women & children's
health research institute

2017
Research Day
Abstract Book

The Power of Partnership

UNIVERSITY OF ALBERTA

Alberta Health Services

STOLLERY CHILDREN'S HOSPITAL FOUNDATION

LOIS HOLE HOSPITAL FOR WOMEN

Acknowledgements

Thank you

These amazing research projects, and all the other services and supports that WCHRI offers, wouldn't be possible without the continued partnership of the University of Alberta, Alberta Health Services, the Stollery Children's Hospital Foundation and the supporters of the Lois Hole Hospital for Women.

Through the support of our partners, we are able to gather some of the most brilliant minds in research together to collaborate and share ideas that will make the future of both women and children brighter.

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DISCLAIMER:
While the abstracts have been slightly modified for consistency, each abstract has been predominantly printed exactly as originally submitted.

Abstract #:	1
Presenter:	Tiffany Kim
Supervisor:	Simon Urschel
Title:	Alterations in naïve Treg cells in thymectomized children predispose for allergic disorders after heart transplantation
Authors:	Tiffany Kim, Nicholas Avdimiretz, Lavinia Ionescu , Ingrid Larsen, Faye Murdoch, Bruce Motyka, Susan Gilmour, Lori West, Simon Urschel
Affiliations:	University of Alberta
Research Activity:	Children's Health and Well-Being

Background: Pediatric heart transplant (HTx) recipients are at higher risk for allergic disorders than non-transplanted children. We found young age at HTx and thymectomy (TE) to be risk factors. We hypothesized that TE and immunosuppression at an early age affect development of T- and B-cell subsets, especially regulatory T-cells (Tregs), which are key in maintaining peripheral tolerance. We investigated the impact of TE and lymphocyte-depleting induction on lymphocyte subsets, and allergic disorders after HTx.

Methods: Flow cytometry phenotyping was used to determine lymphocyte subset proportions in peripheral blood from pediatric HTx patients. Demographic and clinical data were collected in standardized questionnaires and from medical charts. An age-matched, immune suppressed but non-TE liver transplant (LTx) comparison group was included.

Results: 69% of TE patients experienced new or worsening asthma and eczema post-transplant, compared to 33% of non-TE patients. CD45RA+CD27+ naïve Treg proportions within the CD4+CD25+CD127low Treg population was lower in TE patients although not significantly. Patients with asthma and eczema had significantly lower naïve Treg proportions than patients without ($p=0.038$), and showed increased memory CD4+ populations with age. Memory CD4+ and CD5+CD1d+ "B10" populations were higher in TE patients although not significantly. 71% of TE patients were EBV carriers compared to 29% of non-TE patients. Comparison to the LTx group is pending due to small sample size.

Conclusions: Lower percentages of naive Tregs are found in children with allergic disorders after pediatric HTx and likely result from TE. Persisting EBV infection was more common after TE and may impact T-cell maturation. Memory and "B10" populations may also contribute. A larger sample size may help quantify the independent risk of these factors and allow us to stratify the type and intensity of immunosuppression.

The Power of Partnership

Abstract #:   2
Presenter: Victor Mocanu
Supervisor: Michael Hawkes
Title: Lipopolysaccharide binding protein is inversely correlated with endothelial activation markers in vertically HIV-1 infected children.
Authors: Victor Mocanu, Jeremy Soo, Jason Brophy, Fatima Kakkar, Ari Bitnun, Lindy Samson, Stanley Read, Hugo Soudeyns, Michael Hawkes
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Destruction of gut immune defenses in human immunodeficiency virus 1 (HIV-1) infection permits microbial translocation (MT) that drives chronic systemic inflammation and endothelial activation (EA). Lipopolysaccharide binding protein (LBP) is a plasma protein produced by the liver which complexes with lipopolysaccharide and CD14 in the innate immune response to gram-negative bacterial infection. While data for adult cohorts exist, the link between LBP and levels of EA markers in HIV-1 infected children remains undocumented, to our knowledge. HIV-infected children face lifelong systemic immune activation that may predispose to cardiovascular disease. We hypothesized that MT and decreased plasma LBP would be associated with elevated plasma levels of EA markers in pediatric HIV-1 infection.

Methods: Cross-sectional analysis of quantitative plasma concentrations of LBP and EA markers: angiopoietin-2 (Ang-2), soluble vascular endothelial growth factor receptor 1 (sVEGFR-1) and soluble endoglin (sEng). Plasma samples were collected from vertically HIV-1 infected children enrolled in the Early Pediatric Initiation – Canadian Child Cure cohort study (EPIC4) at 9 tertiary health care centres across Canada. All participants achieved sustained viral suppression (<40 copies/mL) with combination antiretroviral therapy (cART). Samples were analyzed using commercial ELISA (R&D Systems).

Result: We included 63 vertically HIV-1 infected children, 35/63 (56%) girls, with median age of 13 years (range 4-19). EA markers were correlated with each other: Ang-2 with sVEGFR-1, Ang-2 with sEng, sVEGFR-1 with sEng (ρ>0.4, p< 0.001 for all comparisons). LBP was negatively correlated with sVEGFR1 (ρ=-0.48, p=0.03) and sEng (ρ=-0.67, p<0.001).

Conclusion: Decreased plasma LBP, indicative of increased MT, is associated with increased plasma levels of EA markers in pediatric HIV-1 infection. This suggests that gut barrier dysfunction and MT may be drivers of EA, a recognized risk factor for cardiovascular disease and possibly cancer, the leading causes of mortality in HIV-1 infected individuals with well controlled viral replication. Future studies should assess long-term outcomes including cardiovascular events in HIV-1 infected children with decreased plasma LBP.

The Power of Partnership

Abstract #:   3
Presenter: Deliwe Ngwezi
Supervisor: Lisa K Hornberger
Title: Exploring exposures to developmental toxicants and effects on congenital heart disease in urban and rural Alberta
Authors: Deliwe Ngwezi, Lisa K Hornberger, Jesus Serrano-Lomelin, Charlene Nielsen, Deborah Fruitman, Alvaro Osornio-Vargas
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Preliminary evidence is emerging suggesting associations between environmental pollutants and CHD development however it is still inconclusive. The aim of this study was first to explore the effect of exposure to multipollutant groups of industrial developmental toxicants (DTs) and CHD and secondly to explore the effect of socio-economic status (SES) on CHD in urban and rural Alberta.

Methods

We identified eighteen DTs emitted to air in Alberta from the National Pollutant Release Inventory and 2, 413 CHD cases from Provincial echocardiographic databases (2003-2010) using the postal code as the unit of analysis. We used Principal Component Analysis to derive 3 multipollutant groups of DTs comprised of: 1) organics and gases, 2) organics and 3) heavy metals. Exposure to DTs was assigned to each postal code in Alberta as the sum of the product of multiplying the amounts of DT (tonnes) emitted from any industrial facility within a 10 km radius, by the inverse distance from the facility to the centroid of the postal code. Exposures were categorized into deciles from 1=lowest to 10=highest for group 1 DTs and tertiles for groups 2, 3 DTs and the SES index (1=lowest to 3 =highest). We conducted our analysis for the whole 8 years. CHD counts were calculated for the deciles and tertiles of DT exposure and Poisson regression models were used to calculate risk ratios (RR) and 95% CI accordingly, adjusted for SES index and surrogates for traffic-related pollution (NO_2, $PM_{2.5}$).

Results

Effect of DT Exposure: The risk ratio for Group 1 DT was increased in urban and rural regions only in the 10th decile of exposure [adjusted RR= 1.85(1.5, 2.3), 2.67(1.04, 6.8)], respectively. Group 2 risk ratio was increased only in urban 3rd tertile [adjusted RR =1.45(1.3, 1.6)]. Group 3 DTs were associated with increased risk ratio in urban and rural regions in the 3rd tertile of exposure [adjusted RR =1.16(1.04, 1.3), RR = 2.8(1.14, 7.1)], respectively.

Effect of SES: SES was independently associated with an increased risk ratio of CHD in urban lowest SES tertile, [adjusted RR=1.13(1.0, 1.3)] and rural lowest and middle SES tertile, [adjusted RR=2.9(1.9, 4.8) and RR=1.6(1.1, 2.6)], respectively.

Conclusions

Our findings suggest that very high exposures to multipollutant groups of DTs and Low SES are independently associated with an increased risk of CHD in urban and rural Alberta. In particular SES had a greater impact in rural compared to urban regions.

The Power of Partnership

Abstract #: 4
Presenter: Victor Do
Supervisor: Lisa Hornberger
Title: Persistent aortic stiffness and left ventricular hypertrophy in children of pregestational diabetic mothers at 3-8 years of age
Authors: Victor Do, Luke Eckersley, Lily Lin, Sandra Davidge, Michael Stickland, Tiina Ojala, Lisa Hornberger
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Infants of diabetic mothers (IDMs) develop left ventricular (LV) hypertrophy and diastolic dysfunction before birth, and are at increased risk long-term of cardiovascular disease (CVD). We have previously shown in this cohort of infants of diabetic mothers (IDM) and age-matched control pregnancies that at late infancy (6-12 months of age), IDMs had persistent mild intraventricular septum (IVS) and left ventricular posterior wall (LVPWd) thickening. IDMs also had increased aortic pulse wave velocity (PWV), independent of blood pressure changes. Interestingly IDM aortic PWV demonstrated a strong correlation with maternal third trimester HbA1c, while aortic PWV correlated strongly with ventricular hypertrophy. These findings led us to further study this cohort in early childhood.

Methods: Children and families who had previously participated in this prospective longitudinal study and were now 3-8 years of age were invited to return for follow-up assessment. Height, weight and right arm blood pressures were recorded. A full functional and structural echocardiogram was performed. Children also underwent peripheral arterial endothelial function assessment measured as a Vascular Reactivity Index using the VENDYS device (digital thermal monitoring). Offline analysis of the echocardiograms was performed with a specific focus on LV wall thickness, diastolic function and aortic PWV. Participants also completed a demographics and clinical history survey, HAES physical activity questionnaire and provided a 3-day diet log.

Results: Twenty-five IDM children and 20 children from control pregnancies have completed their assessments (n= 41) or have bookings for upcoming studies (n=4). Mean age of IDM children was 5.6 ±1.7 years and 5.3±1.3 years for control children (NS). Preliminary analysis has shown that IVS z-scores were increased in IDMs compared to controls (1.2± 0.6 vs 0.5± 0.3, respectively, p=0.006), with 5 (20 %) of the IDMs having an IVS z-score of >2, consistent with hypertrophy. LVPWd z-scores also tended to be greater in IDMs versus controls (0.6± 0.4 vs 0.2± 0.2, respectively, p=0.06), but none had a z score of >2. Measures of diastolic function did not differ. Aortic PWV continued to be increased in IDMs compared to controls (3.2± 0.6m/s vs 2.2± 0.4m/s respectively, p= 0.001), while blood pressures did not differ. The Vascular Reactivity Index was similar between the two groups. There was a strong correlation between IVSd z score and aortic PWV (R^2=0.81, p=0.001).

Conclusions: Preliminary analysis indicates there may be mild persistent septal hypertrophy and increased aortic stiffness but no evidence of endothelial dysfunction in IDMs in early childhood.

The Power of Partnership

Abstract #:   5
Presenter: Frances Sobierajski
Supervisor: Margie Davenport
Title: Maternal physical activity is associated with improved blood pressure regulation during late pregnancy
Authors: Frances Sobierajski, Graeme Purdy, Charlotte Usselman, Rachel Skow, Marina James, Radha Chari, Rshmi Khurana, Michael Stickland,
                   Sandra Davidge, Maureen Devolin, Craig Steinback, Margie Davenport
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Background: Cardiovagal baroreflex gain reflects an individual's ability to buffer swings in blood pressure when it is both rising and falling. There is evidence to suggest that cardiovascular adaptions during pregnancy result in a blunting of the baroreflex. However, it is not well understood how this mechanism is influenced by physical activity in pregnancy. Since pregnant women tend to engage in low levels of moderate-to-vigorous physical activity (MVPA) and high levels of sedentary behaviour, we sought to determine the influence of MVPA and sedentary behaviour on baroreflex gain and mean arterial pressure in pregnancy.

Methods: 58 third trimester (31.9±3.0 weeks) normotensive pregnant women (31.2±2.8 years) were tested. Heart rate (HR, electrocardiogram) and blood pressure (systolic blood pressure [SBP] and mean arterial pressure, finger photoplethysmography) were collected on a beat-by-beat basis, and averaged over three minutes of rest. Spontaneous baroreflex gain was calculated as the slope of the relationship between fluctuations in SBP and HR. Objective measures of MVPA and sedentary behaviour were collected over a 7-day period using Actigraph accelerometry (wGTX3-BT).

Results: Participants spent 67.5±7.9% of waking hours engaged in sedentary behaviour, and performed 68.6±91.9minutes of MVPA/week. After stratifying women according to *Canadian Physical Activity Guidelines for Adults*, 11 of the 58 women were classified as ACT, while the rest were INACT. Sedentary behaviour was not related to baroreflex gain (r=-0.035, p=0.793) or mean arterial pressure (r=-0.033, p=0.803). However, MVPA was positively associated with baroreflex gain (r=0.315, p=0.016), but not mean arterial pressure (r=-0.115, p=0.389). The association between MVPA and baroreflex gain remained significant after controlling for age, pre-pregnancy body mass index, gestational age and wear time (r=0.338, p=0.013), indicating that women who engaged in greater amounts of MVPA demonstrated increased baroreflex gain. Indeed, between group differences demonstrated that ACT women had increased baroreflex gain compared to INACT women (ACT: 29.5 ± 10.1ms/mmHg, INACT: 20.5 ± 10.6ms/mmHg, p=0.013).

Conclusions: Our data suggests that increased MVPA, but not necessarily reduced sedentary behaviour may be beneficial for blood pressure regulation during pregnancy.

The Power of Partnership

Abstract #: 6
Presenter: Brandon Chan
Supervisor: Richard Schulz
Title: MMP inhibitors attenuate doxorubicin-induced heart failure by preventing cardiac titin proteolysis
Authors: Brandon Chan, Andrej Roczkowsky, Nils Moser, Mathieu Poirier, Ramses Ilarraza, Henk Granzier, Richard Schulz
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Heart failure remains a major, long-term complication with doxorubicin (DXR) chemotherapy in women and children. We investigated the mechanism of DXR cardiotoxicity in order to develop new strategies to prevent heart injury when treating pediatric cancer patients. DXR enhances oxidative stress and activates two intracellular isoforms of matrix metalloproteinase-2 (MMP-2) in neonatal cardiac myocytes. Intracellular MMP-2 is known to exacerbate myocardial oxidative stress injury by cleaving specific sarcomeric proteins including titin. We determined whether MMP-2 mediated titin proteolysis contributes to DXR-induced heart failure in vivo.

Methods: 8-week old male C57BL/6J mice were treated with DXR (6 mg/kg/wk, i.p.) or saline vehicle (control) ± MMP inhibitors doxycycline (15 mg/kg/day, gavage) or ONO-4817 (60 mg/kg/day, gavage) for 4 weeks. Cardiac function was assessed by M-mode echocardiography before and after treatment (n=10 per group). The hearts and plasma were collected following post-treatment echocardiography and MMP-2 protein levels and activity were measured by western blot and gelatin zymography, respectively. Titin (T1) and its degradation product (T2) levels were measured by agarose gel electrophoresis. Data are represented as mean ± SEM (n animals) and statistical analysis was performed using one-way ANOVA followed by Tukey's post-hoc test.

Results: DXR caused systolic and diastolic dysfunction marked by a significant reduction in left ventricular ejection fraction (64.0±2.3% vs. 45.5±2.4%, p<0.0001), fractional shortening (34.5±1.7% vs. 22.3±1.4%, p<0.0001), and E/A ratio (1.07±0.04 vs. 0.85±0.06, p<0.05) compared to control. Doxycycline or ONO-4817 prevented these changes. DXR trended to increase MMP-2 activity by two-fold in hearts (p=0.062, n=9) and this was not observed in doxycycline or ONO-4817 hearts (n=10 each). In plasma, DXR increased MMP-2 activity by two-fold (p<0.05, n=10) and protein levels by 225% (p<0.01, n=8) relative to control. ONO-4817, but not doxycycline, attenuated DXR-induced MMP-2 activity and protein levels in plasma (p<0.05, n=8-10). T2/T1 titin ratio was increased by 258±7% (n=8, p<0.05) in DXR hearts and this was reduced by ONO-4817 (169±10%, n=8, p<0.05), but not doxycycline (203±16%, n=8), relative to control.

Conclusions: MMP-2 contributes to DXR-induced heart failure in mice by proteolyzing cardiac titin and this was prevented by ONO-4817, which is a more potent MMP inhibitor than doxycycline. Prophylactic use of orally available MMP inhibitors may be a potential therapeutic strategy to prevent heart failure in pediatric cancer patients undergoing chemotherapy.

The Power of Partnership

Abstract #:   7
Presenter: Felipe Ganz
Supervisor: Lesley Pritchard-Wiart
Title: Sedentary behaviour in children with physical disabilities: A scoping review
Authors: Felipe Ganz, Nevin Hammam, Lesley Pritchard-Wiart
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Increased sedentary behaviour (SB) is a concern in pediatric health care because of rising obesity rates and long-term adverse health effects including increased risk of cardiovascular disease and stroke. Since children with physical disabilities are even more sedentary than their peers without disabilities, there is growing concern over how to decrease SB in this group of children. The purpose of this scoping review was to review the evidence related to SB in children with physical disabilities to answer the following questions: (1) what is known about SB patterns in children with physical disabilities? (2) What strategies for decreasing SB with children with physical disabilities are discussed in the literature? (3) What is the current state of the evidence regarding the interventions to decrease SB in children with physical disabilities?

Methods: A scoping review was conducted using the methodology described by Levac et al. (2010). Articles were considered for inclusion if participants were aged 0–18 years, had physical disabilities, and the focus of the articles was sedentary behavior. Full text of articles was obtained and each article was reviewed and data were extracted independently by two reviewers. The reviewers met to discuss discrepancies and reach consensus.

Results: Forty-three articles were selected for inclusion in the review. Of these articles, the majority of the studies were observational studies describing SB patterns (n=31) (objective 1). Strategies for decreasing SB (objective 2) were discussed in ten papers. Only two studies conducted to evaluate interventions for decreasing SB (objective 3) were included. Most of research has been conducted in children with cerebral palsy. Older children and adolescents were the main focus of the studies with few addressing SB in infants and preschool children. There was a lack of longitudinal studies and no research examined the long-term health outcomes of SB in these children. Only two interventional studies have been conducted to evaluate strategies to decrease SB. There is no evidence to support the effectiveness for strategies to reduce SB in children with physical disabilities. Accelerometry was the most common objective measure of sedentary behavior used however, questionnaires, survey and interviews were also used.

Conclusion: Research to evaluate interventions related to decreased sedentary behaviour in children with physical disabilities is needed. Future research should also consider the use of validated measures and longitudinal studies to understand long-term health effects of sedentary behaviour.

The Power of Partnership

Abstract #:   8
Presenter: Jennifer Hermann
Supervisor: Shannon MacDonald
Title: Immunization coverage of Albertan children in care of the Government
Authors: Jennifer Hermann, Kimberley Simmonds, Christopher Bell, Shannon MacDonald
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Background: Children in care of the child welfare system ('children in care') are a vulnerable population who access preventive health services less than other children.

Objective: To assess immunization coverage of a cohort of children in care and compare it to children who have never been in care.

Methods: This retrospective cohort study assessed immunization status at age two (N=44 206) and seven (N=42 241) for children in the 2008 Alberta birth cohort. Population-based administrative health databases were utilized to assess coverage for three vaccines (diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type b[DTaP-IPV-Hib]; meningococcal [Men-C]; and measles, mumps, rubella [MMR]) for children in care compared to those in the general population. A child was considered to be in care if they spent any time in care before the age of assessment. Logistic regression was used to compare immunization status between groups.

Results: Immunization coverage for children in care at age two ranged from 54.3% (DTaP-IPV-Hib) to 81.4% (MMR), compared to those not in care which ranged from 74.2% (DTaP-IPV-Hib) to 87.4% (MMR). Coverage for children in care at age seven ranged from 53.1% (DTaP-IPV) to 65.3% (MMR), compared to those not in care which ranged from 76.6% (DTaP-IPV) to 83.4% (MMR). For all vaccines at both ages, the odds ratios (OR) for being under immunized were higher for children in care (e.g. DTaP-IPV-Hib OR: 2.43; 95% confidence interval [CI]: 1.72-3.44). Further analysis compared coverage among children in care to children not in care subdivided into two groups, those with characteristics often associated with low coverage (e.g. highly mobile lifestyle) and those without such characteristics. Compared to the two groups of children not in care, children in care still had the lowest coverage, with the highest OR of being under immunized (e.g. DTaP-IPV-Hib, OR: 2.72; 95% CI: 1.93-3.86).

Conclusion: Children in care have consistently lower immunization coverage than children not in care. Policies and practices should be examined to ensure optimal access to immunization for these children.

The Power of Partnership

Abstract #:   9
Presenter: Atsushi Kawaguchi
Supervisor: Allan deCaen
Title: Impact of physicianless pediatric critical care transport: What do triage physicians need to know in making a decision?
Authors: Atsushi Kawaguchi, Charlene Nielsen, Yutaka Yasui, Allan deCaen
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

1) To explore the impact of a physicianless pediatric critical care transport program, and 2) to identify factors associated with the selection of specific transport team compositions.

Methods

Children under 18 years of age who were transported to a Canadian academic Children's Hospital were included. Two eras (PT-era: Physician-accompanying transport era; 2000-2007, when physicians commonly accompanied the transport team; and PLT-era: Physicianless transport era; 2010-2015, when a physicianless team was increasingly used) were compared with respect to transport and PICU outcomes. Transport and patient characteristics were examined to identify factors associated with the selection of a physician-accompanying transport team composition, using multivariable logistic regression with triage physicians as random effects.

Results

In total, 2,667 transports met our inclusion criteria. In the PLT-era compared to the PT-era, fewer patients had their heart rates improve or remain within age-appropriate normal ranges during transport, and more patients had their respiratory rates deteriorate. The probability of PICU admission was significantly lower and patient outcomes (including mortality and PICU length of stay) were not significantly worse.

In the PLT-era, significant associations were noted between the selection of a physicianless transport team and specific transport characteristics. There was appreciable variability in decision-making among the seven-triage physicians for the selection of a physicianless transport team, after adjusting for patient characteristics.

Conclusions

Increasing use of a physicianless transport team did not impact negatively on patient outcomes. Selection of transport team compositions was influenced by clinical and system factors, but appreciable variation still remained among triage physicians.

The Power of Partnership

Abstract #:   10
Presenter: Tasneem Siyam
Supervisor: Nese Yuksel
Title: Perspectives and decision-making about menopausal therapies in women who had an early surgical menopause: A focus group study
Authors: Tasneem Siyam, Sue Ross, Tami Shandro, Shelly Hagen, Lori Battochio, Nese Yuksel
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: Women who have had a premenopausal bilateral oopherectomy (surgical menopause) struggle with severe menopausal symptoms as the surgery results in an abrupt drop in hormone levels. In addition, these women may be at risk for long term health consequences such as osteoporosis, cardiovascular disease and cognitive impairment. Although, current guidelines recommend the use of hormone therapy (HT) in women with early menopause and without contraindications to HT, until the average age of menopause, its use is greatly underutilized among surgically menopausal women. The objective of this study is to address a clinical area where there is little information in the literature: the perspectives and decision-making of women who have had an early surgical menopause (< 50 years) on the use of menopausal therapies.

Methods: We used a descriptive qualitative research design. Women who had an early surgical menopause were purposefully selected from the Edmonton Menopause Clinics. Focus groups were held, each with 6 to 9 participants and lasted for 1.5 hours. All sessions were audio-recorded and transcribed verbatim. Data was analysed using qualitative content analysis.

Results: We conducted five focus groups from Jun 30 to Jul 21, 2016 (N = 37). One-third of the women had the surgery within the last 5 years. Almost all women had a concurrent hysterectomy (97%) and were current users of hormone therapy (HT) (70%). Four main themes identified were: "perceptions of surgical menopause", "perceptions of support", "being my own advocate", and "concept of adequate support". Women shared that the experience was worse than their expectations and did not feel they were given adequate support to prepare them to make therapy decisions. Women had to "be their own advocates" and seek support from within the healthcare system and outside, to cope with their health issues. To make an informed decision about treatments post-surgery, women expressed a need to learn more about the symptoms of surgical menopause, treatment options, resources, avenues for support and stories of similar experiences, preferably before the surgery.

Conclusion: We identified several modifiable deterrents to decision-making in early surgical menopause which can help inform the development of a patient decision aid for this context.

The Power of Partnership

Introduction. Parents play an important role in the early detection and treatment of their child's urinary tract infection (UTI). To inform the development of knowledge translation tools for parents, we systematically reviewed the literature on their self-reported experiences and information needs related to pediatric UTIs.

Methods. We searched Ovid Medline, Ovid PsycINFO, CINAHL, and ProQuest Dissertations and Theses Global for relevant literature. We included studies of any design published in 2000 or thereafter. Two reviewers independently screened the records. From the included studies, we extracted characteristics of the: publication; study design and data collection method(s); population; UTI type and severity; and setting. We summarised the quantitative data narratively and the qualitative data thematically. Two reviewers independently appraised study quality using the Mixed Methods Appraisal Tool.

Results. We identified 1,493 independent records from the searches. We included 25 records after title and abstract screening, and four after full text inspection: two quantitative, one qualitative, and one mixed methods. The studies were generally good quality, however there was potential for bias in participant selection and low response rates in two studies. In the qualitative and mixed methods studies, reflexivity was not evident. The studies were heterogeneous with respect to sample size (range: 20 to 2,726) and geographic setting. Most (83%) participating parents were mothers. The children ranged in age from <1 to 12 years and had experienced one to >10 UTIs. Parents were not always aware of the symptoms of pediatric UTIs and some did not know that long-term health complications could result. Most parents received little information from their health care provider (HCP). Parents commonly sought information on the Internet, but also desired information via traditional sources, like pamphlets and presentations. Parents were often not confident in their HCP's knowledge of pediatric UTIs, and were frustrated by delays in diagnosis and treatment. Inadequate information about diagnostic procedures sometimes resulted in fear and non-compliance.

Conclusions. There is a need for increased research into parents' experiences and information needs related to UTIs. Information for parents should aim to improve their confidence to identify UTIs, and empower them to make treatment decisions based on knowledge and not fear. Continuing education for HCPs should focus on the uptake of evidence-based guidelines, and on the skills necessary to communicate pertinent information in a way that suits parents' self-identified needs.

The Power of Partnership

Abstract #:   12
Presenter: Maira Quintanilha
Supervisor: Maria & Rhonda Mayan & Bell
Title: Using integrated knowledge translation to effectively promote maternal health of migrant women
Authors: Maira Quintanilha, Maria Mayan, Rhonda Bell
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: The ENRICH Research Program began in 2013 with the overall purpose of promoting appropriate maternal body weight in pregnancy and postpartum through healthy eating among diverse groups of women in Alberta. With the recognition that low income and sociocultural barriers can negatively affect many aspects of a healthy pregnancy, one of ENRICH's objectives was to explore migrant women's perceptions and experiences of health during pregnancy and postpartum while receiving support from the Multicultural Health Brokers (MCHB) Cooperative in Edmonton. In 2014-2015, we found that Northeast African women faced various life adversities (e.g., low income, social isolation) that made being healthy during pregnancy and postpartum more challenging in Canada. In contrast, women described that services and supports offered through MCHB facilitated their pregnancy and postpartum health. We describe here how we used an integrated Knowledge Translation (iKT) approach to integrate and disseminate research findings, and develop meaningful strategies to support maternal health of migrant women.

Methods: By using an iKT approach we involved both knowledge users and researchers, as equal partners, in data collection, analysis and knowledge translation. We held frequent meetings with stakeholders (i.e., health brokers) from MCHB in which we discussed and co-developed strategies aiming to increase migrant women's access to healthy foods during pregnancy and postpartum.

Results: As a result of the partnership between the ENRICH Research Program and MCHB Cooperative, the position of a Community Resource Coordinator (CRC) was established to develop and implement novel strategies to address food insecurity among migrant women and families. One of these strategies – the Grocery Run Program (GRP) – entails collecting donated foods, and distributing them to women and their families with same-day food needs. Despite its importance in ensuring these families' human right to food, the GRP does not address low income as the root cause of food insecurity. For this reason, the CRC is also involved in starting a social enterprise among women within MCHB. Additionally, we disseminated our research findings through traditional peer-reviewed publications, and a short whiteboard video that illustrated key findings in a more engaging format (http://bit.ly/maternalhealthofmigrantwomen).

Conclusion: Improving migrant women's diets will require addressing migration as a determinant of health. Using iKT to involve community-based organizations, such as MCHB, can foster opportunities to promote social and economic integration of women and families into Canada, and policy advocacy that can positively impact maternal health.

The Power of Partnership

Introduction

Prenatal fetal hypoxia is a common pregnancy complication that can lead to placental oxidative stress and abnormal cardiovascular function in the offspring. Mitochondria are a major source of oxidative stress in the placenta. We can deliver the mitochondrial antioxidant to the placenta and prevent it from crossing placental barrier to the fetus by using a nanoparticle delivery system. We hypothesize that treating the placenta in a prenatal hypoxia model will lead to improved cardiovascular outcomes in the offspring.

Methods

Pregnant rats were injected with either MitoQ loaded nanoparticles (nMitoQ; 125 µM) or saline via tail vein on gestational day (GD) 15. Rats then were subdivided into two groups exposed to either hypoxia (11% O_2) or normoxia (21% O_2) from GD 15-21 (term; 22 days). Male and female offspring of these pregnancies were assessed separately at 13 months of age for vascular function (wire myography), blood pressure (tail-cuff plethysmography),and *in vivo* cardiac function (echocardiography). A 2-way ANOVA was used for analyses.

Results

Ex vivo mesenteric artery sensitivity to phenylephrine (PE) was not altered by hypoxia. nMitoQ, however, increased sensitivity to PE in male offspring from normoxic and hypoxic pregnancies (pEC$_{50}$ PE: normoxia/saline: 5.54±0.05 vs. normoxia/nMitoQ: 5.66±0.03 and hypoxia/saline: 5.69±0.08 vs. hypoxia/nMitoQ: 5.88±0.03; P=0.0001). This effect was not seen in female offspring. While hypoxia did not alter *ex vivo* mesenteric artery sensitivity to the vasorelaxant methacholine (MCh) in male offspring, sensitivity to MCh was increased by treatment with nMitoQ. In female offspring, hypoxia reduced mesenteric artery sensitivity to MCh which was increased by nMitoQ in both normoxic and hypoxic offspring. Neither hypoxia nor nMitoQ altered blood pressure. Assessment of cardiac function demonstrated that hypoxia led to diastolic dysfunction in male and female offspring. nMitoQ did not improve diastolic function in male offspring but enhanced diastolic function in both normoxic and hypoxic female offspring by increasing the E wave velocity (MV E: normoxia/saline: 847±60 mm/svs. normoxia/nMitoQ: 1204±162 mm/sand hypoxia/saline: 844±75 mm/svs. hypoxia/nMitoQ: 929±88 mm/s; P=0.02).

Conclusion

Using nanoparticles to target antioxidant treatment to the placenta in mid gestation can alter cardiovascular function in offspring later in life. nMitoQ was shown to increase mesenteric artery sensitivity to vasoconstriction in males, increase the sensitivity to vasorelaxation in male and female offspring and improve diastolic function in female offspring. Our data demonstrate that treating the placenta may be a therapeutic strategy to fetal programming of cardiovascular disease.

The Power of Partnership

Introduction

The development of hypertension and proteinuria in preeclampsia (PE) is thought to be due to the release of placental factors leading to maternal endothelial dysfunction. The lectin-like oxidized LDL receptor-1 (LOX-1) is a multi-ligand scavenger receptor that is associated with vascular dysfunction. We have previously shown that LOX-1 expression is increased in women with PE, and that PE plasma factors disturbed vascular function via LOX-1. However, the exact role of LOX-1 in contributing to vascular maladaptations to pregnancy is unknown. Thus, to further investigate a role for LOX-1 in pathological pregnancies, we propose to use genetically modified LOX-1 deficient (knockout; KO) mice. We hypothesize that an absence of the LOX-1 receptor would improve vascular function and benefit pregnancy outcomes.

Methods

C57BL/6 mice (WT; n=7-15) and LOX-1 KO mice (n=8-16) were sacrificed at the end of pregnancy on gestational day 18 (term = day 19). Fetal and placental weights were collected. Uterine arteries were obtained and isolated vessels were incubated overnight in physiological salt solution. Using wire myography, endothelium-dependent (methylcholine; MCh) vasodilation (in the presence or absence of L-NAME, a pan nitric oxide synthase inhibitor), endothelium-independent vasodilation (sodium nitroprusside; SNP) and high potassium physiological salt solution (KPSS) mediated vasoconstriction responses were measured.

Results

No differences in placental or fetal weights were observed between WT and LOX-1KO mice, however, litter size was significantly increased in LOX-1KO mice compared to WT mice (WT 6.7±0.7 vs. LOX-1KO 9.1±0.3; p=0.003). Uterine arteries from LOX-1KO mice were less sensitive to MCh than arteries from WT mice (pEC_{50}: WT 7.1±0.08 vs. LOX-1KO 7.4±0.06; p=0.01). Conversely, the nitric oxide contribution to MCh-induced vasodilation was increased in LOX-1KO mice compared to WT mice (delta AUC: WT 54.8±11.7 vs. LOX-1KO 146.4±34.9; p=0.02). No changes were observed in SNP-induced vasodilation or KPSS-mediated vasoconstriction.

Conclusions

Mice that do not express the LOX-1 receptor show an improved pregnancy outcome, while also displaying a shift in the mechanisms of endothelium-dependent vasodilation. This supports our hypothesis that LOX-1 could play a role in the development of pregnancy complications and indicate that the presence of the LOX-1 receptor may be detrimental for pregnancy. The exact mechanisms, and whether the vascular adaptations in LOX-1KO mice contribute to the improved pregnancy outcome, remain to be further investigated. These data increase our understanding of endothelial dysfunction in PE and contribute to the development of novel treatment strategies in the future.

The Power of Partnership

Abstract #:   15
Presenter: Lauren Zalaski
Supervisor: Radha Chari
Title: Atypical perintatal antibiotic exposure patterns and indications for use in Canada: A population-based study
Authors: Lauren Zalaski, Radha Chari, Anita Kozyrskyj
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

The prevalence of antibiotic exposure during the perinatal period has not been well documented, since mothers may not accurately recall medications administered in hospital, and these medications are not captured by community-based prescription databases. However, such exposures are important, as aberrancies in the early gut microbial profile of infants following antibiotic exposure have been linked with the development of immune-mediated disease. Evaluating the short and long-term impact of antibiotic exposure during the intrapartum period requires complete and accurate documentation of exposures, as cumulative effects may become apparent with further investigation.

Hypothesis

We expect a significant number of neonates are exposed to antibiotics in utero during the intrapartum period. We expect discrepancies from SOGC guidelines when multiple indications are present.

Methods

A retrospective review of the hospital charts of 995 mother–neonate pairs enrolled in the Canadian Healthy Infant Longitudinal Development study was conducted. The main outcome measures included the following: type of maternal and neonatal antibiotic use, indications for use, documentation of risk factors, drug allergy and mode of delivery.

Results

Over 40% of mothers were administered antibiotics during the perinatal period. Indirect antibiotic exposure to the neonate was significant, with the majority of administration occurring intrapartum. Additionally, many scenarios do not resemble expected exposures, with 22.5% of women undergoing emergent Caesarean section (CS) receiving both GBS and CS prophylaxis, or 15.5% of mothers receiving GBS prophylaxis being administered an alternative to Penicillin.

Conclusion

A significant proportion of neonates are exposed to antibiotics during the intrapartum period. There is a paucity of evidence examining the consequences of non-typical or aggregate exposures, despite these accounting for nearly 25% of intrapartum prophylactic exposures in our data. It is prudent to continue to be vigilant in tracking trends in GBS disease, antibiotic usage, and develop longitudinal studies evaluating the long-term consequences of intrapartum antibiotic exposure as new prophylactic regimens are implemented.

The Power of Partnership

Abstract #:   16
Presenter: Anthony Reardon
Supervisor: Jonathan Martin
Title: Association of perfluoroalkyl acids (PFAAs) and maternal thyroid hormone status: a longitudinal assessment of gestation and postpartum relationships
Authors: Anthony J. F. Reardon, Elham Khodayari-Moez, Irina Dinu, Susan Goruk, Catherine J. Field, David W. Kinniburgh, Amy MacDonald, Jonathan W. Martin
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Perfluoroalkyl acids (PFAAs) are persistent organic contaminants that are associated with the disruption of thyroid hormone (TH) homeostasis. Maternal TH status is critical for healthy fetal brain development during pregnancy, particularly during the early stages when the fetus is entirely dependent on a maternal supply of THs. The aim of the current investigation is to determine if maternal PFAA exposure is associated with altered TH levels measured at multiple time points in a Canadian birth cohort while considering thyroid-specific conditions and the potential for mixture effects from mercury co-exposure.

Methods

Maternal blood samples (n = 501) were collected at 3 trimester-specific timepoints and at three months postpartum from participants enrolled in the Alberta Pregnancy Outcomes and Nutrition (APrON) birth cohort. Second trimester plasma or blood samples were analysed for PFAAs or mercury and mixed effects regression models were used to investigate potential associations with trends in THs across all time points. Thyroid peroxidase antibodies (anti-TPO), a marker of autoimmune hypothyroidism, and mercury were both included in PFAA-TH models as interaction terms.

Results

Perfluorohexane sulfonate (PFHxS) and isomers of perfluoroctane sulfonate (PFOS) were both significantly positively associated with thyroid stimulating hormone (TSH). Moreover, these associations were time dependent, with the greatest effect early in pregnancy and diminishing as pregnancy progressed. In addition to these findings, PFHxS was observed to be negatively associated with free thyroxine (FT4) and significant differences were found for numerous PFAA-TH associations when comparing outcomes during gestation to post-pregnancy. Mercury was found to be significantly inversely associated with free triiodothyronine (FT3), but neither mercury or anti-TPO were found to significantly alter established associations when included as interaction terms in PFAA-TH models.

Conclusions

These results suggest that background exposure to specific PFAAs and mercury in the blood of the Canadian population are high enough to significantly influence maternal thyroid hormone homeostasis in the most highly exposed individuals. The greatest association was found for PFHxS, the strongest binding PFAA to the TH transport protein transthyretin. As associations of PFAAs and thyroid hormones were found to be trimester-dependent, these findings may explain discrepancies in published literature.

The Power of Partnership

Abstract #:   17
Presenter: Andrew Woodman
Supervisor: Stephane Bourque
Title: Perinatal iron-deficiency causes sex-dependent early onset vasoconstrictor hypersensitivity in aging offspring
Authors: Andrew Woodman, Ronan Noble, Sareh Panahi, Ferrante Gragasin, Stephane Bourque
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: Epidemiological and animal studies on the developmental origins of health and disease (DOHaD) have shown that susceptibility to non-communicable chronic disease in later life may be 'programmed' by stressors during pregnancy. Our group studies the effects of maternal iron-deficiency (ID), which is the most common nutritional deficiency worldwide. In Canada an estimated 23% of women become iron-deficient during pregnancy, and as many as 50-80% in the developing world. Offspring with perinatal ID develop hypertension and salt sensitivity, and these perturbations are evident even in childhood. The mechanisms through which ID causes hypertension are currently poorly understood. Hypertension is often characterized by a reduction in the bioavailability of nitric oxide (NO), which may contribute to a constrictor phenotype in systemic blood vessels. We hypothesize that prenatal ID results in a reduction of NO and vasodilatory capacity coupled with an increase in vasoconstrictor response and hypertension.

Methods: Sprague Dawley rats were fed either an iron replete (control group) or low iron diet (iron-deficient [ID] group) 2 weeks prior to and throughout pregnancy. Upon giving birth, all dams were fed an iron replete diet. Offspring were anesthetized and instrumented with indwelling arterial catheters on postnatal day (PD) 7, 14, 21, and 180. Vascular function was assessed with intravenous administration of: (i) endothelium-dependent vasodilator methacholine, (ii) NO donor sodium nitroprusside (SNP), and (iii) adrenergic agonist phenylephrine (all in the presence or absence of nitric oxide synthase inhibitor L-NAME).

Results: ID resulted in 31% decrease in maternal hemoglobin (Hb), ~55% decrease in PD1 offspring Hb, and 21% reduction in PD1 bodyweights compared to controls. Mean arterial pressure (MAP) in ID offspring was not different from controls at any time point assessed, although MAP rose continually with age from PD7 to PD180. Vascular reactivity to SNP and methacholine was not altered by ID, either in the presence or absence of L-NAME. Female ID offspring had reduced hemodynamic responses to phenylephrine on PD7, which normalizes by PD14, and was enhanced by PD180. In contrast, male offspring exhibit enhanced responsiveness to phenylephrine PD14 through PD180.

Conclusions: These results show sex-specific programming effects of perinatal ID on vascular reactivity in aging offspring. Although increases in blood pressure were not observed in our offspring while under anesthesia, enhanced reactivity to vasoconstrictors may play a role in the increased blood pressure observed by others. Interestingly, reduced NO bioavailability does not appear to be implicated in the observed hypersensitivity to phenylephrine.

The Power of Partnership

Abstract #:   18
Presenter: Jessica Krahn
Supervisor: Vera Caine
Title: Developing an evaluation for pregnancy pathways: Principles, challenges, and progress
Authors: Jessica Krahn, Vera Caine
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Each year in Edmonton approximately 100 pregnant women are homeless or unstably housed. Women who are homeless have a higher risk of trauma, mental illness and substance use that threatens their health, as well as the health of their children (Chambers et al., 2014; Schuster et al., 2011). High levels of chronic stress during child development, like those associated with homelessness, are linked to altered brain structures that lay a poor foundation for future learning, behaviour, and health (Siegel et al., 2012). *Pregnancy Pathways* is a transitional housing program for pregnant and early parenting women experiencing homelessness that aims to interrupt the cyclical pattern of family homelessness and to improve the mental and physical health of women and their children in vulnerable life circumstances. While the need for supportive housing programs for this population is clear, there is very little empirical evidence to establish what housing models (Krahn, Caine, Singh, & Chaw-Kant, in review) and principles can be linked to positive outcomes. In developing an evaluation model for *Pregnancy Pathways,* we explored potential evaluation tools that would reflect program principals of harm reduction, trauma informed care, and cultural safety.

Methods

An extensive literature search was conducted to identify evaluation tools measuring outcomes related to *Pregnancy Pathway*'s principles. Related programs across Canada were also contacted and community stakeholders were consulted. Identified tools were assessed based on their feasibility and fit with the principals. Several tools were presented to a group of women with lived experiences, along with service providers to gather input on the tools' acceptability and utility.

Results

Over 60 tools were identified in the search. After the initial assessment, the list was narrowed down to ten tools measuring outcomes reflective of the program's principles. After further discussions decisions were made about the utility and acceptability of the tools. Throughout this process notes were kept about the challenges and possibilities encountered. In particular we took note of the tension between outcome driven and principal based evaluation efforts.

Conclusions

The development of the *Pregnancy Pathways* program along with its evaluation framework fills significant gaps in service provision in Edmonton for a complex and often vulnerable population. While engaging in program development it is important to attend to key foundational principals. Tools that are linked to outcome evaluation indicators must be carefully selected to ensure that they reflect the assumptions inherent in the principles selected and that their use is acceptable to the population receiving services.

The Power of Partnership

Abstract #:   19
Presenter: Emma Zwaigenbaum
Supervisor: Eytan Wine
Title: Factors secreted from infected epithelial cells promote Citrobacter rodentium clearance by macrophages
Authors: Emma Zwaigenbaum, Michael Bording-Jorgensen, Heather Armstrong
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Inflammatory Bowel Diseases (IBD) are chronic debilitating intestinal disorders with increasing incidence in Canada, notably in children. While IBD have been linked to genetic and environmental factors, and their interactions with intestinal microbes, the precise causes remain unknown. One of the identified IBD associated genetic variation involves the inflammasome complex, NLRP3. This complex is involved in the detection of pathogen associated molecular patterns (PAMPs) and when activated, releases the proinflammatory cytokines IL-1β and IL-18. In IBD, there is a characteristic hypoproduction of IL-1β due to a proposed under activation of the inflammasome; how this relates to disease pathogenesis is unclear. Our lab has recently shown that ATP activation of the inflammasome in macrophages improves bacterial clearance. However, currently little research exists on the role of the inflammasome in intestinal epithelial cells.

Methods: Our study focused on whether inflammasome activation in epithelial cells would increase their ability to clear adherent bacteria. The mouse pathogen *Citrobacter rodentium*, a commonly used infection model for colitis,was used to infect CMT-93 mouse colonic epithelial cells. ATP was applied to activate the inflammasome. Gentamicin protection assays (GPA) were used to determine the difference in bacterial clearance between ATP activated and non-activated epithelial and macrophage cells. Using enzyme-linked immunosorbent assays (ELISA) we quantified the levels of IL-1β and IL-18 secreted by epithelial cells and macrophages to assess the immune response to infection with and without inflammasome activation.

Results: In contrast to our hypothesis, direct activation of the inflammasome with ATP in epithelial cells infected with *C. rodentium* did not increase bacterial clearance or secretion of IL-1β and IL-18 in 4-hour infections. However, addition of supernatants from epithelial cells previously infected with *C. rodentium* for 24 hours increased bacterial clearance in macrophages, suggesting that factors secreted from infected epithelial cells could impact the ability of macrophages to kill bacteria in an inflammasome-dependent fashion. Similar effects were seen on cytokine secretions.

Conclusions: While activation of the NLRP3 inflammasome in epithelial cells does not appear to promote epithelial cell clearance of bacteria; epithelial cell signals to macrophages are able to increase macrophage bacterial clearance ability. The epithelial cell secretions discussed would be relevant in future research into treatment of inflammation in children with IBD as an inability to clear pathogenic bacteria in the intestine leading to inflammation is a proposed etiology of IBD. Improving bacterial clearance is a potential novel therapy for IBD.

The Power of Partnership

Abstract #:   20
Presenter: Nicole Ofosu
Supervisor: Paul Veugelers
Title: Long-term effects of comprehensive school health on health behaviours and weight status of adolescents
Authors: Nicole N. Ofosu, Kerry A. Bastian, John P. Ekwaru, Sarah Loehr, Kate Storey, John C. Spence, Paul J. Veugelers
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: APPLE Schools is a comprehensive school health (CSH) project for schools in socio-economically disadvantaged neighbourhoods. APPLE Schools have been shown to be successful in improving diet and physical activity (PA), preventing obesity among students and bringing them at par with students in other schools. However, it is unknown whether the benefits of CSH projects such as APPLE Schools are sustained when children grow into adolescence.

Objective: To assess the effects of APPLE Schools on health-related knowledge, attitudes, self-efficacy, diet, PA, and weight status, seven years after the start of the project, when students are in junior high and high school.

Methods: In the 2015/16 school year, junior high and high school graduates (grades 7-12) in Northern Alberta, Canada participated in a youth health survey. Participants included graduates from APPLE elementary schools (n = 202) and comparison elementary schools (n=338). Health-related knowledge, attitudes, self-efficacy, diet (24-hour dietary recall), PA (pedometer step count) and weight status were assessed. Multilevel regression methods were used to assess differences in knowledge, attitudes, self-efficacy, diet, PA, and body weights between APPLE School graduates and comparison school graduates. Temporal cross-sectional comparisons of self-efficacy, PA and weight status between elementary school (2008/09) and junior high/high school (2015/16) were also examined.

Results: APPLE School graduates did not significantly differ from comparison school graduates for the outcomes of knowledge, attitudes, self-efficacy, diet, PA, and weight status. In the temporal comparisons of self-efficacy, PA and weight status between elementary school (2008/09) and junior high/high school (2015/16), there was also no statistically significant differences between the two groups.

Conclusions: Our findings suggest that the benefits of CSH may continue into adolescence. However, this could also be the result of the new school environment having an equalizing effect on all students. Since lifestyle practices are adopted throughout childhood and adolescence, an extension of CSH into junior high/high schools should be considered in order to consolidate healthy lifestyle messages and practices.

The Power of Partnership

Abstract #:   21
Presenter: Pierrette Elias
Supervisor: Kate Storey
Title: Care provider's perception and their role in promoting healthy eating and physical activity for children in the after-school care setting
Authors: Pierrette Elias, Genevieve Montemurro, Kate Storey
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

After-school care (ASC) programs have garnered interest in recent years as the hours of 3-6pm are an opportune time for children to engage in healthy behaviours. School's Out…Let's Move (SOLMo) is an ASC intervention which applies the evidence-based comprehensive school health (CSH) framework to improve healthy eating (HE) and physical activity (PA) for children attending ASC programs. Within the ASC setting, care providers are important influencers and have the ability to impact the social and physical environments for children. The purpose of this study was to explore the role of care providers and their ability to promote HE and PA opportunities for children within the SOLMo intervention.

Methods:

Focused ethnography was employed for this study. Multiple data generating strategies were applied: participant observation, reflexive journaling, and semi-structured interviews. Convenience sampling was used to invite care providers from intervention sites (n=4) to participate in interviews. Individual interviews with ASC providers (n=13) were audio recorded and transcribed verbatim. Latent content analysis was completed using NVivo v11 software. Peer debriefing with research team members and use of critical friend aided in the development of codes and themes during the analysis phase and helped to ensure trustworthiness.

Results:

Findings revealed multiple themes regarding the impact of SOLMo on ASC providers' roles and ability to promote HE and PA. ASC providers expressed a comprehensive view on care to ensure children's well-being. Overall provider experiences of the SOLMo project were reported as positive, indicating their participation as beneficial to the promotion of HE and PA. Specifically, providers reported: (1) enhanced awareness by ASC providers for the promotion of HE and PA opportunities for children, (2) improved programming of HE and PA, (3) confirmation of their role as an essential instrument in the promotion of HE and PA opportunities in the ASC setting, (4) a need for community connections for quality ASC programs, and (5) a perceived role tension, internal and external, of being both a child minder and educator.

Conclusions:

Care providers are essential to improving HE and PA opportunities for children in the ASC setting. Multiple themes emerged in this study, which confirms the suitability of a CSH approach to positively affect ASC provider's ability to promote HE and PA opportunities for children in the ASC setting. This research contributes to the literature on 'better practices' for ASC programs to improve health behaviours in school-aged children.

The Power of Partnership

Abstract #: 22
Presenter: Hein Min Tun
Supervisor: Anita Kozyrskyj
Title: Birth mode and infant gut microbiota sequentially mediate the association between maternal and child overweight
Authors: Hein Min Tun, Sarah Bridgman, David Guttman, Allan Becker, Piush Mandhane, Stuart Turvey, Padmaja Subbarao, Malcolm Sears, James Scott, Anita Kozyrskyj
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: Childhood overweight is a global public health concern. In Canada, over 20% of preschool children are overweight. Also on the rise is maternal obesity during pregnancy. Although children born to obese mothers are at higher risk for obesity, the mechanisms behind this association are not fully delineated. The transmission of obesogenic microbiota is recently hypothesized as a novel possible pathway. The current study examined whether birth mode and infant gut microbial diversity are mediators in the association between maternal and child overweight.

Methods: The study comprised a large sub-sample of 999 infants enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) population-based birth cohort. Maternal BMI was calculated from data taken from hospital records or pre-pregnancy recall, or measurements taken at 1 year if the former were not available. Maternal overweight/obesity was classified as > BMI 25.0. Gut microbial diversity and composition of 3-month old infants was assessed using high-throughput 16S rRNA sequencing. At age 3 years, age-gender BMI-z scores were generated from measured weight and height according to WHO criteria. Child overweight/obesity was defined as >97th centile BMI z score. Data on maternal smoking, birth mode, breastfeeding and antibiotic exposure were retrieved from administered questionnaires or birth charts. A multiple mediator path model was evaluated to examine the indirect effects of birth mode (M1) and infant gut microbial diversity (M2) as mediators of the maternal –childhood obesity association. Statistical analyses were performed in SAS V9.4.

Results: One in 5 toddlers born to overweight/obese mothers were overweight at age 3 years versus 5% of children born to normal weight mothers. This translated into a 5-fold increased risk of overweight/obese at age 3 years (OR: 4.9, 95%CI: 2.8-8.7). Maternal overweight was associated with increased infant gut microbiota richness indices at 3 months of age including total microbiota species richness and Firmicutes richness (P<0.01). Increases in these indices elevated risk of overweight in toddlers more than two times. Moreover, overweight mothers were more likely to give birth by CS (OR 1.4, 95%CI: 1.1-1.9). Compared to vaginal delivered infants, CS-delivered infants had lower total microbiota species richness but higher Firmicutes richness and diversity at 3 months (P<0.05). The multiple mediator path modeling revealed that birth mode and infant gut microbiota (especially total species and Firmicutes richness) sequentially mediated the association of maternal overweight with childhood overweight (P<0.05).

Conclusion: This study provides evidence of a novel sequential mediator pathway involving mode of delivery and infant gut microbiota for the association between maternal overweight and childhood overweight.

The Power of Partnership

Abstract #:	23
Presenter:	Brittany Matenchuk
Supervisor:	Anita Kozyrskyj
Title:	Association between infant sleep duration and gut microbiota composition at 3 months of age
Authors:	Brittany Matenchuk, Ted Konya, Hein Tun, Allan Becker, Piush Mandhane, Stuart Turvey, Padmaja Subbarao, Malcolm Sears, Anita Kozyrskyj
Affiliations:	University of Alberta
Research Activity:	Maternal and Infant Healthy Development

Introduction

Infancy is a critical period for gut microbiota colonization. In infants and toddlers, sleep and gut microbiota composition have been independently linked to future risk for asthma and obesity. The relationship between sleep duration and negative health outcomes may be explained by an altered gut microbiota composition. This study aims to explore the relationship between short sleep duration and gut microbiota composition in the 3-month-old infant.

Methods

Sleep duration was assessed at 3 months of age using the Brief Infant Sleep Questionnaire in 339 infants whose mothers were enrolled during pregnancy between 2009 and 2012 in the Sleep, Learning, Education, and Environment Project - Edmonton(SLEEP-E) sub-study of the Canadian Healthy Infant Longitudinal Development(CHILD) study. Infant gut microbiota were profiled by Illumina 16S rRNA sequencing from faecal samples collected at 3.3(mean) months of age. Nonparametric tests were used to compare the median relative abundance, richness, and diversity of bacterial taxa groups according to sleep duration. Significant taxa were confirmed with regression modelling.

Results

Median sleep duration was 14.50hrs (range: 5.50-20.00hrs). Maternal race/ethnicity, breastfeeding exclusivity, infant antibiotic use, birth mode, and solid food intake were not significantly associated with sleep duration. In infants born vaginally without intrapartum antibiotic prophylaxis(IAP), sleep duration ≤14hrs was associated with a 2.7-fold greater likelihood of a high abundance of unclassified genera in the *Enterobacteriales* family (Odds Ratio[OR]=2.690, 95% Confidence Interval[CI], 1.430-5.061; P=0.002) and a 54% reduced likelihood of high abundance of unclassified genera in the *Lachnospiraceae* family (OR=0.465, 95% CI, 0.240-0.903; P=0.024). In infants born by emergency cesarean section(CS), total sleep duration ≤12hrs was associated with a 6.7-fold increased likelihood of a high abundance of *Pasteurellales* (OR=6.722, 95% CI, 1.687-26.784; P=0.007). These associations were independent of maternal race/ethnicity, breastfeeding exclusivity, infant antibiotic use, and solid food intake.

Conclusions

The National Sleep Foundation recommendation for infant sleep duration is 14-17 hours per day. Sleep duration below this recommendation is associated with an increased likelihood of a high abundance of *Enterobacteriales,* which is positively associated with eczema in infancy and overweight in childhood. Optimal-high infant sleep duration (>14hrs) is associated with an increased likelihood of a high abundance of unclassified genera of the *Lachnospiraceae* family, which has been positively associated with lower long-term weight gain in adults. Programs to increase infant sleep duration may provide novel courses of action for the prevention of obesity, asthma and allergic disease in childhood through the manipulation of the gut microbiome.

Abstract #:   24
Presenter: Megan Beggs
Supervisor: R. Todd Alexander
Title: Capacity for intestinal calcium absorption is greater in suckling versus mature mice
Authors: Megan R. Beggs, Allein Plain, R. Todd Alexander
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Infants and children must maintain a positive calcium balance for appropriate growth. Intestinal absorption is the sole mechanism mediating uptake of dietary calcium. Intestinal absorption can occur via active transcellular pathways or paracellular diffusion, driven by an electrochemical gradient. This occurs through the tight junction proteins claudins-2, -12, and -5. Prior work in the Alexander laboratory identified significant transcellular absorption in the lower small intestine that exists only prior to weaning. However, it is currently not known whether the paracellular pathway is altered during postnatal development as well. We, therefore, aimed to determine if paracellular calcium transport is increased in the distal small bowel prior to weaning.

Methods

Wildtype FVB/N mice 14 (± 4) days or 6 weeks (± 2 weeks) were used to represent pre and post weaning, respectively (N = 6 - 12). Gene expression: *Cldn2*, and *Cldn15* were examined using quantitative PCR. Protein abundance of CLDN2 was assessed by immunoblot and quantified using ImageJ. Ussing chamber studies were used to measure ^{45}Ca flux and calcium permeability across *ex vivo* sections of mouse ileum. Transcellular calcium flux was blocked using 10µM nifedipine.

Results

Cldn2 expression was 9-fold greater in p14 mice although no significant difference was observed at the protein level. In contrast, *Cldn15* expression was 4-fold higher in the older mice. Basolateral to apical ^{45}Ca flux measured under conditions lacking a paracellular driving force is representative of Ca^{2+} permeability. Under these conditions, no difference was observed between ages. However, direct measurement of calcium permeability assessed by bi-ionic diffusion potentials revealed a 4-fold higher calcium permeability in pre-weaned mice relative to mature mice. This observation was consistent under conditions of pharmacological blockade of transcellular calcium flux.

Conclusions

Paracellular calcium absorption is significantly higher in the distal small intestine prior to weaning. This pathway likely contributes to the positive calcium balance achieved in early postnatal development. Future studies will similarly examine other segments of the small intestine.

The Power of Partnership

Introduction:

The most severe pain following a fracture occurs within 48 hours of discharge and over 80% of children experience compromise in at least one functional domain. A third of parents are dissatisfied with pain management at home and fail to provide analgesia. Multimedia platforms may improve caregiver knowledge surrounding management of children's fracture pain at home.

Objectives:

We sought to determine whether a novel educational video (VID) was superior to a novel interactive web-based module (WBM) and verbal instructions, the standard of care (SOC).

Methods:

This open-label, randomized, controlled, superiority trial included caregivers of children presenting to the emergency department (ED) with non-operative fractures. Primary outcome was the gain score (pre-post intervention) on a novel 21-item questionnaire testing knowledge surrounding pain recognition and management for children with fractures. Secondary outcomes included a survey of caregiver confidence in managing pain (five-item Likert scale), number of days with difficulty sleeping, number of days before return to a normal diet, and number of days of work/school missed.

Results:

We analyzed the results of 311 participants (WBM 99; VID 108; SOC 104) with a mean (SD) age of 9.6 (4.2) years, of which 125/311 (40.2%) were female. The SOC group had a significantly lower mean gain score than both the VID group (delta = -2.3, 95% CI: -3.3, -1.2; p < 0.001) and WBM group (delta = -1.6; 95% CI: -2.6, -0.5; p = 0.002). The mean gain score on in the VID group was not significantly greater than WBM group (delta = 0.7; 95% CI: -0.3, 1.8; p = 0.25). There were no significant differences in caregiver confidence (p=0.4), number of absent school days (p=0.43), number of nights with difficulty sleeping (p=0.94), number of days before return to a normal diet (p=0.07), or workdays missed (p=0.95).

Conclusions:

Web-based platforms are superior to verbal instructions for improving caregiver knowledge on management of children's fracture pain, with no differences in functional outcomes. Future studies should be adequately powered to detect changes in functional outcomes.

The Power of Partnership

Abstract #:   26
Presenter: Lily Lin
Supervisor: Nee Khoo
Title: Elucidating mechanisms of tricuspid valve adaptation to chronic increased pressure and volume loading of the right ventricle in a swine model
Authors: Lily Lin, Sanaz Hatami, Yashu Coe, Timothy Colen, Consolato Sergi, Elena Di Martino, Ziad Abu Sara, Darren Freed, Nee Scze Khoo
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Tricuspid valve (TV) regurgitation is a mortality risk factor in children with Hypoplastic Left Heart Syndrome (HLHS), who has a 20-30% mortality risk in their first 10-years. Significant TV regurgitation develops in 25-35% of children with HLHS and the pathophysiology leading to TV failure is unknown. We currently lack innovative strategies for preventing or repairing TV regurgitation in HLHS. Previous longitudinal study on HLHS TV function showed increased leaflet size and annulus during chronic increased preload and afterload, not simply explained by somatic growth. Recent data from mitral valve studies support the concept of valve adaptive response by leaflet growth and thickening, to loading stress. We propose a novel piglet model with similar HLHS physiology to study of TV adaptation in response to chronic increased preload and afterload, for newer insights and therapy innovation. We hypothesize that TV will demonstrate adaptive changes to maintain valve competency by rapid leaflet expansion and chordal thickening in response to loading stressors.

Methods

We used 4-5 week piglets to achieve a human infant model of increased RV preload and afterload. The study has 2 phases, (1) develop a piglet model and (2) assess TV changes following exposure to 4-weeks of increased load. In phase 1, piglet is anaesthetized and via left thoracotomy with echocardiographic guidance, pulmonary regurgitation to increase RV preload is achieved using a bioptome. Pulmonary artery banding is then performed to increase RV afterload to 2/3 systemic pressure. Phase 2 consists of 7 sham and 7 intervention piglets. Both will undergo phase 1 with the sham not having the interventions. Both groups are recovered for 4 weeks prior to data collection and sacrifice for comparison. We will assess (a) in-vivo TV anatomy and function using 3D Echo, (b) in-vitro histopathology, (c) biaxial mechanical leaflet tensile properties, (d) leaflet extracellular matrix architecture using Second Generation Harmonic (SHG) microscopy and (e) immunohistochemistry of extracellular matrix remodeling enzymes.

Results

Phase 1 is completed, achieving acute procedural success and anesthesia recovery. Feasibility of proposed assessments on TV was demonstrated in 3DE imaging of piglet TV, biaxial planar mechanical stress testing and SHG microscopy.

Conclusions

A novel piglet infant model of increased RV preload and afterload is feasible. This allows in-vivo and in-vitro study of TV structure and adaptive function in response to chronic stress. Project findings will spur future directions in HLHS TV research and lay the foundation for future studies of TV in children.

The Power of Partnership

Abstract #:   27
Presenter: Marisha McClean
Supervisor: Lisa Hornberger
Title: Echocardiographic predictors and outcomes of branch pulmonary artery stenosis patients with pulmonary atresia.
Authors: Marisha McClean, Timothy Colen, Mohammed AlAklabi, Lisa Hornberger
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

Branch pulmonary artery (PA) stenosis due to ductus arteriosus tissue (DA-PS) contributes to morbidity and mortality associated with pulmonary atresia (PAtr). As preoperative predictors of DA-PS in PAtr remain poorly defined, we sought to identify preoperative echo features that predict DA-PS in PAtr.

Methods:

Neonates with PAtr and a ductal-dependent pulmonary circulation surgically managed in our program from January 2009 to June2015 were included. DA-PS was diagnosed as a discrete proximal stenosis of the branch PA ipsilateral to the DA requiring intervention. Preoperative echocardiograms were reviewed to assess 3 features: 1) proximal branch PA diameters, 2) an abnormal relationship between the branch PAs (an inability to image their origins on the same plane), 3) a horizontal course of the ipsilateral PA with a more obtuse posterior angle between the branch PAs. Following review of their clinical course, comparisons were made between those with and without DA-PS.

Results:

Seventy-six patients met inclusion criteria. At initial intervention, 51 had an aorto-pulmonary shunt, 23 a biventricular repair and 2 pulmonary valve radiofrequency perforation. DA-PS was found in 41(54%) patients of whom 22 had angioplasty at initial surgery and 34 developed DA-PS postoperatively (including 15 despite surgical angioplasty). On pre-operative echo, patients with DA-PS had a smaller proximal PA ipsilateral to the DA (Z-score -4.0±2.1 vs no DA-PS -1.0±1.9, p<0.0001), a more frequent abnormal branch PA relationship (24(59%) vs 2(6%), p<0.0001) and a more obtuse angle between the PAs (112°±32° vs 90°±32°, p=0.007). The ipsilateral PA had a horizontal course in 30(73%) of those with DA-PS versus 3(9%) of those without (p<0.0001). An abnormal PA relationship and/or horizontal course of the ipsilateral PA best predicted DA-PS with a sensitivity, specificity and positive predictive value of 81%, 91% and 92%, respectively.

Conclusions:

In patients with PAtr, diagnosis of DA-PS may be improved by identification of pre-operative echo features, including an inability to image the PAs on the same plane and a horizontal course of the PAs. These findings should guide initial surgical management and postoperative surveillance.

The Power of Partnership

Abstract #:   28
Presenter: Jayani Abeysekera
Supervisor: Lisa Hornberger
Title: Umbilical arterial blood flow in the 3rd trimester and its association with neurodevelopmental outcomes in children with congenital heart disease
Authors: Jayani Abeysekera, Dora Gyenes, Charlene Robertson, Gwen Bond, Irina Dinu, Dianne Creighton, Joseph Atallah, Ivan Rebeyka
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction Children with congenital heart disease are at increased risk of adverse long-term neurodevelopmental outcomes believed in part secondary to a prenatal insult. Altered fetal middle cerebral arterial (MCA) Dopplers suggestive of brain sparing (low Pulsatility Index, PI) as well as placental pathology have been documented in fetal heart disease. In this study, we investigated the relationship between MCA and umbilical arterial, UA, flow patterns in fetal transposition of the great arteries (TGA) and hypoplastic left heart syndrome (HLHS) on growth and 2-year neurodevelopmental outcomes.

Methods We identified children with d-TGA and HLHS within the Western Canadian Complex Pediatric Therapies Follow-Up Program who had a 3rd trimester fetal echocardiogram between October 2004 and August 2014. Participants with inadequate fetal Doppler data or death prior to 2-year follow-up were excluded. MCA and UA PI measurements were obtained via offline analysis of 3rd trimester fetal echocardiograms. The relationship with birth and 2 year somatic measures, and 2 year Bayley Scales of Infant and Toddler Development III composite scores were analyzed using two-sided Pearson correlations (r). Univariate regression models were used to screen for variables associated with our outcomes. Multiple linear regression models are currently being constructed to evaluate the magnitude of the observed relationships.

Results Children with d-TGA (n=24) and HLHS (n=36) were included. MCA PI did not correlate with birth somatic measures or 2-year neurodevelopmental outcomes. UA PI, however, inversely correlated birth and 2 year head circumference (r=-0.36, p=0.005 and r=-0.25, p=0.05), length (r=-0.27, p=0.039 and r=-0.40, p=0.001) and weight (r=-0.31, p=0.015 and r=-0.44, p=0.001), and 2-year cognitive (r=-0.30, p=0.019), language (r=-0.30, p=0. 022) and motor scores (r=-0.27, p=0.04). Sub-group analysis between d-TGA and HLHS participants demonstrated a higher UA PI, lower MCA PI, smaller birth/2 year weights, and lower Bayley-III scores in the HLHS group.

Conclusions A higher UA PI, suggestive of placental insufficiency, in fetal HLHS and d-TGA is associated with worse 2-year growth and neurodevelopmental outcomes. These relationships were more pronounced in the HLHS cohort. This could represent an additional insult that contributes to long-term outcomes in critical neonatal heart disease. Understanding these risk factors allows for early identification and intervention to ultimately improve outcomes.

The Power of Partnership

Abstract #:   29
Presenter: Daniela M. Isaac
Supervisor: Dr. Justine Turner
Title: Effect of n-3 fish oil versus n-6 soybean oil parenteral lipid emulsions on hepatic neutral lipid, fatty acid and phytosterol composition in piglets
Authors: Daniela M. Isaac, Abeer S. Alzaben , Celeste Lavallee, Vera C. Mazurak, Jason Yap, Pamela R. Wizzard , Patrick N. Nation, Consolato Sergi , Paul W. Wales
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Determining the optimal lipid emulsion for parenteral nutrition (PN) in pediatric intestinal failure patients remains an important clinical question given the risk of PN associated liver disease (PNALD). Hepatic steatosis is a clinically relevant histopathologic finding in PNALD. This study examined hepatic neutral lipid (NL), fatty acid (FA) and phytosterol composition in piglets receiving parenteral nutrition with n-3 fish oil (FO) containing or n-6 soybean oil (SO) predominant lipid emulsions.

Methods: Ten neonatal piglets received iso-caloric, iso-nitrogenous parenteral PN at 5 g/kg/day with variation only in the lipid emulsion provided: SO (n=5) versus FO (n=5). Liver tissue was assessed on day 14 of PN for: 1) histology, 2) NL accumulation using Oil Red O staining, 3) hepatic FA composition including triglyceride (TG), total phospholipid (TPL), phosphatidylcholine (PC) and phosphatidylethanolamine (PE) fractions, and 4) phytosterol composition. GGT, ALT, bile acids and total bilirubin were also assessed. Descriptive data were expressed as mean with standard deviation. Independent t-test was used to compare blood chemistries, hepatic FA and phytosterol composition.

Results: Total serum bile acids were 3-fold higher in SO versus FO piglets (30 ± 19 µmol/L vs 11 ± 5 µmol/L, p=0.06). Liver histology scores were not different between FO and SO groups (3.8 ± 0.8 vs 4.6 ± 0.9, p=0.18). Oil Red-O staining showed a two-fold higher trend in NL staining in the SO compared to the FO group (2.0 ± 1.0 vs 0.8 ± 0.8, p=0.07). Total FA in the TPL fraction was significantly lower in the FO compared to the SO group (4852 ± 472 µg/g vs 7333 ± 1177 µg/g, p<0.01). The proportion of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) was significantly higher in the FO versus SO piglets in the TG, TPL, PC and PE fractions (p<0.05). The FO group was lower in campesterol (FO 1.3 ± 0.2 µg/mg vs SO 8.2 ± 1.1 µg/mg, p<0.0001), stigmasterol (FO 0 µg/mg vs SO 3.7 ± 0.7 µg/mg, p<0.0001) and β-sitosterol (FO 0 µg/mg vs SO 14.5 ± 1.4 µg/mg, p<0.0001).

Conclusions: FO lipid emulsion was associated with lower FA and phytosterol accumulation, and higher proportions of EPA and DHA in the liver of neonatal piglets. There was a trend to higher bile acids and NL accumulation in the SO piglets suggesting an increased risk for cholestasis. Alterations in hepatic lipid, FA and phytosterol composition in PN fed piglets given SO lipid emulsion may contribute to PNALD.

The Power of Partnership

Abstract #:   30
Presenter: Sylvie Cormier
Supervisor: Michael van Manen
Title: Exploring paediatric residents' perceptions of competency in neonatal intensive care
Authors: Sylvie Cormier, Melissa Chan, Maryna Yaskina, Michael van Manen
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Background: Assessment and stabilization of the newborn is an expected competency of trainees graduating from Canadian paediatric residency training programs. There is limited evidence, regarding the optimal approach to training these competencies, and whether such competencies are actually achieved by graduates.

Method: A national, cross-sectional survey was developed and employed to explore paediatric residents' perspectives of competencies in neonatal procedures and resuscitation skills. Survey questions were constructed based on review of the Royal College of Physicians and Surgeons of Canada objectives of training in paediatrics to include activities necessary in the assessment and stabilization of the newborn. Likert scales were used to quantify self-reported competence. The survey was distributed to residents across Canada.

Results: A total of 138 participating residents from fifteen Canadian paediatric residency programs completed the survey. Of the different procedural skills, only lumbar puncture was reported as an activity that residents on average were competent in by year 3 and 4. Our study showed a relationship between the number of completed blocks of NICU and competence, suggesting that more time spent in the NICU leads to residents achieving competence. We found an inverse relationship between the exposure to cross-cover calls and competence. Increasing autonomy in the NICU as well as considering neonatology as a sub-specialty were not statistically associated with competence.

Conclusions: Our study showed that a majority of paediatrics residents do not feel confident in neonatal resuscitation skills, and do not meet competence criterion. As residency programs are transitioning towards competence-based education, it is important to gain more insights with respect to strengths, deficiencies, and opportunities for a paediatrics residency training program in terms of NICU experiences.

The Power of Partnership

Abstract #:   31
Presenter: Melissa Tremblay
Supervisor: Rebecca Gokiert
Title: Supporting the health and well being of teen families
Authors: Melissa Tremblay, Rebecca Gokiert, Bethan Kingsley, Karen Mottershead, Rob Appleyard, Gary Benthem, Karen Caine
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Teen parents often struggle to attain safe and secure housing, which can significantly impact the health and wellbeing of their children. Recognizing the complex challenges involved in teen parenting, the Terra Centre for Teen parents and Brentwood Community Development Group partnered to collaboratively develop the Successful Families (SF) program, which offers safe, secure, and affordable housing in combination with wraparound supports.

The organizations contacted the Community-University Partnership for the Study of Children, Youth and Families at the University of Alberta to research the SF program. Together, we co-created a community-based participatory research project to study the impacts of the program on the health of teen mothers and their children.

Methods

Our project has used multiple methods. For the current presentation, we will focus on our use of the qualitative photovoice method (Wang & Burris, 1997) to capture teen mothers' perspectives. As part of our photovoice process, we engaged a total of thirteen teen mothers in twelve group discussions over a five-month period. We asked teen mothers to take photos in response to two research questions: (1) how has participation in the SF program helped you to be a healthy parent? and (2) what do you need in order to help your children grow and develop in healthy ways? Group discussions were audio recorded and transcribed verbatim. Using thematic analysis (Braun & Clarke, 2007), we organized our qualitative data into meaningful themes and sub-themes relevant to understanding how the health of teen mothers and their children can be best supported.

Results

Data from our photovoice process were organized into three categories: (1) independent living; (2) structured support; and (3) community. Within each of these categories, participants discussed the opportunities and challenges involved in raising their children with the support of the SF Program. They also captured powerful photographs that shed light on the realities of teen families. Our results are organized into a conceptual model which will be discussed during our presentation. Importantly, the results of this project, including the photos taken by teen mothers, were featured in multiple media outlets including CBC and CTV news stations.

Conclusions

Our results shed light on how to best support the health and wellbeing of teen families, from the perspective of teen mothers, and within the context of a supportive housing program. Ultimately, this program model could inform programming and policy across sectors, and be used to optimize housing services for teen families.

The Power of Partnership

Abstract #:   32
Presenter: Kathleen Kennedy
Supervisor: Damien Cormier
Title: An examination of the math interactive learning experience (MILE) program for children with neurodevelopmental disorders and learning difficulties
Authors: Kathleen E. Kennedy, Damien C. Cormier , Jacqueline Pei , Carmen Rasmussen
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

Young children experiencing learning difficulties in mathematics are at a higher risk for experiencing difficulties in the subject in their later school years. Early math interventions which target both developmental level and underlying cognitive factors specific to mathematics including working memory and visual-spatial skills are therefore of critical importance to later mathematics achievement. The Math Interactive Learning Experience (MILE) was developed to improve math ability and focuses on the underlying cognitive skills involved in math, and has been highly effective for children with Fetal Alcohol Spectrum Disorder (FASD; Kable et al., 2007). Further research is required to examine the effectiveness of MILE in educational settings, and in a small group format for children with varying neurodevelopmental disorders and/or learning difficulties, not limited to FASD. Therefore, we aimed to determine the effectiveness of the MILE program in an educational setting and small group format in children with neurodevelopmental disorders and/or learning difficulties.

Method:

Participants (N = 14, 6 females, 8 males), aged 5 to 8 years old (M = 6.93 years) participated in the MILE program in three schools. All participants had documented learning difficulties or a neurodevelopmental diagnosis. Over two months, each child participated in 14 MILE sessions (Session length = approx. 30-50 mins) conducted in small groups in their classroom setting administered by an educator or research assistant Participants were completed a battery of math and cognitive tests (pre and post intervention). Curriculum Based Measures (CBMs) were used to measure each child's learning progress over the course of the intervention in the areas of oral counting, number identification, missing number and quantity discrimination.

Results:

Performance on the CBMs demonstrated that the sub-skill areas of growth varied considerably across participants according to slope values calculated using the Theil-Sen Slope Method calculations. Participants, demonstrated growth in at least one area (e.g., Oral Counting) however the magnitude of the median slope values were small.

Conclusions:

The CBM results indicated that progress across the course of the intervention varied considerably across participants. CBMs have proved to be effective tools in progress monitoring (Deno, 1985). However, participants did show improvement on other standardized measures of math following the intervention. Therefore, more research is required to determine which measures are most appropriate for use in interventions with children with neurodevelopmental disorders and/or learning difficulties.

The Power of Partnership

Abstract #:   33
Presenter: Andy Le
Supervisor: Debra Andrews
Title: Developing skills for developmental disabilities: Teaching module improves medical students' confidence even in different settings
Authors: Andy Le, Stephanie Penner, Alexis Fong-Lebouef, Debra Andrews
Affiliations:
Research Activity: Children's Health and Well-Being

Introduction:

Medical students feel inadequately trained in caring for patients with developmental disabilities (PWDD) (Troller et al. 2016; Salvador-Carulla et al., 2015). Inadequate education about care for PWDD can affect provision of timely and empathetic care (Sahin & Akyol, 2010). To address this issue, we developed a pre-clinical 12-hour elective, "Developing Skills with Developmental Disabilities" (DSDD), to improve student knowledge, skills, and attitudes toward pediatric PWDD. The first two student cohorts worked with pre-schoolers; we demonstrated the elective's effectiveness in improving student confidence working with this population (Penner et al. 2017). The current project compared the efficacy of DSDD using a hospital-based day-school for elementary-aged children to previous cohorts.

Methods

The DSDD module was an elective offered to preclinical medical students for credit. Students were given 6 hours of didactics on child development, assistive technologies, and breaking bad news. Students also participated in 6 clinical hours at the Glenrose Rehabilitation Hospital, where they observed school-aged PWDD in a classroom and interacted with an interdisciplinary team. Students also interviewed children's families during medical intakes.

Participating students were given pre- and post-module surveys administered on a 5-point Likert scale. Survey questions pertained to students' self-perceived comfort and knowledge regarding PWDD. Scores pre- and post-elective were compared using t-test analysis. This data was compared to data collected from previous years of the elective, which used the same survey.

Results:

This year, 24 students signed up for the module, and 23 completed it (96%); however, one student's surveys were lost and another student was a coordinator of the elective whose responses were withheld from the data, leaving 21 surveys for analysis. Statistically significant ($p<0.01$) increases were present in 9 of 10 self-reported scores this year, with the statistically insignificant score pertaining to confidence using positive reinforcement techniques. In previous years, statistically significant ($p<0.01$) increases were present across all 10 self-reported scores. There was no significant difference in improvement from pre-elective to post-elective scores when comparing this recent cohort and past cohorts across all 10 scores.

Conclusions:

The DSDD module may be a useful tool for medical schools to incorporate into curricula. The critical components were maintained across the setting change with significant ($p<0.01$) increases in students' self-reported confidence and knowledge in working with PWDD. Ultimately, this elective has demonstrated effectiveness in different settings and with different age groups of children. The general structure and principles of DSDD may be modified and applied in various formats to improve medical education.

The Power of Partnership

Abstract #:	34
Presenter:	Sarah Raza
Supervisor:	Lonnie Zwaigenbaum
Title:	The short quantitative checklist for autism in toddlers (Short Q-CHAT) as an early "red flag" screen for autism spectrum disorder
Authors:	Sarah Raza, Kyle Reid, Lori-Ann Sacrey, Susan Bryson, Jessica Brian, Isabel Smith, Wendy Roberts, Peter Szatmari, Tracy Vaillancourt, Lonnie Zwaigenbaum
Affiliations:	University of Alberta
Research Activity:	Children's Health and Well-Being

Introduction

Identifying early risk markers of Autism Spectrum Disorder (ASD) is crucial in order to facilitate earlier detection and diagnosis of ASD, and implement targeted interventions to improve functional outcomes. Although numerous "red flag" screening instruments have been developed to identify toddlers who may be on a developmental trajectory for ASD, many of these measures are arguably too lengthy to be used in community practice. Thus, the development and implementation of brief screening tools are warranted. The purpose of this study was to examine the effectiveness of a parent-reported questionnaire, the Short Quantitative Checklist for Autism in Toddlers (Short Q-CHAT), as a rapid screen for ASD in a high-risk sibling population.

Methods

Participants: Three groups of toddlers: (1) HR siblings who <u>did not</u> receive an ASD diagnosis at 36 months (HR-N; *n*=72), (2) HR siblings who <u>did</u> receive an ASD diagnosis at 36 months (HR-ASD; *n*=20), and (3) low-risk toddlers with no family history of ASD (LR; *n*=44). *Parent-Report Questionnaire:* The Short Q-CHAT is a 10-item questionnaire shortened from the Q-CHAT that assesses a broad range of ASD symptomology (Allison et al., 2012). Parents of HR and LR toddlers completed the Short Q-CHAT at 18 and 24 months. *Statistical Analyses:* Performance on the Short Q-CHAT was compared between groups (HR-ASD, HR-N, LR) at 18 and 24 months using a series of one-way ANOVAs. Group effects were explored using Benjamini & Hochberg (1995) corrections for multiple comparisons.

Results

Higher total score on the Short Q-CHAT differentiated the HR-ASD group from HR-N and LR groups at both 18 ($q\leq0.001$) and 24 months of age ($q\leq0.001$), indicating greater frequency of ASD symptoms at these time points. Estimates of sensitivity and specificity were 0.78 and 0.55 at 18 months, and 0.87 and 0.56 at 24 months, respectively.

Conclusion

The findings support the effectiveness of the Short Q-CHAT in predicting ASD diagnostic outcomes as early as 18 months of age in at-risk toddlers, which may lead to earlier detection and identification of ASD symptomology and help guide busy healthcare professionals in the referral pathway for ASD. Although the specificity estimates of the Short Q-CHAT were poor, this is likely attributed to higher rates of developmental problems among HR toddlers in our prospective study. Future work will explore alternate Short Q-CHAT cutoffs and ASD classifications.

The Power of Partnership

Abstract #:   35
Presenter: Lori Sacrey
Supervisor: Lonnie Zwaigenbaum
Title: Parent and clinician agreement of early behavioural signs of autism: A high-risk sibling cohort
Authors: Lori Sacrey, Lonnie Zwaigenbaum, Susan Bryson, Jessica Brian, Isabel Smith, Wendy Roberts, Peter Szatmari, Tracy Vaillancourt, Caroline
                   Roncadin , Nancy Garon
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Identifying early impairments in children who will subsequently be diagnosed with Autism Spectrum Disorder (ASD) is crucial to ensure that they gain timely access to interventions that will improve functional outcomes. Although prospective studies of high-risk infants have focused on direct observation of infants' behaviour during clinical assessments, parent reports may provide valuable and complementary information. The purpose of this study was to examine parent and clinician agreement for early signs of ASD.

Methods: *Participants*: High-risk infants (HR; have an older sibling diagnosed with ASD) were divided into two groups based on an independent expert clinical assessment using the ADOS and ADI-R at 36 months of age: HR siblings who <u>did not</u> receive an ASD diagnosis (HR-N; n = 155) and HR siblings who <u>did</u> receive a diagnosis of ASD (HR-ASD; n = 68). *Assessments*: The clinician observational assessment, the Autism Observation Scale for Infants (AOSI; Bryson et al., 2008), and the parent-report questionnaire, the Autism Parent Screen for Infants (APSI; Sacrey et al., 2016), which was modeled in content from the AOSI, were compared. These assessments share 19 items that cover early symptomatology of ASD and were completed at 12 months of age. *Statistical Analyses*: Performance on the APSI and AOSI was compared between the two HR groups using independent t-test analyses. Agreement between parents and clinicians for the shared 19 items was analyzed using intraclass correlations (ICC).

Results: Intraclass correlations indicated poor agreement between parents and clinicians, with ICC < .04 for the combined group, the HR-ASD group alone, and the HR-N group alone. Item-level comparisons using independent t-tests indicated: (1) six items were informative in predicting diagnostic outcomes on both the AOSI and APSI, (2) six items were informative on the APSI only, and (3) seven of the items were not informative on either assessment.

Conclusion: Prospective parent report is informative for early signs of ASD by 12 months and complements what may be observed during a clinical assessment. Thus, some clinically informative behaviour may be more likely detected by parents based on their day-to-day observations than during a brief clinical visit.

The Power of Partnership

Abstract #:   36
Presenter: Graham Little
Supervisor: Christian Beaulieu
Title: Sex differences in patterns of brain volume reduction in children with prenatal alcohol exposure
Authors: Graham Little, Christian Beaulieu
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Although many brain imaging studies of fetal alcohol spectrum disorders (FASD) combine male and female participants, quantitative MRI has suggested that prenatal alcohol exposure may impact brain structure such as regional volumes differently in males relative to females. However, these studies examine each brain region separately rather than considering that there may be global patterns of brain differences with sex. Machine learning algorithms can be applied to "learn" models from imaging data that may predict a grouping (e.g. FASD or control).

Purpose: Can multi-variate models of brain volume identify individuals with FASD and how do they differ between males and females?

Methods: Brain imaging (3D MPRAGE) was acquired from two independent projects: (i) NeuroDevNet including FASD (N=79, 12.7±3.2 years, 5-19 years, 44 females) and controls (N=83, 11.9±3.4 years, 5-19 years, 50 females); (ii) CIHR including FASD (N=57, 10.6±3.1 years, 5-20 years, 24 females) and controls (N=57, 10.6±3.1 years, 5-20 years, 30 females). Volumes of 81 brain regions were extracted (Freesurfer version 5.3) keeping left and right separate per subject. FASD predictive models were generated separately for males and females by inputting brain volumes from the NeuroDevNet dataset into a learning algorithm (linear support vector machine). The two models were evaluated using the CIHR dataset based on accuracy, sensitivity, and specificity. The 5 most important (weighted) brain volumes per model were compared between male and females.

Results: Both models showed moderate performance in predicting FASD: males accuracy 68%, sensitivity 70%, and specificity 67%; females accuracy 68%, sensitivity 64%, and specificity 72%. The 5 regions that provide the most distinction in the models were left/right caudate, left pallidum, right hippocampus, and right superior parietal for males and left superior parietal, left insula, left pericalcarine, right bank of superior temporal sulcus, and left transverse temporal cortical gray matter for females.

Conclusion: Sex specific model performance using brain volumes to predict FASD was similar between males and females, but the unique regional brain patterns suggest sex differences of prenatal alcohol exposure.

The Power of Partnership

Abstract #:   37
Presenter: HanHyung Lee
Supervisor: David Olson
Title: Peripheral neutrophils invade the mouse uterus in a IL1b-induced model of preterm birth (PTB)
Authors: HanHyung Lee, Meghan Onushko, Xin Fang, David Olson
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Neutrophil invasion of the gestational tissues precludes every term birth. Their role is unclear, but they may play an important role in activating the contractile mechanisms of the uterus and softening the cervix for fetal expulsion through the expression of inflammatory cytokines and matrix metalloproteases respectively. Our lab has recently demonstrated that neutrophil invasion of the mouse lower uterus (mUL) is predominant at gestational day (GD) 18.5, but whether this phenomenon occurs during PTB is unknown. In this current study, a mouse model of interleukin 1b (IL1b)-induced PTB was used to study whether IL1b induces neutrophil invasion of the mUL, and whether this response could be blocked with 101.10, an IL1R inhibitor.

Methods

Timed-pregnant mice at GD16 were anesthetized under isoflurane, and injected with either IL1b (3 µg) or vehicle in the right horn of the mUL between two fetal membranes. The mice were injected with 101.10 (1 mg/Kg/12h) or vehicle subcutaneously in the neck 30 minutes before IL1b administration. Blood and mUL samples were collected at GD17 or GD18.5. mRNA for IL1b, IL6, IL10, TNFa, and CCL2 was detected in mouse leukocytes by RT-qPCR. mUL was cryosectioned (7 mm) and stained for neutrophils using anti-Ly6G. Stained mUL were visualized under a confocal microscope. Chemoattractants were extracted from the mUL using homogenization and density centrifugation, and normalized to tissue weight. Total human leukocytes were isolated from women at term in spontaneous labor, and used to assess the strength of mouse chemoattractant in a modified Boyden Chamber: leukocytes underwent chemotaxis toward chemoattractant across a polycarbonate membrane (3 µm pores), and were quantified using Hoescht 33342, a DNA-binding fluorescence dye.

Results

In normal mouse pregnancies, neutrophils were detected in the mUL significantly higher at GD18.5 than GD17 (p<0.05). The strength of mUL chemoattractants was also significantly higher at GD18.5 than GD17 (p<0.05). IL1b induced PTB within 24 hours (n=6) and 101.10 blocked this action every time (n=6). 101.10 alone (n=6) nor the sham control (n=6) induced PTB. Similarly, only the PTB-induced group experienced an invasion of neutrophils in the mUL (p<0.001). No significant difference wasfound for the strength of mUL chemoattractants between experimental groups. Rather, there was increased detection of mRNA for inflammatory markers in the neutrophils in the PTB-induced group.

Conclusions

Neutrophils invaded the mUL in a IL1b-induced model of PTB, and this action was blocked by the subcutaneous injection of 101.10. This was not the action of increased chemoattractants in the mUL, but most likely a function of a priming effect on peripheral neutrophils to respond to chemoattractants. The increased detection of mRNA for inflammatory cytokine mRNA in peripheral neutrophils suggests that they are more active. Previous work by our lab has demonstrated that neutrophils are more active the closer a woman approaches spontaneous term labor. This phenomenon most likely occurs in our IL1b-induced model of preterm birth in the mouse. Whether this priming effect is specific to uterine chemoattractants or universal is not yet understood.

The Power of Partnership

Abstract #:   38
Presenter: Kelycia Leimert
Supervisor: David Olson
Title: Co-culture of human fetal membranes and uterine myocytes induce a cytokine chain reaction promoting transitioning of the uterus for parturition
Authors: Kelycia Leimert, Angela Messer, Theora Gray, Xin Fang, David Olson
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: Transformation of the pregnant uterus into the uterus of delivery is essential for parturition, and is marked by increases in uterine activation proteins (UAPs: FP, OTR and COX-2) and pro-inflammatory mediators (IL-6). IL-1b has an influential role in this transition; recent data demonstrated an up-regulation of 98 genes in uterine myocytes stimulated with IL-1b. We developed a co-culture method to explore maternal and fetal gestational tissue interactions, involving term non-labouring primary human myometrial smooth muscle cells (HMSMC) and human fetal membrane explants (FME). We hypothesize that crosstalk between tissues promotes pro-inflammatory expression and therefore uterine transitioning for parturition.

Methods: HMSMC are plated in 12-well plates alone or with 6mm FME in transwell inserts. Via shared culture medium, these tissues can be simultaneously stimulated with IL-1b (1 ng/mL), followed by collection of supernatant for multiplex assay and RNA extraction of FME/HMSMC for RT-PCR. UAP and cytokine/chemokine relative expression levels are measured in each tissue separately, as well as products released into shared supernatant, in response to both monoculture and co-culture conditions. N=5-7, two-way ANOVA, $p<0.05$.

Results: After 24h in co-culture, HMSMC showed 34x and 523x increased *COX-2* and *IL-6* mRNA, respectively, compared to HMSMC alone. Co-incubated FME had 13x higher *IL-6* and 17x higher *COX-2* than FME alone (all $p<0.001$). IL-1b strongly up-regulates *IL-6* and *COX-2* in both monocultures, but in co-cultures, IL-1b incubation only induces a slight additional effect. Co-culture resulted in a 3.2x and 2.2x increase in FME *FP* and *OTR*, and a 3x increase in HMSMC *OTR*, but this effect was not significant ($p>0.05$). Supernatants from HMSMC alone, FME alone and HMSMC/FME co-cultures were analyzed via multiplex. Co-culture induced a synergistic increase in the release of 18 different cytokines/chemokines (including IL-6, IL-8, CCL2, CXCL1 and TNFa), producing outputs much greater than the sum of each monoculture ($p<0.001$).

Conclusions: A better understanding of labour physiology, especially the role of inflammatory mechanisms, is crucial. Our model studies *in vitro* interactions between gestational layers using adjacent layers of gestational tissues at term. After only 6h, indirect contact via shared medium results in amplified production of a series of pro-inflammatory cytokines/chemokines. After 24h co-culture, we see significantly increased *IL-6* and *COX-2* (and increasing trends in *FP* and *OTR*) in both HMSMC and FME. These data suggest that 'crosstalk' between the tissues initiate a 'cytokine chain reaction' that results in up-regulation of *IL-6* and *COX-2*, promoting uterine transitions. Acknowledgements: WCHRI, CIHR.

The Power of Partnership

Abstract #:   39
Presenter: Charlene Nielsen
Supervisor: Alvaro Osornio-Vargas
Title: Spatio-temporal hot spots – how do the patterns compare for subnormal birthweight and outdoor pollutants?
Authors: Charlene Nielsen, Alvaro Osornio-Vargas, Carl Amrhein, Jesus Serrano-Lomelin, Osmar Zaiane
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction/Objectives: Disorders related to short gestation and low birth weight are the 2nd cause of infant death in Canada and have been increasing, especially in Alberta. Individual maternal risks are important but environmental exposures during pregnancy may restrict fetal growth. This contributes to small for gestational age (SGA: < tenth percentile weight for pregnancy duration) and low birth weight at term (LBWT: <2500 grams at ≥37 weeks-gestation). We examined the spatial-temporal patterns of SGA and LBWT with patterns of pollutants at conception, second trimester, and birth.

Methods: We aggregated postal code locations of mothers' residences from the 2006-2012 birth registry in to space-time bins to analyze emerging hot spots. We applied the space-time pattern analysis on 70 industrial chemical emissions from the National Pollutant Release Inventory (NPRI) in estimated three month intervals. Then we statistically associated the classified patterns of SGA/LBWT with the pollutant patterns using the kappa statistic to determine how much the hot spot categories agree. The difference between kappas indicated which trimester would be more important for which chemical.

Results: There was an increasing trend for SGA (consecutive hot spots) and for LBWT (sporadic hot spots) in major urban centers. There was an increasing trend for 15 chemicals (varying hot spots). 28 chemical patterns had a kappa index greater than 0.2 with SGA or LBWT patterns. Although there is poor agreement between the space-time patterns, the maximum kappa values occurred mostly with LBWT and during the last trimester.

Conclusions: Patterns of chemicals identified in published literature (e.g. particulate matter, CO, and SO2) agreed more with timing around conception; however, there were additional pollutants with maximum kappa during the birth trimester. Our research is moving us toward a better understanding of the spatial-temporal link between environment and early health.

The Power of Partnership

Abstract #:   40
Presenter: Bonnie Woolnough
Supervisor: Tarek Motan
Title: Effect of follicular flushing during oocyte retrieval in assisted reproductive techniques
Authors: Bonnie Woolnough, Larissa Shapka, Ariadne Daniel, Tarek Motan
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction:

Follicular flushing is a common procedure during oocyte retrieval in many assisted reproductive technology (ART) clinics. Previous studies have provided conflicting results on its utility. This study aimed to assess whether follicular flushing during assisted reproductive technologies improved the oocyte yield, number of good quality blastocysts or utilization rates of blastocysts among women who responded well to ovarian stimulation. We aimed to assess if the stimulation protocol used in our centre, unique from prior studies, would make a difference in outcomes.

Methods:

A retrospective cohort study was carried out, reviewing patients from August 2016 to February 2017 in a single clinic. Patients who were normal responders to ovarian stimulation were recruited. They were used as their own controls with alternating daily allocation of the left or right ovary to have ovarian follicular aspiration followed by follicular flushing. The other ovary had follicles retrieved using standard aspiration. Statistical analysis was carried out using paired T-tests for comparison of flushed and non-flushed ovaries.

Results:

The mean number of oocytes retrieved from the flushed ovary was 9.5 as compared with the unflushed ovary at 8.8 (mean difference 0.71, 95% CI: -0.20, 1.63). The mean number of mature (M2) oocytes retrieved was 7.5 from the flushed ovary, compared with 6.9 from the unflushed ovary (Mean difference 0.62, 95% CI: -0.18, 1.41). Blastocysts of good quality obtained from the flushed and unflushed ovaries were 2.5 and 2.1, respectively (mean difference 0.39, 95% CI: -0.17, 0.95). Utilization rates from the flushed and unflushed ovaries were 0.56 and 0.51, a mean difference of 0.05 (95% CI: -0.02, 0.12) .

Conclusions:

Neither the primary nor secondary outcomes showed a statistically significant difference between the flushed or unflushed ovary. This is concordant with the results from previously published systematic reviews showing no difference. This study adds to current knowledge given that in our centre, the majority of ART cycles (96%) are done with gonadotropin releasing hormone (GnRH) antagonist stimulation and GnRH agonist trigger, while previous studies all used GnRH agonist protocols. It suggests that the stimulation protocol does not make a difference to the oocytes obtained or embryos used with or without follicular flushing.

The Power of Partnership

Abstract #: 41
Presenter: Jesus Serrano-Lomelin
Supervisor: Alvaro Osornio-Vargas
Title: Urban-rural variations in the prevalence of maternal risk factors for preterm birth and small for gestational age in Alberta
Authors: JESUS SERRANO-LOMELIN, MARIA OSPINA, CHARLENE NIELSEN, ALVARO OSORNIO-VARGAS
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction. The prevalence of preterm birth (PTB) and small for gestational age (SGA) in Alberta have been among the highest in Canada during the last decade. Multiple risk factors relate with PTB and SGA, such as young/advanced maternal age, high blood pressure, diabetes, obesity, cigarette smoking, and alcohol/drug use. A better understanding of the distribution of these known risk factors in the province is necessary for developing strategies aimed to mitigate their impact and inform targeted prevention.

Methods. We conducted a population-based retrospective cohort study of mothers having singleton live births from 2006 to 2012, in Alberta. We estimated the prevalence of 1) spontaneous preterm birth (S-PTB), 2) SGA and 3) pre-pregnancy obesity, gestational hypertension/diabetes, smoking/substance use during pregnancy in both urban and rural settings. We calculated annual and period prevalence, according to maternal age groups: < 20 years old; 20 to 34 years old, and ≥ 35 years old.

Results. We studied a total of 330,957 singleton live births with gestational ages between 22 and 42 weeks. **Key differences between urban and rural settings were:** (i) the period prevalence of S-PTB was higher in the groups of younger (8.6%) and older (7%) mothers when compared with the 20-34 years old group (6.4%) only in urban settings; (ii) the period prevalence of SGA was 9.5% vs. 6.9% in rural settings. The SGA annual prevalence increased over time in the younger and older maternal age groups in urban settings; (iii) the period prevalence of gestational diabetes was higher in urban than rural settings, particularly in older mothers (10.2% *vs.* 7.4%, respectively) and increased over time; (iv) the period prevalence of pre-pregnancy obesity was lower in urban (8%) than rural settings (10.5%); the same pattern was observed for smoking (22% *vs.* 28%, respectively) and substance use during pregnancy (5.3 *vs.* 7.5%, respectively); (v) annual prevalence of smoking during pregnancy decreased over time, except for mothers aged ≥ 35 years in rural settings; (vi) the period prevalence of gestational hypertension was ≈5% in both urban and rural settings; although annual prevalence decreased over time only in urban settings for young mothers and in the 20-34 age group.

Conclusions. We observed different patterns in the prevalence of S-PTB, SGA and associated maternal risk factors between urban and rural settings, suggesting that targeted interventions could be designed to mitigate the impact of these known risk factors on S-PTB and SGA in Alberta.

The Power of Partnership

INTRODUCTION: Observational studies on the association between gestational age/birth weight and respiratory health have increased over the last decade. Systematic reviews (SR) and meta-analyses have synthesized this body of research with variations in primary study types, populations and outcomes. This overview synthesizes the evidence from meta-analyses (MA) on the magnitude and direction of the association between gestational age/birth weight, and a variety of respiratory outcomes occurring in childhood and adulthood.

METHODS: A PROSPERO protocol was developed *a priori* (CRD42017072745). Comprehensive searches were conducted in four electronic databases up to July 2017. Two independent reviewers screened the records to identify SR with at least one MA of categorical or numeric data about the association between preterm birth (PTB), small for gestational age (SGA), and birth weight (low/high birth weight [LBW/HBW]) and respiratory outcomes (diagnosis and lung function) in children and adults. Risk of bias was independently assessed using ROBIS and R-AMSTAR tools. The magnitude and direction of pooled estimates were summarized. **RESULTS:** Of 1,479 records identified by the searches, 11 SRs with MA data were included. Most of them focused on the relationship between LBW and asthma (11 MA) with pooled odds ratios (pOR) between 1.13 (95% CI 1.01, 1.27) and 1.59 (95% CI 1.29, 1.98). Also frequent were MAs of the association between HBW and asthma (8 MA), with pOR between 1.04 (95% CI 0.92, 1.19) and 2.77 (95% CI 1.56, 4.95). Pooled estimates (OR) for PTB and wheezing (7 MA) ranged between 1.34 (95% CI: 1.25, 1.43) and 3.00 (95% CI 2.61, 3.44). For PTB and asthma (4 MA), pOR ranged between 1.074 (95% CI 1.072, 1.075) and 1.40 (95% CI 1.18, 1.67); while pOR for LBW and wheezing (4 MA) were between 1.10 (95% CI 1.00, 1.21) and 1.63 (95% CI 1.32, 2.01). Others reported associations between HBW and wheezing (2 MA, pORs 1.02 [95% CI 0.99, 1.04] and 2.40 [95% CI 1.53, 3.7]) and SGA and asthma (1 MA; pOR 1.10 (95% CI, 1.01, 1.37). Lung function outcomes (FEV1) were also reported. The majority of SRs were of moderate quality and varied in their selection criteria of primary studies.

CONCLUSIONS: There are consistent (but small) associations between LBW, PTB, SGA and risk of asthma and wheezing across MA. Results for HBW and asthma and wheezing are inconsistent. The relationship between duration of pregnancy and birth weight and other respiratory outcomes has not been assessed in SRs.

The Power of Partnership

Abstract #:   43
Presenter: Cary Ma
Supervisor: Michael Hawkes
Title: The utility of handheld point-of-care lactate measurement to predict mortality in Ugandan children hospitalized with pneumonia
Authors: Cary Ma, Austin Ericson, Sophie Namasopo, Robert Opoka, Andrea Conroy, Michael Hawkes
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

Pneumonia is the leading cause of death among children <5 worldwide. Most deaths occur in low-income countries in Africa and Asia. Healthcare professionals in resource-limited countries often use clinical risk scores to triage and risk-stratify their patients. Lactate, a product of anaerobic metabolism, is a known clinical indicator of perfusion status and illness severity. In this context, we investigated the prognostic value of point-of-care lactate, in comparison to several clinical risk scores, in children admitted to hospital with pneumonia.

Methods:

We conducted a prospective cohort study of children <5 years admitted for pneumonia in Uganda. Lactate was measured at admission and daily during hospitalization with a rapid handheld point-of-care device, the Lactate Scout Analyzer. Clinical data and outcome (death or survival) were recorded. Clinical risk scores were calculated: Bedside PEWS, Pediatric Early Death Index for Africa (PEDIA), Lambarene Organ Dysfunction Score (LODS), Signs of Inflammation in Children that can Kill (SICK), and Fluid as Expansive Supportive Therapy Pediatric Emergency Triage (FEAST PET). Receiver operator characteristic (ROC) curve analyses was used to compare lactate as a prognostic marker was compared and clinical risk scores. Kaplan-Meier analyses was used to study survival, which was stratified by admission lactate level.

Results:

Between September 2013 and July 2015, we enrolled 155 children with pneumonia admitted to the Jinja Regional Referral Hospital and Kambuga District Hospital. In-hospital mortality was 22/155 (14%). Median [range] lactate level was 2.4 [0.9-25] mmol/L among children who survived versus 5.3 [1.6-20] mmol/L among children who died (p=0.0001). Lactate was a clinically informative prognostic marker of mortality, with an area under the ROC curve (AUROC) greater than or equal to that of any single clinical sign or composite clinical risk score (AUROC 0.76, [95%CI 0.65 to 0.87], p=0.0001). Lactate also augmented the ability of the leading clinical risk score, PEDIA, to predict mortality (AUROC 0.82 [95%CI 0.69 to 0.94], p=0.001). Lactate level at admission accurately risk-stratified children, with 5-day mortality of 2%, 11% and 26%, among children with lactate of <2.0, 2.0–4.0, and >4.0 mmol/L, respectively (p=0.001).

Conclusion:

Handheld point-of-care lactate measurement is a superior predictor of mortality than any single clinical sign or composite risk score among children hospitalized with pneumonia. This may be a valuable, convenient tool for triage and risk stratification in resource-limited hospitals for pneumonia, the leading killer of children <5 worldwide.

The Power of Partnership

Abstract #:   44
Presenter: Bridget Wiafe
Supervisor: Peter Metcalfe
Title: Co-culture with mesenchymal stem cells inhibits hypoxia-induced inflammatory and fibrotic pathways in bladder smooth muscle cells
Authors: Bridget Wiafe, Adetola Adesida, Thomas Churchill
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Abstract

Introduction: Partial Bladder Outlet Obstruction (pBOO) results in significant morbidity across childhood. In children with severe disorders, such as spina bifida and posterior urethral valves it can result in a lifetime risk of renal failure. Bladder deterioration is fundamentally driven by hypoxia, whereby the constant contraction of bladder smooth muscles and elevation of intra-vesical pressure results in the compression of capillaries and decreased blood flow to the bladder wall. We have characterized hypoxia's role as a single stressor and found that hypoxia is sufficient to induce an intense inflammatory and profibrotic switch in bladder smooth muscle cells (SMCs).

Current clinical management of pBOO is cumbersome and carries significant risk of morbidity. Meanwhile, mesenchymal stem cells (MSCs) therapy is known to have a huge potential in the treatment of hypoxic, inflammatory and fibrotic conditions. Therefore, we aimed to investigate if these hypoxia-signaling pathways can be mitigated using stem cells as well as elucidate the molecular mechanisms of interplay.

Methods: SMCs was cultured under hypoxic conditions for 72 hours with either the direct or indirect co-culture with bone marrow derived MSCs. High pore density transwells were used for indirect co-cultures in order to prevent physical contact between the SMCs and MSCs. This way, the interaction between the two cell types was limited to the diffusion of soluble factors across the membranes. RNA was extracted for gene expression analysis whiles the Mesoscale multiplex assay (U-PLEX) was used for secreted cytokines and growth factor measurements. Total collagen contents were also measured using the Sirius Red collagen assay.

Results: Hypoxia-induced HIF3α transcripts and VEGF in SMCs were unaltered by MSCs co-culture. Both direct and transwell co-cultures inhibited > 50% of hypoxia-induced TGFβ1 and IL-6 expression ($p<0.001$). Also, both MSCs co-culture techniques induced >200% increase in IL-10 protein ($p<0.0001$) and inhibited hypoxia-induced αSMA, collagen 1&3 transcripts as well as total collagen proteins ($p<0.0001$). Contrastingly, the hypoxia-induced IL-1β and TNFα levels were inhibited by only the direct MSCs co-cultures ($p<0.05$).

Conclusion: MSCs co-culture with bladder SMCs potently mitigates hypoxia-induced inflammatory and profibrotic pathways. This study throws light on cell-cell contact and paracrine immunomodulatory mechanisms of MSCs action which is imperative for therapeutic intervention.

The Power of Partnership

Abstract #: 45
Presenter: Powel Crosley
Supervisor: Mary Hitt
Title: Combination of apoptosis-activating agents that hold potential for treatment of ovarian cancers
Authors: Powel Crosley, Kate Agopsowicz, Anniina Farkkila, Mary Hitt
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: Granulosa cell tumour (GCT) is a rare form of ovarian cancer (~5% of ovarian neoplasms), which generally responds poorly to chemotherapy.

Procaspase activating compound-1 (PAC1) is a small-molecule drug shown *in vitro* to sequester inhibitory zinc ions from the Caspase-3 (CASP3) zymogen allowing CASP3 to auto-mature and execute apoptosis.

TNF-related apoptosis-inducing ligand (TRAIL) is a pro-apoptosis ligand that can bind membrane-bound death receptors and trigger the extrinsic apoptotic pathway resulting in activation of CASP3 to execute its proteolytic role in programmed cell death.

Methods: The GCT cell line KGN was separately treated *in vitro* with a range of PAC1 and TRAIL concentrations for 48 hours to establish a dose-response curve. Calculated EC_{50} PAC1 (20 μM) along with low-dose TRAIL (10 ng/mL) was used to evaluate the biologic response of simultaneous treatment with PAC1 and TRAIL, or TRAIL applied 24 hours after PAC1 treatment. Independently, cells from fresh primary and recurrent GCT samples were cultured *in vitro* for 5 days, then treated with the same regimen. Cell viability was measured 48 hours after PAC1 treatment.

Results: Dose-response assays indicate treatment with PAC1 strongly reduces viability of KGN cells compared to untreated control ($p<0.05$) while TRAIL only significantly reduces viability of KGN cells at the highest concentration tested (1 μg/mL). Two-way dose-response assays in KGN combining simultaneous PAC1 with TRAIL showed the combination of PAC1 20 μM with TRAIL 10 ng/mL was significantly effective in reducing viability of KGN cells ($p < 0.05$). Similar assays in fibroblast and kidney cells (N60 and NKC, respectively) showed the PAC1/TRAIL combination to be less toxic in normal cells. Kinetic assays of treated KGN cells by high-content screening suggest that PAC1 requires ~24 hours to manifest effect, while TRAIL is more rapid in affecting target cells. KGN and patient-derived primary GCT cells were assayed withPAC1 20 μM and TRAIL 10 ng/mL either alone,concurrently, or TRAIL applied 24 hours after PAC1. The combination of PAC1 with delayed TRAIL was dramatically more cytotoxic than TRAIL or PAC1 treatment alone ($p<0.05$), especially in the patient-derived cells.

Conclusion: Results *in vitro* suggest combining CASP3 activator PAC1 with apoptosis-inducing TRAIL holds potential as an effective strategy for treatment of GCT at dosages that are nontoxic in normal cells. Future directions include investigating the use of an oncolytic vaccinia virus expressing a TRAIL transgene on PAC1-pretreated cells. This could enhance selectivity for, and toxicity in, cancer cells.

The Power of Partnership

Introduction: An estimated 6600 Canadian women were diagnosed with uterine cancer in 2016, with 20% of women succumbing to the disease. One of the most lethal subsets of uterine cancer is dedifferentiated endometrial carcinoma (DDEC). DDEC tumors possess both well-differentiated and undifferentiated regions. The majority of metastatic disease is made up of cells from the undifferentiated component of DDEC yet it is unclear how these poorly differentiated regions are initiated and sustained within the carcinoma. Examining the well-differentiated and undifferentiated components of DDEC tumors in terms of mutation profiles, we demonstrated that 80% of the undifferentiated regions in DDEC lesions lack the expression of core chromatin remodeling proteins, BRG1 or ARID1A and ARID1B. We hypothesize that the loss of these proteins, which are known regulators of transcription, may lead to the induction and/or maintenance of stem cell-like gene expression programs that drive dedifferentiation, metastasis and therapy resistance.

Methods: BRG1-deficient or ARID1A/B co-deficient cell line models were generated by CRISPR and validated using immunofluorescence and immunohistochemistry. qRT-PCR and immunofluorescence will be used to assess the level of expression and localization of markers of epithelial-to-mesenchymal transition (EMT), stemness and endometrial lineage. The ability of the generated knockouts to proliferate and form spheres will be evaluated, as well as an examination of the response of these BRG1-deficient or ARID1A/B co-deficient cell line models to chemotherapy and current clinically relevant epigenetic inhibitors (vorinstat and tazemetostat). Tumor formation in immune-compromised mice will be monitored to ascertain any histological differences between wildtype and BRG1 or ARID1A/B knockout endometrial cancer cells.

Results: Endometrial cancer cells lacking BRG1 expression have significantly reduced E-cadherin and estrogen receptor levels while also possessing increased levels of the stemness associated marker, Oct4. Interestingly, the ability of the BRG1 deficient cell line model to form spheres was significantly reduced in comparison to BRG1 intact cell lines.

Conclusions: BRG1 deficient endometrial cancer cell lines have been shown to partially undergo EMT and recapitulate the clinical DDEC phenotype. Determining the extent to which loss of BRG1 or ARID1A/B contributes to the acquisition of dedifferentiated endometrial carcinoma is a criticial step towards improving diagnostic and treatment practices for aggressive stem-like forms of gynecological cancers.

The Power of Partnership

Abstract #:   47
Presenter: Babak Nami
Supervisor: Zhixiang Wang
Title: Epigenetic signature of ERBB2 gene enhancer elements governs HER2 expression status in epithelial and mesenchymal context
Authors: Babak Nami, Zhixiang Wang
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: HER2 (encoded by *ERBB2*) receptor tyrosine kinase that is overexpressed in approximately 20% of all breast cancers (BCs) is a poor prognosis factor and target for trastuzumab. Approximately, 60-70% of HER2+ BCs develop de novo resistance to trastuzumab due to the loss of expression of HER2 on their tumor cells. Mesenchymal breast cancer (BC) cells are generally HER2-negative therefore resistant to anti-HER2 therapies. We previously suggested that HER2 signaling can promote epithelial to mesenchymal transition (EMT) in a negative feedback fashion that results emerging resistant mesenchymal cells. We hypothesize that EMT may be a mechanism of de novo resistance to anti-HER2 therapies.

Methods: Bioinformatic analysis of RNA-seq data of 1642 breast tumors from The Cancer Genome Atlas (TCGA), ChIP-seq data from ENCODE and Cistrome Projects and super-enhancers data from dbSUPER databases were done to investigate epigenetics regulation of *ERBB2* gene expression in epithelial and mesenchymal BC cells.

Results: RNA-seq analysis revealed a significant negative correlation between expression of mesenchymal key transcription factors and *ERBB2* gene. Epigenetic analysis revealed a high enrichment of active chromatin modifications (DNase hypersensitivity, H3K4me1, H3K4me2, H3K4me3, H3K9ac and H3K27ac) at the promoter of *ERBB2* in both HER2+ and HER2-negative cell lines. However, active chromatin at *ERBB2* gene enhancer elements was found in only HER2+ cell lines. In addition, high enrichment of general transcription factors (EP300, CTCF, MED1, BRD4 and RNA Polymerases) was observed at the regulatory elements of *ERBB2* gene in HER2+ cell lines, which was correlated with high occupancy of mesenchymal key transcription factors FOXA1, FOXA2, FOXM1, FOXP2, MAX and MYC at *ERBB2* gene regulatory elements in HER2+ cell lines but not in HER2-negative cells. Moreover, super-enhancers were found near *ERBB2* gene in HER2+ but not HER2-negative cell lines/tissues.

Conclusion: findings suggest that, 1) high expression of HER2 in HER2+ BC cells may be attributed to activity of super-enhancers near *ERBB2* gene, and 2) low expression of HER2 in mesenchymal cells may be due to abrogation of *ERBB2* super-enhancers by epigenetics which dramatically suppresses expression of *ERBB2* gene despite high expression level of upstream key transcription factors. We conclude that EMT-mediated epigenetic regulation may be a bona fide mechanism of HER2 depletion, therefore, de novo resistance to anti-HER2 therapies.

The Power of Partnership

Introduction

Cytomegalovirus (CMV) infects 40-70% of women, but has been reported in >90% of breast cancer patients. Breast tumors cause inflammation, which stimulates autotaxin (ATX) secretion from surrounding adipose tissue. ATX produces lysophosphatidate, which through six G protein-coupled receptors further increases inflammation in a feed forward cycle. CMV infection produces inflammatory stimuli like interleukin 6 (IL-6) and cyclooxygenase-2 (COX-2). Our preliminary results from treating mouse breast adipose tissue with mouse CMV (mCMV) in culture showed an increased gene expression of IL-6, COX-2, and ATX. We hypothesized that CMV infection enhances the inflammatory cycle in the breast, which promotes tumor progression.

Methods

Syngeneic mouse breast cancer models were established by injecting E0771 or 4T1 breast cancer cells into the mammary fat pad of C57Bl/6J or Balb/c mice, respectively. A transgenic MMTV-PyVT mouse model with spontaneous tumor growth was also used. Mice were either infected with mCMV or mock infection (virus removed by filter) 10 weeks prior to tumor inoculation or spontaneous tumor development to establish a presumed latent infection status. Tumor development and growth was monitored by caliper measurements at regular intervals. Tumor characteristics including volume, mass and vascularity were determined at the endpoint. Lung metastasis was also examined. Tumors, tumor-associated adipose tissues and contralateral adipose tissues were collected to analyze expression of inflammatory mediators by RT-PCR and ELISA.

Results

The C57Bl/6J mice infected with mCMV showed suppression of tumor growth for ~12 days, but this was then followed by rapid growth similar to uninfected controls. However, the onset of this growth was unpredictable and for some mice it was delayed up to an additional 20 days. ATX expression showed ~1.5-fold increase in tumor-associated adipose tissues from CMV-infected mice, suggesting enhanced inflammation. In Balb/c mice, mCMV infection led to a ~3-fold increase in the number of nodules on lung surface, indicating greater metastasis. In MMTV-PyVT model, CMV-infected mice showed a trend of increased total tumor burden at the endpoint. Phenotypes of the tumors in this model were also affected by mCMV infection, including increased tumor vasculature and multiple tumor lobes.

Conclusions

mCMV infection plays a role in breast tumor progression and metastasis by modulating the host inflammatory responses. Detailed mechanisms of these observations are being investigated through analysis of inflammatory mediators and immune cell subtypes.

The Power of Partnership

Abstract #:   49
Presenter: Kenji Rowel Lim
Supervisor: Toshifumi Yokota
Title: Efficacy of early treatment with exon skipping in an animal model of Duchenne muscular dystrophy
Authors: Kenji Rowel Lim, Yusuke Echigoya, Mutsuki Kuraoka, Tetsuya Nagata, Masanori Kobayashi, Yoshitsugu Aoki, Terence Partridge, Shin'ichi Takeda, Toshifumi Yokota
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction. Duchenne muscular dystrophy (DMD) is a fatal X-linked recessive disorder that begins in early childhood, with patients experiencing progressive muscle degeneration. DMD is caused by loss-of-function mutations in the *DMD* gene, which codes for dystrophin, a muscle membrane-stabilizing protein. A promising approach to treat DMD is exon skipping (ES) using antisense oligonucleotides (AOs), called morpholinos, to restore the *DMD* reading frame and enable dystrophin synthesis. While an FDA-approved ES AO, called eteplirsen, is now available for certain DMD patients, its efficacy is poor, with less than 1% normal levels of dystrophin expression observed, and its therapeutic utility is currently under dispute. Studies are thus geared towards improving the efficacy of ES drugs. Here, we investigate whether early ES treatment will lead to therapeutic improvement in an animal model of DMD.

Methods. Canine X-linked muscular dystrophy in Japan (CXMD$_J$) animals were treated thrice intravenously with a 4-morpholino cocktail at 1, 3, and 5 weeks of age; we designed the cocktail to skip *DMD* exons 6-8. Blood samples were collected weekly. Two-to-three weeks after the final injection, animals were functionally evaluated and muscle samples were collected. Muscles were analyzed for ES efficiency (RT-PCR), dystrophin restoration (Western blot, immunostaining), histopathological improvement, and AO uptake (ELISA).

Results. Variable ES efficiencies were observed across skeletal muscles but were highest in the hindlimbs and diaphragm, with up to 14% normal levels of dystrophin expression observed. Treated skeletal muscles showed marked improvements in histopathology, with a significant decrease in centrally nucleated fibers, an indicator of muscle degeneration/regeneration, in respiratory muscles. Minimal ES and dystrophin protein restoration was found in cardiac muscles. The extent of AO uptake correlated with the observed treatment efficacy across muscles; surprisingly however, AO uptake was found to be high in the heart. No evidence of toxicity was found from blood tests. Treated animals significantly improved compared to non-treated controls in the standing test, but not for other functional tests.

Conclusions. Early ES treatment resulted in significant improvements in muscle histology and the standing test. Importantly, it was shown to be potentially beneficial for the treatment of respiratory muscles. A longer-term study might be required to more appropriately demonstrate the utility of early ES treatment.

The Power of Partnership

Abstract #:   50
Presenter: Mahdieh Khodaei
Supervisor: Edmond Lou
Title: Reliability of spinal flexibility measurements using ultrasonic imaging method on children with adolescent idiopathic scoliosis (AIS)
Authors: Mahdieh Khodaei, Rui Zheng, Lawrence Le, Edmond Lou
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Adolescent Idiopathic Scoliosis (AIS) is a 3D spinal deformity. Knowing spinal flexibility helps both surgeons and orthotists for treatment planning. Currently, spinal flexibility is calculated based on the lateral curvature of spine on standing radiograph relative to supine side bending radiograph. However, exposing children to ionizing radiation is undesirable, and the traditional method includes gravitational effect which may not truly reflect the spinal flexibility. Thus, a new ultrasound (US) imaging method has been developed. This study aimed to determine the reliability of the spinal flexibility measurements using ultrasound imaging method.

Methods

One hundred and eight (93 F; 15 M) AIS subjects were recruited and consented. At maximum, four US scans including standing, prone, voluntary maximum right and left sides prone bending were acquired. Spinal flexibility indices, prone relative to standing index (PRSI), bending relative to standing index (BRSI) and bending subtract prone relative to standing index (B-PRSI) were introduced and assessed. The BRSI is the traditional method to assess spinal flexibility by using subjective corrective force. The PRSI provides the gravitational effect and the B-PRSI provides the force effect to report spinal flexibility. Two experienced raters, (R1) and (R2), measured the lateral curvature of spine on the 4 US scan images. The inter-rater reliability of the flexibility indices was analyzed by using the Intra-class correlation coefficient (ICC) [2, 1], and the standard error of measurements (SEM). Also, the mean absolute difference (MAD) and standard deviation (SD) of the flexibility indices between raters were reported.

Results

Among 108 subjects, 173 curves were identified from both raters. The range of PRSI, BRSI, and B-PRSI from R1 versus R2 were (0.05 - 1.17, 0.43 - 3.67 and 0 - 3.13) versus (0.05 - 0.94, 0.38 - 3.62 and 0.03 - 3.00), respectively. Higher the index value meant more flexible of the curve. The ICC [2, 1] values of the inter-rater reliabilities of PRSI, BRSI, and B-PRSI were 0.70, 0.94 and 0.87, respectively. Among the three indices, the B-PRSI had the highest SEM values 0.07, while BRSI had the lowest SEM 0.04. The MAD ± SD between the two raters of PRSI, BRSI and B-PRSI, were 0.13±0.11, 0.16±0.17 and 0.21±0.21, respectively.

Conclusions

The PRSI, BRSI and B-PRSI, could be measured reliably on US images. Although the B-PRSI is slightly worse than the traditional method (BRSI), the different is insignificant. More importantly the B-PRSI provides a better information to clinicians on treatment planning.

The Power of Partnership

Abstract #:   51
Presenter: Kenwick Ng
Supervisor: Edmond Lou
Title: A novel 3D printed spinal orthosis for the treatment of adolescent Idiopathic Scoliosis
Authors: Kenwick Ng, Edmond Lou, Kajsa Duke
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Adolescent Idiopathic Scoliosis (AIS) is a three-dimensional spinal deformity. This deformity affects 1-3% of growing children. Girls are eight times more likely to have progressive scoliosis. Currently, bracing is the only proven non-surgical treatment and its effectiveness is correlated with adherence and wear tightness. However, brace manufacturing technology has not changed in the last 40 years where most of the braces are rigid plastic jackets. The adherence is usually poor due to bulkiness, lack of ventilation and conspicuous nature. On the other hand, wear tightness affects brace interface pressure on the torso. As 3D printing technology matures, applications in the clinical setting such as creation of patient-specific prostheses can implement positive changes in the health care arena. Success with the application of 3D printing in the medical field motivates this study to investigate the feasibility of printing a dynamic spinal brace for scoliosis.

Methods

Three 3D printed braces made of ABS-M30, ULTEM1010, and Nylon12 were manufactured from Stratasys. The braces were designed with voids and had thicknesses of 2.29mm for ABS-M30 and 2.54mm for both ULTEM1010 and Nylon12. Recently, ABS-M30 and ULTEM1010 braces were received and tested by two orthotists. Orthotists evaluated the braces based on feasibility of modification, attachment of accessories and breakage with excessive bending. Furthermore, mechanical tests were conducted to compare the strength and stiffness of the 3 materials with traditional polypropylene brace material. Also, a dynamic brace pad made of VeroClear was 3D printed in-house. The brace pad could easily deform to brace shape and had an inflatable rubber cover which allowed changing pressure dynamically.

Results

The printed thicknesses of ABS-M30 and ULTEM1010 braces were 2.31±0.09mm and 2.55±0.06mm, respectively. Similar to the traditional brace, both braces were modifiable, trimmed to shape, and attached with lining and buckles. Orthotists also reported that both braces had adequate stiffness. From the mechanical tests, the 3 materials all had higher yield strength than polypropylene. Also, the ULTEM1010 had the highest stiffness while the Nylon12 had the lowest. The 3D printed dynamic brace pad was easy to attach to the 3D printed brace and it could handle pressure higher than the typical pad pressure of 80-120 mmHg without leaking.

Conclusions

A 3D printed spinal brace is feasible demonstrated by the three 3D printed dynamic spinal braces being thinner and lighter than the traditional brace. Among the 3 tested materials, Nylon12 is suggested with its material properties closest to polypropylene.

The Power of Partnership

Abstract #:   52
Presenter: Andrew Chan
Supervisor: Edmond Lou
Title: Measurement accuracy of 3D ultrasound system for adolescent Idiopathic Scoliosis surgery
Authors: Andrew Chan, Eric Parent, Edmond Lou
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Adolescent idiopathic scoliosis is a spinal deformity involving lateral curvature and axial rotation of the spine, affecting patients aged 10-18. Severe scoliosis requires surgical treatment to prevent deformity progression and detrimental effects to patient self-image and physiologic functioning. Surgery involves attaching instrumentation to the spine using pedicle screws. High accuracy in screw insertion is critical to prevent spinal neurologic and vascular injury. Motion capture of surgical tools combined with intraoperative CT scans has been used to guide screw insertion but requires bulky equipment and radiation exposure for young patients. 3D spinal ultrasound has been suggested as an alternative image guidance method. The objective of this study is to determine the accuracy of linear and angular measurements from a custom developed spinal 3D-ultrasound system using motion capture and handheld ultrasound.

Methods: Optitrack Prime 13W cameras were selected to provide motion capture capabilities of within 0.25mm and 3.5° for 150mm and 60° movements within a $0.6 \times 0.6 \times 0.8 m^3$ capture volume. An Ultrasonix SonixTablet ultrasound imager with a 6.67 MHz, 38mm transducer was used to acquire images. A custom holder was 3D printed to attach motion capture markers to the transducer. Software was developed in Matlab to stream data from both motion capture cameras and ultrasound systems together and to process images for 3D reconstruction. The accuracy of reconstructions was tested on four 3D-printed phantoms. Each phantom was reconstructed three times. Measured dimensions ranged from 5-25mm and $5-35^{\circ}$ and were measured three times each. Positional accuracy of reconstructions was completed in twenty trials, comparing virtual position of phantom landmarks with physically measured positions.

Result: Reconstruction accuracies from 234 linear measurements were: across the ultrasound aperture direction (X-direction) 0.55±0.15mm, axially along the penetration direction (Y-direction) 0.10±0.05mm and along the transducer moving direction (Z-direction) 0.55±0.15mm. Angular accuracies from 84 measurements were $0.70 \pm 0.30^{\circ}$ for angles in the X-Y plane, and $0.65 \pm 0.30^{\circ}$ in the Z-Y plane. Positional accuracies were 0.10±0.15mm in the X direction, 0.05±0.15mm in the Y direction and 0.30±0.30mm in the Z direction. Both accuracies lie within the clinical standard of 1mm and 5° for adequate image guidance in pedicle screw insertion.

Conclusion: The custom developed 3D ultrasound system has linear reconstruction accuracies within 0.55mm, angular accuracies of within 0.70° and positional accuracies within 0.30mm when scanning and reconstructing 3D printed phantoms. Further work in imaging vertebrae-mimicking phantoms is planned for continued validation of the 3D ultrasound system.

The Power of Partnership

Abstract #:   53
Presenter: Robert J. Reklow
Supervisor: Gregory D. Funk
Title: ADO sensitivity and ADK activity in the central inspiratory network may contribute to developmental changes in depression of breathing by hypoxia
Authors: Robert J. Reklow, Gregory D. Funk
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: Exposure to low oxygen (hypoxia) evokes a biphasic hypoxic ventilatory response (HVR) comprising of an initial increase in ventilation followed by a secondary depression. The secondary depression is much stronger and life-threatening in premature infants and it is implicated in apneic events (Apnea of Prematurity). Despite the clinical significance, mechanisms underlying this secondary depression are poorly understood. During hypoxia, astrocytes in the preBötzinger complex (preBötC, a key brain region for generating inspiratory rhythm) release ATP which increases breathing and attenuates the secondary depression. However, ATP is rapidly metabolized into adenosine (ADO), which is implicated in the secondary depression. Thus, the overall effects of ATP are determined by a balance between its excitatory actions and the inhibitory actions of its by-product ADO. Our overall goal is to determine if factors that control this balance change during development, potentially contributing the greater hypoxic depression of breathing in neonates and its decline with development. My objectives were to test i) whether the sensitivity of the preBötC to ADO changes developmentally; ii) whether ADO kinase (ADK, an intracellular enzyme that converts ADO into AMP so that ADO can continually be transported into cells thereby reducing ADO_e), influences basal ADO tone and preBötC inspiratory activity; and iii) whether the effects of ADK change developmentally.

Methods: Using medullary slices of mice (0-3 and 10-12 days old), the inspiratory activity generated by preBötC was recorded from the slice surface and hypoglossal nerve rootlets. We assessed the effects of injecting ADO (500 µM, 30 s) into the preBötC, and in separate experiments assessed the effects of an ADK inhibitor (ABT 702, 10 µM) on baseline rhythm during development.

Results: ADO evoked a ~30% depression in P0-3 mice, whereas the depression was ~16% at P10-12. When ABT 702 was bath-applied, the depressive effect on basal frequency increased from ~25% in P0-3 mice to ~40% in P10-12 animals.

Conclusion: These results suggest the sensitivity of the preBötC to ADO decreases during development. Data also suggest that the ability of ADK to remove ADO from the extracellular space is not fully developed at birth, but increases in the first two weeks of life. These factors may contribute to the greater sensitivity of premature mammals to the depression of breathing by hypoxia. Studying ADK activity in the central inspiratory network may reveal a novel target to counteract the depression of breathing by hypoxia and life-threatening apneas in premature infants.

The Power of Partnership

Abstract #:   54
Presenter: Nils Koch
Supervisor: Silvia Pagliardini
Title: Chemogenetic inhibition of preBötzinger complex to impair respiratory function during sleep
Authors: Nils Koch, Annette Pisanski, Silvia Pagliardini
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Respiratory activity is a fundamental biological function controlled by central pattern generators located in the brainstem. Reduced activity of the respiratory pattern generators may result in altered breathing function, especially during sleep when excitatory neuromodulation is reduced. Sleep disordered breathing (SDB), defined by respiratory impairment during sleep, is prevalent in the general population with increased incidence in certain patient populations such as preterm infants, congestive heart failure and neurodegenerative disorders. Current models of SDB are crude and not representative of the condition. Selective ablation of neurons expressing neurokinin 1 receptors in the preBötzinger complex (preBötC), the inspiratory rhythm generator, has been shown to increase the length of respiratory disturbances (RD) in all states of arousal. Increased number of respiratory disturbances during REM sleep were also reported.

Methods

In this study we have taken advantage of a recently developed chemogenetic approach to depress activity of the rat inspiratory rhythm oscillator, the preBötC, across sleep wake cycles. This approach takes advantage of a mutated opioid receptor (KORD) that is only activated by an exogenous ligand. Viral constructs expressing KORD were delivered to the preBötC.

Results

Activation of KORD viruses in preBötC hyperpolarized respiratory neurons for several hours and caused recurrent spontaneous apneas following systemic application of the exogenous ligand. Apneas occurred preferentially during sleep, in particular during REM sleep.

Conclusion

Our results indicate that KORD chemogenetic activation of preBötC neurons across sleep wake cycle is able to create a model of sleep disordered breathing, with frequent spontaneous apneas, occurring particularly in REM sleep. This model can be further used to test therapeutic interventions designed to potentiate inspiratory drive and promote breathing in presence of sleep-related respiratory depression.

The Power of Partnership

Abstract #:   55
Presenter: Nicole Anderson
Supervisor: Catherine J. Morgan
Title: Post-operative fluid overload as a predictor of hospital outcomes in the pediatric heart transplant population
Authors: Nicole Anderson, Ari R. Joffe, Christine MacDonald, Simon Urschel
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Pediatric patients undergoing cardiac surgery, including heart transplantation have a number of factors predisposing them to become fluid overloaded. There is limited data on fluid overload (FO) epidemiology specific to pediatric heart transplant recipients and the impact of FO on hospital outcomes.

Methods: Secondary analysis of data from a prospective cohort study. We evaluated 72 children (birth to 6 years old) who had heart transplant between 2000 and 2012 and determined 1) the extent, timing, and predictors of post-operative FO and 2) the impact of FO on clinically important outcomes including duration of mechanical ventilation and length of stay in cardiac pediatric intensive care unit (CPICU). FO was defined as a cumulative fluid balance (in the first 5 post-operative days) greater than 10% of body weight. Associations were tested using regression when assumptions were met and non-parametric methods for non normal data. Poisson regression was used for evaluating the association between fluid overload and outcomes.

Results: Of the 72 children, 2 were excluded due to incomplete fluid balance data. FO occurred in 21% of patients. In those with FO, 67% were overloaded within 48 hrs postoperative. Donor ischemic time was associated with increased risk of FO. Children with postoperative fluid overload had a 1.5 times longer length of CPICU stay (p<0.0001) and were ventilated 2.2 times longer (p<0.0001) than those without fluid overload. Longer ventilation time and PICU length of stay were also associated with longer time to first negative fluid balance (p=0.005)

Conclusions: FO was common after pediatric heart transplant and was associated with worsened clinical outcomes including prolonged CPICU stay and longer mechanical ventilation requirements. Prolonged time to negative fluid balance was also associated with longer time requiring mechanical ventilation and CPICU length of stay. More research is needed to explore safe and effective ways to reduce FO in this specific population.

The Power of Partnership

Abstract #:   56
Presenter: Esther Jun
Supervisor: Samina Ali
Title: A survey of caregiver perspectives on opioid use for children's acute pain management
Authors: Esther Jun, Megan Fowler, Naveen Poonai, Kathryn Dong, Amy Drendel
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Pain secondary to acute injury is one of the most common presenting complaint to pediatric emergency departments (EDs). There has been significant effort to improve pediatric pain assessment and management; however, studies have shown that children are still under-treated for pain despite evidence regarding the dangers of oligoanalgesia. Although opioids are safe and effective for management of moderate to severe acute pain in the ED, caregivers often refuse them for their children. Given that caregivers are often the gate-keepers to their children's' pain management, understanding their reason for opioid refusal in this context is essential. We aimed to determine caregivers': a) willingness to accept opioid analgesia in various hypothetical situations, b) possible reasons for objecting to opioid analgesia, and c) past experiences with opioids.

Methods

We conducted a descriptive, cross-sectional survey developed following Burns et al. methodology guidelines and CHERRRIES checklist. We collected data from the University of Alberta Stollery Children's Hospital (Edmonton, Alberta) and the Children's Hospital at London Health Sciences Center (London, Ontario) EDs. We consecutively enrolled 215 caregivers presenting to the Stollery pediatric ED with a child between the ages of 3-16 who had a MSK injury that occurred within 1 week of ED presentation. Data collection is ongoing at the London site. Biostatistical analysis will be completed at the University of Alberta.

Results

To date, of our 215 caregivers enrolled in the study, their child's mean age was 9.6 years (SD=3.6), with more males (61%) than females (39%). The caregivers' mean age was 40.3 years (SD=7.3), with the majority being mothers (71%). The most common presenting MSK injuries were upper limb (52%) and lower limb (37%) injuries. Nearly 93% of caregivers stated that they worry to some extent about their child receiving opioid pain medications. The greatest reason for concern appears to be the side effects of the opioids (94%), followed by addiction risk (80%), and overdose risk (80%). Further secondary analysis is pending.

Conclusions

Our results support our hypothesis that caregivers are unwilling to accept opioid pain medications for their child in acute injuries. Common barriers identified thus far include concerns about the opioids' side effects, overdose risk, and addiction risk. Further secondary analyses are ongoing. Understanding caregivers' attitudes toward opioid analgesia could improve pediatric pain management through tailored family education, improved communication, and a more family centered approach in the ED.

The Power of Partnership

Abstract #:   57
Presenter: Hayley Turnbull
Supervisor: Michael Hawkes
Title: Development of a novel device for objective respiratory rate measurement in low resource settings
Authors: Hayley Turnbull, Claude Kasereka Masumbuko , Israel Amirav, Eugenie Sahika Sivasivugha , Ian Solomon, Yossi Aldar, Michael Hawkes
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Pneumonia is a leading cause of child mortality worldwide, causing close to a million deaths per year in children under 5 years of age. In low-resource settings (LRS), the majority of pneumonia-related deaths occur in the community. An instrument to facilitate accurate respiratory rate (RR) measurement at the community level could improve pneumonia diagnosis and case management. We aimed to develop and evaluate a novel device (Respimometer[TM]) for objective measurement of respiratory rate in LRS.

Methods

The study took place at four pediatric health care facilities in Butembo, DR Congo. This study provides a description of prototype development, with proof-of-concept pilot field study. The instrument was tested in healthy adult volunteers (N = 10) and Congolese children (N = 42) and compared to timed breaths (adults) or by reference comparator capnography (children). Correlation and Bland-Altman plots were generated for paired measurements.

Results

In adult volunteers, the correlation coefficient between the delivered RR and the Respimometer[TM] measurement was median 0.992 (IQR 0.980-0.999). Measurement bias was -0.50 min^{-1} (95%CI -1.1 to +0.07, p=0.093), with upper and lower limits of agreement of -5.2 min^{-1} and 4.2 min^{-1}, respectively. Among Congolese children, there was no evidence of bias: mean difference in RR +1.0 min^{-1} (95%CI -2.1 to +4.1, p=0.52). The upper and lower limits of agreement were -18 and +20 min^{-1}, respectively.

Conclusion

The Respimometer[TM] can accurately measure the respiratory rate in healthy adults and African children. A simple and accurate instrument could facilitate the diagnosis of pneumonia by community health workers (CHWs) in low-and middle-income countries leading to reduced pneumonia-related deaths.

The Power of Partnership

Abstract #:   58
Presenter: Cielle Wachnian
Supervisor: Dr. Aisha Bruce
Title: Cold external temperatures and Sickle Cell morbidity in children: A retrospective analysis
Authors: Cielle Wachnian, Nicholas Thompkins, Dr. Mark Belletrutti, Dr. Catherine Corriveau-Bourque , M Yaskina, Dr. Aisha Bruce
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Patients with Sickle Cell Disease (SCD) experience vaso-occlusive crisis, which results in extreme pain, often requiring opioids and admission. Genetic and environmental factors affect the frequency and severity of these episodes. Previous research has born conflicting evidence on whether environmental temperature is contributory. Edmonton, Alberta is the most northern city in North America with a population over a million and has an increasing sickle cell population exposed to extreme winter conditions. This provides a suitable population and atmosphere to study the influence on cold external temperatures in SCD.

Hypothesis: This study sought to identify if pediatric patients with SCD, experience greater morbidity in cold external temperatures.

Methods: We performed a Heath Research Ethics Board approved retrospective case control series. Patients were identified through a clinical database, and emergency visit, phone call and admission data was collected over a five-year period. The average and minimum and change in temperature on day of presentation, 24 and 48 hours prior, was collected from the Government of Alberta, and will be statistically analyzed using descriptive statistics, to determine the relation to vaso-occlusive events.

Results: 118 patients were identified, and 258 VOC events reviewed. The mean patient age was 6.6 years of age with a range from 0.3-17 years old. The female to male ratio was equivalent with 133 female (51.6%) and 125 male (48.4%) VOC events. Eight records (3%) had documented cold exposures. The analysis between the temperature and the frequency of events did not yield significant correlation. Average and minimum temperature on day of admission had the largest percentage of VOC events occur at mild temperatures, from -4.99 to 20 °C and -4.99 to 5 respectively. Change in temperature on day of admission, 24 and 48 hours had the largest percentage of VOC events was at a mild to moderate in temperature of 10-15 degrees. Data at 24 & 48 hours prior to admission show similar results.

Conclusions: There was no correlationof average, minimum or change in temperature on day of admission, 24 or 48 hours prior. Multiple cofounding factors likely contribute to these results. As it was a retrospective study many confounding and precipitant factors may not be recorded or identified. A prospective study to better record specific cold exposure is warranted.

The Power of Partnership

Abstract #:   59
Presenter: Richelle Wright
Supervisor: Lola Baydala
Title: Promoting awareness of First Nations child health issues through resident education
Authors: Richelle Wright, Melissa Tremblay, Lola Baydala
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

The health disparities facing Indigenous children in Canada are well known and unfortunately pervasive. Indigenous children are subject to inequalities in infant mortality, early childhood development, chronic medical conditions and mental health. One strategy to decrease these disparities is educating medical trainees about health issues specific to Indigenous children. The Maskwacis Pediatric Outreach Clinic (MPOC) provides General Pediatric residents the opportunity to learn in an outpatient pediatric clinic directly on a First Nations reserve. Our research project was designed to analyze resident experiences at MPOC and to determine if such a clinic augments training with respect to Indigenous child health issues.

Methods:

A survey based methodology was used. General Pediatric residents at the University of Alberta completed voluntary surveys following each clinical day at MPOC over an 18-month period. In addition, a focus group was held consisting of seven residents who had worked at MPOC. Our surveys contained qualitative reflections and quantitative Likert-scale questions. Survey analysis consisted of content based qualitative description and simple descriptive statistics (not yet finalized). Focus group analysis utilized thematic analysis through coding.

Results:

Residents reflections identified the following benefits of MPOC most frequently: MPOC allowed them to recognize the importance of social determinants of health for children, MPOC increased their awareness of the limited child health resources on a First Nations reserve, and MPOC provided exposure to child health concerns that are less frequently encountered in other clinical settings. These concerns included severe skin infections, overcrowded or unsafe housing, extreme poverty, and domestic violence.

Common themes identified in our focus group were that through MPOC residents learned about and witnessed the barriers, disparities, and social determinants of health experienced by Maskwacis children and that residents learned they must maintain sensitivity to the diversity of personal circumstances when working with First Nations children.

Conclusions:

Direct clinical exposure to Indigenous child health issues was considered to be a valuable educational experience by General Pediatric residents at the University of Alberta. We identified that clinical work on a First Nations reserve emphasized the importance of social determinants of health and fostered a deeper appreciation of why health disparities exist for Indigenous children. Future directions for this work include assessing if exposure to MPOC altered resident mentality and clinical practise when caring for Indigenous children in a hospital setting and if working at MPOC increases the likelihood of directly providing Indigenous children health services after completing residency.

The Power of Partnership

Abstract #:   60
Presenter: Noureen Ali
Supervisor: Sujata Persad
Title: Active Beta Catenin (ABC) as a prognostic marker for Osteosarcoma (OS) progression
Authors: Noureen Ali, Geetha Venkateswaran, Elizabeth Garcia
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Osteosarcoma (OS) are aggressive primary bone malignancies having peak incidences in children and young adolescents. Outcome remains poor for most patients with metastatic disease which develops in 1 of every 5 cases. Presently, there are no widely recommended screening tests for early diagnosis of OS and no reliable prognostic marker for aggressive/metastatic disease. We investigated the putative role of the Wnt/β-catenin pathway, specifically the transcriptionally active form of β-catenin, Activated β-Catenin (ABC), in OS progression.

Methods: We used two pairs of cell lines that simulate OS progression: Saos2/Saos2-LM7 and HOS/ HOS-143B. MMP2 and MMP9 activity were used to confirm the greater metastatic potential of Saos2-LM7 & HOS-143B compared to SaOS2 and HOS. Total cellular/nuclear levels/localization of ABC/β-catenin were evaluated by Western blot and immunofluorescence (IF) analysis. High Content analysis of IF (x10) was used for quantification of cellular/nuclear levels of ABC/β-catenin. Transcriptional activity of ABC/β-catenin was evaluated by RT-qPCR of target genes (MMP2, MMP9, Cyclin D1, VEGFA) and TopFlash activity.

Results: Results show significantly higher cellular levels of ABC in the SaOS2-LM7 and HOS-143B cell lines compared to the respective parent cell lines (SaOS2 & HOS). Additionally, ABC exhibited a more prominent nuclear localization in the SaOS2-LM7 and HOS-143B cell lines compared to SaOS2 & HOS, respectively. No significant differences in cellular levels and localization of β-catenin were observed. SaOS2-LM7/HOS-143B exhibited significantly greater transcriptional activity.

Conclusion: The strong correlation between cellular/nuclear ABC levels/activity and OS progression supports the potential for ABC to serve as a prognostic marker for OS progression.

The Power of Partnership

Introduction

Neuroblastoma and Wilms tumor are the most common solid tumors in pediatric patients and primarily effect children under the age of 5. Cancers are classified as advanced when they metastasize from the primary site to other places in the body. In blood-borne metastasis, migrating cancer cells are believed to induce the formation of fibrin rich microemboli providing the tumor cells with a physical shield which protects against shear forces and immune recognition by cytotoxic natural killer cells. Only Tissue factor (TF) has been shown to be expressed by tumor cells and the current thinking is that TF interacts with the hemostatic factors present in the plasma which results in fibrin formation. We hypothesized that hemostatic factors involved in fibrin formation are expressed by cancer cells, thereby facilitating metastasis. To determine this, we assessed the expression of genes associated with the hemostatic system in pediatric cancer cell lines using RT-qPCR.

Method

We used tissue culture methods to assess the pediatric cancer cell lines,

1) Neuroblastoma (CCL-127) derived from 13 month old male and

2) Wilms tumor (CRL-1441) derived from a 3 month old male.

RT-qPCR technique was done to determine the expression of hemostatic system genes.

Results

Both cell lines expressed the following genes:

i) Procoagulant factors; Prothrombin, Thrombin receptor, TF, FVIII, FXII, von Willebrand factor

ii) Procoagulant inhibitors; Tissue factor pathway inhibitor, Antithrombin, Protein C Receptor,

iii) Fibrinolytic system; Tissue plasminogen activator, Alpha 2-antiplasmin, Plasminogen activator inhibitor-1.

In addition, the Wilms tumor cells expressed Factor V, Fibrinogen beta chain and Fibrinogen gamma chain.

Conclusion

We report a novel observation of expression of hemostatic factor genes in Neuroblastoma and Wilms tumor cells. Determining the role of tumor based hemostatic factors in metastasis and further understanding this mechanism is essential in establishing novel therapeutic methods and reducing mortality rates.

The Power of Partnership

Abstract #:   62
Presenter: Mirna Matta
Supervisor: Dr. Lawrence Richer
Title: Exploring the feasibility of remote delivery of an exercise program in patients with postural orthostatic tachycardia syndrome (POTS)
Authors: Mirna Matta, Eric Mathieu, Meghan Linsdell, Dr. Lawrence Richer
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

Postural tachycardia syndrome (POTS) is a condition characterized by an inability to stand for long periods due to excessive tachycardia causing dizziness and generalized weakness. Exercise has shown to be an effective intervention based on limited adult studies, however these interventions require large time commitments and expensive equipment – yielding poor adherence. This study's goal was to investigate the feasibility and tolerability of an exercise program comprised of short duration - high intensity circuits, no equipment requirement, and personalized to the participants' symptoms. *Feasibility* and *tolerability* were primarily defined as participant ability to complete and willingness to continue the program.

Methods:

Participants (n=9), aged 13-18 years and diagnosed with POTS, completed surveys to evaluate their symptom burden and beliefs about exercise before and after the 28-day exercise program. Adherence was tracked via daily exercise logs while functional outcomes were measured via a 6-minute exercise circuit videotaped at home. In a post-study debriefing session, participants evaluated the quality of the program.

Results:

Based on preliminary results, five participants completed the program with an additional two due to complete it by September 2017. Of those who have completed the program, 80% indicated a desire to continue the exercises along with their regular activities. Reasons for not continuing included general disinterest in exercise. All participants were able to modify and perform the exercises at home. However, monitoring performance via videos was difficult due to issues with uploading videos and not wanting to be filmed.

Conclusions:

Overall, the results demonstrate that the exercise program is feasible to complete and well tolerated by participants; however, future intervention studies need to explore other methods of remotely monitoring performance.

The Power of Partnership

Abstract #:   63
Presenter: Morgan Sosniuk
Supervisor: Lori West
Title: It's all under control: Using standardized immune flow cytometry phenotyping to create comprehensive pediatric reference ranges
Authors: Morgan Sosniuk, Anne Halpin, Juanita Wizniak, Artur Szkotak, Simon Urschel, Lori West
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

INTRODUCTION: Studying pediatric patients includes challenges such as difficulty obtaining samples, limited normal control data and small sample volume. Adult reference ranges are established using standardized flow cytometry (FC) phenotyping, but comparable pediatric control data do not exist. Our group had the opportunity to collaborate with the clinical hematology laboratory to obtain normal pediatric samples. Our objective is to establish a reference dataset to be available for pediatric studies using standardized, comprehensive, fresh whole blood, flow cytometry panels. This study is also a useful trial of this methodology for potential implementation in the clinical laboratory. Beckman Coulter provides standardized panels to explore extensive lymphocyte markers. Where pediatric phenotyping data do exist, comprehensive reference ranges across the age spectrum have not been established in fresh blood for certain subsets of interest. For markers such as the programmed cell death protein 1 (PD-1), often noted as a measure of T cell exhaustion, and for gammadelta T Cells and their associated markers Vd1 and Vd2, increased granularity of standardized phenotyping data is necessary.

METHODS: Using only 700uL of blood, DuraClone IM flow cytometry phenotyping was performed to garner a comprehensive immune phenotype of pediatric patients ranging from 66 days to 16 years of age (n=12).

RESULTS: Samples were tested in 5, 10-colour immunophenotyping panels. Preliminary analyses show age related trends in gammadelta and PD-1 + T cells.

CONCLUSIONS: Duraclone is a rapid and effective method for defining pediatric immune phenotypes. These results provide versatile control data and suggest that DuraClone shows promise for application in the clinical flow cytometry laboratory. Although limited by small patient numbers, our data suggest age-related trends in proportions of PD-1+ T cells, which will be explored as we continue to test additional samples and investigate this and other trends across the age spectrum. Other subsets of interest may be explored, for example these immunophenotyping panels may be a useful tool for gaining more insight into the subsets of gammadelta T cells present at the onset of juvenile diabetes. The use of fresh whole blood in this project differs from published pediatric reference range studies utilizing frozen cells and ensures populations are not lost during isolation or freeze thaw cycles. This unique partnership between the research and clinical labs not only provides unparalleled access to otherwise difficult to obtain samples; it also provides a valuable opportunity to define pediatric patients' immune phenotype and clinical applications of this methodology.

The Power of Partnership

Introduction: Pediatric heart and kidney transplant recipients (pHTx, pKTx) appear to have lower physical fitness than healthy children (HC). This study sought to quantify the fitness level of transplant recipients and investigated clinical and lifestyle factors that may affect physical fitness.

Methods: pHTx, pKTx, and a control group of HC were included in the study. Age-specific questionnaires were used to assess quality of life (PedsQL 4.0) and physical activity (PAQ). Body composition (fat and fat-free mass) was measured using air-displacement plethysmography. Aerobic capacity was assessed by six-minute walk test (6MWT), and muscle strength of deltoid, abdominals and quadriceps muscle by hand-held dynamometry. Muscle endurance of upper (push-ups), core (curl-ups), and lower (wall-sit) body muscle groups were measured. Clinical data regarding transplant course, medications, participation in physical therapy, and underlying diagnosis were collected from medical records.

Results: The transplant groups (pHTx n=7, pKTx n=2, HC n=8) were age-matched with controls (pHTx=9.3±3.9 y, pKTx=11±4.0 y, HC=12±2.7 y, p=0.13). Time post-transplant was 7.1 y (1.86-15.1) for heart, and 6.5 y (0.91-12.2) for kidney. Transplant recipients and controls had comparable levels of physical activity (p=0.13), but pHTx had lower fat-free mass than HC (25.9±12.8 kg vs 38.6±10.6 kg, p=0.042). Some fitness measures were reduced in pHTx and pKTx vs HC: 6MWT distance and number of curl-ups were significantly impaired in pHTx vs HC (83±3% vs 101±14% predicted, p<0.01; 13±13 vs 35±16 curl-ups, p<0.05). Wall-sit time was lower in pKTx vs HC (11±0.7 vs 91±59 s). Quality of life data was not yet completely analyzed.

Conclusions: Aerobic capacity and core muscle endurance were impaired in pHTx versus HC. Lower body muscle endurance was impaired in pKTx versus HC. Since physical activity is similar between groups, muscle function in transplant recipients is likely impaired by other factors, such as medications or function of the transplanted organ. A larger sample will allow further investigation of the effect of pediatric transplantation on fitness, and the clinical factors affecting fitness.

The Power of Partnership

Abstract #:   65
Presenter: David Fung
Supervisor: Lori West
Title: Exploiting activated T cells for a rapid cytokine suppression assay for assessment of regulatory T cell potency
Authors: David Fung, Esmé Dijke, Lori West
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Regulatory T cells (Tregs) have been proposed as a therapy to prevent and/or treattransplant rejection, graft-vs-host disease and autoimmune disease due to their immunosuppressive ability. Our lab has shown that abundant, highly suppressive Tregs can be isolated and expanded from discarded human thymus, routinely removed during pediatric cardiac surgery. Current suppression assays to assess the potency of expanded Tregs is based on suppression of T cell proliferation over four days, a timeframe that limits clinical use. We sought to establish a one-day suppression assay involving the suppression of T cell cytokine production by expanded Tregs. We hypothesize that re-stimulation of activated T cells will cause rapid cytokine production within a few hours which can be tested as a substrate for suppression by the addition of expanded Tregs.

Methods

For this pilot study, peripheral blood mononuclear cells were isolated from blood of healthy volunteers (n=4). T cells were isolated by magnetic bead separation, stimulated using anti-CD3/CD28 beads (ratio 10 cells:1 bead), and cultured for 7 days. Supernatant was obtained daily and a cytokine assay (MSD Multispot Assay) was performed. In addition, T cells were stimulated with anti-CD3/CD28 beads for two days. On day 2, cells were collected and washed. One group of stimulated T cells was re-stimulated and the other was not re-stimulated. Supernatant was taken at 2, 4, and 6 hr timepoints and assessed by cytokine assay.

Results

Cytokine concentrations peaked at day 3 and 6 for IFNγ (range: 1567-2488 pg/mL), and day 2 for IL-10 (7.8-14 pg/mL), IL-2 (259-353 pg/mL) and TNFα (78-100 pg/mL). Since the highest production of most cytokines occurred on day 2, we performed re-stimulation on this day. Cytokine production began as soon as 2hr after re-stimulation of the previously stimulated T cells with a steady increase in cytokine production from 2 hr to 6 hr. The re-stimulated T cells secreted higher levels of cytokines than the non-re-stimulated T cells at each timepoint.

Conclusion

Re-stimulation of activated T cells resulted in rapid production of cytokines on the scale of hours indicating that cytokine analysis of re-stimulated T cells may be exploited for the development of a one-day suppression assay. In future experiments, re-stimulated T cells will be cultured with or without expanded Tregs to assess suppression of cytokine secretion. A reproducible rapid suppression assay would be a powerful tool to check the potency of therapeutic Tregs for clinical use.

The Power of Partnership

Introduction: SGLT2 inhibitors, such as empagliflozin, are used as a treatment for diabetic patients to reduce blood glucose levels. The EMPA-REG trials showed cardioprotective effects of empagliflozin in humans, concomitant with increased blood ketone levels. Ketones have been proposed to be a superfuel, which can increase the efficiency of cardiac metabolism in these patients. We therefore determined whether empagliflozin affects ketone oxidation and cardiac efficiency in the hearts of diabetic *db/db* mice.

Methods: *db/db* mice were fed food with (*db/db*+emp) or without (*db/db*+veh) 10mg/kg body weight of empagliflozin starting at 18 weeks of age for 4 weeks. A third group of C57BL mice were fed the diet with vehicle. Isolated working hearts were perfused using 0.8mM palmitate, 5mM glucose, 500µM β-hydroxybutyrate (β-OHB), and 500µU/mL insulin to measure fatty acid oxidation, glucose oxidation, β-OHB oxidation, glycolysis, O_2 consumption, and cardiac efficiency (cardiac work/O_2 consumption).

Results: d*b/db*+veh mice had elevated fasting basal blood glucose levels, and this was significantly decreased in *db/db*+emp treated mice. Compared to C57BL, *db/db* mice had a decreased cardiac function and efficiency, which was associated with increased fatty acid oxidation, and decreased glucose oxidation and β-OHB oxidation. Empagliflozin improved cardiac function, but did not affect cardiac efficiency, fatty acid oxidation, or glucose oxidation, nor did it increase β-OHB oxidation.

Conclusion: Empagliflozin treatment increases cardiac function but this is not related to a stimulation of ketone oxidation.

The Power of Partnership

Abstract #: 67
Presenter: Nevin Hammam
Supervisor: Lesley Pritchard-Wiart
Title: Association of red blood cell distribution width (RDW) with physical activity and sedentary behavior in children and adolescents
Authors: Nevin Hammam, Victor Ezeugwu, Trish J. Manns , Lesley Pritchard-Wiart
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Increased red blood cell distribution width (RDW), a measure of the range of red blood cell volume, has been associated with cardiovascular disease (CVD) in adults. Reduced physical activity (PA) and prolonged sedentary behavior (SB) are also associated with CVD. RDW is correlated with PA and SB in adults, but it is unclear if this relationship is present in children. Determining the relationship between RDW and PA and SB in children and adolescents would provide some insight into the potential role that RDW plays in the contribution to CVD and may have implications for early identification of children at risk. We explored the relationship between RDW, PA and SB among children and adolescents, and whether these relationships were independent of CVD risk factors.

*Method:*Data from participants aged 10-19 years in the 2003–2006 National Health and Nutrition Examination Survey, which includes a representative sample of the American population, were included in the analysis. Participant socio-demographic characteristics, anthropometric and clinical measurements, caloric intake, and laboratory data were obtained from the database. The average proportion of time sedentary and at light, moderate and vigorous activity levels were calculated. Multivariate regression analyses (adjusted for potential covariates) were used to explore the associations between RDW with SB and PA. Statistical analyses were performed using Stata software.

*Results:*2,143 (1,080 boys and 1,063 girls) children and adolescents were included in the analysis. There was a significant difference between RDW quartiles (RDW-Q) and anthropometric parameters for girls. In addition, non-Hispanic/black ethnicity and lower PIR were associated with higher RDW in girls. Among boys, younger age, lower educational level, being non-Hispanic/black and lower PIR were significantly associated with the highest RDW-Q. In the fully adjusted linear regression model for boys, SB was positively associated with RDW (ß=0.116, P=0.004) while moderate PA was negatively associated with RDW (ß=-0.082, P=0.048). In girls, there were no significant association between SB and different PA intensities with RDW.

*Conclusions:*The results of this study provide preliminary evidence of an association between prolonged SB and decreased PA with RDW in boys. Additional research is required to understand the role of prolonged SB and higher RDW in the development of cardiovascular disease.

The Power of Partnership

Introduction: Adult studies demonstrated that three-dimensional echo (3DE) quantification of MR is equivalent to MRI, and superior to two-dimensional echo (2DE), however the mechanisms of MR in adults differ considerably from pediatrics. There are no studies to date assessing the feasibility & precision of 3DE in quantifying MR in children. This pilot study aims to compare the accuracy of 2DE and 3DE to the reference standard of MRI in quantifying MR.

Method: Children with MR were prospectively recruited for cardiac MRI and transthoracic 2DE and 3DE on the same day. Mitral valve effective regurgitant orifice area (EROA) and regurgitant volume (Rvol) were measured with 2DE & 3DE. 2DE EROA was estimated from biplane vena contracta area and PISA method, using parasternal long axis & 4-chamber views. 3DE EROA was calculated from vena contracta area, using planimetry from 3DE color Doppler and multiplanar reconstruction. 2DE & 3DE Rvol was calculated as EROA x MR velocity time integral. MRI Rvol was the difference between left ventricular stroke volume and aortic flow. 2DE & 3DE were compared to MRI using Pearson correlation and Bland-Altman plot.

Result: Fifteen patients were enrolled, 1 was excluded for poor-quality MRI. Of the 14 patients included (9-18y); 4 had mild MR and 10 had moderate or greater MR. 3DE Rvol (r=0.86, p<0.0001) and 3DE EROA (r=0.84, p=0.0002) had a strong correlation with MRI R vol. 3DE EROA also had a moderate correlation with MRI LV end diastolic volume (r=0.63, p=0.01). 2DE EROA by parasternal long axis PISA (r=0.60, p=0.02) and 4-chamber PISA (r=0.60, p=0.02) had a modest correlation with MRI Rvol, and 2DE EROA by biplane vena contracta area (r=0.10) had no correlation. Compared with MRI Rvol 3DE overestimated Rvol by 5.5% and 2DE by 17-27%. 2DE overestimated Rvol by 11-20% relative to 3DE. Bland-Altman plot showed close agreement between 3DE and MRI Rvol (bias -2.3 +/- 9.7, limits -21.2 to 16.7).

Conclusion: Quantification of MR Rvol by 3DE in children is feasibile and closely correlates to MRI. Overestimation of Rvol by 2DE may reflect the more eccentric and elliptical shape of the vena contracta in pediatric population. 3DE can quantify the degree of MR and assess the progression of MR, which may improve our ability to stratify children for medial and surgical repair.

The Power of Partnership

Introduction

CD36 is a transmembrane glycoprotein found in a wide variety of cells including macrophages, platelets, endothelial, and muscle cells. It contributes to angiogenesis, immunity, inflammation, atherosclerosis, and lipid metabolism. There is evidence to support a role for CD36 in the uptake of fatty acids, but this role is controversial due to CD36's structural differences with the family of fatty acid transport proteins, and the possibility that CD36 initiates signaling for another molecule to uptake fatty acids. Recent crystal structures of CD36 support the hypothesis that fatty acids are transferred through a hydrophobic cleft that spans the length of CD36. We hypothesize that polymorphisms in the transmembrane hydrophobic cleft in membrane bound CD36 can affect the rate of fatty acid uptake, which may ultimately contribute to metabolic disorders.

Methods

Mutations within the hydrophobic cleft in CD36 have been designed, changing certain amino acids hydrophobicity, size, and/or charge. To determine if fatty acid uptake is reduced, these mutated proteins will be expressed in HEK293 cells, which do not contain fatty acid binding proteins, and assayed for fatty acid uptake. To determine if the proteins function normally through signaling, they will be expressed in HEK Blue cells, which contain a known signaling partner, TLR2, and will undergo a secreted embryonic alkaline phosphatase assay.

Results

Two out of eight proposed mutations in the hydrophobic cleft in CD36 have been designed, created, and expressed in HEK293 cells. Future directions include assaying them for fatty acid uptake and signaling abilities. The remaining six mutations will follow.

Conclusions

Uptake of fatty acids is important for cellular oxidation, storage, structure, and signaling. Abnormalities in uptake can influence how a cell behaves and contribute to metabolic disorders including diabetes, obesity, and non-alcoholic fatty liver disease. A link between CD36 mediated fatty acid uptake and sudden infant death syndrome is also being investigated in a funded Heart and Stroke Foundation Grant in Aid. Determining CD36's role in fatty acid uptake could be used to implement genetic testing on newborns which would prompt increased awareness and care from the parents or guardians. This knowledge could also be used to identify new targets for pharmaceuticals which would significantly increase health outcomes for all aforementioned disorders.

The Power of Partnership

Introduction

Children rely heavily on object exploration to learn about the world and develop cognitive and social skills. However, children with motor impairments have difficulty with object manipulation and miss out on important developmental opportunities. Through assistive robotics, children with motor impairments can better manipulate objects, compensating for physical limitations that normally impair exploration.

Unfortunately, previous robotic systems only allow visual feedback for the user. In addition, many properties of objects are only explored through touch. By adding haptic (touch) feedback to the robotic interface we will offer an active touch experience to enhance children's development. However, we must first determine if a haptic interface can accurately inform users about objects around them. Electrodermal Activity (EDA) will be used to indicate difficulty/cognitive arousal when using the interface. We hypothesize that a haptic robotic interface will be accurate for comparison of object properties.

Methods

We optimized the PHANToM haptic robotic interface and ran trials, presenting eleven children aged 5-6 years with contrasting object pairs and asking them to assess the objects based on a particular feature. Subjects assessed four object properties (roughness, hardness, shape, and size) during four separate tasks. All tasks were completed both with the haptic interface and with the subject's hands in a "no tech" control condition. EDA was recorded and analyzed using cvxEDA MATLAB algorithm to assess the subject's cognitive arousal during each task. Analyzing behavioral data determined subjects' accuracy and confidence in their performance.

Results

Children were not as accurate when performing shape and roughness tasks compared to hardness and size tasks in the "no tech" condition. Children's average accuracy was significantly lower when using the haptic interface than when using their hands. There was no significant difference in subjects' reported confidence between tasks or conditions. There was no correlation between subjects' accuracy and reported confidence. Four of the EDA recordings were accepted for analysis. There appeared to be no difference in cognitive arousal either between no tech and haptic conditions or between tasks. Statistical analysis of EDA was not performed due to low n.

Conclusions

Our results suggest that the haptic robotic interface was somewhat accurate for object exploration; however, future improvement in the interface is necessary for determination of object properties to be comparable to using one's hands. There does not appear to be a difference in cognitive arousal between the conditions or tasks completed, however more data is required to discern potential trends.

The Power of Partnership

Abstract #: 71
Presenter: Osnat Wine
Supervisor: Alvaro Osornio Vargas
Title: Collaborative research, capacity building and knowledge translation development for health and the environment research
Authors: Osnat Wine, Jude Spiers, Michael van Manen, Katharina Kovacs Burns, Alvaro Osornio Vargas
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Working in collaborative and interdisciplinary teams is an increasingly common practice for researchers. The benefits of collaborative research support co-production of new knowledge responding to complex questions as well as facilitation of knowledge translation and exchange. Integrated knowledge translation (KT) is a collaborative approach that builds on participation of different disciplines and perspectives of researchers, stakeholders and knowledge users who provide their experience and expertise to enhance the depth and breadth of research and to facilitate knowledge translation. Understanding the components that impact team building processes can contribute to supporting ongoing and future collaborative efforts. Based on the DoMiNO project (Data mining & Neonatal outcomes) we present major components that contributed to building team capacity for knowledge creation and development of a knowledge translation plan.

Methods

The DoMiNO project explores the relationship between environment and health. We use this project's integrated KT process as a case study in a qualitative evaluation of the ongoing research collaboration (experience and learnings). Here, we focus on how the KT plan evolved following team engagement in the research process (e.g., meetings, informal interactions). Participants included all 24 DoMiNO team members. Data were collected through interviews, focus groups, surveys and participant observations, all adding to the cumulative understanding of the collaborative research process and the KT plan evolution. All data were coded and analyzed using thematic analysis procedures.

Results

Findings highlight some of the components of building capacity to support the progress of research, and co-production of new knowledge alongside the KT plan development. These components include readiness (commitment, balancing perspectives), and communication (co-learning and developing interdisciplinary literacy, transparency), which contribute to establishing relationships and trust, optimizing team work and building capacity. While Early KT plans were vague, through spontaneous and dedicated discussions, main messages and attainable KT goals were identified as the research progressed and identified components advanced. The KT plan was then articulated to identify potential users, audiences, and strategies (e.g., workshops with researchers and government representatives).

Conclusions

Several components contribute to capacity building and the development of the KT plan. In this complex context, it is an ongoing iterative process that evolves through time, as the team works and builds capacity. In the case of DoMiNO, it required four years to progress from the original perspectives of the different disciplines and sectors to a mature plan. Identifying and supporting the essential components of team development could optimize capacity building.

The Power of Partnership

The Canadian Pediatric Society (CPS) has identified Aboriginal communities in Canada as being at increased risk for health disparities. These health disparities include an increased prevalence of a number of medical conditions, infant deaths, substance abuse and childhood developmental delays. Furthermore, Aboriginal children and youth are at higher risk of chronic disease, which contribute a tremendous burden on Aboriginal families and their communities as well as the health care system.

In 2013, the Maskwacis Pediatric Outreach Clinic (M-POC) was established to provide access to health services for children and youth in Maskwacis Four Nations region of Alberta. Many First Nations communities, including the Maskwacis Four Nations, do not have access to consistent, reliable health care services. Pediatricians and pediatric residents, working in the Maskwaics 4 Nations have a unique opportunity to identify medical conditions that contribute to poor health and to advocate for and contribute to improved health outcomes.

The goal of this research project is to improve health outcomes for the children and youth who attend the Maskwacis community.

Objectives

1) To gain a better understanding of the medical conditions in the children and youth who attend the M-POC.

2) To engage community decision makers and community members in focus group discussions on how best to respond to the findings of the prospective chart review.

3) To provide an opportunity for pediatric residents to engage with the Maskwacis community to advocate for improved resources for the pediatric population.

Methods

The project will use a mixed methods approach consisting of a prospective chart review and focus groups.

The prospective chart review will occur at the Maskwacis Pediatric Outreach Clinic. The chart review will include pediatric patients between the ages of 0-18 years. Outcome information including patient age, gender, medical diagnosis, treatment and resources required will be anonymously recorded. Recording will be done by the pediatric residents and one of two pediatricians who attend the clinic.

After data collection, two focus groups will be conducted to discuss findings from the chart review. Focus groups will be conducted using the method of qualitative inquiry and analyzed using interpretive description. The purpose of the focus groups is to explore ideas, encourage discussion and prioritize issues in response to the chart review findings.

Outcomes

The outcome of this project is to consider and take initial steps to develop prevention interventions and treatment programs to target identified needs based on the prospective chart review.

The Power of Partnership

Abstract #:   73
Presenter: Paige Reeves
Supervisor: Shanon Phelan
Title: Constructions of disability in inclusive education settings: A qualitative exploration of parent and child experiences
Authors: Paige Reeves, Meghan Harris, Shanon Phelan
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Intro: Past research on educating children with disabilities has been entrenched in a deficit discourse. Although more recent research has shifted from an emphasis on impairment towards examining environmental factors and school level structures; powerful, potentially oppressive, underlying assumptions surrounding disability remain unchallenged. Through the application of a critical lens, this study (1) explores child and parent experiences of inclusion in school settings, (2) examines the construction of disability in inclusive settings, and (3) illuminates implicit assumptions surrounding disability in schools today.

Method: Framed in critical social theory (Eakin, Robertson, Poland, Coburn & Edwards, 1996) and critical disability studies perspectives (Barnes, Oliver & Barton, 2002; Shakespeare, 2014), this collective case study (Stake, 2006) examines the experiences of 9 parents and 9 school aged children in inclusive education settings. Individual, in depth, semi structured interviews were conducted with parent-child dyads. The medical, social, affirmative, tragedy, and relational models of disability were used as sensitising concepts to guide data analysis (Bowen, 2006).

Results: The following 3 themes emerged from the data: systemic level constructions of disability, school level constructions of disability, and parent and child constructions of disability. Systemic and school level influences were found to cultivate medical and tragedy based, deficit oriented, discourses of disability and consequently shaped parent and child experiences. Simultaneously, parent and child narratives were found to assert disability as affirming and identified the built environment, staff and school attitudes, and sociocultural expectations as disabling.

Conclusions: Despite the intentions of promoting inclusion in the school context, current school-based policies and structures unintentionally perpetuate negative disability discourses and negate an affirmative perspective on disability and identity. These negative valuations of disability have significant negative implications for child mental health and well being. Findings from this study call for critical reflexivity on current inclusive education policies and practices to consider the exclusionary effects of inclusion today.

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The Power of Partnership

Abstract #:   74
Presenter: Aamena Kapasi
Supervisor: Jacqueline Pei
Title: Improving self-regulation in adolescents with fetal alcohol spectrum disorder
Authors: Aamena Kapasi, Jacqueline Pei, Michael-Anne Markham, Katy Flannigan, Sandra Hodgetts , Danielle Mattson, Carmen Rasmussen
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

It is common for individuals with Fetal Alcohol Spectrum Disorder (FASD) to have difficulty with self-regulation, which is the ability to manage thoughts, behaviours, and emotions. Self-regulation is a product of multiple executive functions (i.e. neurologically based processes that help facilitate goal oriented behaviour) working in harmony. The Alert Program$^{®}$, developed by Williams & Shellenberger (1996), is a self-regulation intervention that has reported positive outcomes for children with FASD (Nash, 2015).

Methods:

In this study, the Alert Program$^{®}$ was adapted for use withadolescents with FASD. Pilot data from seven adolescents with diagnosed FASD (M_{age}=13.1 years, range=11-17; 6 females, 1 male) were examined from a parent report measure: the Behaviour Rating Inventory of Executive Function, Second Edition (BRIEF-2). After participating in a self-regulation program, it is hypothesized that adolescents with FASD will improve in three areas of regulation measured by the BRIEF-2: cognitive, behavioural and emotional regulation. The Cognitive Regulation Index (CRI) is comprised of working memory and the abilities to initiate, plan, organize, and task monitor. The Behavioural Regulation Index (BRI) is comprised of the ability to self-monitor and the ability to control impulses. The Emotional Regulation Index is comprised of the ability to move freely from one situation to another, and have emotional control.

Results:

An exact sign test was used to compare the differences pre and post intervention. There was no statistically significant median difference found on the CRI, BRI, or the ERI ($p>0.05$). However, given the small sample size and consequential limitations in analysis, it is difficult to make conclusions at this time. There were decreases in mean t-scores from pre- to post test in in all four measures of regulation (CRI pretest=76.7, posttest=74.4; BRI pretest=75.8, posttest= 72.9; ERI pretest=75.3, posttest=67.8), indicating possible group level improvements. Data will be additionally analyzed in comparison to a control group, and results will be discussed.

Conclusions:

Exploring the effects of a self-regulation intervention for adolescents with FASD allows for the development of more effective intervention initiatives that may help adolescents with FASD best access their strengths and support improved overall outcomes for them. Increasing the abilities to self-regulate in adolescents with FASD may help these individuals stay calm, focused, and alert, and thus may ultimately contribute to reducing the risk of adverse outcomes common in the FASD population and helping them move more successfully into adulthood.

The Power of Partnership

Abstract #: 75
Presenter: Lisa Lemieux
Supervisor: Pamela Brett-MacLean
Title: Exploring developmental pediatrics: an evolving field
Authors: Lisa Lemieux, Pamela Brett-MacLean
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Developmental pediatrics emerged as a certified specialty relatively recently. Informed by a broad knowledge base, developmental pediatricians work primarily in interdisciplinary teams to diagnose conditions and coordinate care aimed at optimizing a child's function in the home and in the community. Given the overlapping scope with general pediatrics, psychiatry, neurology, and adolescent medicine, it is unclear how developmentalists make sense of their specialty and enact their professional identity. In conducting this research, we sought to understand both the commonalities amongst developmental pediatricians and the differences between practitioners, to aid in articulating a description of the professional community to those in it and to the broader community, all in a broader aim to best support the care of children with developmental differences.

Methods: In-depth interviews were conducted with 10 developmentalists practicing in tertiary care centers in Alberta. We explored practitioners' values, beliefs, and motivations in relation to their understanding of the field. Interviews were transcribed. Qualitative data was coded and analyzed following a constant comparative method.

Results: Characterizing developmental pediatrics as a "broadly-based specialty area," all participants struggled to locate themselves within this evolving field. The position of developmental pediatrics at the intersection of several overlapping fields was seen as a strength. In this, the importance of a developmentalists' comfort managing complexity was a core theme across many interviews. In contrast, participants also described several tensions in trying to articulate a core identity: 1) the entwining of two historically separate branches (developmental-behavioral and neuromotor pediatrics); 2) the breadth of knowledge required contrasted with the depth of specialized knowledge needed in certain areas; 3) the chronic care approach required arising from a largely acute care training model; 4) the value placed on having a holistic approach challenged by the resource and time pressures of a consulting practice; 5) participating in interdisciplinary collaboration which requires flexibility in understanding the physician role.

Conclusions: Our findings offer a framework for articulating core constructs and apparent contradictions within the field. Recognizing the dialectical tensions can help practitioners locate themselves and thus affirm a professional identity. It is hoped that further articulation of the roles and tensions in the field helps others to understand the work, and helps with the recruitment of physicians well-matched to the field, to serve an every growing population of children who would benefit from the work of a developmental pediatrician.

The Power of Partnership

Abstract #:	76
Presenter:	Keon Ma
Supervisor:	Samina Ali
Title:	iPad distraction during intravenous placement in the pediatric emergency department: A randomized clinical trial
Authors:	Keon Ma, Samina Ali, Nadia Dow, Amir Issawi, Shannon Scott, Tanya Beran, Timothy A.D. Graham, Sarah Curtis, Hsing Jou, Lisa Hartling
Affiliations:	University of Alberta
Research Activity:	Children's Health and Well-Being

Introduction: Intravenous (IV) cannulation is a common procedure for children seeking medical attention, particularly in the emergency department (ED), often causing significant pain and distress. Distraction has been shown to significantly reduce child-reported pain, yet there is currently little published research on the use of iPad technology as distraction. Our **primary objective** was to compare the reduction of pain and distress with the use of distraction (via the iPad) versus current standard care in children aged 6 to 11 years. The **secondary objectives** were to assess the reduction of parental anxiety related to their child's use of distraction, and to examine the association between parental anxiety and child outcomes (pain, distress). We hypothesized iPad use would reduce pain and distress for children undergoing IV insertion in the ED, and reduce anxiety for their parents.

Methods: This randomized controlled trial (RCT) was conducted at the Stollery Children's Hospital ED from October 2015-December 2016. Eligible children were aged 6 to 11, required IV placement, were fully conscious and alert, and were proficient in English. Children were excluded if they had hearing, visual, sensory impairments, neurocognitive delays, or at the discretion of the attending staff. The intervention was child-appropriate games on an iPad. The control group received standard care, such as topical anesthetic cream. The primary outcomes were patient-reported pain and distress, measured using the Faces Pain Scale-Revised (FPS-R) and the Observed Scale of Behavioral Distress-Revised (OSBD-R), respectively. Two research students independently observed digital videos of each child and recorded the frequency of operationally-defined distress-related behaviours for each 15-second interval.

Results: Eighty-five children were enrolled, with 42 children receiving iPad intervention and 43 children standard of care. There were 40 females (47.1%) with a mean age of 8.32 ± 1.61 years. For the intervention arm, the median pre-procedure pain score was 2 (IQR 0,6) and post-procedure was 2 (IQR 0,6). For the standard care arm, the median pre-procedure pain score was 2 (IQR 0,4) and post-procedure was 2 (IQR 2,6). This study is currently undergoing more detailed statistical analyses.

Conclusions: The intent of this project is to provide groundwork for a larger, multi-armed, multi-center, technology-based RCT that we plan to submit for national funding. We plan to disseminate the results of this project through standard methods including peer-reviewed publications in a high impact journal, and presentation at scientific meetings. Further, our team will actively disseminate the findings to key engaged stakeholder groups.

The Power of Partnership

Abstract #:   77
Presenter: Jingyi Ma
Supervisor: Ordan Lehmann
Title: Inhibition of the glaucoma-causing gene, WDR36, affects ciliary structure and function
Authors: Jingyi Ma, Ordan Lehmann
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Mutations in *WDR36* cause primary open angle glaucoma, and contribute to complex glaucoma inheritance patterns. *WDR36* is part of a large family, characterized by highly conserved WD-repeat domains. For those members with reported disease phenotypes, an unusually high proportion of *WDR* genes induce ciliopathies or ciliopathy phenotypes [10 of 29]. In this context, together with cilia having key roles in movement of extracellular fluid, I investigated whether *WDR36* mutation caused the glaucoma phenotype by impacting ciliary structure/function.

Methods

I inhibited *WDR36* in murine fibroblasts [NIH3T3] by transfecting cells with 4 separate shRNAs [short hairpin RNAs], and measured *WDR36* expression levels with qPCR. Next I used confocal microscopy to measure cilia length after immunostaining cells with appropriate antibodies for the basal body and cilia. Finally, to assess the function of a major cilia-mediated pathway [Hedgehog (Hh) signaling], I stimulated cells with 3nM Smoothened agonist [SAG] and measured the response by quantifying Gli1 levels [a key effector of Hh pathway].

Results

shRNA inhibition induced a ~25% reduction in *WDR36* mRNA levels, and this in turn was associated with a 9% alteration in ciliary length. Preliminary data from a single experiment demonstrated an 8%reduction in Gli1 protein levels.

Conclusion

These preliminary data are consistent with the hypothesis that *WDR36* influences ciliary structure and function. The results require validation in replicate experiments, in which *WDR36* is inhibited by shRNA, and separately over-expressed. Such analyses are in progress, together with studies to determine WDR36's cellular position, and whether it localizes to the ciliary axoneme or basal body.

The Power of Partnership

Abstract #:   78
Presenter: Daniel Fung
Supervisor: Susan Gilmour
Title: Social determinants of life and medical adherence as predictors for health-related quality of life in the pediatric liver transplant population
Authors: Daniel Fung, Cheri Robert, Susan Gilmour, David Nicholas
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Progress in immunosuppression and surgical technique has led to increased survival for pediatric patients requiring liver transplant (LTx) to alleviate their primary disease. However, patients are left with a chronic condition including the lifelong need for immunosuppression and medical follow-up. Long-term concerns for LTx include medical non-adherence (MNA); MNA is a leading cause for mortality and morbidity in the adolescent transplant population. The complex association of social, physical and emotional constructs that surround patients are known as social determinants of health (SDOH) and influence both health-related quality of life and MNA. The present study aims to define SDOH and MNA as predictors for health-related quality of life in the pediatric LTx population at the Stollery Children's Hospital using the Pediatric Liver Transplant Quality of Life questionnaire (PeLTQL).

Methods:

Patients between 8-17 years of age who received LTx at least 6 months prior, and continue to receive regular medical follow-up with the Stollery Children's Hospital were included. Between March 2014 and July 2017, thirty-eight (n=38) patients completed the PeLTQL questionnaire as part of their clinical assessment. Retrospective chart review allowed for the extraction of factors for SDOH and MNA. MNA was defined as patients with less than 80% clinic and blood work attendance in the calendar year leading up to the completion of the PeLTQL. Planned analysis for PeLTQL questionnaire scores involve exploring their relationship with factors of SDOH and MNA through bivariate and multivariate analysis.

Results:

Our preliminary results show PeLTQL patient-reported scores for medically non-adherent patients were lower in all domains and the overall PeLTQL score (61.8 ± 13.5) compared to adherent patients (73.9 ± 9.6 p<0.05). Further bivariate analysis showed that children actively followed by any rehabilitation service at the time of the questionnaire, had elevated liver function tests in the last 12 months, or had changed their place of residence in the past 12 months had lower overall PeLTQL scores. Patients who had changed schools in the past 12 months also had lower scores in all domains and overall PeLTQL scores (60.0± 16.2) than those who had not (69.3 ± 11.7, p< 0.05).

Conclusion:

The results suggest medical non-adherence and specific factors of social determinants of health are strong predictors of lower overall health-related quality of life for the pediatric LTx population at the Stollery Children's Hospital. The current research may highlight areas of MNA and SDOH for further monitoring and modification to optimize patient outcomes.

The Power of Partnership

Abstract #:   79
Presenter: Ellen Rafferty
Supervisor: Shannon MacDonald
Title: Accuracy in parental reporting of childhood vaccination status in the All Our Babies cohort over time
Authors: Ellen Rafferty, Syrose Aujla, Erin Hetherington, Shannon MacDonald, Deborah McNeil, Vineet Saini, Sheila McDonald, Suzanne Tough
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Accurate and reliable indicators of vaccine coverage are needed to ensure the optimization of vaccination programs. Parental reporting of childhood vaccination status is often used for policy and program evaluation and research purposes. Many factors can bias parental reporting of childhood vaccination status, however, to our knowledge, no analysis has assessed whether time since vaccination impacts reporting accuracy. Therefore, using the Calgary electronic vaccine registry (PHANTIM) as the gold standard, we aimed to test the accuracy of parental reporting of childhood vaccination status at three different time-points since vaccination.

Methods: This study was a sub-analysis of the All Our Babies (AOB) cohort study. The AOB study asked parents to report their child's 2, 4, 6, 12 and 18 month vaccines (vaccination time-point) on questionnaires given when the child was 12, 24 and 36 months of age (survey time-point). We linked the AOB parental reporting of vaccination status to the PHANTIM registry, and measured the sensitivity and specificity, and negative and positive predictive values of parental vaccine recall for the five vaccination time-points at each of the three survey time-points. Furthermore, we calculated the difference in coverage estimates between PHANTIM and AOB at each vaccination and survey time-point combination.

Results: We found uniformly high sensitivity across all vaccination and survey time-points. In comparison, at all vaccination time-points but the 2 month vaccines there was a decreasing trend in the specificity of parental reporting of childhood vaccination from the 12 months to 36 months surveys, with the specificity in the 12 and 18 month vaccines being statistically significantly lower at the later survey time-points. The difference between AOB and PHANTIM coverage rates was very low in the 2, 4 and 6 months vaccines (<1%) but then jumped dramatically for 12 and 18 months vaccines (4-12%), with the AOB coverage rates consistently higher than the PHANTIM estimates.

Conclusion: Time since vaccination may be an important consideration when designing and implementing a vaccination survey. However, we also identified other factors that may contribute to the bias associated with parental reporting of vaccination status, including, the complexity of the vaccine schedule, changes to the schedule over time, and the wording and structure of the questionnaires.

The Power of Partnership

Abstract #:   80
Presenter: Lu Kun Chen
Supervisor: Joseph Casey
Title: Red blood cell senescence antigen develops through a major conformational change in membrane protein band 3 (AE1)
Authors: Lu Kun Chen, Katherine Badior, Joseph Casey
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction

As red blood cells (RBCs) circulate, they become increasingly damaged and dysfunctional. Clearance of aged RBCs is essential to maintenance of circulatory function. Anion Exchanger I (AE1) is a senescence marker for red blood cells. During senescence, circulating immunoglobin G antibodies bind to two sites on AE1, signalling the cell for macrophage degradation. Two regions of AE1 were identified as accessible on the extracellular surface, but a recently published crystal structure shows intracellular localization of one of the antigens. To reconcile these inconsistencies, we propose that senescence antigen forms when the cytosolic antigen becomes transiently accessible extracellularly upon a significant conformational change of AE1.

Methods

To test this, we will attempt to trap this conformation, using a disulphide bond. Cysteine residues were introduced into the two halves of the antigen (one half is outside and the other is intracellular prior to conformational change). Cysteine double mutants were cloned using the Q5 mutagenesis kit on a cysteine-free AE1 cDNA background. These mutants were expressed in HEK 293 cells. Crosslinking of cysteine residues requires the use of the oxidizing agent, Cu-o-phenanthroline.

Results

To identify crosslinked products on SDS-PAGE gels, AE1 was proteolysed at K743 site, between the two antigenic regions. Crosslinked fragments indicate that the two Cys residues in the antigen came together, indicating a major conformational change to form the senescence antigen.

Conclusion

Understanding the process of RBC senescence antigen formation has significance for understanding biological clocks and in storage of banked blood.

The Power of Partnership

Abstract #:   81
Presenter: Liane Kang
Supervisor: Anita Kozyrskyj
Title: Maternal pre and postnatal distress trajectories and age-specific fecal Immunoglobulin A concentrations in infants
Authors: Liane Kang, Petya Koleva, Catherine Field, Angela Chow, Allan Becker, Piushkumar Mandhane, Stuart Turvey, Padmaja Subbarao, Malcolm Sears, James Scott
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Evidence has been accumulating on the negative impact of maternal distress on the development of allergy in children. Previous studies have shown changes in gut microbiome (less lactic acid bacteria) and reduced mucosal immunity of offspring when exposed to distress, but little is known about the stress-microbiome-immunity pathways in humans. Lower concentrations of fecal secretory Immunoglobulin A (sIgA), a marker of immune maturation, have been associated with allergies and maternal depression in previous studies. In this study, we investigated the association between maternal distress trajectories (Persistent, Antepartum, Postpartum, Never) and infant fecal sIgA concentrations in different age groups (2-3, 3-4 and 4-8 months).

Methods

A subsample of 888 term infants from the Vancouver, Edmonton and Winnipeg sites of the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort were included. Pregnant mothers were enrolled and were asked to report perceived distress through scored-scales administered at recruitment, 36 weeks gestation and 6, 12, 18 and 24 months of infant age. Center for Epidemiologic Studies Depression (CES-D) scale determined depressive symptoms, while the Perceived Stress Scale (PSS) determined stress. From infant stool collected at a mean of 3.7 months, fecal sIgA was quantified using the Immundiagnostik sIgA ELISA kit. Maternal distress trajectories were created using M-plus. Using SPSS version 24, multiple linear and logistic regression models tested the associations of interest.

Results

About 5%, 7% and 2% of women in our sample were classified as having antepartum, postpartum and persistent depression trajectories. Four percent had higher stress antepartum, 21% had stress postpartum and 6% of mothers had persistent stress during pregnancy and postpartum. Infants of the Antepartum depression group had significantly lower median sIgA than the Never group (3.63 (IQR=1.54–8.08) versus 6.62 (IQR=3.44–11.72)mg/g feces; p=0.001). Significant odds ratios for sIgA at the lowest quartile were found with antepartum and persistent depressive symptoms not independently of breastfeeding status. In infants who had stool collected at 2-3 months, there was a 2-fold greater likelihood of lowest quartile sIgA concentrations when the mother had postpartum stress (95% CI 0.98–4.24). Multiple linear regression models indicated antepartum depressive symptoms were negatively associated with sIgA after adjusting for age at sampling, breastfeeding, infant sex and pets (β=-0.067, p=0.029).

Conclusions

Infants born to mothers experiencing antepartum depression trajectories are negatively associated with fecal sIgA independently of breastfeeding status. Due to the association with lower sIgA, prenatal depression may put infants at higher risk of allergic disease.

The Power of Partnership

Abstract #:   82
Presenter: Shweta Pipaliya
Supervisor: Joel Dacks
Title: Informatic characterization of membrane trafficking proteins in Giardia intestinalis and related fornicates
Authors: Shweta Pipaliya, Elisabeth Richardson, Dayana Salas-Leiva, Andrew Roger, Joel Dacks
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Giardia intestinalis is a fresh water-contaminating parasite responsible for the dysenteric illness Giardiasis, also known as 'beaver-fever' in North America. This diplomonad protist is the cause of the most common intestinal parasitic infection in Canada with approximately 26 cases per 100,000 annually. Children aged 0-9 are particularly susceptible to this infection due to their frequent contact with fecal material in daycare and school settings. *Giardia*, along with its diplomonad relative, *Spironucleus* salmonicida, possess unusual modifications within their membrane trafficking organelles which aid in the overall infection process and lifecycle establishment. Examples of these modifications include presence of unstacked Golgi bodies, a functional merging of the ER and endosomal compartments, and a separate multi-functional endolysosomal organelle, the peripheral vacuole. The molecular machinery underpinning the membrane-transport pathways is clearly reduced in *Giardia*, and yet sequence divergence has made robust classification of the specific components into their protein sub-families difficult to obtain. Free-living relatives that are less divergent are a fruitful way to tackle parasite evolution and comparative cell biology. We have used the basal, free-living, diplomonad relative, *Carpediemonas membranifera*, as a model system for studying both *Giardia assemblages* and *related diplomonads, Spironucleus salmonicida and Trepomonas sp. PC1. C. membranifera* possesses a standard set of membrane-trafficking organelles and encodes much less diverged protein sequences than *Giardia*. Therefore, we hypothesized that membrane-trafficking coat loss has occurred at the free-living to parasitic transition in diplomonads, with *C. membranifera* possessing a larger complement of vesicle coats than its relatives. In order to study these systems, we took a bioinformatics approach to analyze newly obtained genomic scale data for the identification coat proteins associated with endosomes and the Golgi. Results revealed a structured pattern of loss in the adaptor proteins complexes (AP). From a reconstructed complement of 5 AP complexes in the metamonad ancestor, we confirm the presence of AP1-3 in *C. membranifera*, *S. salmonicida*, and *Trepomonas sp. PC1* and at least AP1-2 in the various *Giardia* genomes examined, including the mice pathogen, *Giardia muris*. These results have fundamental implications in our understanding of the evolution of membrane trafficking from free-living lineages to parasitic lifestyles with modified endosomes coats within the Diplomonads. Together, a comprehensive understanding of the cell and evolutionary biology of the parasitic diplomonads is vital in the development of drug targets.

The Power of Partnership

Narratives Of Marital Relationships Post Immigration: Experienced Through The Eyes Of Immigrant Women In Canada

Introduction

In the pursuit of a higher standard of living, new opportunities, or for financial or political reasons, individuals often immigrate to a new country. While immigration may have several benefits, the process also encompasses many challenges and requires adjustments. These challenges may impact the relationship of married couples that immigrate together in many ways. Given that men and women may experience immigration differently, this qualitative study used narrative inquiry to specifically explore how immigrant women experience and narrate their marital relationships post immigration to Canada. The research question guiding this study was, "What was your marital relationship like after immigrating to Canada?"

Methods

Rather than focus on the experiences of immigrant women from a specific country, participants were required to have immigrated to Canada from a predominantly non-English speaking country and to have been married prior to immigration. Recruited individuals also identified to have at had at least one child in their country of origin, to have resided in Canada for a minimum of three years, and to be able to read and write in English. The study was limited to one-on-one semistructured interviews with only two adult female participants.

Results

The focus of this study was on the co-construction of meaning between participant and researcher resulting in 12 to 16 individual themes for each participant and 6 common themes: (a) lagging behind and feeling unsupported by spouse in Canadian integration; (b) experiencing disengagement with spouse and longing to connect; (c) experiencing positive changes with coparenting; (d) growing as an individual and gaining independence from spouse, (e) changing views about love, romance, and partnerships; and (f) feeling dependent on spouse during integration. Holistic-content and categorical-content approaches based on verbatim transcripts were used to construct the individual and common themes narratives.

Conclusions

The themes developed in this study present an in-depth understanding of immigrant women's experiences of their marital relationships after moving to Canada. They contribute to mental health work by offering insight on the relationship challenges immigrant women face and hence suggest the kind of service provision, community support and counselling focus that are required. Future research may benefit from recruiting a larger number of participants and from investigations that focus exclusively on recruiting participants from specific countries of origin.

The Power of Partnership

Abstract #:   84
Presenter: Michelle Gates
Supervisor: Lisa Hartling
Title: A descriptive analysis of non-Cochrane child-relevant systematic reviews published in 2014
Authors: Michelle Gates, Sarah Elliott, Cydney Johnson, Lisa Hartling
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Systematic reviews (SRs) specific to children are essential to inform evidence-based practice. Child-relevant SRs in the Cochrane Database of Systematic Reviews (CDSR) have been characterized (2009, 2013), showing: limited child-specific evidence; variable methodological and reporting quality; some out-of-date evidence; and few SRs originating from developing countries. It is unknown whether SRs published outside of the CDSR may be complementary and/or suffer similar shortfalls. We aimed to characterize all non-Cochrane child-relevant SRs published in 2014.

Methods: We searched four electronic databases for child-relevant SRs. A single reviewer screened articles for inclusion using a two-stage process (title/abstract, then full text); a second reviewer verified excluded studies only. Three reviewers independently extracted 3 broad categories of data: general characteristics; included study characteristics; methodological approaches. We checked all data for variables with <85% inter-reviewer agreement. We calculated descriptive statistics and presented the findings narratively.

Results: We identified 1,598 child-relevant SRs (>4 published per day) containing a median (IQR) 19 (11, 33) studies. The SRs originated primarily from high income countries (n = 1,246, 78.0%) in North America (n = 534, 33.4%) or Europe (n = 535, 33.5%), and provided coverage over 47 of the 53 Cochrane Review Groups (CRGs). Fifty-three percent of SRs fell into the top eight CRGs: Developmental, Psychosocial and Learning Problems (n = 216, 13.5%); Metabolic and Endocrine Disorders (n = 132, 8.3%); Pregnancy and Childbirth (n = 124, 7.8%); Common Mental Disorders (n = 110, 6.9%); Airways (n = 70, 4.4%); Anaesthesia, Critical and Emergency Care (n = 69, 4.3%); Public Health (n = 67, 4.2%); Infectious Diseases (n = 61, 3.8%). Most SRs synthesized therapeutic (n = 753, 47.1%) or epidemiologic (n = 701, 43.9%) evidence. Though half of the SRs included evidence either for children only (n = 628, 39.3%) or pregnancy (n = 176, 11.0%), relatively few were published in pediatric journals (n = 273, 17.7%). Reporting quality varied; few SRs mentioned an *a-priori* protocol (n = 246, 15.4%) or registration (n = 111, 6.9%), and only 23.4% specified a primary outcome. There were few updates (n = 32, 2.0%); more commonly, new SRs disregarded the availability of previous evidence syntheses on the same topic. Many SRs relied solely on evidence from non-RCTs (n = 796, 49.8%). Less than two-thirds of SRs (n = 953, 59.6%) appraised the quality of included studies and assessments of the certainty of the body of evidence were rare (n = 102, 6.4%). The synthesis method used in SRs was roughly equally split between narrative (n = 741, 46.4%) and statistical (n = 857, 53.6%).

Conclusion: There exists a wealth of child-relevant evidence from non-Cochrane SRs that may complement evidence contained in the CDSR, though there remain topics that appear understudied (e.g., Haematological Malignancies, Neuromuscular, Hypertension, Stroke, Urology, and Schizophrenia groups all contained <10 SRs, each representing <1% of the total sample). Many non-Cochrane SRs suffer methodological and reporting shortfalls, despite the availability of guidance for reviewers.

The Power of Partnership

Abstract #:   85
Presenter: Aireen Wingert
Supervisor: Lisa Hartling
Title: Screening for asymptomatic bacteriuria in pregnancy: A systematic review and meta-analysis
Authors: Aireen Wingert, Jennifer Pillay, Robin Featherstone, Michelle Gates, Meghan Sebastianski, Kassi Shave, Ben Vandermeer, Lisa Hartling
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Background: Asymptomatic bacteriuria (ASB) is a significant amount of bacteria in urine, without symptoms of infection. Pregnant women may be at higher risk of developing ASB leading to pyelonephritis and adverse perinatal outcomes. We conducted a systematic review and meta-analysis to inform recommendations by the Canadian Task Force on Preventive Health Care (CTFPHC) on screening for ASB in pregnancy.

Methods: A staged approach was used based on the quality of evidence when applying Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods. A reduction in the following outcomes would favor screening: maternal mortality, maternal sepsis, pyelonephritis, perinatal mortality, spontaneous abortion, neonatal sepsis, preterm delivery, low birthweight, and serious harms. Stage 1 examined a) benefits and harms of screening compared with no screening, b) benefits and harms of different screening programs, and c) women's valuation of benefits and harms of screening and treatment in pregnancy. Based on very low quality evidence from Stage 1, Stage 2 was undertaken to examine effectiveness of antibiotic treatment for pregnant women with bacteriuria.

Results: Four non-concurrent cohort studies compared outcomes before and after the introduction of a screening program for ASB: three studies comparing screening with no screening showed a reduction in pyelonephritis (RR 0.28, 95% CI 0.15-0.54; ARR 1.3%; NNS 77, 95% CI 65-121), with no significant differences found for perinatal mortality, spontaneous abortion, preterm delivery and fetal abnormalities; one study comparing frequent with one-time screening found no significant difference for pyelonephritis or preterm delivery. Indirect evidence on women's outcome valuation reported conflicting opinions about antibiotic use during pregnancy. Fifteen trials comparing antibiotic treatment with no treatment or placebo found a significant difference in pyelonephritis (12 trials, RR 0.24, 95% CI 0.13-0.41; ARR 17.6%; NNT 6, 95% CI 5-7) and low birth weight (7 trials, RR 0.63, 95% CI 0.45-0.90; ARR 4.4%; NNT 23, 95% CI 15-85); no significant differences were found for other maternal and neonatal outcomes.

Interpretation: Very low quality evidence from studies on screening provided little certainty in effect estimates for maternal and neonatal outcomes. No direct evidence was found for how women weigh the benefits and harms of screening for ASB. Antibiotic treatment may reduce incidence of pyelonephritis and babies born at low birth weight; however, we have limited certainty about the magnitude of effects and applicability to screening populations. Very low quality evidence was found for other maternal and neonatal benefits and harms.

The Power of Partnership

Abstract #:   86
Presenter: Stephanie Kowal
Supervisor: Tania Bubela
Title: Parental decision-making processes in pediatric trial enrollment: recommendations for informed consent in gene and stem cell research
Authors: Stephanie Kowal
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Clinical trials for novel interventions, including cell therapies and devices, for Type 1 diabetes are beginning to recruit pediatric participants. It is, therefore timely to consider how to communicate risks and potential benefits of trial participation with parents who make clinical decisions on behalf of their child. Parents have high expectations for new treatment options, which may encourage them to pursue clinical trial opportunities or join risky movements. For example, the Do It Yourself Pancreas System uses open access coding communities to share unproven automated insulin delivery via smartphones.

Methods: We conducted 16 qualitative interviews with parents of children with Type 1 diabetes to explore information gathering, decision-making processes, and knowledge of clinical trial conduct by parents. We used the constant comparison method to code interview transcripts for themes, using NVivo qualitative analysis software.

Results: Parents' decision-making processes followed Protection Motivation Theory. This theory posits that parents will use available information to balance the risks of trial participation against the risks of current disease management. This balancing helps them decide whether trial enrollment may protect the health of their child better than current management methods. However, the Theory needs to account for the overly optimistic information about treatment research accessed by parents on traditional and social media. In general, parents are risk-adverse and express a preference for complete and accurate information to make fully informed decisions.

Conclusion: Parents can differentiate between hope and expectation for trial outcomes. However, their preference for accurate information means that clinicians must clearly communicate therapeutic potential, likelihoods of risks and benefits, as well as uncertainty. Recommendations for clinical investigators to develop communication protocols that ensure parents receive all necessary risk and benefit information will ensure that parental consent for pediatric clinical trials is, in fact, informed.

The Power of Partnership

Introduction: Inflammation and maternal stress influence the birth process, with interactions between the local neuro-endocrine and immune system playing essential roles in parturition. We developed a two-hit stress model in which parental generation (F0) rats receive psychological and/or immune stress in late gestation and demonstrated that two-hit stress increases adverse pregnancy outcomes compared to either stressor alone. Furthermore, stressors differently influence cytokine mRNA expression in F0 and F1 uteri, with Interleukin (IL)-1β mainly increasing abundance in dams. In contrast, interactions were only present in offspring tissues, mediating stress effects. We hypothesize that distinct stressors influence F0/F1 uterine expression of stress-related genes differently when combined than either alone and propose that these effects are transferred intergenerationally and are generation-dependent.

Methods: F0 dams underwent psychological (restraint/forced swimming) and/or immune stress (IL-1β, 5µg/day, i.p.) on gestational days 12-18 and 17-delivery respectively. F0/F1 animals were divided into: no stress/saline (N/Sa), no stress/IL-1β (N/IL), stress/saline (S/Sa), stress/IL-1β (S/IL). Uteri were collected from F0 animals at weaning and from virgin adult F1. mRNA abundance was evaluated by qRT-PCR for *Crh* and receptors *Crhr1/2*, the gluco- and mineralocorticoid receptors *Nr3c1/2* and both isoforms of the corticosterone-metabolizing 11β-hydroxysteroid dehydrogenase, *Hsd11b1/2*, normalized to housekeeping gene CyclophilinA. Two-way ANOVA with *posthoc* testing, $P \leq 0.05$ deemed significant.

Results: IL-1β respectively doubled and tripled the mRNA abundance of *Crh* ($P<0.01$) and *Crhr1* ($P<0.05$) in F0 uterine tissues, whereas in their daughters expression of both was downregulated by gestational Stress (both $P<0.05$). No interaction was present, although S/IL offspring displayed the lowest expression. *Nr3c2* had a similar expression pattern in F1 but was not changed in maternal uteri. *Hsd11b1* was significantly downregulated in S/IL as compared to S/Sa and N/IL progeny ($P=0.001$), with the interaction reducing abundance to levels similar to those in N/Sa animals.

Conclusion: Effects of prenatal stress are also visible on stress-related genes, which are an important part of local regulation of uterine quiescence and contractility. While our results strengthen the hypothesis that multiple-hit stress has different effects than single stressors, these outcomes are not straightforward and appear dependent on the nature of the stressor(s), timing since exposure and generation. The observation that stress-outcomes appear dampened in adult F1 progeny, while increasing adverse pregnancy outcomes could fit in the match/mismatch hypothesis of fetal programming, with offspring preparing for an expected stressful pregnancy. Putting F1 offspring through gestation may reveal whether these are a form of maladaptation or a sign of resilience.

The Power of Partnership

Abstract #:   88
Presenter: Meghan Onushko
Supervisor: David Olson
Title: Predicting pre-term labour before it is to late: An investigation of the fetal membrane interaction with the blood
Authors: Meghan Onushko, Han Lee
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction:

The uterus experiences a broad range of changes from pregnancy to birth. Inflammatory proteins, known as chemoattractants, can stimulate circulating white blood cells, causing the cells to invade the uterus. An event that occurs at some point in every birth. In some cases, this may cause the early onset of labour. With over 15-million occurrences annually, pre-term birth is the primary cause of death among infants. Though it is infrequently fatal, it is responsible for the upwards of one million deaths per year. Of the babies that survive, many are at risk of serious health complications including difficulty breathing, changes in brain development, and other long-term disabilities. Antenatal care or intervention during pregnancy could prevent three-quarters of these births (World Health Organization, 2016). Researchers can use *in vitro* tools to characterize the cell signalling pathways in preterm birth (<37 weeks) weeks before any symptoms appear and blocking these pathways may assist in preventing preterm birth. Few studies have looked at the relationship between white blood cells and fetal membranes, and the pathway is not completely understood. We know that in preparation for birth, the fetal membranes release specific proteins that attract white blood cells in to the uterus.

Methods:

We have developed a migration test that uses the increasingly responsive white blood cells to predict the timing of delivery.

Hypothesis:

The potential causes for the growing responsiveness of the white blood cells include: an increased number of receptors for protein molecules on the white blood cells, interactive mechanisms that enhance communication between the different maternal tissues, or more effective methods of white blood cell migration. Since it has been determined that inflammatory protein receptors on muscle layer surrounding the uterus (myometrium) change when labour begins, it is likely that the same process is occurring on the fetal membranes. We hypothesize that an increased number of receptors for protein molecules causes white blood cells to invade the uterus before (or on) the expected delivery date.

Results:

We have shown that fetal membrane contains chemoattractant, and the strength of this chemoattractant can be amplified two-fold with interleukin 1-b. As well, we have demonstrated that spontaneous term labour (STL) leukocytes responds better to STL fetal membrane chemoattractant. Finally, we have found that leukocyte invasion to the lower uterus is significantly greater an interleukin 1-b stimulated mice.

Conclusions:

In the broader context, this knowledge could be used to develop a simple clinical test, which could serve as an identification tool for the mothers at risk of preterm labour.

The Power of Partnership

Introduction

Iron deficiency (ID) is the most common nutritional deficiency worldwide with pregnant women most at risk. ID has been shown to impact growth and development of the fetus, in part by affecting oxidant status in fetal tissues. Indeed, prenatal ID is associated with increased reactive oxygen species (ROS) production in rodent kidneys, though it is not clear whether other tissues (e.g. liver) are similarly affected. Interestingly, female tissues have a higher antioxidant capacity, suggesting males may be more susceptible to ROS generation.

We hypothesized ID would cause sex-dependent increases in superoxide production in fetal kidneys and liver in the rat.

Methods

Dams were fed either a control, moderately iron-restricted or severely iron restricted diet throughout gestation. Dams and fetuses were euthanized at the end of pregnancy, and tissues were collected. Kidneys and livers were sectioned and stained with markers for cytosolic (DHE) and mitochondrial superoxide (MITO-SOX), and quantified by fluorescence microscopy.

Results

Cytosolic superoxide was increased in ID kidney (P=0.02) and livers (P=0.01) from male, but not from female fetuses (P=0.56 and P=0.60, respectively). In contrast, there was no evidence of increased mitochondrial superoxide production either male or female kidney or livers.

Conclusions

These results suggest prenatal ID causes sex-dependent patterns of oxidative stress, with males more affected than females.

The Power of Partnership

Abstract #: 90
Presenter: Stewart Rowe
Supervisor: Maria B. Ospina
Title: A systematic review of the measurement properties of indices of adequacy of prenatal care
Authors: Stewart Rowe, Zahra Karkhaneh, Isaiah MacDonald, Thane Chambers, Sana Amjad, Alvaro Osornio-Vargas, Radha Chari, Manoj Kumar, Maria B. Ospina
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

INTRODUCTION: Prenatal care has long been recommended for healthy pregnancies. Evidence from systematic reviews show inconsistencies on the optimal components of prenatal care (i.e., content, frequency, and timing of visits) associated with its effectiveness to avoid adverse outcomes for mothers and babies. An accurate measurement of adequacy of prenatal care (APC) is critical to inform its relationship with pregnancy outcomes. A variety of indices of APC have been developed, each employing different algorithms based on time of initiation and frequency of prenatal care. It is unknown which index has the best scientific evidence to support its use. The objectives of this systematic review (SR) were: 1) to describe the frequency and characteristics of use of APC indices in the scientific literature, and 2) to summarize the evidence about the measurement properties of indices assessing APC.

METHODS: A comprehensive search was conducted up to June 2017 in four electronic databases (PROSPERO protocol CRD42017067110). Studies were included if 1) they used at least one APC index, and/or 2) evaluated at least one of their measurement properties. SR outcomes were: 1) frequency and purpose of use, and 2) evaluation of reliability, validity, and responsiveness of the indices. The methodological quality of studies evaluating the measurement properties of APC indices was appraised using COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN).

RESULTS: From 2,582 studies initially screened, 220 used at least one APC index. The most frequently used were the Kotelchuk/Adequacy of Prenatal Care Utilization Index (APNCUI; 57.2%), the Kessner Index (40.4%) and the Revised-Graduated Prenatal Care Utilization Index (R-GINDEX; 6.3%). The majority of indices were used for descriptive/discriminative (88.6%), predictive (35.9%) and evaluative purposes (18.6%). Thirteen studies evaluated measurement properties of APC indices. Measurement properties of the APNCUI index were evaluated in all 13 studies, while those of Kessner and R-GINDEX were evaluated in eight and two studies, respectively. Construct validity was the most frequently evaluated property (12 studies) while reliability (n = 2) was seldom assessed. Criterion validity was evaluated in one study only. Responsiveness to change was not evaluated. The quality of the evidence on the measurement properties of all APC indices was poor.

CONCLUSIONS: Limited and low-quality evidence currently informs the selection of indices of APC for research and practice. Lack of good evidence about which index is the best to measure APC has important implications for tracking health care utilization and for formulating prenatal care recommendations.

The Power of Partnership

#wchriRD2017   **Women and Children's Health Research Institute**

Abstract #:   91
Presenter: Ayanna Rocke
Supervisor: Robin Clugston
Title: Congenital diaphragmatic hernia and maternal Vitamin A status: Investigating the retinoid hypothesis
Authors: Ayanna Rocke, Timothy Dalmer, Tianna Clarke, Robin Clugston
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: Congenital Diaphragmatic Hernia (CDH) is a birth defect that occurs in approximately 1 in every 3000 births. In CDH, the integrity of the diaphragm is compromised as it fails to form properly during development of the fetus. CDH is known to cause breathing problems in newborns, leading to significant mortality, and long-term morbidity in survivors. The cause of CDH is poorly understood and is thought to be multifactorial, including teratogenic, dietary and genetic hits. Vitamin A is a fat- soluble vitamin that is an essential component of the diet and has many critical roles in the day-to-day functioning of the body. Research has shown that Vitamin A and Retinoic Acid (a product of Vitamin A) plays a substantial role in the development of CDH; a concept that has been formulated into the so-called "Retinoid Hypothesis". CDH can be induced in offspring of mice treated with teratogens such as 2,4-Dichlorophenyl 4-nitrophenyl ether (Nitrofen) and N,N'- bis (dichloroacetyl)- 1,8- octamethylenediamine (Bisdiamine). With the knowledge that these chemicals can cause CDH and that Vitamin A has been associated with the formation of CDH, we hypothesized that maternal Vitamin A (retinoid) status influences the formation of teratogen-induced CDH.

Methods: This hypothesis was tested in three groups of female mice with different Vitamin A status: 1) marginal, 2) sufficient and 3) excess. Vitamin A status was confirmed in maternal tissues by HPLC. Mice were mated, and pregnant animals were treated with a combination dose of Nitrofen and Bisdiamine. Offspring were collected via dissection and we recorded the effect of different doses of the teratogenic combination on the formation of CDH, including incidence and severity. *Results:* We have determined that teratogen treatment has a dose-dependent effect on the induction of CDH in mice. We have established three groups of mice with different vitamin A status (marginal, sufficient and excess), and are validating this through the measurement of maternal hepatic vitamin A levels. Studies are continuing into the effect of maternal vitamin A status on teratogen-induced CDH.

Conclusion: Teratogen treatment induces CDH in mice. We expect that offspring of the mothers on a Vitamin A excess diet will have reduced incidence of CDH, while the mothers on a Vitamin A marginal diet will have an increased incidence. This research will help support the Retinoid Hypothesis and highlight the need for future studies to focus on the role of Vitamin A and its derivatives on diaphragm development.

The Power of Partnership

Abstract #:   92
Presenter: Sana Amjad
Supervisor: Maria Ospina
Title: Social determinants of health and adverse maternal and birth outcomes in adolescent pregnancies: A systematic review
Authors: Sana Amjad, Isaiah MacDonald, Thane Chambers, Alvaro Osornio-Vargas, Sujata Chandra, Don Voaklander, Maria Ospina
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

INTRODUCTION: Adolescent pregnancy poses significant health risks for both the mother and the infant. Adverse outcomes in teen pregnancies have been associated with both biological immaturity and social determinants of health (SDOH). We present preliminary results of a systematic review that evaluate the evidence of the association between SDOH and adverse maternal and birth outcomes in adolescent mothers.

METHODS: A comprehensive search was conducted from database inception up to August 2017 in four electronic databases (PROSPERO protocol # 42017068749). Two independent reviewers screened retrieved records to identify studies that evaluated the association between SDOHs (place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status, and social capital from the PROGRESS-PLUS framework) and the risk of adverse maternal and birth outcomes in adolescent mothers. Methodological quality of the primary studies that met inclusion criteria, was independently assessed with the New Castle-Ottawa Scale adapted to the study design. Unadjusted odds ratios (OR) were pooled in a random-effect model meta-analysis.

RESULTS: From 3,151 studies initially screened, 31 studies met the inclusion criteria. Studies from 11 countries were reviewed. The most frequent SDOH evaluated in individual studies were race/ethnicity (n=20), socioeconomic status (n=10), education (n=9), place of residence (n=7), and occupation (n=7). Caesarean section was the most commonly reported maternal outcome (n=11), while preterm birth (PTB) was the most commonly reported birth outcome (n=20). We report in this abstract, only the meta-analysis of the association between race and adverse birth outcomes. Evidence from 4 retrospective cohort studies showed that black teenage mothers had increased odds of PTB compared to white teens (pOR 1.67; 95% confidence interval [CI] 1.59, 1.75). Similarly, a meta-analysis of 4 retrospective cohort studies showed that black teenage mothers had a 53% increase in the odds of low birth weight compared to white teens (pOR 1.53; 95% CI 1.45-1.62).

CONCLUSIONS: Preliminary results suggest that race is associated with adverse maternal and birth outcomes in adolescent pregnancy. Particularly, our findings show that black adolescent mothers are at a high risk of adverse birth outcomes. These findings have implications for service providers and policy makers and will assist them to effectively design and deliver informed perinatal health care services for adolescent mothers.

The Power of Partnership

Abstract #:   93
Presenter: Esha Ganguly
Supervisor: Sandra Davidge
Title: Treating the placenta with a nanoparticle-linked antioxidant to improve pregnancy outcomes in a rat model of fetal hypoxia
Authors: Esha Ganguly, Jude Morton, Raven Kirschenman, Christy Cooke, Patrick Case, Sandra Davidge
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Pregnancy complications leading to fetal hypoxia are linked to the development of adult cardiovascular disease in offspring. We have previously shown that a prenatal hypoxic insult reduces placental perfusion, induces hypoxia and increases oxidative stress in the placenta associated with fetal growth restriction. Factors released from a stressed placenta affect the development of key fetal organ systems (e.g. heart). MitoQ is an antioxidant which, when attached to nanoparticles (nMitoQ), can be used to target maternal and placental oxidative stress without crossing the placenta. We hypothesized that nMitoQ treatment will improve oxygenation and reduce associated oxidative stress in both placental and fetal cardiac tissues in a sexually dimorphic manner, ultimately leading to better pregnancy outcomes

Methods

Pregnant rats were exposed to either hypoxia (11% O_2) or normoxia (21% O_2) from gestational day (GD) 15-21; term=22 days. On GD15, rats were intravenously injected with saline or nMitoQ. Placentae and fetal tissues were collected from both sexes on GD21. Tissue hypoxia was assessed by Hypoxyprobe-1 staining, which binds to thiol groups at oxygen tensions below 10 mm Hg. Reactive oxygen species (ROS) were assessed by dihydroethidium and MitoSOX staining in placenta and fetal cardiac tissues.

Results

nMitoQ treatment improved oxygen delivery in placentae of female but not male offspring. Prenatal hypoxia increased mitochondrial ROS in placentae (normoxia: 0.021±0.001 a.u. vs. hypoxia: 0.025±0.001 a.u.; $p < 0.05$), and tended to increase cardiac hypoxia, in only male offspring. nMitoQ reduced mitochondrial ROS in prenatally hypoxic placentae of only female offspring. nMitoQ treatment reduced cardiac hypoxia in both sexes. Evidence of cardiac oxidative stress was greater in male (normoxia: 0.017±0.0002 a.u. vs. hypoxia: 0.019±0.0005 a.u.; $p < 0.05$) hypoxia exposed offspring while nMitoQ treatment reduced cardiac ROS in female but not male offspring.

Conclusions

Treatment with nMitoQ at the time of a prenatal hypoxic insult prevented both placental hypoxia and reduced mitochondrial ROS production in female but not male offspring. Without crossing the placenta, nMitoQ exerted a sexually dimorphic protection against fetal cardiac oxidative stress. Treatment targeted to the placenta could lead to improved cardiovascular outcomes in offspring.

The Power of Partnership

Abstract #:	94
Presenter:	Paul Li
Supervisor:	Sandra Davidge
Title:	The role of LOX-1 in the development of vascular dysfunction in preeclampsia
Authors:	Paul Li, Floor Spaans, Jude Morton, Anita Quon, Sandra Davidge
Affiliations:	University of Alberta
Research Activity:	Maternal and Infant Healthy Development

INTRODUCTION

Preeclampsia (PE) is a pregnancy complication diagnosed by *de novo* hypertension, proteinuria, and/or end organ failure. PE is the leading cause of maternal morbidity and mortality. Although the pathophysiology remains poorly understood, there is considerable evidence that vascular endothelial dysfunction plays a central role in the disease. The lectin-like oxidized LDL receptor 1 (LOX-1) is a multi-ligand scavenger receptor that has been associated with vascular dysfunction. Further, LOX-1 expression is increased in arteries from women with PE. A dysfunctional vascular renin-angiotensin system has also been associated with PE. Interestingly, recent studies have suggested that activation of LOX-1 enhances angiotensin II signalling via the angiotensin II receptor AT-1. In order to investigate the hypothesis that an interaction between the AT-1 receptor and LOX-1 contributes to vascular dysfunction in PE, we assessed vascular function in LOX-1 overexpressing (LOX-1 OE) mice.

METHODS

Pregnant LOX-1 OE (n=2) and wildtype (WT; n=3) mice were sacrificed at gestational day 18 (term = 19 days). Nonpregnant LOX-1 OE (n=2) and WT (n=3) mice were used as age-matched controls. Mesenteric arteries were isolated and vascular function was assessed using wire myography. Endothelium-dependent vasodilation responses to methylcholine were assessed, and vasoconstriction responses to angiotensin II in the presence or absence of the AT-1 receptor antagonist candesartan or the LOX-1 ligand oxidized LDL (oxLDL). Sections of artery were snap frozen and used for immunohistochemical staining of LOX-1 and AT-1 receptors.

RESULTS

No changes were found in vasodilation responses to methylcholine between arteries from pregnant or nonpregnant mice, nor between the LOX-1 OE and WT mice. In arteries from pregnant LOX-1 OE mice, vasoconstriction responses to angiotensin II were increased compared to pregnant WT mice and both strains of nonpregnant mice. This increase in angiotensin II responsiveness in arteries from pregnant LOX-1 OE mice was exaggerated after oxLDL treatment. OxLDL stimulation had no effect in the other groups. Angiotensin II-induced vasoconstriction responses were blocked by candesartan in all groups. Immunohistochemical staining suggested potential co-localization of LOX-1 and AT-1 receptors in the endothelium.

CONCLUSIONS

LOX-1 overexpression appears to predispose mice to angiotensin II induced vascular dysfunction during pregnancy. This was shown to be AT-1 receptor mediated and could be the result of co-localization between LOX-1 and AT-1 receptors. The results will be confirmed with increased numbers. These data help further define the pathways leading to vascular dysfunction in pregnancy and contribute to the development of novel therapeutic strategies in the future.

The Power of Partnership

Abstract #:   95
Presenter: Zenah Gheblawi
Supervisor: Susan Armijo-Olivo
Title: The effectiveness of exercise therapy on decreasing pain in women with TMD and how their brains respond: A pilot randomized controlled trial
Authors: Zenah Gheblawi, Vaishali Sharma, Musa Tashfeen, Angela Fung
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: Due to physiological differences between men and women, pain is experienced differently between the two sexes. Chronic pain disorders, notably temporomandibular disorders (TMDs), disproportionately affect women in diagnosis, and pain severity in opposition of their male counterparts. TMDs are a type of musculoskeletal disorder that target the masticatory muscles, temporalis muscle, and temporomandibular joints, causing considerable orofacial pain which can usually be referred to the neck and back. Therapeutic methods are scarce, and are not TMD-centered, with the latest research suggesting that subjects with chronic musculoskeletal pain disorders have abnormal alterations in the grey matter of their brains which can be remedied with exercise, and thus, decreasing the pain experienced. The aim of our study is to investigate the effects of exercise therapy in TMD female patients experiencing chronic jaw pain, and to assess the consequential effects on brain activity.

Methods: In a randomized controlled trial, we will test the effectiveness of an exercise program to improve brain alterations and clinical outcomes in women with TMD pain. Women with chronic TMD pain will be randomized to either an intervention arm or a placebo control group. Women in the intervention arm will receive 8 weeks of progressive exercise of motor control training using visual feedback (MCTF) of the cervical muscles, twice per week. Women in the placebo arm will receive innocuous transcutaneous electrical nerve stimulation during 8 weeks as well.

Our primary outcomes will be changes in:

1) **pain**, measured with the Visual Analogue Scale

2) **brain structure and networks**, measured by fractional anisotropy (brain structure) and the blood-oxygen-level dependent signal (brain networks)

Outcomes will be measured at baseline, after 8 weeks of treatment, and 4 months after treatment ends.

Expected Outcomes. Measure effectiveness of MCTF in managing TMD, through improved clinical outcomes. Results will directly inform and guide clinicians in prescribing more effective interventions for women with TMD.

Results: This study is underway and no results are available at this point.

Conclusions: The results of this study will have substantial implications on the advancement in understanding the scope of plasticity the brain has in regards with pain, and how it can be used to improve the treatment and pain of women with TMD, and more generally, other musculoskeletal disorders.

The Power of Partnership

Abstract #:   96
Presenter: Saba Rehman
Supervisor: R. Todd Alexander
Title: Activation of the calcium sensing receptor attenuates SP1 activity to increase Claudin-14 expression
Authors: Saba Rehman, Jawad F. Alzamil, R. Todd Alexander
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

INTRODUCTION

Calcium regulation is critical for normal cell function, neuronal transmission, membrane stability, bone structure, blood coagulation and intercellular signaling. Calcium is therefore maintained under tight control in plasma. To do so, the calcium sensing receptor (CaSR), which is expressed in kidney along the renal tubule, senses plasma calcium levels and when they are too high mediates increased urinary calcium excretion, by increasing the expression of claudin-14 which blocks tubular reabsorption. However, the signaling pathway between CaSR activation and claudin-14 expression is completely unknown. We therefore set out to delineate this pathway.

METHODS

We used quantitative real time PCR to determine which claudin-14 transcript variant was regulated by CaSR activation. We then cloned increasingly longer fragments 5' of the first exon of this variant into the pGL3 basic vector until we found the sequence with promoter activity. To confirm that it was CaSR sensitive, after transfection into HEK cells, they were incubated with the CaSR agonist Cinacalcet. Next, to tease out the signaling pathway downstream of CaSR activation, cells expressing the CaSR sensitive promoter were incubated with either vehicle, Cinacalcet, blockers of various signaling pathways or Cinacalcet and the blocker. We tried a number of inhibitors including Mithramycin (SP1 inhibitor), U-73122 (PLC inhibitor), Staurosporine (PKC inhibitor) and U0126 (MEK 1 & 2 inhibitor). Transcription factors including Sp1 were also cotrasnfected with the promoter containing vector to assess the effect on reporter activity.

RESULTS

We identified the first variant of claudin-14 to be sensitive to CaSR activation, the other 4 variants were not. Next we determined that the promoter was between 1000 and 1500 bp 5' to the first exon of claudin-14 variant 1. This 1500 bp fragment containing the promoter was CaSR sensitive. The PLC, PKC and MEK inhibitors did not alter claudin-14 reporter expression, nor did they attenuate the increase in expression induced by CaSR activation. However, we found that Mithramycin increased claudin-14 expression but not more than that of Cinacalcet. Consistent with this, a significant decrease in reporter activity was observed when SP1 was co-transfected with the CaSR sensitive reporter.

CONCLUSION

Together these studies have identified the 1500 bp 5' of the first exon of the first transcript variant of claudin-14 to contain the promoter and to be responsive to CaSR activation. Moreover, Sp1 appears to be critical to this pathway. This knowledge can help design therapeutics to decrease urinary calcium excretion and help prevent kidney stone formation.

The Power of Partnership

Introduction: Youth who participate in sport are at increased risk of knee injuries. The most frequent knee injury is an anterior cruciate ligament (ACL) tear. A common treatment pathway for active youth who sustain a complete ACL tear and desire to return-to-sport is to undergo ACL reconstruction (ACLR) and rehabilitation. There is a paucity of information on how knee-related quality-of-life (QOL) is impacted by physical activity and other modifiable factors over the first year following youth sport-related ACLR.

Objectives: The primary objective of this pilot prospective cohort study is to investigate the association between self-reported QOL, and moderate-to-vigorous physical activity (MVPA) and sedentary behaviour over the first year following youth sport-related ACLR. Secondary objectives include assessing the relationship between self-reported QOL, and self-reported knee symptoms and kinesiophobia.

Methods: Forty youth with isolated, first-time, sport-related ACL tears who elected to undergo ACLR with a desire to return-to-sport were monitored at 3-month intervals for 1-year following ACLR. Knee-related QOL was assessed with the Knee Injury and Osteoarthritis Outcome Score QOL subscale ($KOOS_{QOL}$). Other variables included: weekly MVPA and sedentary minutes (tri-axial accelerometer), KOOS symptoms subscale ($KOOS_{sx}$), and Tampa Scale of Kinesiophobia (TSK). Descriptive statistics (mean (95% CI), median (range), or proportion (exact 95% CI)) were calculated for all outcomes at each time point (baseline, 3, 6, 9 and 12-months). Wilcoxon-matched pair tests and minimal clinically important differences (MCID) were used to examine 12-month changes in all variables. Spearman's correlation coefficient (r) was used to assess the association between $KOOS_{QOL}$ and each variable at all time points. To ensure adequate adjustment for multiple comparisons, the significance level was set at $\alpha=0.002$.

Results: Mean participant age was 18.1 years (95% CI; 15.1, 20.5) and 65% were female. 12-month change in $KOOS_{QOL}$ score exceeded the reported MCID (median score (range)) vs MCID; 19 (–6-69) vs 7.2. Although there was no evidence of an association between $KOOS_{QOL}$ and MVPA, sedentary time, or $KOOS_{sx}$, a significant negative association was identified between $KOOS_{QOL}$ and TSK scores (3-month $r=-0.68$, p<0.001; 6-month $r=-0.69$, p<0.001; and 9-month $r=-0.66$, p=0.002).

Conclusion: These preliminary analyses indicate that self-reported knee-related QOL improves over the year following ACLR in an active youth cohort. Kinesiophobia may be an important modifiable factor as it can negatively impact knee-related QOL during ACLR rehabilitation. More research is needed to understand the determinants of QOL in the first year following ACLR in active youth.

The Power of Partnership

Abstract #: 98
Presenter: Jacqueline Crossman
Supervisor: Tarek El-Bialy
Title: The effect of therapeutic ultrasound on TMJ condylar cartilage in arthritic mice
Authors: Jacqueline Crossman, Nadia Alzaheri, Mohamed-Nur Abdallah, Faleh Tamimi, Patrick Flood, Tarek El-Bialy
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Juvenile arthritis, arthritis that affects children, can involve different joints, including the jaw joint, the temporomandibular joint (TMJ). TMJ arthritis can result in TMJ cartilage destruction/bone erosion, leading to craniofacial growth disturbances, and causing an underdeveloped lower jaw, and jaw movement pain. These can negatively affect the children's quality of life. Current treatments of TMJ arthritis include physiotherapy, medications, and surgery, however, these treatments only affect some patients, research evidence is lacking, and surgery is painful and risky. Low intensity pulsed ultrasound (LIPUS) is commonly used in therapeutic medicine. It accelerates bone fracture healing, has an anti-inflammatory effect, and stimulates lower jaw growth in animals and humans. This study's aim was to evaluate LIPUS's effect on TMJ condylar cartilage in a mouse model that develops TMJ arthritis.

Methods

Sixteen 9-week old MRL-lpr/lpr mice were divided into 4 groups (n=4). Group 1: LIPUS treatment (20 minutes/day, 30 mW/cm^2 intensity, 1.5 MHz frequency, 1kHz pulses) to the right TMJ area for 2 weeks; group 2: LIPUS treatment to the right TMJ for 4 weeks; groups 3 and 4: no LIPUS treatment for 2 and 4 weeks, respectively (control). H&E staining was performed on the condyles to analyze condylar cartilage. Articular, chondrogenic, and hypertrophic cell layer thicknesses were measured. The articular surface was analyzed for cartilage destruction. One-way ANOVA (SPSS 16.0) was used to statistically analyze this data.

Results

The articular layers of the right condyles in the 2-week LIPUS group were significantly thicker compared to the right condyles in the 4-week LIPUS group (p < 0.05). The hypertrophic layers of the right condyles in the 2-week LIPUS group were significantly thicker compared to the left condyles (no LIPUS) and to the right condyles in the 2-week control group (p < 0.01). No differences were observed in the chondrogenic layers. Less cartilage destruction was observed in the right condyles in the 4-week LIPUS group compared to the right condyles in the 2-week LIPUS group, and in the right condyles (LIPUS group) compared to the left condyles (no LIPUS).

Conclusions

These results suggest that LIPUS treatment may have had a preventative/reparative effect on articular layers and may decrease cartilage destruction. It is suggested that the thicker hypertrophic layer may indicate that LIPUS may have an effect on increasing TMJ osteogenesis (bone formation). This study's limitations include the number and age of mice used. Future studies should increase the sample size and investigate LIPUS's effect on a juvenile, growing animal model.

The Power of Partnership

Abstract #:   99
Presenter: Phuong-Thuy Nguyen
Supervisor: Lawrence Le
Title: Correlation of tibial ultrasonic velocity with DEXA-based bone mineral density
Authors: Phuong-Thuy Nguyen, Tho Tran, Mauricio Sacchi, Jacob Jaremko, Lawrence Le
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: Osteoporosis is a skeletal disease in which the density of bone is reduced, leading to weakness of the skeleton and increased fracture risk. Gold standard method for the assessment of bone strength is based on bone mineral density (BMD) measurement by dual-energy X-ray absorptiometry (DEXA). While BMD is an important predictor of bone strength, additional factors are required to explain bone characteristic more accurately. Quantitative ultrasound (QUS) is a good candidate to study bone tissue with some advantages of being radiation free, inexpensive, and portable. The ultrasonic axial transmission technique has been developed to characterize the cortical long bones such as radius or tibia.

Objectives: The aims of this study were to determine the speed of ultrasound (SOU) from human tibia data and to correlate the tibial ultrasonic velocity with BMD at hip and spine of the subjects.

Material and Methods: The ultrasound data were collected from patients of a local Medical Imaging Consultant (MIC) clinic with consent. The ultrasonic device (TomoScan FOCUS LT^{TM}) was used with a 16-element 2.25 MHz transmitting probe and a 64-element 2.25 MHz receiver. The transducer was excited at 1 MHz. Data were obtained at the tibia by axial transmission technique and each subject was scanned 3 times using different beam steering configuration (0^0, 20^0, and 30^0). First arriving signal (FAS) was defined as the head wave traveling in the cortex along with the interface of soft tissue. The arrival time of FAS was picked for all receiving channels subjects to their visibility. The SOU was then measured by the slope of the best fit line using linear regression. The correlation between SOU and BMD at hip and spine were evaluated.

Results: This pilot study included 18 healthy subjects. The calculated SOU varies from 2,791 to 4,198 m/s. SOU show an increasing trend with BMD at spine and hip with R^2 = 0.02 - 0.03.

Conclusion: SOU was found to increase mildly with BMD i.e. velocity of ultrasound is sensitive to osteoporosis-related change in bone. Axial transmission is a potential technique for cortical bone assessment and osteoporosis monitoring and diagnosis.

The Power of Partnership

Abstract #:   100
Presenter: Alejandra Arguelles Lopez
Supervisor: Dr. Anna Farmer
Title: Child care educators' needs and recommendations for improving implementation of Alberta nutrition guidelines for children and youth in child cares
Authors: Alejandra Arguelles Lopez, Dr. Anna Farmer, Dr. Geoff Ball
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Child care educators are key players in the promotion of healthy eating in children. In 2008, the Government of Alberta launched the *Alberta Nutrition Guidelines for Children and Youth* (ANGCY) to equip child care centres with the tools needed to promote healthy food choices and healthy eating behaviours. Previous research conducted in Alberta found there is room for improving child care educators' knowledge and use of ANGCY in child care centres. Since the guidelines were released nearly a decade ago, it is time to revisit the factors and resources that are needed to support implementation of the ANGCY.

The objective of this study was to explore key informants' perceptions of child care educators' educational needs and their recommendations to improve implementation of the ANGCY.

Methods

A cross-sectional study design was used to consult a group of key informants composed of child care educators (n=8), child care directors (n=3), parents of children attending child care (n=29), dietitians working in the child care setting (n=6), and experts in child care food environments working in academia and government (n=7). The consultation was conducted through an online survey with open-ended questions, and responses were analyzed qualitatively using conventional content analysis.

Results

Dietitians and experts indicated that there is room for improving child care educator's knowledge and use of ANGCY. All key informants emphasised these as factors likely influencing child care educator's knowledge and practice of ANGCY: 1) ANGCY are unpractical, unclear and difficult to understand; 2) lack of dissemination strategies and guidance in implementing the guidelines; and 3) inconsistent adoption of the ANGCY in child care centres. Key informants recommended that the ANGCY be updated; Alberta Health Services should provide guidance and more resources to assist child care centres to overcome barriers on implementing the ANGCY; and training on the use of ANGCY should be added into child care educators training curriculum.

Conclusions

The findings of this study point out to the need for a comprehensive approach to nutrition promotion in child cares that includes improved training and organizational supports to enable the adoption and implementation of the ANGCY.

The Power of Partnership

Abstract #:   101
Presenter: Prachi Shah
Supervisor: Eytan Wine
Title: Burkholderia cepacia as an invasive pathogen in the gut of pediatric IBD patients
Authors: Prachi Shah, Heather Armstrong, Michael Bording-Jorgenson, Eytan Wine
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Inflammatory bowel diseases (IBD), including Crohn Disease (CD) and Ulcerative Colitis (UC), are characterized by chronic inflammation of the bowel and affect an estimated 1 in 150 Canadians, of which 25% of cases occur in children. Previous studies have shown that there is a change in microbial composition in IBD patients compared to non-IBD. It remains unknown whether this is due to the inflammatory environment or if the inflammation is caused by the altered microbiota. Previous work by our lab showed that increased binding of the antibody immunoglobulin G (IgG) to certain microorganisms may be indicative of their pathogenic role in the gut. As a current study of pediatric patients identified *Burkholderia cepacia* to have increased IgG binding in UC compared to non-IBD, we hypothesized that *B. cepacia* would demonstrate pathogenic potential in the human bowel.

Methods: Caco2 and HT29-MTX-E12 human intestinal epithelial cell lines were utilized as models of infection. FISH assays and in-and-out staining visually demonstrated invasion of *B. cepacia* into epithelial cells, while gentamicin protection assays were performed to obtain quantifiable data on the level of bacterial invasion into the cells. IL-1B and IL-6 ELISAs, performed on supernatant cell secretions, examined epithelial cell immune activation in response to infection.

Results: Infection of human epithelial cells with *B. cepacia* allowed us to visually identify bacteria inside the intestinal epithelial cells upon imaging, suggesting pathogenic potential of these IgG-bound bacteria. Furthermore, the quantifiable results obtained using gentamicin protection assays demonstrated similar levels of infection using the *Burkholderia* strains compared to the known pathobiont *adhesive invasive Escherichia coli* (AIEC).

Conclusions: Results from this study demonstrate that *B. cepacia*, a bacterial strain identified to have increased binding by IgG in UC, has pathogenic and invasive potential in human intestinal epithelial cells. No IL-1B or IL-6 secretions were detected which may mean there is no immune activation or we may have to repeat the assays. Understanding the interaction of the microorganism strains identified in our pediatric cohort with their host environment is essential to improving our ability to advance treatment options for patients suffering from IBD. Further examination of *B. cepacia's* ability to penetrate the gut mucosa will improve our understanding of the role this bacterium plays in IBD pathogenesis. Similarly, future research will focus on other bacterial species that we identified to have altered IgG binding in IBD patients compared to non-IBD.

The Power of Partnership

Introduction

First Nations children in Canada are at an elevated risk for obesity and obesity-related chronic disease. One strategy to improve the diets of children and address obesity within school environments is the use of a school nutrition policy (SNP). A SNP may be especially important in First Nations communities where parents often struggle to provide their children with nutritious food due to economic and environmental limitations. However, there is little research concerning successful SNP implementation in First Nations communities, or the influence that perceptions of parents and students themselves may have on SNP outcomes.

A First Nations school in Alberta has implemented a SNP to improve nutrition for children. This community-based participatory research aims to understand 1) student and parental perceptions of the policy, and 2) student and family factors acting as enablers and barriers to its adoption.

Methods

This focused ethnography uses both quantitative and qualitative methods to deliver a holistic understanding of the complex factors influencing SNP adoption. Paper surveys were completed by parents (n=83) and students (n=94), followed by semi-structured interviews with parents (n=10) and students (n=20).

Results

Preliminary findings indicate that the majority of children and parents are supportive of a policy that allows only healthy food to be served or sold at the school. When given the option, most students also choose to be sold and served healthy foods (e.g. fruit and vegetables) more often than unhealthy foods (e.g. chocolate bars and candy). However, most students and their parents perceive their eating habits to be average or unhealthy, and the majority of children are not engaging with their teachers or parents about healthy eating.

Conclusions

This research aims to strengthen the current SNP to reflect the health beliefs and perceptions of the community, thereby minimizing barriers to adoption and improving children's access to healthy food choices at school. This knowledge will further provide recommendations for developing comprehensive school health in First Nations schools to promote healthy eating and healthy weight among First Nations children in Canada.

The Power of Partnership

Introduction: Weight bias is the tendency to negatively judge a person simply based on his or her weight. Ingrained in society, weight bias has many serious physical, mental, and social health consequences, such as disordered eating, depression, and physical activity avoidance. Overweight and obesity affect one-quarter of Canadian children, who are vulnerable to weight bias in all domains of life, including at school. In Canadian schools, weight is the most common cause of bullying. However, in Alberta, weight bias is not addressed in school policies or curricula. Furthermore, little research has examined strategies to reduce weight bias, particularly in children. The objective of this research is to develop, implement, and evaluate the impact of a school-based program in reducing weight bias in Grades 1–3 students in an Edmonton public school.

Methods:

Phase 1 (Fall 2017/Winter 2018): Participatory, formative research will be completed in partnership with an elementary school to tailor the program to the school's needs. Using focused ethnography, a qualitative method employed to understand a contextually specific problem, one-on-one interviews will be conducted to explore school staff perspectives regarding strategies to address weight bias, analyzing the data inductively to identify themes and categories.

Phase 2 (Spring/Summer 2018): Informed by Phase 1 findings, program resources (e.g., lesson plans) will be developed with the Canadian Obesity Network, an organization which aims to reduce societal weight bias.

Phase 3 (Fall 2018-Spring 2019): The program will be piloted over eight months. Proposed components, derived from promising weight bias interventions to-date, include anti-weight bias policies and student, school staff, and parent education, although these will depend on Phase 1 findings. The impact on students' weight biases will be evaluated pre- and post-intervention using multiple qualitative techniques, such as draw-and-write, photo interviews, and participant observation.

Results: Knowledge translation will aim to inform school policy change and curricular development to address weight bias, by sharing findings and resources with key decision-makers within the school community, the Edmonton Public School Board, and Alberta Education. Given that Alberta in the midst of curriculum redesign, this research is timely.

Conclusions: Reducing weight bias in schools can foster positive social environments that promote children's health and well-being. This program has the potential to be scaled up for Grades K–12 in schools across Alberta, and even Canada. Such research is needed to create effective strategies to reduce weight bias in schools, a public health issue affecting many Canadian children.

The Power of Partnership

Understanding the impact of maternal overweight on metabolic function of infant gut microbiome at 3-4 months using shotgun metagenomic approach

Introduction: Obesity is one of the most worrisome diseases throughout the world. Over 20% of children are overweight or obese in the United States and Canada. It has been widely accepted that infant gut microbiome plays critical roles in mechanisms of overweight, and it is also strongly influenced by maternal weights in pregnancy. The compositional differences of gut microbiota have been observed between infants born to normal weight and overweight mothers by using 16S rRNA sequencing data. However, answering "*who is there*" is often not enough for us to fully understand the metabolisms involved, especially metabolic pathways responsible for the overweight transmission from mother to offspring.

Methods: In this study, ten selected samples (5 infants born to normal weight mothers and the others born to overweight mothers) from the Canadian Healthy Infant Longitudinal Development (CHILD) study cohort were investigated for the question of "*what are they doing*" by using shotgun metagenomic sequencing at NexSeq platform. Infant fecal samples were collected at 3-4 months old. High-quality metagenomic reads were first analyzed using the HUMAnN2 pipeline to infer the functional and metabolic potentials of individual microbial communities. Then, non-parametric comparisons were done using the STAMP software to identify pathways and their related microbes that distinguish between the two groups.

Results: Our statistical analysis revealed that *E. coli* contributes not only the largest portion of the infant gut microbiome, but also the most significant differences between infants born to normal weight and overweight mothers. Many fatty acid biosynthesis related pathways, such as "superpathway of fatty acid biosynthesis initiation (*E. coli*)", "pyruvate fermentation to propanoate I", "octanoyl-[acyl-carrier protein] biosynthesis (mitochondria, yeast)", *etc.*, tend to enriched in the normal weight group, while various sugar degradation pathways, such as "glucose and glucose-1-phosphate degradation", "myo-, chiro- and scillo-inositol degradation", "L-rhamnose degradation I", "pentose phosphate pathway (non-oxidative brance)", *etc.*, are enriched in the overweight group.

Conclusions: Although there is no significant difference in the overall relative abundance of *E. coli*, their encoded functions and metabolic pathways are different between the two groups. It is important to study the metabolic role of *E. coli* that responsible for overweight and obesity in infants.

The Power of Partnership

Abstract #: 105
Presenter: Alena Frankish
Supervisor: Carla Prado
Title: Accuracy of a portable indirect calorimeter for measuring resting energy expenditure in women with class II/III obesity
Authors: Alena Frankish, Sarah Purcell, Carlene Johnson Stoklossa, Amanda Purkiss, Carla Prado
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Department of Agricultural, Food and Nutritional Science (AFNS), Human Nutrition Research Unit, University of Alberta

Introduction: The adverse effects of obesity on women's health are well known. A crucial factor in managing obesity is determining resting energy expenditure (REE), the largest component of total daily energy needs. Women with obesity often have high rates of comorbidities and would benefit from targeted energy recommendations. The objective of the current analysis was to assess the accuracy and reliability of a portable technique which estimates REE (Fitmate GS™). This indirect calorimeter with a ventilated hood was compared against a state-of-the-art whole-body calorimetry unit (WBCU) in women with obesity.

Methods: Women with class II/III obesity (body mass index, BMI ≥ 35 kg/m^2) aged 18-55 years were recruited for the study. REE values were obtained from WBCU and compared with Fitmate GS values performed on the same day. Fitmate GS measurements were completed twice for each participant. A brief medical history, anthropometric measurements and basic demographic data were collected for each individual. Group-level agreement between the Fitmate GS and WBCU measurements were assessed via dependent samples t-test. Bland-Altman analysis was used to assess both group-level (bias, average difference) and individual-level agreement (limits of agreement, bias ± two standard deviations). The minimum and maximum differences were also reported to contextualize the results to clinical practice. Test-retest reliability was assessed using intraclass correlation coefficient with two-way random effects.

Results: Preliminary data for 15 females (BMI = 40.3 ± 8.4; age = 35 ± 10y) was collected as part of an ongoing study. On average, REE measurements from the Fitmate GS were lower than the WBCU (1613 ± 259 vs. 1948 ± 325 kcal/day, p < 0.001) and individual values differed from -680 to -77 kcal/day (-34 to -4%). Bland-Altman analysis showed an overall underestimation of REE (bias: -334kcal/day) and wide limits of agreement (-656 to -13 kcal/day). Comparison of two Fitmate GS measurements from the same subject showed a difference up to -770 kcal. The intraclass correlation coefficient was 0.643 ("moderate" agreement according to the literature) with 95% confidence interval from 0.214 to 0.864.

Conclusion: Our preliminary finding suggests the Fitmate GS was not an accurate or reliable tool for measuring REE on a group and individual level in women with class II/III obesity.

The Power of Partnership

Abstract #: 106
Presenter: Usha Rai
Supervisor: Anita Kozyrskyj
Title: Duration of labour and the infant gut microbiota
Authors: Usha Rai, David S. Guttman, Allan B. Becker, Piushkumar J. Mandhane, Stuart E. Turvey, Padmaja Subbarao, Malcolm R. Sears, James A. Scott, Haqq M. Andrea, Chari Radha
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

INTRODUCTION

Microbial colonization of the infant gut plays pivotal role in immune programming. Birth by Cesarean section (CS) is associated with divergent gut microbial colonization (Azad et al 2015). Since protracted labour is the leading cause of primary CS (Barber et al 2011), hypothetically it may affect the microbial seeding of newborn gut and future disease risks. We studied the association between duration of labour and gut microbial composition of infants at 3 to 4 months of age.

METHODS

This study used a subset of 999 infants from the Canadian Healthy Infant Longitudinal Development (CHILD) national birth cohort. Data on labour and birth characteristics were obtained from hospital charts. Fecal samples were collected at 3 to 4 months after delivery, and fecal microbiota were characterized by Illumina high-throughput sequencing of 16S rRNA gene. Microbiota taxon abundances were compared between infants based on duration of labour using Mann-Whitney U-test, and logistic regression models adjusted for delivery mode, intrapartum antibiotic prophylaxis, gestational age and breastfeeding status.

RESULTS

For the first stage of labour, 56.5% of infants (N= 564) were born after ≤ 6 hours (Reference), whereas 26.7% and 8.7% were born after > 6 to ≤13 hours and >13 hours respectively. Longer durations (> 6 to ≤13 hours and >13 hours) in the first stage of labour were associated with decreased abundance of *Bifidobacterium* [aOR 0.57 (95%CI=0.42 - 0.78) and aOR 0.57 (95%CI=0.42-0.77), respectively].

For the second stage of labour, 66.8% of infants (N= 667) were born after ≤ 1 hour (Reference), whereas 12.5% and 16.3% were born after > 1 to ≤2 hours and >2 hours respectively. Longer durations (> 1 to ≤2 hours and >2 hours) in the second stage of labour were associated with increased abundance of Clostridium [aOR 1.59 (95%CI=1.06 -2.39) and aOR 1.84 (95%CI=1.28 -2.65), respectively].

CONCLUSION

Our findings provide evidence of association between duration of labour and changes to infant gut microbial composition at 3 to 4 months of age. Decreased *Bifidobacterium*, which has been linked to childhood atopy, was observed after longer first stage of labour. Increased *Clostridium*, which has been associated with immune homeostasis and improved gut health, was observed after longer second stage of labour.

The Power of Partnership

Abstract #:   107
Presenter: Arnaldo Perez
Supervisor: Dr. Geoff Ball
Title: From whom to where? Referral making to pediatric weight management services in Alberta
Authors: Arnaldo Perez, Maryam Kebbe, Andrea Eaton, Chenhui Peng, Katerina Maximova, Alison Connors, Nicholas Spence, Rena LaFrance,
                  Kristine Godziuk, Geoff Ball
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Canadian guidelines recommend that children with overweight or obesity should be referred to specialized services for weight management, especially when primary care-based services have proven unsuccessful. To date, little is known about whether referral providers (*e.g.,* physicians) in Canada follow these guidelines, which is an important first step to identify areas for improving weight management services. The purpose of our study was to characterize referral providers and the children referred to outpatient nutrition counselling (ONC) and multidisciplinary care (MC) for pediatric weight management in Alberta Health Services (AHS).

Methods: This retrospective, cross-sectional study included all 2–18 year olds referred to ONC and MC in Alberta from April 2013 to July 2017. Referral data were obtained from standardized referral forms received and processed by AHS. Additional information regarding referral providers (*e.g.,* sex) was retrieved from publically available, online sources. Descriptive statistics were used to characterize referral providers and children they referred for weight management.

Results: During the study period, 6,510 referrals were received. Similar proportions of children were referred to ONC (n=3,435; 52.8%) and MC (n=3,075; 47.2%). Physicians made most of the referrals (n=6,100; 93.7%), followed by nurse practitioners (n=58; 0.9%). In total, 1,427 and 38 unique physicians and nurse practitioners, respectively, referred children for weight management; most referrers (55.1%) were female. Approximately two-thirds (n=4,236; 65.1%) of referred children (mean age: 10.7 years old) were ≤12 years old, most of whom (n=2,546; 60.1%) were referred to ONC. The number of children referred varied by age group (2–5 years old; n=557; 8.6%; 6–12 years old; n=3,381; 51.9%; 13–18 years old: 2,569; 39.5%). Most children (n=4792, 81.5%) met the criteria for severe obesity. No differences (p>0.05) were observed between children referred to ONC *versus* MC regarding age or weight status.

Conclusions: Many children with overweight or obesity in Alberta do not fully benefit from ONC and MC because they are either not referred or timely referred by physicians and nurse practitioners. Supporting eligible referral providers, particularly nurse practitioners, in referring eligible children, especially 2–5 year olds and those at lower levels of overweight or obesity, may increase the likelihood that children who are eligible for care choose to enroll in and derive benefit from weight management services.

The Power of Partnership

Abstract #: 108
Presenter: Yong Zhang
Supervisor: Gregory Funk
Title: Towards an understanding of how ATP excites the brainstem inspiratory rhythm generator during hypoxia to reduce the hypoxic depression of breathing
Authors: Yong Zhang, Alexander Gourine, Sergey Kasparov, Tucaaue Alvares, Gregory Funk
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: The ventilatory response to hypoxia comprises an initial increase in ventilation followed by a profound secondary depression, largely attributed to the inhibitory actions of adenosine in the brain, that can be life-threatening in premature infants (apnea of prematurity). Thus, there is great interest in understanding the mechanisms underlying this response. We have shown that ATP is released within the preBötzinger Complex (preBötC, critical site for inspiratory rhythm generation), during hypoxia where it acts via $P2Y_1$ receptors to attenuate this depression. The goal of my study was to test the hypothesis that $P2Y_1$ receptors excite breathing by activating a G_aq-signaling pathway and potentiate a specific current, the H-current, in the membrane of preBötC inspiratory neurons.

Methods: I used a well-established in vitro model in which the preBötC is isolated in a brain slice and placed in a dish where it continues to generate inspiratory-related rhythm. Inspiratory network activity was recorded from XII nerves and the activity of inspiratory preBötC neurons was recorded via whole-cell recording. Effects of $P2Y_1$ agonists on network and neuronal activity were compared, before and after addition of specific blockers for each step of the G_{aq}-signaling pathway and also the H-current.

Results: Blocking different steps in the G_{aq}-signaling pathway with U73122 (phospholipase C inhibitor, 20 μM), 2-APB (inositol trisphosphate receptor inhibitor, 100 μM) and chelerythrine (protein kinase C inhibitor, 10 μM) either shortened the duration of MRS2365 ($P2Y_1$R agonist, 100 μM)-evoked frequency increase of inspiratory activity (U73122) or reduced the frequency increase by 40~60 % (2-APB and chelerythrine). Intracellular dialysis of the same agents (U73122 2 μM, 2-APB 50 μM, chelerythrine 20 μM) as well as endoplasmic reticulum Ca^{2+}-ATPase blockers thapsigargin (4 μM) and cyclopiazonic acid (20 μM) attenuated ATP (5 mM)-induced inward currents in inspiratory neurons by 20~40 %. Characterization of the $P2Y_1$R-evoked current (MRS2365, 100 μM and 1 mM) revealed that it potentiated an H-current in a subset of inspiratory neurons (33%). Block of the H-current with ZD 7288 (25 and 100 μM) almost completely blocked the network effect of MRS2365.

Conclusion: These data suggest that ATP excitation of the preBötC network is produced, at least in part, via activation of a G_{aq}-signaling pathway and potentiation of an H-current in a subset of inspiratory neurons, and identify two potential targets that could be activated to counteract the depression of breathing caused by hypoxia.

The Power of Partnership

Abstract #:   109
Presenter: Cara McLean
Supervisor: Anita Kozyrskyj
Title: Systematic review: Impact of maternal smoking on the infant gut microbiome and its association with child overweight
Authors: Cara A McLean , Hein M Tun, Anita L Kozyrskyj
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: Childhood obesity is a growing public health concern that will affect 60 million children globally by 2020. Maternal smoking is linked to low birth weight, however, rapid catch up in weight is observed in postnatal growth patterns, which increases the risk of obesity in later life. Moreover, infant gut microbiota also plays an important role in childhood adiposity. This systematic review summarizes current literature on the impact of maternal smoking on the infant gut microbiome and its association with child overweight.

Methods: The PRISMA guidelines for systematic reviews were used to ensure exhaustive, complete and transparent reporting. One investigator searched for relevant scientific publications from all fields of two databases (Medline, and Pubmed). The last search was performed on August 15th, 2017 using key terms ((smoking OR maternal smoking OR cigarettes OR tobacco OR second-hand smoke OR prenatal smoke OR household smoke OR postnatal smoke OR nicotine) AND (microbiota OR microbiome OR organism OR meconium OR dysbiosis OR microbes OR metagenome)). All studies used fecal samples to detect gut microbiota. Animal studies were excluded. There were no language restrictions.

Results: No studies examined these three criteria: maternal smoking, infant gut microbiome and child overweight. Therefore, a narrow-structured focus was done on maternal smoking and the infant gut microbiome. Two prospective cohort studies were identified using high-throughput 16S rRNA gene sequencing to assess the infant and neonatal gut microbiome on a total of 320 infant/neonatal participants. Both studies confirmed that maternal smoking was associated with composition of the infant/neonatal gut microbiome. Neonates (1 month old) exposed to environmental smoke had a higher abundance of *Ruminococcus* and *Akkermansia* (p <0.01), while infants (6 month old) of mothers who smoked currently and during their entire pregnancy had an increased abundance of *Bacteroides* and *Staphylococcus* (p<0.01). Meconium of neonates measured at birth of women who smoked during their entire pregnancy was found to be less diverse and dominated by *Enterobacteriaceae* (*Escherichia/Shigella*) (p=.099) bacteria.

Conclusion: The limited evidence to date warrants further larger studies to explore the impact of maternal smoking on the infant gut microbiome and its relation to child overweight.

The Power of Partnership

Abstract #:   110
Presenter: Andreana Marcinkow
Supervisor: Nese Yuksel
Title: Quality of online information regarding combined oral contraceptives: A content analysis
Authors: Andreana Marcinkow, Polina Parkhomchik, Alyssa Schmode, Nese Yuksel
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Quality of online information regarding combined oral contraceptives: A content analysis

Andreana Marcinkow, Polina Parkhomchik, Alyssa Schmode, Nese Yuksel

Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta

Introduction: Combined oral contraceptives (COC) remain a popular choice among women. The Internet is an accessible and popular source of information on contraception options. The objective of this study was to evaluate the quality of information provided on COC's on the Internet.

Methods: A quantitative content analysis was completed on websites containing patient health information on COC. A Google search was completed in October 2016 using "birth control pill", "oral contraception", "oral birth control", "birth control", and "pregnancy prevention" as search terms. Websites were excluded if they were for health care professionals, forums, personal blogs, videos or news articles. The first 3 pages of search results were screened according to inclusion and exclusion criteria. Only websites in English which contained health information on COC for a lay audience were included. The DISCERN instrument was used to determine content quality. Websites were analyzed independently by two coders; discrepancies were resolved by a third coder.

Results: Of the 155 websites identified, 32 were eligible for review. Eighty-one percent of sites mentioned contraceptive benefit, yet only 53% reported effectiveness in preventing pregnancy. Most commonly identified non-contraceptive benefits were dysmenorrhea (88%) and menstrual blood loss (84%). Breakthrough bleeding was the most common side effect listed (97%). Most common risks mentioned were VTE (81%), stroke (56%) and MI (47%), however most sites failed to mention factors that increased a woman's risk. Contraindications were listed in just over half of the sites. Information gaps were identified as less than half of sites mentioned COC start methods (47%) and the quick start method (25%). As well, only 22% of sites provided sufficient detail for management of missed pills. Mean total DISCERN score was 46.3(±9.37), indicating 'fair' quality.

Conclusion: Online information on COC's was variable in quality, often missing key information to make informed decisions. Health care professionals should be aware of information gaps to ensure that patient counseling is tailored accordingly.

The Power of Partnership

Abstract #:   111
Presenter: Cailey Turner
Supervisor: Beate Sydora
Title: A scoping review observing walking exercise in menopausal women
Authors: Cailey Turner, Alexandra Malley, Beate Sydora , Sue Ross, Tami Shandro
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

INTRODUCTION: Menopause is a natural stage in every woman's life that is often accompanied with physical and psychosocial symptoms, along with an increased risk to certain conditions (e.g. osteoporosis, weight gain, cardiovascular disease). The mainstay treatment for menopause is hormone therapy, but many women are reluctant to take hormones due to the potential risk of breast cancer. There is emerging evidence that exercise can greatly improve the quality of life in menopausal women and significantly impact their general health, however, so far there is no conclusive evidence.

OBJECTIVE: Our goal was to conduct a literature search for published therapeutic walking programs for menopausal women to identify features (adherence by women, health improvements, etc.) that have resulted in successful outcomes.

METHODS: Six databases were searched for articles up to June 1st, 2017. Databases included Medline, EMBASE, CINAHL, Sport Discus, Scopus, and Web of Science. The keywords used were peri-menopause, post-menopause, menopause, climacteric, menopause and climacteric symptoms, menopause transition, walking-exercise, - therapeutic, -program. Data was collected into EndNote X8 reference manager to identify and remove duplicates. Included in the final selection were all English language articles that studied walking as a health intervention during menopause or the transition during menopause and articles that used a walking therapy as a control with relevant data provided. The exclusion criteria included abstracts, commentaries, thesis, reviews, and walking used merely as a test or in combination with other interventions, such as drugs or additional exercises. Articles that mentioned walking exercise retrospectively in surveys without describing details of the walking program were also excluded. Data was extracted using the inclusion/exclusion criteria and charted according to the publication year, author, participant characteristics, medical reason under investigation, walking intervention specifics, and results and outcomes from these interventions.

RESULTS: 3244 papers were collected from the six databases. After removing duplicates and using the inclusion/exclusion criteria 86 articles were included in the final analysis. The average length of the walking intervention was 24 weeks with a frequency of 3.7 times a week. Overall, 89.5% of these studies showed a beneficial outcome in at least one medical category.

CONCLUSION: Walking appears to have a positive impact on menopausal health and is both an easy and an inexpensive exercise for post-menopausal women.

The Power of Partnership

Abstract #:   112
Presenter: Onouma Thummapol
Supervisor: Tanya Park
Title: Access to health care services from the perspectives of Indigenous women living in northern and rural Thailand
Authors: Onouma Thummapol, Tanya Park, Sylvia Barton
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: Access to equitable and responsive health care services for Indigenous women remains a persistent public health and policy challenge. The recently released Sustainable Development Goals, in particular Goal 5 shines a light on this worldwide concern. The purpose of this study was to understand the inequities in health that arise from challenges experienced by socially and economically marginalized Indigenous women living in northern Thailand, when healthcare services are needed.

Method: Focused ethnography was used to guide the research project and to inform the retrieval of information about culture and intersecting components that illuminated the experiences of participants. The 21 women from a northern village, engaged in face-to-face, in-depth, semi-structured interviews. Data were analyzed using the principles of thematic analysis and interpretive description.

Results: Three themes emerged from the interview data: 1) the reasons why, when, and where women sought health care services; 2) Indigenous women's experiences with accessing health care services; and 3) factors associated with access to health care.

Conclusions: Indigenous women living in northern Thailand continue to experience discrimination in the provision of health care and face greater barriers in accessing essential health care services such as excessive waiting times and lack of transportation to health care facilities. Improving access to health care, by providing outreach services to the rural and isolated communities and establishing transport system is one way that the current barriers could be reduced/changed. Implications of these findings are discussed in relation to the role of stakeholders such as policy makers, nurses, and allied health care professional in designing culturally appropriate health care policies, interventions, and support services, that are responsive to priorities and unique health needs of Indigenous women. Recommendations shed light on the need for reflective practice among nurses and allied health professionals regarding the impact of their attitudes and performance on patients' health status and adherence, satisfaction with care and care seeking. By doing so, this may improve the lives and health of Indigenous women, contributing to the achievement of the SDGs.

The Power of Partnership

Abstract #:   113
Presenter: Daniel Krys
Supervisor: Frank Wuest
Title: Hypoxia-induced regulation of membrane transporters in breast cancer
Authors: Daniel Krys, Ingrit Hamann, Stephanie Mattingly, Melinda Wuest, Frank Wuest
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Hypoxia-inducible factor (HIF)-1 is the master homeostatic regulator during hypoxia in human cancer cells. Reduced oxygen supply in cancer cells leads to tumor hypoxia, activates HIF-1a, which then controls the expression of multiple target genes, including membrane transporters like GLUT1. Recently we have also demonstrated regulation of fructose transporter GLUT5 via HIF-1a in breast cancer (BC).

To determine if and how tumor hypoxia regulates other membrane transporters in BC, we studied protein expression and functionality of nucleoside transporter hENT1 and amino acid transporter LAT1 under normoxic and hypoxic conditions. Cellular uptake experiments were performed with radiolabeled nucleoside [^{18}F]FLT and radiolabeled amino acid [^{18}F]FDOPA in ER(+) MCF7 and triple-negative MDA-MB231 BC cells.

Higher [^{18}F]FLT uptake was observed in MDA-MB231 cells (241±10% radioactivity/mg protein) compared to ER(+) MCF7 cells (147±18% radioactivity/mg protein) at 60 min. This also corresponded with detected higher hENT1 protein expression levels in MDA-MB231 versus MCF7 cells. Data also indicated that [^{18}F]FLT uptake and hENT1 expression levels were not influenced significantly by hypoxia. In contrast, LAT1 expression was higher in ER(+) MCF7 versus MDA-MB231 cells. Initial cell uptake experiments with [^{18}F]FDOPA revealed no difference between both BC cell lines under normoxic conditions, whereas a ~50% increased uptake in MDA-MB231 was observed under hypoxia.

We found that nucleoside transport via hENT1 is not regulated by hypoxia, while hypoxic regulation amino acid transporter LAT1 still needs further investigation.

The Power of Partnership

Sonia Sultan- Masters of Management in Health Care Administration (Robert Morris University)

INTRODUCTION:

Developing countries are facing many difficulties due to a rise in population. High fertility rates have posed increased health risks for mothers and child's health, resulting in poor quality of life. According to WHO (2015) approximately 225 million women in developing countries want to limit childbearing but are unable to do because of unmet needs, lack of resources, limited access to family planning (FP) services, religious beliefs and illiteracy. FP can play an imperious role in stabilizing the issues in developing countries. The purpose of this literature review was to explore and synthesize articles on knowledge, attitude, and practices of FP services with correspondence to three determinants including education, resources, and poverty in low and middle income countries.

METHODOLOGY:

This systemized literature review was conducted from the period of Oct to Dec 2016 in PUBMED, CINAHL and Allied Health Literature based on predefined search terms. Eligibility criteria included: **original researches, review articles and perspective, opinion, and commentary articles.**

RESULTS:

The key findings from literature review suggested that education regarding family planning is essential. Moreover, it is fundamentally important to introduce the concept, knowledge, awareness, practice and availability of contraceptive measure and family planning services. However, women in developing countries are struggling for the use of modern contraceptive methods but are lagging far behind due to scarcity of resources. It is imperative to make contraceptive methods more accessible and available in resource-scarce countries.

CONCLUSION:

FP determinants such as education, lack of poverty, and accessibility to resources can be used to empower women and men in under developed nations. It also helps to change their attitudes and practices towards family planning, thus, leading to better quality of life.

The Power of Partnership

Abstract #:   115
Presenter: Bukola Salami
Supervisor: Kathy Hegadoren
Title: The incidence of family violence in immigrant women in Edmonton
Authors: Kathleen Hegadoren, Bukola Salami, Gerri Lasiuk, Nicole Pitre
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: Despite increased public awareness, under-reporting of family violence (FV) is a significant problem, particularly in immigrant women who are typically under-represented in epidemiological studies and government census reports. A research partnership with an Edmonton non-governmental community agency that provides service specifically for immigrant women created an opportunity to complete a multi-year file audit of the counselor's interactions with women who seek services at this agency. Our primary research questions were (a) What is the incidence of FV in this group of immigrant women, based on agency records (N=1729) and (b) What individual and environmental factors are associated with risk of FV in this population?

Methods: Data were extracted from paper files from 2006 to 2015 using standardized definitions of each quantitative variable and entered into a newly created database. The data files consisted of the agency staff's notes and included demographics, immigration status, services requested and/or provided for each woman who had requested time with the staff counsellor.

Results: The majority of women were Eastern Mediterranean (22.9%), married and had permanent residency status (in Canada. Forty-two % of women reported FV, which is higher than reported in Canadian epidemiological studies and population surveys. Similar to data with non-immigrant populations, separated women are at higher risk of experiencing FV. Seeking services related to FV added significant workload for the agency as this group of women needed multiple other services, such as housing, financial and legal assistance. The women did not see the health care system as providing any FV-related services, despite that FV is recognized as a global public health issue. Anecdotally, suggestions regarding seeking help from women's shelters were often declined.

Conclusions: These data provide evidence that immigrant women face many of the same challenges related to FV that non-immigrant women do and some unique challenges related to immigration status. However, the availability of and funding for culturally appropriate targeted resources are much more limited. FV has many long-term physical health and psychosocial effects on those who experience violence and children who witness such events. It is imperative that more coordination between public health agencies and community support agencies occur that will allow immigrant families to fully participate in Canadian society.

The Power of Partnership

Abstract #:   116
Presenter: Julia Boell
Supervisor: Denise Guerreiro Vieira da Silva
Title: Associations among psychosocial factors and resilience in women with diabetes in urban Brazil
Authors: Julia Estela Willrich Boell, Kathleen Hegadoren, Denise Guerreiro Vieira da Silva Maria
Affiliations: Other
Research Activity: Lifelong Women's Health

Introduction

Promoting self-care among people living with DM has been a challenge for health professionals, especially when it comes to women, since they have worse glycemic control, measures of self-care and quality of life compared to men. Resilience is a construct that contributes to quality of life in those with chronic diseases. We examined associations among psychological factors and resilience scores in women with diabetes.

Method

The research design involved a cross-sectional study with 230 women with diabetes treated in Primary Health Care in a municipality in southern Brazil. Data collection included a sociodemographic questionnaire and measures related to stress, anxiety, depression, social support, hope, and resilience. Descriptive analyses and bivariate correlations were completed.

Results

Participant characteristics included: mean age of 63.5 years (SD 11.2) and most reported being in a stable relationship (44%), held strong religious beliefs (91%) and were retired from paid work (55%). The majority had elementary schooling (60%) and reported low household income (76%). The mean duration since diagnosis was 12 years (SD 10.6). The majority (72%) reported also being treated for hypertension. Higher stress scores ($p < 0.001$), more anxiety ($p < 0.001$) and depression symptoms ($p < 0.001$) were significantly related to lower resilience scores. Higher hope scores ($p < 0.001$) were significantly related to high scores of resilience. Strong correlations were observed between resilience and stress ($r = -0.559$), and depression ($r = -0.603$), while moderate correlations were observed between resilience and anxiety ($r = -0.476$), social support ($r = 0.399$), and hope ($r = 0.494$).

Conclusions

The strong relationship between resilience and psychological factors observed in this study highlight support and direction to develop and test targeted gender specific psychosocial interventions as a component of care to women who have diabetes. Assessment of mood and anxiety symptoms and ongoing interpersonal support must be part of routine care. Those assessed as being at risk for going on to develop mood and anxiety disorders need treatment in timely manner. Future research examining relationships between psychosocial factors, resilience and glycemic control would provide further evidence of the relevance of mental health in chronic diseases management.

The Power of Partnership

Abstract #:   117
Presenter: Nicole Rodriguez
Supervisor: Vivian Huang
Title: Does pregnancy adversely impact the health related quality of life among women with IBD?
Authors: Lindsy Ambrosio, Reed Sutton, Dieleman Levinus, Brendan Halloran, Karen Kroeker, Farhad Peerani, Karen Wong, Richard Fedorak,
                      Vivian Huang
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Background: Women with Inflammatory Bowel Disease (IBD) are at risk of flaring during pregnancy, and are associated with adverse maternal and neonatal outcomes. In addition, active IBD has been associated with poor health related quality of life (HRQoL). However, whether pregnancy-related changes also influence HRQoL of life is still unknown.

Objectives: To assess the impact of pregnancy on the health related quality of life (HRQoL) among women with IBD and the impact of IBD disease activity on HRQoL in pregnant women with IBD.

Methods: Adult (>18years) women with Crohn's disease (CD) and ulcerative colitis (UC), and healthy volunteers who were either preconception or pregnant participated in a quality of life research study, and followed until delivery. Participants completed disease activity indices, such as Harvey Bradshaw Index (HBI) for CD or partial Mayo score (pMayo) for UC. Clinically active disease was defined as mHBI>5 or pMayo >2; whereas CRP >8.0 units and FC >250mg/kg were laboratory parameters for active disease. Short IBD quality of life (SIBDQ) survey was administered at each time point and compared between groups for diagnosis and disease activity. All statistical analyses were performed using SPSS statistical program, version 24.0.

Results: A total of 70 women completed at least one SIBDQ survey during the follow up period. There were 11 (15.7%) healthy volunteers, 36 (52.4%) women with UC, and 23 (32.9%) women with CD. SIBDQ scores were lower in IBD patients than in healthy participants in T2 of pregnancy. Furthermore, SIBDQ scores were significantly lower in patients who had clinically active disease in T2 and T3. No statistically significant differences were found between patients when grouped by objective disease activity.

Conclusions: Overall, HRQoL was reduced in women with IBD and especially during clinically active disease during pregnancy. Women with inactive IBD during pregnancy have similar IBD related quality of life as women without IBD. Our findings encourage further research on the interaction of IBD and pregnancy to improve patient and physician related knowledge in optimizing pregnancy outcomes in IBD patients.

The Power of Partnership

Introduction:

Neuroblastoma or NB is a childhood cancer that develops from neuroblasts, immature nerve cells in the sympathetic nervous system, derived from neural crest cells. Of cancer deaths in children, about 15% are due to NB. Identifying and understanding proteins in pathways that contribute to the initiation and progression of NB can provide potential drug targets for NB treatment. One such protein Beta-Catenin, the primary effector of the Wnt signalling pathway. This pathway plays an important role in normal neural crest stem cell proliferation and differentiation, but is involved in the development of neuroblastoma when deregulated. β-Catenin is a transcription factor for genes involved in proliferation, it therefor has oncogenic activity when deregulated. The Wnt pathway doesn't regulate β-Catenin at the transcriptional or translational level, but through phosphorylation/de-phosphorylation of 4 amino acid residues. Therefore, we hypothesize that higher levels of the transcriptionally Active β-Catenin (AβC), which two amino acids of the possible four are phosphorylated, likely contributes to higher levels in aggression, invasion and metastasis of certain NB tumours. The goal of this study is to determine whether up-regulation of AβC is involved in the progression of NB and if it can be used as a prognostic marker.

Methods:

To test our hypothesis, several NB cell lines were arranged into panel in order of least to most aggressive. This was done by measuring migratory and invasive abilities of the cell lines using migration and invasion assays. This data was combined with existing information on each cell line's morphology and cytogenetics and the original tumour. The amount of Active-β-Catenin in each cell line was determined via Western Blotting of cell lysates.

Results:

Preliminary results suggest a correlation between a cell lines aggressiveness, ie ability to migrate and invade, and AβC levels. Levels of overall β-Catenin do not seem to be significantly different between cell lines.

Conclusion:

The correlation between AβC and aggressiveness needs to be confirmed via other methods of protein quantification, and immunohistochemistry should be performed to confirm whether the AβC is localized to the nucleus. Adding further cell lines to the panel should be considered. Causation should be tested by over expressing a reporter protein, which mimics AβC but cannot be "turned off," in neuroblasts to determine if AβC is sufficient to cause NB progression.

The Power of Partnership

Abstract #:   119
Presenter: Rebecca Clark
Supervisor: Yan Yuan
Title: Examining the relationship between premature menopause in childhood cancer survivors and cancer treatment exposures
Authors: Rebecca Clark, Yan Yuan
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction

Childhood cancer survivors are often faced with chronic conditions in their adulthood resulting from the toxicities of their treatment. Female survivors are at an increased risk of developing non-surgical premature menopause (NSPM), where ovarian function is retained for at least 5 years after diagnosis but amenorrhea presents for a minimum of 6 months before age 40. The proportion of childhood cancer survivors developing NSPM is estimated to be 9%, compared to only 1% in the general population. NSPM negatively impacts quality of life and can significantly reduce potential reproductive years, emphasizing an urgent need to properly counsel survivors on their individual risk. Identified risk factors for NSPM in childhood cancer survivors include an older age at cancer diagnosis, treatment with high doses of alkylating agents and radiation to the abdomen and pelvis. My objective is to develop a model that will predict the absolute risk of an individual childhood cancer patient developing NSPM at pre-specified ages. This estimate can help physicians, patients and their families have informed discussions of the need for early interventions to preserve reproductive ability.

Methods

Preliminary research was performed using data from 3604 female participants in the original cohort of the Childhood Cancer Survivor Study. Descriptive statistics including means, frequencies and medians were obtained for various baseline characteristics. Competing risks regression was used to assess the relationship between NSPM and each individual risk factor.

Results

Competing risks regression confirmed the relationship between NSPM and previously identified risk factors. Increasing age of diagnosis by 5 years (SHR: 1.249, 95% CI: 1.114-1.399), increasing exposure to doses of alkylating agents by 1000 mg/m^2 (SHR: 1.024, 95% CI: 1.013-1.036) as well as increasing radiation doses by 10 Gy to the pelvis (SHR: 1.251, 95% CI: 1.147-1.365) and abdomen (SHR: 1.261, 95% CI: 1.153-1.378) were identified as significant risk factors for the development of NSPM.

Conclusions

Simple univariate analysis using competing risks regression confirmed the relationship between NSPM and exposure to high doses of alkylating agents, radiation to the abdomen and pelvis as well as an older age at diagnosis. Future directions involve investigating these covariates in the development of multivariate risk prediction models.

The Power of Partnership

Abstract #:   120
Presenter: Mahsa Mohseni
Supervisor: Joseph Brandwein
Title: Targeting STAT5 in acute leukemic cells with siRNA
Authors: Mahsa Mohseni, Cezary Kucharski, Remant Bahadur KC, Hasan Uludag, Joseph Brandwein
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

Development of novel acute leukemia therapy is urgently needed due to poor prognosis and high relapse rates of the current therapy[1], [2]. Transcription factors including Signal Transducer and Activator of Transcription (STAT) protein family members are key molecular targets for acute leukemia, since they can activate expression of oncogenes leading to aberrant proliferation and migration of cancer cells[1]. In hematological malignancies, downregulation of STAT5 can decrease proliferation of leukemia cells[1], [2]. Small interfering RNA (siRNA) mediated silencing of these targets has become a promising alternative due to its specificity and high degree of safety[3]. However, development of clinically relevant siRNA carriers is needed since siRNA molecules are highly unstable in serum and their anionic nature prevents them to traverse cellular membranes[3]. In this study, we evaluated therapeutic role of STAT5 inhibition in acute leukemic cell lines by polymeric siRNA delivery systems.

Methods:

Acute myeloid MOLM13 leukemia cells and Acute lymphocytic NALM-6 leukemia cells were selected for *in vitro* studies. Lipid-modified low molecular weight polyethyleneimine (PEI) polymers were used as siRNA carriers. Cell proliferation was assessed using MTT and DNA assays. Cellular uptake of siRNA was evaluated by Flow Cytometry and STAT5 knockdown was investigated at the mRNA level by RT-qPCR.

Results:

Specific lipid substituted 2 and 1.2 kDa PEI (2PEI and 1.2PEI) displayed excellent complexation properties with siRNAs to form nanoparticles and gave high siRNA uptake in both cells with negligible toxicity. There was a good correlation in uptake between the two cell types. Cell growth was reduced (90%) by STAT5 siRNA delivery in MOLM13 cells using 1.2PEI-lipid polymer, however, STAT5 downregulation was not enough to cause cell death in NALM6 cells. Though some polymers showed higher uptake, STAT5 gene expression was strongly downregulated (60-70%) with leading polymers and the silencing effect was higher on day 6.

Conclusions:

We have demonstrated effective delivery of STAT5 siRNA by polymeric nanoparticles into leukemia cells, accompanied by marked inhibition of STAT5 gene expression. Further experiments will be directed at evaluating STAT5 protein silencing by siRNA therapy and exploring the effect of STAT5 downregulation on leukemic patient samples. The STAT5 knockdown by polymer/siRNA complexes in patients with acute leukemia will be a promising approach to address limitations of current therapies. The low toxicity and controlled delivery of siRNA using efficient delivery systems such as modified polymers can be beneficial to apply siRNA therapy to treat and improve quality of life in cancer patients.

The Power of Partnership

Abstract #: 121
Presenter: Mervin Burnett
Supervisor: Consolato Sergi
Title: PathVisio analysis of miRNAs playing a role in Osteosarcoma
Authors: Mervin Burnett, Consolato Sergi
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

PathVisio Analysis of miRNAs playing a role in Osteosarcoma

Mervin Burnett, Consolato Sergi

Department of Laboratory Medicine and Pathology

Stollery Children's Hospital, University of Alberta, Edmonton, Alberta, Canada

Introduction: Osteosarcoma is the most common primary malignant bone tumor, comprising about 20% of primary bone sarcomas with a predilection for the pediatric and juvenile age group. There has been a significant increase in the 5-year survival rates of patients with osteosarcoma due to the advances in clinical management of patients. MicroRNAs (miRNAs) are small single strand, non-coding RNA molecules, usually between 18 to 25 nucleotides in length that are found in eukaryotic cells. MiRNAs have been found to be involved in the pathogenesis of cancer, including osteosarcoma as they have the ability to function as tumor suppressors, oncogenes or both. There is increasing evidence that miRNA may play a role in determining the response to chemotherapy in the treatment of osteosarcoma. Several miRNAs have been found to be involved in osteosarcoma, with some molecules being overexpressed while others downregulated. We aim to clarify the osteosarcoma pathways involving miRNA using bioinformatic tools.

Methods: WikiPathways is an open, collaborative platform for drawing, editing, and sharing biological pathways, built using the same software underlying Wikipedia. WikiPathways can be used to integrate, visualize, and analyze system-wide transcriptomics, proteomics, and metabolomics measurements using the open source pathway analysis tool PathVisio.

Results: Significant differences were observed between the good responders and poor responders to ifosfamide with miR-92a, miR-99b, miR-193a-5p, and miR-422a increased, and miR-132 decreased in good responders. There is a significant increase of miR-221 in osteosarcoma cell lines when compared with osteoblasts.

Conclusion: The biological properties of miRNAs have the potential to make these molecules a useful diagnostic and prognostic tool in the management of osteosarcoma.

The Power of Partnership

Abstract #:   122
Presenter: Janet Zhou
Supervisor: Lori West
Title: Proof of concept: A bead-based platform for ABO antibody assessment
Authors: Anne Halpin, Jean Pearcey, Todd Lowary, Christopher Cairo, Gour Daskhan, Bruce Motyka
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

ABO-incompatible (ABOi) organ transplantation is possible in pediatric patients due to the delayed development of naturally occurring ABO antibodies. Therefore, determination of ABO antibody titers is important in the assessment of immunological risk for the patient pre- and post-transplant. ABO titres are traditionally measured by hemagglutination. However, hemagglutination has limited ability to differentiate between Ig subclasses and does not readily distinguish between the 18 different subtypes of ABO antigens, which are expressed differently on grafts *vs* erythrocytes. The goal of this study was to create a Luminex bead-based assay to detect ABO antibodies with finer specificity than the traditional hemagglutination method.

Methods:

Phase 1: Human blood group antigen subtype A-II tetrasaccharide was synthesized and conjugated to bovine serum antigen (BSA). BSA-A-II was coupled to Luminex beads using a carbodiimide reaction. Antigens were detected with IgG and IgM anti-A monoclonal antibodies either directly labeled with phycoerythrin (PE) or indirectly, with PE-labeled secondary antibodies. Different amounts of antigen were coupled to optimize mean fluorescence intensity (MFI) output on a Luminex-200 cytometer.

Phase 2: Experiments from Phase 1 were repeated using ABO antigen subtypes A-III and A-IV with additional beads. The multiplexing ability of the assay using the three coupled antigens was also tested.

Phase 3: Dilutions of PE-labeled anti-human IgG secondary antibody were tested against dilutions of anti -A plasma (blood group B donor) in a checkerboard titration using BSA-A-II coupled beads. Blood group A donor plasma was included as a negative control.

Results:

The coupling of BSA-A-II, -III and -IV was successful as demonstrated by a linear increase in MFI with doubling concentrations of primary antibody. MFI values approaching 20,000 and plateau of MFI values were achieved, indicating bead fluorescence saturation. Beads were successfully labeled with monoclonal anti-A antibody when multiplexed. Based on the patient serum results, the assay was able to detect anti-A IgG antibodies with increasing sensitivity depending on the dilution of patient plasma and secondary antibody.

Conclusions:

This novel assay has the potential to be adopted by clinical histocompatibility laboratories for rapid, specific, and sensitive assessment of IgM/IgG subtype-specific ABO antibodies in ABOi transplantation as the expertise and instrumentation already exist. We will continue to optimize the assay, include additional controls, and assess additional ABO subtypes. We are also testing other bead-based platforms. The results from these platforms will be compared to the existing microarray technique already shown to provide additional valuable information in transplantation.

The Power of Partnership

Abstract #:   123
Presenter: Ali Hajar
Supervisor: Simon Urschel
Title: The phenotype and regulatory capacity of IL10-secreting B-cells in humans
Authors: Ali Hajar, Lavinia Ionescu, Ying Ling, Lori West, Simon Urschel
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Background: Infants show better graft survival and need for less immunosuppression after heart transplantation. The CD5+CD1d+ B-cell subset contains IL10-producing "B10 cells" with immune regulatory capacity in animals, and we found this subset to be up to ten times more prevalent in infants than adults. Transitional (CD24+CD38+) B-cells also secrete IL10 and improve graft survival in animals. We hypothesized these populations contribute to the tolerogenic environment in infants, and aimed to describe the phenotype of human IL10-producing B-cells, and their impact on B- and T-cell proliferation.

Methods: Splenocytes were sorted by flow cytometry to separate CD5+CD1d+ or CD24+CD38+ B-cells from remaining B-cells and obtain 4 populations, which were separately cultured with stimuli reflecting T-dependent (TD; aIgM+CD40L) or T-independent (TI; CpG) activation. IL10 secretion was measured by ELISA. To assess effects on proliferation, CellTrace™-marked splenocytes were stimulated with Staphylococcal enterotoxin B, aIgM+CD40L, CpG, or aCD3+aCD28 in absence of either CD5+CD1d+ or CD24+CD38+ B-cells as well as in 1 (natural proportion, CONTROL), 2 and 5 times their natural proportions. Peripheral blood mononuclear cells (PBMC) were activated in a TD or TI manner for 5 and 48 hours to determine alteration of the phenotypes of IL10+ and IL10- B-cells.

Results: CD5+CD1d+ B-cells produced IL10 following TD activation, while non-CD5+CD1d+ B-cells produced even higher amounts of IL10 after TI activation. Compared to the CONTROL, B-cell proliferation after TD activation was 27% higher in CD5+CD1d+ depleted cultures ($p = 0.081$), with strongest effects being on non-class-switched memory (CD27+IgM+) B-cells ($p = 0.059$). Results regarding the IL10 secretion and suppressive capacity of CD24+CD38+ B-cells, as well as the phenotypes of IL10+ B-cells are currently being analyzed.

Conclusion: CD5+CD1d+ B-cells encompass many, but not all, IL10-producing B-cells. Their presence decreases the proliferation of TD-activated B-cells, especially those that are non-class-switched memory cells.

The Power of Partnership

Introduction

The early years (0-5), are recognized as the period of greatest brain vulnerability to adverse events, including those stemming from early complex cardiac surgery. While limited, the research also indicates that children following complex cardiac therapies are at risk of ongoing adverse neurocognitive, behavioral, emotional, and academic outcomes as they progress into their school years. We set out to 1) determine the extent to which regression occurs in pre-academic and academic functioning after life-saving therapies at $\leq$ 6 weeks of age and to 2) develop a practical, workable framework of intervention to prevent regression in the child's developmental trajectory.

Method

We determined a mean lack of expected progression of functional skills and a regression of skills (loss of ability) using the parent-completed Adaptive Behavioral Assessment System II (domain, mean$\pm$sd, 10$\pm$3; delay = <4). Focus Groups consisting of health care professionals, allied health workers and parents engaged in active dialogue about prevention of regression under the sub-topics of: at the bedside, in follow-up, early childhood, school-readiness, and school age.

Result

Pre-academic and Academic scores were 8.9(3.1), 8.2(3.4) and 6.4(3.3) at 2, 4,and 8 years of age respectively. The proportion of children with delay increased, 4.1%, 9.7%, 32% at these ages relative to peers. The Focus Groups yielded well organized and helpful approaches to intervention.

Conclusion

Lack of progression and regression of skills occurs in children after complex cardiac therapies. Evaluation and intervention for functional deficits for these children requires collaborative care early on in the child's life. This study informs our developing framework to enable all children to have support both before and after school entry. Functional abilities are a very important consideration in developmental evaluations of children assessed for school readiness.

The Power of Partnership

Abstract #:   125
Presenter: Sunjidatul Islam
Supervisor: Andrew Mackie
Title: Health care resource utilization among children with congenital heart disease in Alberta
Authors: Sunjidatul Islam, Padma Kaul, Andrew Mackie
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Data regarding healthcare resource utilization (HRU) among children with congenital heart disease (CHD) are scarce. Therefore, we sought to describe the extent of HRU (outpatient visits and hospitalizations) among children with CHD <5 years of age in Alberta.

Methods: A population based retrospective cohort study was conducted among all live births between 2005 and 2014 in Alberta. We identified all live births from Alberta Vital Statistics Birth file and linked to Alberta Health Administrative Databases. CHD was classified as simple, moderate-complex, or single ventricle (SV). Results were compared to children without CHD. In order to assess 1-year and 5-year HRU, birth cohorts of 2005-2014 and 2005-2010 time periods were created. All continuous variables were presented as median (IQR) and compared across groups using the nonparametric Kruskal-Wallis tests. Rates were compared using Poisson regression models.

Results: Overall, 7,546 of 490,120 children born in Alberta between 2005 and 2014 were diagnosed with CHD (incidence rate=1.5%). Among children with CHD, 1-year hospitalization rate/100 person-years was 399 in SV patients, 243 in moderate-complex patients, 165 in simple patients, and was significantly higher than that of non-CHD children (110/100 person-years) ($p<0.001$). The number of hospitalizations, including birth hospitalization, in the first year of life was 3 (2 – 5) in SV, 2 (1 – 3) in moderate-complex CHD, 1 (1 – 2) in simple CHD, and 1 (1 – 1) in non-CHD children ($p<0.001$). Total length of hospitalization stays in days were significantly longer among CHD children [54 (27 – 99) in SV, 22 (9 – 47) in moderate-complex CHD, and 7 (2 – 28) in simple CHD] vs. 2 (1 – 3) among non-CHD children ($p<0.001$). Children with CHD had more frequent clinic-based outpatient visits than children without CHD in the first year of life [43 (20 – 65) in SV, 19 (7 – 38) in moderate-complex CHD, 4 (1 – 14) in simple CHD, and 0 (0 – 1) in non-CHD children; $p<0.001$]. These differences remained through the first five years of life. In addition, hospitalization rates (per 100 children) were consistently higher in CHD children than non-CHD children in every year of age (62-243 vs. 11 in first year and 12-80 vs. 2 in fifth year of life).

Conclusions: Health care resource utilization is high among children with CHD <5 years of age and increases with increasing CHD severity. Our data implies that CHD children, compared to non-CHD children, require a continuum of health care in the first 5 years.

The Power of Partnership

Background: ABO-incompatible heart transplantation (ABOi-HTx) is safe during infancy and allows increased donor access. B-cell tolerance develops to donor A/B-antigen(s) (Ag) after ABOi-HTx by mechanisms remaining unclear. We developed transgenic mice (A-Tg) constitutively expressing human A-Ag on vascular endothelium and erythrocytes (RBC) to study anti-A antibody responses. CD22 participates in B-cell tolerance and we found that B cells express high-levels of CD22 in human B cells, decreasing with age. Here we used a mouse model to study the anti-A response in the context of MHC syngeneic, allogeneic and xenogeneic stimulation, and the impact of CD22 expression.

Methods: Part I: Adult wild-type (WT) C57BL/6 (B6/H-2^b), BALB/c (BALB/H-2^d), C3H/He (C3H/H-2^k), or CD22-deficient B6 (CD22KO) mice received intraperitoneal injections of B6 or BALB A-Tg blood cells or human-RBC membranes (100ul/10%v/v) from blood group-A (hu-A) or O (hu-O); or A-incompatible heart allografts. Serum anti-A Ab was measured by hemagglutination and ELISA (IgG and IgM); graft survival was assessed by palpation. Part II: a) To assess requirement of foreign protein to stimulate anti-A, hu-O RBC/syngeneic A-Tg cells or allogeneic A-Tg blood were co-injected in WT mice; b) to assess T cell dependence of anti-A response, CD4+ T cells were depleted from WT B6 mice before hu-A RBC injection. Part III: To assess the role of CD22, A-Tg or hu-A-RBC, were injected into CD22KO mice with or without CD4+ T-cell depletion.

Results: Part I: Exposure to *allogeneic* A-Tg blood cells/heart graft or xenogeneic hu-RBC induced anti-A production (**Table**), whereas *syngeneic* A-Tg blood cells did not. Part II: a) mixture of syngeneic A-Tg/hu-O RBC did not induce anti-A; b) after CD4+ T-cell depletion, hu A-RBC failed to elicit anti-A. Part III: Hu A-RBC induced a very high anti-A in CD22KO mice compared to WT B6. In contrast to WT B6 mice, anti-A Ab was elicited in CD22KO mice following injection with A-Tg blood cells or hu A-RBC with CD4+ T cell depletion.

Conclusions: Our results show that in WT mice, anti-A antibody production depends not only on exposure to A-antigen but also co-engagement with foreign protein and a requirement for CD4+ cells; consistent with a T-dependent anti-A response. Conversely, in CD22KO mice there was no requirement for foreign protein or CD4+ cells to elicit an anti-A antibody response; consistent with a T-independent anti-A response. These findings suggest an important role for the regulatory CD22 receptor in the B cell response to ABH antigens.

Table
Part I:
Syngeneic

Treatment	Recipient	n	Anti-A titer
B6 A-Tg blood	WT B6	12	<4
BALB A-Tg blood	WT BALB	3	<4

Allogeneic

Treatment	Recipient	n	Anti-A titer
B6 A-Tg blood	WT BALB	3	512
B6 A-Tg blood	WT C3H	3	64
BALB A-Tg blood	WT B6	3	512
B6 A-Tg HTx (rejected day 8-10)	WT BALB	3	512
B6 A-Tg HTx (rejected day 8-11)	WT C3H	3	256

Xenogeneic

Treatment	Recipient	n	Anti-A titer
Human A-RBC	WT B6	9	512
Human A-RBC	WT BALB	4	1024

Part II:
a)

Treatment	Recipient	n	Anti-A titer
Human O-RBC	WT B6 (control)	3	4
Human O-RBC + B6 A-Tg blood	WT B6	6	8

b)

Treatment	Recipient	n	Anti-A titer
Human A-RBC	WT B6 (control)	3	<4
Human A-RBC + anti-CD4	WT B6 (CD4 T cells depleted)	6	<4

Part III:
a)

Treatment	Recipient	N	Anti-A tier
No treatment	CD22KO B6	6	4-128
Human A-RBC	CD22KO B6	6	512-8192
A-Tg blood	CD22K9B6	8	16-1024

b)

Treatment	Recipient	N	Anti-A tier
Human A-RBC + anti-CD4	CD22KO B6 (CD4 T cells depleted)	7	2048-8192
A-Tg blood + anti-CD4	CD22KO B6 (CD4 T cells depleted)	7	64-8192

The Power of Partnership

Abstract #:	127
Presenter:	Jordana Fersovich
Supervisor:	Lori West
Title:	Investigation of ABO tolerance in a mouse model following neonatal treatment with a novel A-antigen glycoconjugate
Authors:	Jordana Fersovich, Bruce Motyka, Brendon Lamarche, Kesheng Tao, Jean Pearcey, Gour Daskhan, Christopher Cairo, Todd Lowary, Lori West
Affiliations:	University of Alberta
Research Activity:	Children's Health and Well-Being

Introduction: ABO-incompatible heart transplantation (ABOi HTx) is safe during infancy and allows increased donor access. Post-ABOi HTx, B cell tolerance develops to donor blood group antigen(s) by mechanisms not fully defined. We developed A-transgenic (A-Tg) mice that express A-antigen on vascular endothelium and erythrocytes (RBCs) and demonstrated A-antigen specific tolerance following HTx into young (4 wk) wild-type (WT) mice. Intentional induction of tolerance to A/B-antigen(s) in infancy may allow later ABOi HTx. Here, we explored intentional tolerance induction using a novel bifunctional glycoconjugate (GC) displaying AG10, a small molecule shown to increase the *in vivo* half-life of molecules it is bound to, and human A subtype II antigen (A(II)-AG10).

Methods: Neonatal (<24 hours after birth) WT BALB/c mice were intravenously injected with 100 μg A(II)-AG10 GC (n=7) or left untreated (n=7). In an attempt to elicit anti-A antibody, mice at 5 wk of age were injected intraperitoneally with human A-RBC (100 μL, 20% vol/vol, weekly ×5). Serum anti-A antibodies were assessed by hemagglutination and ABH-glycan microarray.

Results: A-sensitization resulted in high-levels of IgM and IgG antibody specific to A(II) with no significant difference between A(II)-AG10 GC treated or untreated groups (IgM, p=0.944; IgG, p=0.528). Levels of antibodies specific to all A-subtypes (I-VI) were also similar in treated and untreated groups (IgM, p=0.185; IgG, p=0.185).

Conclusion: Neonatal treatment with A(II)-AG10 GC in this model did not result in tolerance to A(II)-antigen. As CD22-CD22L interactions have been shown to be important in B cell tolerance induction, ongoing studies are accessing tolerance to A-antigen using A-GC containing CD22 ligand (CD22L). Specific parameters of our protocol, such as dose, route, and timing of treatment injections, are also being explored.

The Power of Partnership

Abstract #:   128
Presenter: Kim Ho
Supervisor: Gary Lopaschuk
Title: Ketone bodied can provide additional energy for the diabetic failing heart without compromising cardiac efficiency
Authors: Kim Ho, Sonia Rawat, Cory Wagg, Liyan Zhang, John Ussher, Gary Lopaschuk
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

INTRODUCTION: With global excitement surrounding the class effect of SGLT2 inhibitors improving cardiovascular outcomes, it remains enticingly unclear how the anti-hyperglycemic agent, empagliflozin, confers its cardiovascular benefits to the diabetic heart. In addition to decreasing blood glucose levels, empagliflozin also increases circulating levels of ketones in the blood. Therefore, one proposed explanation for empagliflozin's ambiguous cardioprotection is through optimizing cardiac energy metabolism and deferring the heart's substrate preference from fatty acids and glucose, to the "thrifty" (or efficient) ketones. However, it remains unclear whether an increase in myocardial ketone usage is beneficial for the diabetic heart. Consequently, the aim of our study was to assess the metabolic profile and cardiac efficiency of the diabetic heart in response to ketones [ß-hydroxybutyrate (ßOHB)]. This will help elucidate whether ketones can improve cardiac efficiency and function.

METHODS: Diabetic (*db/db*)23-week-oldmale mice were used to characterize the metabolic profile of the diabetic heart in response to an increase in the availability of ketones. C57BL/6J mice were used as our controls. Isolated working hearts from these mice were perfused for 60 minutes with ^{3}H or ^{14}C labelled glucose (5mM), palmitate (0.8mM), and ßOHB (0mM or 0.6mM) to assess glycolysis rates, and ketone body, fatty acid and glucose oxidation rates, with 100mU/mL insulin added 30 minutes into perfusion. The pulmonary artery was also cannulated during these isolated working heart perfusions, which allowed us to quantify myocardial oxygen consumption rates and calculate cardiac efficiency by normalizing cardiac work to oxygen consumption.

RESULTS: Relative to control, *db/db* hearts had decreased cardiac work and the addition of ßOHB did not affect cardiac work. To add, *db/db* hearts with and without ßOHB had similar rates of glucose oxidation, palmitate oxidation and glycolysis. However, the addition of ßOHB did increase the total amount of energy (ATP) produced by the *db/db* hearts. Interestingly, while energy production increased, oxygen consumption rates in *db/db* hearts did not significantly change in the presence of ketones. As such, cardiac efficiency was not affected by the addition of ketones.

CONCLUSIONS: The cardiac work, metabolic profile and oxygen consumption of the diabetic heart did not significantly change when supplied with ketones. However, ketones can provide additional energy to the diabetic heart without affecting cardiac efficiency. As such, ketones are not a more or less efficient fuel substrate for the diabetic heart but can still be used to increase total energy production.

The Power of Partnership

Abstract #:   129
Presenter: Ashley Radomski
Supervisor: Amanda Newton
Title: An explanatory treatment model of Internet-based cognitive behavioural therapy for anxiety in young persons
Authors: Ashley Radomski, Lori Wozney, Patrick McGrath, Anna Huguet, Lisa Hartling, Michele Dyson, Kathryn Bennett, Purnima Sundar, Amanda Newton
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Recent reviews indicate the potential effectiveness of Internet-based cognitive behavioural therapy (iCBT) for reducing anxiety in young persons. As a 'persuasive technology', iCBT consists of 3 major elements: therapeutic content, technological features, and human-technology interactions. Although recent reviews indicate the potential effectiveness of iCBT for reducing anxiety in young persons, the specific elements used and the treatment effects reported still differ across studies. Thus, it is unclear as to how and for whom iCBT works. The objective of this realist review was to develop an explanatory treatment model that highlights 'iCBT ingredients' (content, technological features, human-technology interactions) that contribute to treatment outcomes for young persons with anxiety.

Methods

A search of published and grey literature was conducted. Documents were appraised for relevance to the review's objective and research studies were assessed for methodological quality. Data extraction was guided by *The Persuasive System Design (PSD) model*—a framework that describes and categorizes technological features proposed to increase the effectiveness of persuasive technologies. iCBT content, technology and PSD features, interactions and delivery components, once coded, were linked to treatment outcomes using meta-ethnographic methods. Sixty-six documents detailing 16 iCBT programs were included. Documents were namely of moderate-to-high relevance and methodological quality.

Results

The analysis revealed that iCBT programs with the highest completion rates and greatest improvements in users' anxiety had: (1) Primary Task Supports that reduced complex content into simple tasks, guided users through the program, provided relevant content, and enabled self-monitoring and skill practice, and (2) Dialogue Supports that had relatable content and design, and encouraged dynamic communication through online/in-person reinforcement, reminders and feedback. The importance of delivery setting, adjunct support, user characteristics and program content on iCBT outcomes was also identified by the analysis.

Conclusions

The explanatory model suggests that, in consideration with delivery, interaction and user factors, certain PSD features may improve the usage and anxiety-related outcomes of iCBT programs. Hypothesis-driven testing of these features is recommended to advance the understanding of how these features contribute to effectiveness.

The Power of Partnership

Abstract #:   130
Presenter: Rika Maruyama
Supervisor: Toshifumi Yokota
Title: Systemic injections of peptide-conjugated morpholinos improve cardiac symptoms of an animal model of Duchenne muscular dystrophy
Authors: Rika Maruyama, Yusuke Echigoya, Akinori Nakamura, Kenji Rowel Q. Lim, Mutsuki Kuraoka, Hong M Moulton, Yoshitsugu Aoki, Terence
                       Partridge, Shin'ichi Takeda, Toshifumi Yokota
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Duchenne muscular dystrophy (DMD) is a lethal genetic disorder caused by an absence of dystrophin protein in body-wide muscles, including the heart. Cardiomyopathy is a leading cause of death in DMD. Exon skipping via synthetic phosphorodiamidate morpholino oligomers (PMOs) represents one of the most promising therapeutic options, yet PMOs have shown very little efficacy in cardiac muscle.

Methods

To increase therapeutic potency in cardiac muscle, we tested next-generation morpholino – arginine-rich, cell-penetrating peptide-conjugated PMOs (PPMOs) – in the canine X-linked muscular dystrophy in Japan (CXMD$_J$) animal model of DMD. A PPMO cocktail designed to skip *dystrophin* exons 6 and 8 was injected intramuscularly, intracoronarily, or intravenously into CXMD$_J$ animals.

Results

Intravenous injections of PPMOs restored expression of dystrophin protein in the myocardium and cardiac Purkinje fibers, as well as skeletal muscles. Vacuole degeneration of cardiac Purkinje fibers, as seen in DMD patients, was ameliorated in PPMO-treated animals. Electrocardiogram abnormalities (increased Q amplitude and Q/R ratio) were also improved in CXMD$_J$ animals after intracoronary or intravenous administration.No obvious evidence of toxicity of PPMOs was found in blood tests throughout the monitoring period.

Conclusions

The present study is the first to report rescue of dystrophin expression and recovery of the conduction system in the heart of dystrophic animals by PPMO-mediated multi-exon skipping, and demonstrates the high clinical potential of systemic PPMO therapy for cardiac symptoms of DMD.

The Power of Partnership

Abstract #:   131
Presenter: Danielle Mattson
Supervisor: Jacqueline Pei
Title: The impact of a math interactive learning experience (MILE) on math abilities in children with neurodevelopmental and learning difficulties
Authors: Danielle Mattson, Kathryn Kryska, Claire Coles, Julie Kable, Gail Andrew, Damien Cormier, Jacqueline Pei, Carmen Rasmussen
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction

Mathematical competence is crucial for success in many areas of daily living. If challenges are not addressed, those with math difficulties may struggle with important life skills such as budgeting, problem solving, and time management. It is especially important to rectify these problems early, as math learning is cumulative and issues can quickly snowball if foundational skills are not mastered. Fortunately, early intervention programs such as the Math Interactive Learning Experience (MILE) can help improve math proficiency. Originally developed to address math deficits in children with fetal alcohol spectrum disorders (FASD), the MILE program uses interactive, individualized tutoring to strengthen basic math skills and the broader cognitions underlying math learning (Kable et al., 2007). Given the positive results this program has shown with the FASD population, the current study aimed to examine whether it is also effective when administered in a school setting to small groups of children experiencing other neurodevelopmental and learning difficulties.

Methods

The pilot study took place in three Edmonton schools with 14 participants aged 5 to 8 years old (mean = 6.93 years) who were identified as experiencing a range of neurodevelopmental and learning difficulties including, but not limited to, FASD. All participants received 14 intervention sessions administered in small groups of two children by a teacher, educational assistant, or research assistant trained in the MILE program. Math abilities were measured using the *KeyMath-3 Diagnostic Assessment: Canadian Edition* at three time points following a waitlist control design.

Results

Upon program completion, 85.7% of participants (12/14) improved by at least one standard deviation in at least one math content area. Eight participants (57.1%) improved by at least one standard deviation in two or more areas, and four participants (28.6%) improved by at least one standard deviation in three or more math content areas.

Conclusions

These results suggest that the MILE program is effective when delivered in a school setting to small groups of children experiencing neurodevelopmental and learning difficulties non-specific to FASD. This information can be used to help inform educational support services for this population and others who may benefit from a math intervention.

References

Kable, J.A., Coles, C.D., & Taddeo, E. (2007). Socio-cognitive habilitation using the math interactive learning experience program for alcohol-affected children. *Alcoholism-Clinical and Experimental Research, 31(8)*, 1425-1434.

The Power of Partnership

Introduction

Children with Obstructive Sleep Apnea (OSA) often present with nasal septum deviation and asymmetrical turbinates. Understanding if and how these abnormalities contribute to airway obstruction is the topic of current investigation, as they might be useful for early diagnosis and better prediction of disease progression. Mice with a neural crest-specific deletion of Bone Morphogenetic Protein 7 (Bmp7) ($Bmp7^{ncko}$) present with similar craniofacial features and develop airway obstruction. As Bmp7 is associated with articular cartilage degeneration and arthritis, we hypothesize that Bmp7 controls the maintenance of the cartilaginous nasal septum and turbinates. Premature loss of cartilage could explain these growth deficiencies leading to midfacial hypoplasia as seen in children with OSA.

Methods

Bmp7fl/fl: Wnt1-Cre ($Bmp7^{ncko}$) mutant mice were obtained by crossing a conditional Bmp7 allele to Wnt1-Cre mice. Microcomputed Tomography (µCT) datasets and were analyzed for morphometric changes in mice. Oxygen consumption was assessed using Comprehensive Lab Animal Monitoring (CLAM) cages and blood serum was screened for metabolite changes. Molecular and cellular processes involved in the nasal septum were identified using histology and immunohistochemistry on 2, 4, and 8-week old mice.

Results

Mice develop initially inconspicuous, however, 70% of the mutant mice die between 3-6 weeks, the period of rapid physiological midfacial outgrowth. Assessment of µCT scans of mice skulls at ages 2 week and 4 week indicated severe midfacial growth reduction. In particular, the perpendicular plate of ethmoid (PPE) initially developed normally but was displaced from the midline by 4 weeks of age. Bmp7 was continuously expressed in PPE and developing turbinates during these times. Histological and immunohistochemical assessment of 2- and 4-week old nasal septum demonstrated differences in cartilage/bone remodeling. Osteopontin, normally expressed in hypertrophic cartilage, was severely reduced in the 4-week-old mutant, and ossification of the PPE was seen at the sites of deviation. CLAM analysis showed that $Bmp7^{ncko}$ mice had extended periods of reduced oxygen consumption and anaerobic metabolism. The metabolomics screen revealed increased levels of hydroxyproline, a marker for bone resorption, in 4-week old $Bmp7^{ncko}$ mice.

Conclusions

This study suggests that altered cartilage/bone remodeling could underlie midfacial hypoplasia and nasal septum deviation. Knowledge of the molecular and cellular changes associated with this remodeling will provide a better understanding of midfacial growth. Lastly, metabolomic changes due to airway obstruction could be useful for early diagnosis of sleep-disordered breathing.

The Power of Partnership

Abstract #:   133
Presenter: Elizabeth Garcia
Supervisor: Alvaro Osornio-Vargas
Title: Particulate matter and its effect on the aryl hydrocarbon receptor (AHR)/CYP1A1 pathway in adherent THP-1 cells
Authors: Elizabeth Garcia, Jesus Serrano-Lomelin, Alvaro Osornio-Vargas
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

INTRODUCTION/OBJECTIVE: Air pollution and Particulate Matter (PM) have recently been classified as human carcinogens. PM is a mixture of compounds including soil, heavy metals and organics like polycyclic aromatic hydrocarbons (PAH). The objective of this study is to evaluate the molecular mechanisms by which the PAH content in PM_{10} (PM with mean aerodynamic diameter ≤10 μm) may influence cell responses. Specifically, we are interested in the Aryl hydrocarbon Receptor (AhR)/CYP1A1 pathway in adherent THP-1 cells.

METHODS: THP-1 cells were cultured in suspension and transformed to macrophages with phorbol-myristate-acetate. The cells were then treated with eight different PM_{10} samples of known soil and PAH content collected from an "industrial" (IND) and a "business" (BUS) area in Mexico City. Q-PCR was conducted to measure gene expression levels of *AHR* and *CYP1A1*. The intracellular localization of AhR and CYP1A1 was evaluated by immunofluorescence microscopy. We also assessed the production of TNFα and IL-6 by ELISA. All experiments also included the use of the following: 1) Polymyxin A against endotoxins, 2) α-naphthoflavone as an AhR inhibitor, and 3) N-acetyl cysteine as a free radical scavenger. One-way ANOVA was used to determine differences between groups. We assessed correlations between PM_{10} soil and PAHs content and the cell responses using Pearson's analysis.

RESULTS: After exposure to PM_{10}, THP-I cells exhibited a significant increase in the expression of CYP1A1 compared to the unexposed cells. A similar effect was not observed in the case of AhR gene expression. In this instance, however, PM_{10} induced the translocation of the AhR receptor to the nucleus accompanied by the expression of CYP1A1. Only α-naphthoflavone significantly decreased the level of CYP1A1 expression (p<0.01). The PM_{10} PHA content correlated with an increased trend in the expression of AhR when using the samples with the highest content of PAHs (IND) (r=0.934, p<0.06). PM_{10}-induced cytokines production correlated with the soil content of the samples (IL-6; r=0.492, p<0.004, TNFα: r=0.669, p=0.000).

CONCLUSIONS: CYP1A1 gene and protein expression are AhR dependent after PM10 exposure. These data demonstrate that PM participates as a xenobiotic in an AhR-mediated signal transduction pathway mediated by the PM_{10} PAH content.

The Power of Partnership

Abstract #:   134
Presenter: Eliza Li
Supervisor: Carmen Rasmussen
Title: Effects of perinatal stroke on visual and verbal reasoning abilities and select academic skills
Authors: Eliza Li, Lisa Smithson, Jacqueline Pei, John Andersen, Jerome Yager, Brian Brooks, Kathleen O'Grady, Anne Dmytryshyn, Edward
                   Armstrong, Carmen Rasmussen
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Perinatal stroke affects 10,000 Canadian children. Studies on intellectual functioning have been contradictory: some have found minimal cognitive impairment; others suggest selectively poor performance on perceptual reasoning and visual-spatial tasks, with language and verbal-based skills preferentially spared. The aim of this study is to address inconsistent findings on the neurocognitive profile of children with perinatal stroke, to better understand the specific, personalized deficits as targets for treatment. It was hypothesized that visual, but not verbal skills would be lower in the perinatal stroke group than in the control group, with math impacted more than reading.

Methods: Data was collected through the Alberta Perinatal Stroke Project, a population-based, prospective, cross-sectional research cohort. Inclusion criteria were children aged 6-16, with clinical-radiographically confirmed perinatal arterial ischemic stroke. A trained research assistant administered two cognitive measures: The Wide Range Intelligence Test, which assessed verbal and visual IQ, and the Woodcock Johnson III Tests of Achievement, which assessed reading and math skills. Multivariate analysis of variance will be used to compare neurocognitive profiles of the two groups.

Results: Data collection is on-going, preliminary results includes 6 children with perinatal arterial ischemic stroke (aged 6-15 years, 67% male) and 7 control participants (aged 6-11 years, 71% male). Preliminary analysis includes descriptive mean comparisons. Verbal IQ was higher in the control group (M = 115.71, SD = 8.85; M = 89, SD = 9.82), as was visual IQ (M = 115.71, SD = 10.83; M = 87.60, SD = 13.94). Additionally, broad reading scores were higher in the control group (M = 111.43, SD = 15.49; M = 86.6, SD = 10.31), as were broad math scores (M = 109.67, SD = 8.19; M = 76.8, SD = 7.22).

Conclusions: Preliminary findings suggest children with perinatal stroke may perform lower on both visual and verbal tasks, though within the low-average range. Neurocognitive outcomes are a strong predictor of functional outcomes, an increased understanding of intellectual and academic deficits in children with perinatal stroke has implications for informing interventions to improve outcomes.

The Power of Partnership

Introduction: Social participation is important for health, development, improved emotional, social and academic outcomes for children, and improved quality of life in adulthood. In particular, children with disabilities, including ASD, identify participation in community leisure and recreation activities as their highest priority when setting personal participation goals. However, children with ASD participate in significantly fewer community-based activities than their typically developing peers. Decreased community participation has been mostly attributed to the influence of family and child factors such as financial resources of the family, and/or the child's emotional and social function. Contextual factors, including attitudes of community members and exclusionary organizational practices and policies, have been infrequently evaluated. In a current study by our research team, investigating parental decisions regarding disclosure and non-disclosure of ASD diagnosis to others, parents reported that perceptions of stigma affect their decisions of whether to disclose their child's ASD diagnosis to community-based programs. This study will be the first to investigate the expectations and perceived outcomes of disclosure of an ASD diagnosis from the perspective of people who work at community recreation programs. Specifically, we aim to better understand:

(1) The expectations of community programs to have parents disclose their children's diagnosis of ASD

(2) The perceptions of the outcomes of disclosure/non-disclosure of an ASD diagnosis

Methods: A multi-layer case study approach was used. Semi-structured interviews (20-45 minutes) were conducted with 6 individuals from community recreation programs in the greater Edmonton area: one program director (administrative), one program manager (administrative/on-site), one head inclusion facilitator, one inclusion support staff, and two general camp counselors. Interviews were audio-recorded, transcribed verbatim, and checked for accuracy. Thematic analysis of these data will provide the opportunity to identify, analyze, and report patterns found within the interview transcripts.

Results: Data analysis is underway and preliminary observations of the data will be presented.

Conclusions: Findings from this study will build understanding of how personal and/or structural practices and policies within community recreation organizations may shape opportunities for participation and inclusion. Gaining a deeper understanding of these expectations and perceived outcomes will facilitate conversation around the varying expectations, assumptions, practices and policies of community organizations related to disclosure. This may also positively support understanding and inclusion in organized or informal community activities for children with ASD, ultimately contributing to improved health for these children and their families, and building towards healthy communities overall.

The Power of Partnership

Introduction: Perinatal stroke is a leading cause of cerebral palsy and lifelong disability. This diagnosis can place significant demands on caregivers. Although some research has been done to identify the psychosocial impact of a perinatal stroke diagnosis on families, more research is needed in this area. In this study, we assessed the impact of perinatal stroke on the caregiver, as well as their attitudes toward perinatal stroke research, providing unique insight into the caregiver experience.

Methods: Participants include primary caregivers and their children aged 5-16 with confirmed perinatal stroke from the Alberta Perinatal Stroke Program (APSP). Caregivers completed the Parental Outcome Measure, which measures the overall psychosocial impact of a perinatal stroke diagnosis on the caregiver, and a caregiver engagement in research questionnaire, which assesses attitudes toward perinatal stroke and cerebral palsy research.

Results: Data collection is underway; to date we have collected data from 7 children with perinatal stroke and healthy control children. Preliminary analysis of the engagement questionnaire indicates that caregivers strongly support research on the prevention and treatment of perinatal stroke, as well as longitudinal research.

Conclusions: Understanding of how a perinatal stroke diagnosis affects caregivers can help guide practitioners in the provision of more effective psychological supports at diagnosis and better on-going support and follow-up. Furthermore, it is important to recognize the research priorities of caregivers to ensure further research is conducted in areas of importance to stakeholders.

The Power of Partnership

Abstract #:   137
Presenter: Kathryn Kryska
Supervisor: Carmen Rasmussen
Title: Cognitive factors that contribute to math difficulties among children with neurodevelopmental difficulties
Authors: Kathryn Kryska, Danielle Mattson, Claire Coles, Julie Kable, Molly Millians, Damien Cormier, Gail Andrew, Jacqueline Pei, Carmen Ramussen
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Background

Understanding cognitive factors that contribute to math difficulties in children allows for the opportunity to provide interventions to children at risk of developing math difficulties. Children's ability to automatically discriminate small quantities (subitizing) has been related to math ability in previous research (Kootnz and Berch 1996). Children with math difficulties tend to struggle with working memory and executive functioning. The objective of the current research was to investigate whether subitizing, working memory, and executive functioning are associated math ability in children with neurobehavioural difficulties.

Methods

Participants included 28 children (18 males) aged 5 - 8 years (M = 6.3 years) who had identified learning and developmental difficulties. Participants completed standardized measures of mathematics (Key Math - 3), working memory (Automated Working Memory Assessment AWMA), and executive functioning (auditory attention and design fluency from the NEPSY – II), as well as a measure of subitizing (Speeded Processing of Small Quantities SPSQ).

Results

The mean total math scores were below average (M = 78.1), with the poorest performance on the subtests measurement and applied problem solving. Subitizing ranged from .48 - 1.85 items per second, with higher scores meaning better and faster subitizing ability. Subitizing was correlated with performance on one math subtest, foundations of problem solving (r = 0.42). All AWMA working memory subtests fell within the average and low average range and most were with highly correlated (r's > .465) with math ability. Measures of executive functioning were also highly correlated (r's > .403) with math ability.

Conclusions

On average the math ability of the children with neurodevelopmental difficulties was low with a variation in strength and weakness on math subtests. Subitizing was found to be the least predictive of math ability as compared to working memory and executive functioning measures. Understanding the cognitive factors that contribute to math difficulty helps to better screen and remediate math difficulties with interventions.

The Power of Partnership

Abstract #:   138
Presenter: Kyle Reid
Supervisor: Lonnie Zwaigenbaum
Title: Use of the Brief Infant-Toddler Social and Emotional Assessment (BITSEA) for early identification of Autism Spectrum Disorder in high-risk populations
Authors: Kyle Reid, Lori-Ann Sacrey, Lonnie Zwaigenbaum, Susan Bryson, Jessica Brian, Isabel Smith, Wendy Roberts, Peter Szatmari, Tracy Vaillancourt, Caroline Roncadin
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Understanding the development of children diagnosed with Autism Spectrum Disorder (ASD) is important for early diagnosis by facilitating referral to intervention programs that can improve functional outcomes. Parents are well-positioned to identify early atypicalities pertinent to an ASD diagnosis. The study objective was to examine whether scores on a parent-reported questionnaire, the Brief Infant-Toddler Social Emotional Assessment (BITSEA), can predict ASD outcomes in a high-risk sibling population ('HR'; older sibling with ASD).

Methods: *Participants*: (1) HR siblings diagnosed with ASD at 36 months (HR-ASD; n=84), (2) HR siblings not diagnosed with ASD at 36 months (HR-N; n=227), and (3) Low-Risk toddlers (LR; without a family history of ASD; n=128). *Parent Report Questionnaire*: The BITSEA is a 42-item parent questionnaire that screens for social-emotional problems and delays in competence. The BITSEA, completed at 18 months of age, has six subscales: Problems, Social Competence, ASD Problems, ASD Social Competence, Total ASD Score, and Red flags. *Diagnostic Assessment*: All toddlers were assessed for ASD at 36 months. *Statistical Analyses*: Performance on the BITSEA was compared by outcome group (HR-ASD, HR-N, LR) using serial one-way ANOVAs. Post hoc assessment was completed using Benjamini & Hochberg (1995) corrections.

Results: All BITSEA subscales differentiated between the HR-ASD group and both HR-N and LR groups (qs < 0.039). Two subscales (ASD and BITSEA Social Competence) differentiated the HR-N and LR groups. Sensitivity and specificity of the Total ASD Screening Score (0.52, 0.84 respectively) suggests it is the best scale for prediction of ASD outcomes.

Conclusion: The BITSEA can differentiate toddlers who will be diagnosed with ASD by 18 months of age. It has utility in a primary care environment as a broadband screening tool for ASD or as a specialized tool to monitor risk for ASD in HR populations. This screener may help in the earlier identification of ASD, potentially supporting access to interventions aimed at remediating atypical development in children with ASD.

The Power of Partnership

Abstract #:   139
Presenter: Tony Ahn
Supervisor: Shannon Scott
Title: Development of an interactive infographic as a knowledge tool for pediatric procedural pain
Authors: Tony Ahn, Xuan Wu, Lisa Hartling, Shannon Scott
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Medical procedures carried out in the emergency department represent one of the most common sources of acutely painful stimuli for children. In many cases, pain and anxiety induced by these procedures could be better managed. Though many evidence-based interventions are widely available to manage procedural pain in children, they remain severely underutilized in pediatric conditions.

Infographics are an innovative, visually engaging strategy to communicate information and hold great potential for making health information more accessible and understandable to the general public. Interactive infographics are expected to make information sharing more engaging by introducing a sense of exploration, with the capacity to store more information compared to a traditional print infographic. This study developed an interactive infographic that aims to provide evidence-based knowledge to parents about how to manage pain and anxiety when their child is undergoing a common medical procedure—needle poke.

Methods:

An infographic was developed based upon a systematic review and a qualitative study on parent experiences and information needs relating to procedural pain in children. Our team's parent advisory group was consulted on the development of the prototype and their key feedback were incorporated in the final version. Currently we are completing usability testing at the Stollery Children's Hospital emergency department to assess parents' perceptions of the tool on 8 evaluation elements, including: 1) usability; 2) aesthetics; 3) language; 4) level of engagement; 5) quality of information; 6) length; 7) preference of form over traditional dissemination venues; 8) value-added. In addition we are also collecting user behavior data while parents navigate through the infographic.

Results/Discussion: We will share the results of our usability testing. Interactive infographics are beginning to emerge as an innovative intervention to enhance knowledge sharing to parents and caregivers.

The Power of Partnership

Introduction

Predicting energy expenditure (EE) in children in the pediatric intensive care unit (PICU) is difficult. The only accurate method to determine EE is indirect calorimetry, which is expensive and often unavailable. As a result, over and under-feeding is common. Over-feeding can cause fatty liver and increased CO_2 production, while under-feeding can cause malnutrition, and impair wound healing, immune function, and muscle strength. Developing a more accessible method to accurately predict EE of children in the PICU may result in better health outcomes.

Hypothesis

The objectives of this study were to determine a) which patient factors are predictors of measured EE, and b) if over or under-feeding is associated with ventilator or PICU days.

Methods

This retrospective study involved reviewing the electronic and paper charts of all non-cardiac patients who had measured EE by indirect calorimetry in the last 3 years (2014-16) at the Stollery Children's Hospital PICU. Variables recorded in the case report form (with an instruction manual) included general demographics, body size, and severity of illness information. Data was entered into a REDCap database. Outcomes were measured EE, ventilator days, and PICU days.

Results

We are in the process of finishing data collection. Univariate and multiple linear [for predicting measured EE] and logistic [for ventilator and PICU days] regressions will determine predictor variables. 100 consecutive patients were identified and included, with no exclusions. Combining our data with patients from Hospital for Sick Children will improve generalizability.

Conclusions

Predicting measured EE without indirect calorimetry has the potential to improve outcomes for children in the PICU by optimizing nutrition support. Future work should validate the developed prediction rule, and determine if it can improve outcomes for patients.

Introduction: The developing retina is supplied by the choroid and transient hyoid vasculature system. The hyaloid vasculature consists of transient blood vessels which regress in the mature retina. Failure of hyaloid vessel regression results in the development of a condition referred to as Persistent Fetal Vasculature (PFV) in newborns. PFV can lead to the development of additional secondary pathologies including cataracts, detached retina, and retinal folding. Neuropilins (*Nrp1* and *Nrp2*) are described as non-catalytic co-receptors for VEGF and class-3 semaphorins. They are critical for vascular and neuronal development. We have found phenotypic similarities between the *Nrp2* knock out (KO) mouse and human PFV. Given the importance of neuropilins in angiogenesis and migration, we hypothesized that Nrp2 may also be necessary for development of the embryonic retinal vasculature.

Methods: We used the Nrp2 KO mouse, of which both heterozygous and mutants are viable and fertile. To understand the temporal and spatial expression of *Nrp2* during ocular development, we performed immunostaining on E13, and E18 retina and X-gal staining (there is a β-galactosidase cassette present in the *Nrp2*-gene-trap mouse) on adults. To examine the overall histology of the eyes in postnatal *Nrp2* mutants, we performed H&E staining. We utilized Optical Coherence Tomography (OCT) to image *Nrp2* KO adult mouse eyes to investigate retinal lamination *in vivo*.

Results: NRP2 expression was found in the transient hyaloid vasculature and the choroidal vasculature at E13. At E18, NRP2 expression was observed in the ganglion cell layer (GCL) and in the remnants of the hyaloid vasculature. In the adult retina, X-gal expression was observed in the GCL as well as the inner nuclear layer. In the E13 *Nrp2* null retina, the neuroblastic layer was expanded and an accumulation of hyaloidal cells was observed in the vitreal space. By E18, a large retrolental mass is present in the vitreous and the GCL is expanded. The *Nrp2* KO eye had substantial retinal folding compared to the WT control. OCT revealed an expanded IPL, Retinal Pigmented Epithelium detachment and dysplasia near optic cup in *Nrp2* null retina compared to the WT controls.

Conclusions: The expression pattern of *Nrp2* suggests that *Nrp2* is required in multiple aspects of ocular development including the development of inner retinal cells and the hyaloid vasculature. Collectively, our results indicate that the loss of *Nrp2* expression results in significant ocular abnormalities including those are typically observed secondary to PFV such as microphthalmia and retinal folding.

The Power of Partnership

Introduction

Severe combined immunodeficiencies are a group of genetic disorders marked by complex clinical presentations and high mortality. We have characterized a new human immunodeficiency disorder in a First Nation family in which comprehensive clinical tests have failed to pinpoint a cause. Combining advanced next generation sequencing techniques we identified the candidate gene, a crucial molecule activating the NF-κB pathway. Upon stimulation, NF-κB translocates into the nucleus to activate immune genes in response to infection. We believe this pathway is impaired in the patient as we have already observed that patient derived fibroblast cells have decreased NF-κB nuclear translocation and lower protein level of the candidate gene compared to controls (carrier and wild type sisters' fibroblasts). We then addressed the following questions: are the candidate gene and other key players in the NF-κB pathway downregulated transcriptionally due to the mutation? Are target genes not activated in patient cells?

Methods

To answer these questions, we employed quantitative real time PCR to measure the transcript levels of selected key players in the NF-κB pathway and compare this expression between patient cells and controls.

Results

We found that whether stimulated or not, there were no significant differences in the transcript levels of the candidate gene and the selected players (NEMO, TAK1, UBC13) indicating they are are not downregulated transcriptionally due to the mutation. The target genes of the pathway involved in immunity (A20, IκBα and IL8) were upregulated significantly after stimulation in wildtype and carrier but not in patient cells.

Conclusion

This is the first time we show the functional consequence of our mutation is at a post-transcriptional level which results in perturbed activation of target genes and provide further evidence for how the mutation is contributing to the pathogenesis of this novel human disorder.

The Power of Partnership

Amarjot Padda (BSc)[1], Corriveau-Bourque, C (MD FRCPC)[1,2], Belletrutti, M (MD FRCPC)[1,2], and Bruce, A (MD FRCPC)[1,2].

[1]Faculty of Medicine University of Alberta, [2]Department of Pediatrics, Stollery Children's Hospital

Introduction: The Canadian Pediatric Society's position statement suggests children with sickle cell disease (SCD) may be at increased risk of complications during air travel and recommend oxygen on flights.There are several factors that may contribute this increased risk, including prolonged hypoxia, dehydration, temperature changes and stress. Current guidelines and evidence are variable and lack consensus.

Objectives:

1) Determine recommendations North American hematology health care providers (HCPs) make to SCD patients regarding air travel.

2) Determine what proportion of HCPs recommend supplemental oxygen to SCD patients.

3) Among HCPs that recommend supplemental oxygen, determine which patient factors influence their decision.

Methods: Using a cross-sectional online survey circulated through CanHaem and ASPHO listservs to North American hematology HCPs, participants were asked to share their air travel recommendations for the SCD population. A total of 81 surveys were returned with 79 evaluable for analysis (response rate 3.7%). Similarly, a patient survey regarding experiences with air travel was circulated through SCDAC listservs and discussion boards.

Results: Results show 82.1% of HCPs do not recommend the use of supplemental oxygen under any circumstance. Among providers recommending supplemental oxygen, 9% recommend it for all SCD patients, 6.4% for only $HbSS/SB^0$, 1.3% for both $HbSS/SB^0$ and HbSC and 1.3% for both $HbSS/SB^0$ and $HbSB^+$ patients. While the majority of respondents did not recommend supplemental oxygen, they did advise patients to increase hydration, carry analgesics, and wear warm clothes to prevent sickling complications. In a small sample of patients, many have experienced a sickle cell crisis during or shortly after air travel. The most common complication noted by patients is VOC.

Conclusion: The majority of HCPs are not routinely recommending supplemental oxygen to their SCD patients as a prophylactic measure to preventing sickling complications. Among HCPs that recommend supplemental oxygen, a number of patient and flight factors influence their recommendations.

The Power of Partnership

Abstract #:   144
Presenter: Alyson Campbell
Supervisor: Shannon Scott
Title: Pediatric parent advisory group (P-PAG): Involving parents in a research program
Authors: Shannon Scott, Xuan Wu, Alyson Campbell, Lisa Hartling
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: The Pediatric Parent Advisory Group (P-PAG) was developed in response to the growing shift towards patient-centred care that actively engages patients and their families in healthcare decision-making. The overarching purpose of the P-PAG is to provide advice, guidance and knowledge from a parent perspective to inform and improve research activities and initiatives in child health research in Alberta.

 Methods: Recruitment of P-PAG members started in June, 2016, targeting caregivers from within the catchment area of the Stollery Children's Hospital. The recruitment process involves 1) the research team posting a brief advertisement via various avenues, both online and offline; 2) parents who are interested to join P-PAG contact the research team for in-person meetings to further determine eligibility and fit. Recruited parents undergo a brief orientation and introduction to become familiar with the operations of the P-PAG. Supported by ECHO Research (Faculty of Nursing), ARCHE and Cochrane Child Health (Department of Pediatrics), P-PAG members volunteer their time and meet 5-6 times a year undertaking one or several of the following activities:

1) Evaluating digital information tools on common pediatric conditions for parents/families;
2) Providing input on research processes to develop resources and decision-making tools for parents/families, physicians, and nurses;
3) Providing input on how to involve parents/families in the research process;
4)Contributing to building the framework for a sustainable P-PAG.
We are also conducting a concurrent evaluation of the P-PAG involving regular, short, anonymous questionnaires, to ensure that the group meets the expectations of its members and that each member's voice is heard.

Results: So far, 14 members joined the group and 5 meetings have been held bimonthly. P-PAG has been actively contributing to various child health initiatives mentioned above. For example, P-PAG was instrumental in the creation and evaluation of several knowledge translation (KT) tools (videos and infographics) on pediatric procedural pain, acute otitis media, and fever. P-PAG members evaluated the KT tools based on a set of questions. The tools were then modified and adapted based on the feedback received from P-PAG and other key stakeholders. Additionally, P-PAG has been accessed by other researchers to take on roles such as collaborators on grant applications and advisors on research instrument development.

Conclusion: Family engagement is integral to children's health care. P-PAG's advice and direction to the research team are instrumental to ensure the application of research evidence is appropriate, relevant, and accessible by parents and families in Alberta.

The Power of Partnership

Abstract #:   145
Presenter: Lauren Albrecht
Supervisor: Lisa Hartling
Title: Knowledge Translation tools for parents on child health topics: A scoping review
Authors: Lauren Albrecht, Shannon D. Scott, Lisa Hartling
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: An emerging field of knowledge translation (KT) research has begun to focus on health consumers, particularly in child health. KT tools provide health consumers with research knowledge to inform health decision-making and may foster 'effective consumers'. Thus, the purpose of this scoping review was to identify previously published effectiveness research on child health-related KT tools for parents/caregivers.

Methods: A health research librarian developed and implemented search strategies in 8 databases. One reviewer conducted screening using pre-determined criteria. A second reviewer verified 10% of screening decisions. Data extraction was performed by one reviewer. A descriptive analysis was conducted and included patient-important outcome classification, WIDER Recommendation checklist, and methodological quality assessment.

Results: 7952 independent titles and abstracts were reviewed, 2267 full-text studies were retrieved and reviewed, and 18 articles were included in the final data set. A variety of KT tools, including single- (n=10) and multi-component tools (n=10), were evaluated spanning acute (n=4), chronic (n=5) and public/population health (n=9) child health topics. Study designs included: cross-sectional (n=4), before-after (n=1), controlled before-after (n=2), cohort (n=1), and RCTs (n=10). The KT tools were evaluated via single primary outcome category (n=11) and multiple primary outcome categories (n=7). Two studies demonstrated significant positive effects on primary outcome categories; the remaining studies demonstrated mixed effects (n=9) and no effect (n=3). Overall, methodological quality was poor; studies lacked a priori protocols (n=18) and sample size calculations (n=13). Overall, intervention reporting was also poor; KT tools lacked description of theoretical underpinnings (n=14), end-user engagement (n=13), and preliminary research (n=9) to inform the current effectiveness evaluation.

Conclusions: A number of child health-related KT tools have been developed for parents/caregivers. However, numerous outcomes were used to assess impact and there is limited evidence demonstrating their effectiveness. Moreover, the methodological rigor and reporting of effectiveness studies is limited. Careful tool development involving end-users and preliminary research, including usability testing and mixed methods, prior to large-scale studies may be important to advance the science of KT for health consumers.

The Power of Partnership

Abstract #: 146
Presenter: Jennifer Pillay
Supervisor: Lisa Hartling
Title: Benefits and harms of antipsychotics in children and young adults: Comparative effectiveness review with meta-analyses
Authors: Jennifer Pillay, Krhista Boylan, Normand Carrey, Amanda Newton, Ben Vandermeer, Megan Nuspl, Tara MacGregor, Robin Featherstone, Lisa Hartling
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: To review the evidence on first- (FGAs) and second-generation antipsychotics (SGAs) for the treatment of psychiatric and behavioral conditions in children and young adults (≤ 24 years). This review was conducted by our Evidence-based Practice Center, in partnership with the American Academy of Child and Adolescent Psychiatry.

Methods: A research librarian searched eight databases. We also searched conference proceedings, Drugs@FDA, trial registries, and reference lists. Two reviewers conducted study selection and risk of bias assessment independently, and resolved discrepancies by consensus. One reviewer extracted, and a second verified the data. We conducted meta-analyses when appropriate and network meta-analysis across conditions for changes to body composition. We rated strength of evidence for pre-specified outcomes.

Results: 135 studies (95 trials and 40 observational studies) were included. None of the evidence was rated as high strength of evidence. Across the five categories of conditions having findings with low or moderate strength of evidence (schizophrenia; bipolar, autism spectrum, tic, and ADHD/disruptive disorders), SGAs improve to some extent key intermediate outcomes for which they are usually prescribed. There may be limited benefit in treatment of depressive phases in bipolar disorder and for symptoms apart from aggression and conduct problems in ADHD. From network meta-analysis, olanzapine was more harmful for gains in weight and BMI than aripiprazole, quetiapine, and risperidone; results were mainly applicable to the short-term. Findings from pair-wise meta-analysis between different SGAs were similar, except for showing no short-term differences between risperidone and quetiapine, or different doses of aripiprazole, asenapine, or quetiapine. FGAs caused slightly less harm for weight and BMI compared with SGAs. There is probably little or no difference in risk for somnolence between different doses of asenapine or quetiapine. There was no significant difference in risk for mortality or prolonged QT interval in the short-term for SGAs as a class. SGAs versus placebo/no treatment increase short-term risk for high triglyceride levels, extrapyramidal symptoms, sedation, and somnolence.

Conclusions: The increased risk for several adverse effects with potentially long-term health consequences lends towards a fine balance of benefits and harms particularly in cases where alternatives exist. Our confidence in the findings from long-term studies was poor. Evidence was sparse for patient-important outcomes (e.g., health-related quality of life) and outcomes for young children (<8 years) and young adults (18-24). This review identified several areas for which the evidence is sparse and which are priorities for future research.

The Power of Partnership

Abstract #:   147
Presenter: Michele Dyson
Supervisor:
Title: The conduct and reporting of child health research: an analysis of randomised controlled trials published in 2012 and evaluation of change over 5 year
Authors: Michele Dyson, Lisa Hartling, Ben Vandermeer, Patrina Caldwell, Despina Contopoulos-Ioannidis, Sarah Curtis, Ricardo Fernandes, Terry Klassen, Katrina Williams, Allison Gates
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction. Randomised controlled trials (RCTs) provide the best evidence to guide clinical practice when carried out appropriately. Especially for pediatric populations, where the quantity of relevant data lags behind that of adults, there is a need for well-conducted and reported RCTs. For child health RCTs published in 2012, we aimed to: describe design and reporting characteristics and evaluate changes since 2007; assess the association between trial design or registration and risk of bias (RoB); assess the association between RoB and effect size.

Methods. We searched CENTRAL and selected a random sample of 300 child-relevant RCTs published in 2012. Two reviewers extracted design and reporting characteristics and assessed RoB using the Cochrane RoB tool. We analyzed trial design and reporting descriptively. We assessed changes in design and reporting from 2007 to 2012 (based on 300 RCTs previously analyzed by our group) using the Fischer's exact test. We tested for associations between RCT design and reporting characteristics and overall RoB and trial registration using the Fisher's Exact, Cochran-Armitage, Kruskal-Wallis and Jonckheere-Terpstra tests. We pooled effect sizes for 201 RCTs with available data using DerSimonian Laird random effects. We assessed differences in effect size by RoB using the chi-square test for subgroups in meta-analysis.

Results. The 2012 and 2007 RCTs differed with respect to many design and reporting characteristics. Compared to 2007, more 2012 RCTs used cluster designs (11% vs. 0%) and fewer used parallel designs (81% vs. 90%) (p<0.001). More 2012 RCTs reported the funding source (80% vs. 65%, p<0.001), specified a primary outcome (62% vs. 41%, p<0.001), and reported findings that favoured the experimental intervention (93% vs. 63%, p=0.007). Fewer 2012 RCTs were industry sponsored (21% vs. 35%, p=0.002). From 2007 to 2012, RoB did not change for random sequence generation and improved for allocation concealment (p<0.001). Fewer 2012 RCTs were rated high overall RoB and more were rated unclear (p=0.03). Only 7.3% of 2012 RCTs were rated low overall RoB. Trial registration doubled from 2007 to 2012 (23% to 46%) (p<0.001) and was associated with lower RoB (p=0.009). Effect size did not differ by RoB (p=0.43).

Conclusion. Random sequence generation and allocation concealment were not often reported, and selective reporting was prevalent. Measures to increase trialists' awareness and application of existing reporting guidance, and the prospective registration of RCTs is needed to improve the trustworthiness of findings from this field.

The Power of Partnership

Introduction

Incomplete information on exact patient age at or time of medical events of interest coarsens knowledge of the rate at which events occur and complicates analyses on the effect of covariates on this rate over time. Accurate estimates are clinically important in developing time- or age-sensitive public health initiatives and medical interventions. Our work investigates how these estimates of age-dependent effects, obtained from marginal regression with events recurring at interval-censored times, are affected by the partial availability of age-related information and assumptions regarding birthdate distribution.

Methods

Hu and Rosychuk proposed a method for the analysis of recurrent event data where incomplete subject birthdates, known only within an interval, make the exact age of subjects at events of interest unknown. Hu et al. applied this method to estimate the age-dependent effect of sex, socio-economic status, and location on the occurrence rate of emergency department (ED) visits for mental health by children at most 18 years old. We use the same method, model, and dataset of 41,159 ED visits by 27,947 individuals to investigate the effect of assumed birthdate distribution, sample size, and the number of recurrent events per patient on age-dependent effect estimates. Using a series of simulation studies, we repeatedly apply the method of Hu et al. while varying the assumed birthdate distribution and subsampling the full dataset, either randomly or by restricting data to subjects with exactly one ED visit. Where random subsampling is used, we examine the effect of sampling variability on time-dependent estimates.

Results

When using the full dataset, effect estimates are greatly similar regardless of the assumed birthdate distribution, except in a naive approach where the left or right birthdate interval endpoints are used as true subject birthdates. Effect estimates are found to deteriorate for sample sizes less than 10,000. The assumed birthdate distribution is more influential for smaller sample sizes when additional age information, such as subject age at fiscal year end, is not present in the data. The restriction to patients with exactly one event also greatly influences estimated effects.

Conclusions

Our studies suggest that assumed birthdate distribution does not greatly influence effect estimates for large datasets and that the assumption of uniformly-distributed birthdates is both a computationally efficient and suitable solution to restricted birthdate information. Our findings may be applicable in more general settings with other methods and motivate future work to establish sample size guidelines to ensure valid time-dependent effect estimation.

The Power of Partnership

Abstract #:   149
Presenter: Ashley Pik
Supervisor: Suzette Bremault-Phillips
Title: Trauma informed care for pregnant women post 2016 Fort McMurray wildfire
Authors: Ashley Pike, Suzette Bremault-Phillips, Joanne Olson, Emily Severson, Ashley Hyde, David M. Olson
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: The Fort McMurray Wood Buffalo 2016 wildfire was the most devastating natural disaster in modern Canadian history. 88,000 people were evacuated from the area, including approximately 1850 women who were pregnant or would soon conceive. The stress as a result of the evacuation, loss of homes and community had the potential to severely impact all those affected, especially the pregnant women and their children. In order for individuals to move on from this event, it was essential to address the trauma. Previous research demonstrated the effectiveness of expressive writing at helping to mitigate the impact of and resolve both acute and past trauma. The aim of this project was to examine both the impact of the wildfire on pregnant women and their children and the effectiveness of an evidence-based expressive writing intervention

Methods: Pregnant women who experienced the wildfire were randomly assigned to an expressive writing, neutral writing or no-writing group. Participants in the expressive writing or neutral writing groups were asked to complete four 15-minute writing sessions. Individuals in the expressive writing group were invited to write about their worst fears, changes in relationships, past traumatic experiences and trauma associated with the 2016 wildfire. Of particular interest is the question, "What is the most traumatic, upsetting experience of your entire life especially that you have never discussed in great detail?" The research team conducted linguistic and thematic analysis of participant responses.

Results: Preliminary results indicate that 64% (18/28) of the women who responded to the trauma-related question reported an incident other than the wildfire as being their most traumatic past experience. 20% of participants in the expressive writing group chose not to answer the trauma-related question (7/35). Qualitative themes discussed included the women's greatest fears, increased or decreased sense of social and emotional connectedness, post-traumatic stress experienced by the women, trauma related and unrelated to the fire and resilience practices and strategies used to help them cope with the evacuation and the aftereffects of the wildfire.

Conclusions: The preliminary results of this study highlight the importance of providing trauma-informed care, particularly when dealing with individuals following a natural disaster affecting a community or larger population. Utilization of interventions such as expressive writing can help individuals work through both acute and past trauma.

The Power of Partnership

Abstract #:   150
Presenter: David Olson
Supervisor:
Title: Prenatal and preconception subjective distress from the 2016 Fort McMurray wildfire in Canada: Comparison to other disasters
Authors: Suzanne King, Ashley Hyde, D.P. Laplante, Guillaume Elgbeili, David M. Olson
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Background: In May 2016, the wildfires around Fort McMurray (FMM), Alberta, Canada forced the evacuation of 88,000 people, including ~1,250 pregnant women and 600 more within a few months of conception. Other natural disaster studies document that prenatal or preconception maternal exposure to natural disasters can result in high levels of maternal objective hardship, subjective distress, and negative cognitive appraisals of the disaster; these can have negative effects on pregnancy outcomes and predict adverse developmental trajectories for the newborn, especially neurodevelopmental and metabolic. The 2016 FMM wildfire presents a new opportunity to replicate previous disaster studies, and to test a brief, online intervention. Our goal was to compare the level of subjective distress experienced by the FMM cohort with those observed in other disaster cohorts.

Methods: Subjects are women who were pregnant during the fire or who conceived since the fire. Recruitment commenced in November 2016 and is on-going, with approximately 200 women recruited by May 2017. Quantitative and qualitative data are collected via a secure online platform. Maternal subjective distress is measured at recruitment using the Impact of Event Scale – Revised to assess post-traumatic stress disorder (PTSD) symptoms, the Peritraumatic Distress Inventory, and the Peritraumatic Dissociative Experiences Questionnaire.

Results: Preliminary results find significantly higher maternal subjective stress relative to our other natural disaster cohorts. Nearly 40% of FMM women reported clinically significant levels of peritraumatic distress, with 42% reporting significant dissociative experiences, at the time of the crisis. These levels are 6.9 and 3.3 times higher, respectively, than those observed in our Queensland Flood cohort and 10.7 and 5.6 times higher than in our Iowa Flood cohort. PTSD symptoms were also significantly higher in our FMM cohort with 26.4% of women screening positive for PTSD, a rate that is 3 times higher than observed in our Project Ice Storm and 7.5 times higher than observed in the flood cohorts. We will report final cohort results.

Conclusions: Given these extreme stress levels, this research will improve understanding of the impact of prenatal stress on maternal and fetal outcomes. Preliminary results suggest that this is the ideal cohort on which to determine the effectiveness of a simple intervention in supporting maternal and fetal resilience. The findings of this study have the potential to inform decision-making and support use of a simple intervention following disasters.

The Power of Partnership

Introduction

Caesarean section (CS) rates are on the rise, both in Canada and other parts of the world. These increases are due to both an increase in primary CS as well as a decrease in vaginal births after caesarean (VBAC). Moreover, labour induction practices may also impact primary CS rate.

Objective

To examine temporal trends in overall CS rates, and repeat CS, and VBAC rates in non-nulliparous pregnancies in a population-based Alberta cohort.

Methods

The study is based on the Alberta pregnancy birth cohort which includes all live births in Alberta between 2005 – 2014. The cohort was developed by linking multiple administrative health databases, including hospitalization data, outpatient data, physician claims data, the Alberta Birth Vital Status registry, and the population health registry. The overall CS rate was calculated and repeat CS and VBAC rates were computed for second-time pregnancies with at least one previous CS in the study cohort.

Results

The study cohort consisted of 438,659 birth events of singleton term infants (≥ 37 weeks) of 289,025 women over the ten-year period. Overall, the CS rate increased from 24.76% to 27.71% with a slight increase in both scheduled CS and emergency CS rate from 8.68% to 10.89% and 16.08% to 16.82% In addition, there was a 1.3 times increase in induction of labour (23.66% to 30.79%). 186,754 (42.57%) birth events were of nulliparous women. The primary CS rate in the nulliparous group had increased from 27.91% to 30%. An increase in emergency CS (25.93% to 27.54%) and labour induction (28.33% to 39%) were also observed in nulliparous women. Among birth events (N=28,840) of women who had a previous CS the rates of repeat CS and VBAC were 83.56% and 16.43%, respectively.

Conclusion

There has been an increase in labour induction and CS rate, particularly the primary emergency CS over time in this population-based study. These statistics highlight the need to reframe the decision-making process in the management of labour induction with the ultimate aim to safely reduce CS rates and improve maternal and newborn health in the short and long term.

The Power of Partnership

Abstract #:   152
Presenter: Laura Reyes
Supervisor: Craig Steinback
Title: Sympathetic neurovascular regulation during pregnancy: A longitudinal case series study
Authors: Laura Reyes, Charlotte Usselman, Rachel Skow, Nisha Charkoudian, Jeffery Staab, Margie Davenport
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

The adaptations of sympathetic nerve activity (SNA) during pregnancy remain poorly understood. An increase in blood volume, cardiac output (Q) and SNA with a concomitant drop in total peripheral resistance (TPR), suggest that during pregnancy there is a reduced transduction of SNA into TPR. Additionally, sex hormones and volume regulatory factors such as vasopressin and the renin-angiotensin-aldosterone system have been shown to play a role in the control of sympathetic outflow in non-pregnant women. The role of these factors during pregnancy remains unknown. The objectives of this case report series were to determine the changes in sympathetic activity and reactivity along with hemodynamics and volume regulating factors before and throughout two healthy pregnancies

Methods

We conducted longitudinal assessments of SNA, hemodynamics, plasma sex hormones, vasopressin and aldosterone in two participants before pregnancy (early follicular phase [EF]); throughout their pregnancies (1st, 2nd, 3rd trimester [early and late]) and two-months postpartum. For all of their visits, participants were asked to abstain for 12 hours from caffeine, alcohol, and strenuous exercise and arrived at the laboratory at 8 am. Mean arterial pressure (MAP) and Q were used to calculate TPR. Sympathetic reactivity was subsequently assessed during a cold pressure test (CPT). Participants were asked to place their left hand in ice water up to their wrist for 3 minutes. SNA was measured using microneurography (peroneal nerve).

Results

There was a gestational-dependent increase in SNA burst frequency (r^2=0.96, p=0.009). Neurovascular transduction, however, decreased 53% in both women. Sympathetic hyperactivity was reversed in the postpartum whereas neurovascular transduction remained lower. During the CPT both participants had a gradual increase in SNA throughout pregnancy (BF increased 47% by the early third trimester) with a concomitant decrease in the systolic blood pressure response (41% by early third trimester). Regarding neurovascular transduction during CPT, we found that there was a decrease in the sensitivity of the vasculature to increases in SNA in early pregnancy, which increased by term. We found that there was a positive correlation of the SNA with aldosterone, vasopressin, estrogen and progesterone.

Conclusions

Pregnancy is characterized by a progressive increase in SNA together with a decrease in neurovascular transduction. We have identified significant associations between SNA, sex hormones and blood volume regulating factors across gestation that suggest that hormonal surges may be associated with a central sympathetic activation during pregnancy. Further studies to elucidate the mechanisms behind these associations are needed.

The Power of Partnership

Abstract #:   153
Presenter: Vivian Nguyen
Supervisor: Vivian Huang
Title: Breastfeeding increases colonic inflammation in infants from healthy moms, which effect is lacking in infants born from moms with IBD
Authors: Vivian Nguyen, Lindsy Ambrosio, Garett Dunsmore, Ambika Agrawal, Naomi Hotte, Leo Dieleman, Brendan Halloran, Karen Kroeker, Richard Fedorak, Shokrollah Elahi
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Breastfeeding (BF) is recommended for at least 6 months postpartum because of the beneficial components of breast milk. Studies show that there is a healthy inflammatory response (measured by fecal calprotectin (FCP)) in healthy full term BF infants. Whether this effect of BF on infant intestinal inflammation is affected by maternal IBD and IBD therapies is unknown. The objective of this study was to compare FCP levels in infants born to and BF by healthy mothers with those born to and BF by IBD mothers.

Methods: Mothers with IBD (CD or UC) and healthy mothers (HC) were consented to collect their infants' stool at delivery, post-partum 3, 6. FCP was extracted and measured by ELISA. BF status was documented as exclusively (EBF) or not exclusively breastfed (non-EBF). IBD medications (no medications, 5-ASA only, thiopurine, biologics) was documented.

Results: There were 21 (5 CD, 12 UC, 4 HC) PP3 months stools and 22 (5 CD, 10 UC, 6 HC) PP 6 months stools. Only 11 infants (4 CD, 4 UC, 3 HC) were exclusively BF until 6 months. As shown in Figure 1, at 3 months post-partum BF non-IBD infants have higher FCP than non-EBF infants or infants from IBD moms, the latter category irrespectively of BF or not. This effect of breastfeeding on infant FCP seems to disappear at 6 months post-partum. As shown in Figure 2, at PP 3, this lack of increased FCP in breastfed infants from IBD moms was not affected by oral 5-ASA or biologics, although the numbers are too small to draw definitive conclusions.

Conclusion: Infant intestinal inflammation is increased by breastfeeding among healthy infants, but not in IBD infants. Further investigation into the infants intestinal inflammation by maternal clinical disease activity, and IBD medications through breast milk are currently in progress.

The Power of Partnership

Introduction

Tetracyclines are known inhibitors of matrix metalloproteinases, important in placental and heart development. High dosage doxycycline in feed has been shown to cause murine placental anomalies and fetal loss. Despite this, many transgenic models use "Tet-On" gene constructs, due to their simplicity in facilitation of gene regulatory control. In preparation for experiments introducing a lentiviral Tet-On system into the murine placenta, we examined the potential for doxycycline to cause placental or fetal heart anomalies at dosage suitable for viral-induced Tet-On induction.

Methods

Seven FVB mice were superovulated with PMSG/HCG and treated from embryonic day 6.5 with either feed containing 200mg/kg doxycycline (Doxy, n=4 maternal mice, 37 fetuses) or usual feed (Ctrl, n = 3 maternal mice, 42 fetuses). Mice were weighed sequentially through gestation. Fetal echocardiography was performed under isoflurane anaesthesia on E11.5, E14.5 and E16.5 - 17.5. Before term, mice were euthanized, placental and fetal weights were taken, and samples were isolated. Data is reported as average of all fetuses and average of each pregnancy ± standard deviation. Student t-tests were performed.

Results

Maternal weight was significantly different at E16.5 (Doxy 36.3±2.8g, Ctrl 43±2.6g, p=0.022). The divergence in weight gain was evident by E11.5-E12.5 (Doxy 29±3.1g, Ctrl 33.3±1.2g, p=0.076). There were on average fewer fetuses in doxycycline treated maternal mice (Doxy 9.8±4.5, Ctrl 19.7±5, p=0.04). Fetal weight was not significantly different averaged by fetus (Doxy 540±100; Ctrl 550±116) or averaged by pregnancy (Doxy n =4, 574±119g; Ctrl n=3, 530±65g). Placental weight was increased when calculated by doxycycline treated fetuses (Doxy 54.5±8.9g, Ctrl 49.4±6.1 p=0.0034), but not by doxycycline treated pregnancies (Doxy 56.3±5.8, Ctrl 49.6±1.3 p=0.116). The placental: fetal weight ratio approached significance calculated by fetus (Doxy 0.104±0.025, Ctrl 0.094±0.023 p=0.0625) but not by pregnancy (Doxy 0.108±0.021, Ctrl 0.089±0.021 p=0.289).

Conclusion

This pilot data suggests there may be fewer fetuses and correspondingly less weight gain in doxycycline treated matenal mice at relatively low dose. Further work will focus on analysis of fetal echocardiographic findings, placental and fetal heart cytoarchitecture and MMP expression.

The Power of Partnership

Abstract #:   155
Presenter: Yuliya Fakhr
Supervisor: Denise Hemmings
Title: The effect of TNF-α on sphingosine-1-phosphate receptor expression in cultured trophoblasts
Authors: Yuliya Fakhr, Martina Mackova, Denise Hemmings
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Preeclampsia (PE) affects 5-7% of pregnant women and is manifested by de novo hypertension, proteinuria, and edema. Tumor Necrosis Factor-α (TNF-α), an inflammatory cytokine, is elevated in placental tissues of mothers with PE. In the placenta, TNF-α increases apoptosis and inflammatory cytokines and inhibits trophoblast syncytialization, all of which occur in PE. Sphingosine-1-Phosphate (S1P) is a bioactive sphingolipid that binds and signals through five S1P receptors (S1PR1-5). S1PR expression is changed in PE placental samples suggesting altered S1P signaling in PE. S1PR1 and S1PR3 mRNA and protein expressions are decreased in placental samples from women with PE compared to those without PE, while S1PR2 is increased. S1PR2 also induces secretion of pro-inflammatory cytokines by extra-villous trophoblasts. Addition of TNF-α to human endothelial cells increases S1PR2 protein expression. It is unknown how TNF-α affects S1PR expression in trophoblasts and whether this is linked to TNF-α-induced placental dysfunctions found in PE. Thus, our goal is to examine the effect of TNF-α on S1PR expression in trophoblasts to understand how TNF-α uses S1P signaling to contribute to pro-inflammatory cytokine release in term trophoblasts. We hypothesized that the addition of TNF-α to cultured term trophoblasts will increase S1PR2 protein expression.

Methods

Double immunohistochemistry staining of human term placentas was used to identify S1PR1, S1PR2, and S1PR3 in Cytokeratin 7 positive trophoblasts. We cultured BeWo cells, a term trophoblast cell line, in TNF-α concentrations ranging from 0 to 100 ng/mL for 24 hrs. The optimum concentration of 10ng/mL was then tested in a time course from 12 to 48 hrs. Cells were lysed, collected, and analyzed for S1PR protein expression by Western Blot with β-actin and α-Tubulin as housekeeping genes.

Results

S1PR1, S1PR2, and S1PR3 were detected in trophoblasts and endothelial cells in human term placentas from normal pregnancies. The addition of TNF-α at 10ng/mL to BeWo cells for 24 hrs decreased S1PR2 protein expression to half its original value. No changes were observed in the expression of S1PR1 and S1PR3. 10ng/mL was the lowest concentration to show a change in S1PR2 protein expression.

Discussion

In this study, we found that BeWo cells respond to TNF-α by reducing rather than increasing S1PR2 expression. BeWo cells, while often used to model trophoblast cells, are choriocarcinoma cells and may respond to TNF-α differently than primary cells. We will focus our future studies on primary trophoblasts isolated from placentas of women with and without PE.

The Power of Partnership

Abstract #:   156
Presenter: Pegah Firouzeh
Supervisor: Lesley Wiart
Title: Ankle foot orthoses in young children with Cerebral Palsy: A scoping review
Authors: Pegah Firouzeh, Lesley Wiart, Lyn Sonnenberg
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Ankle Foot Orthoses (AFOs) are used clinically to improve gait and prevent the development of tendoachilles contracture in children with cerebral palsy. While the focus of research for older children has been on outcomes associated with gait kinematics and kinetics, it is important to also consider the effects on outcomes other than gait for younger children. For example, children under the age of five years are more likely to move around on the floor and AFOs may adversely affect floor mobility. The purpose of this scoping review was to provide updated information on existing literature about the outcomes associated with AFO use for young children and find out what is known about AFO use patterns for young children with cerebral palsy.

Methods: We conducted a scoping review using Levac's six-stage process for scoping studies. Eight electronic databases were searched using the key terms cerebral palsy and ankle foot orthoses. Inclusion criteria were: Articles published in English language that evaluated the effects of AFOs with children with cerebral palsy aged 0 to 5 years 11 months. General information such as authors, year and country of publication, study design, aim of study, participant characteristics (i.e. age, CP sub-type and GMFCS levels) and interventions were extracted. In addition, outcome measures used in the studies were extracted and classified based on the domains of the International Classification of Functioning, Disability and Health (ICF).

Results: Eighteen articles met the inclusion criteria and were included in this scoping study. Of those 18 articles, 8 studies were evaluations of the effects of AFOs on gait, standing (n=3) and sit-to-stand (n=2), most often in clinical settings. Only one article focussed more generally on the gross motor skills of young children. The remaining 4 articles focused on compensatory strategies while wearing orthoses, day or night use of AFOs and the importance of joint alignments while constructing the ankle foot orthoses.

Conclusions: Additional research focussed on assessment of age appropriate outcomes including the effects of AFOs on transitional movements and functional floor mobility and participation in early childhood settings is needed. In addition, the role of ankle foot orthoses in the prevention of tendoachilles contracture in young children with cerebral palsy needs to be explored.

The Power of Partnership

Abstract #:   157
Presenter: Alex Su
Supervisor: Eric Parent
Title: The immediate effect of prone Schroth physiotherapeutic scoliosis-specific exercises on the curve angles of adolescents with idiopathic
                     scoliosis
Authors: Alex Su, Eric Parent, Michelle Goonasekera, Edmond Lou
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction:

Physiotherapeutic scoliosis-specific exercises (PSSE) show promise to prevent curve progression in adolescents with idiopathic scoliosis (AIS). PSSE's require complex postural adjustments and skepticism exists about the amount of in-exercise correction that patients can achieve. Additionally, the effectiveness of different PSSE instructions is unknown. Non-invasive quantification of spinal alignment during exercise is possible with 3D ultrasound imaging (US). Our goal was to determine the immediate effect of Schroth PSSE performed in the prone position on the lateral curve angles of participants with AIS trained in PSSE.

Methods:

Volunteers with AIS having completed at least three months of PSSE training in the Schroth Exercise Trial for Scoliosis (SETS) study were recruited from the Stollery Children's Hospital. The SETS study inclusion criteria were: 10 to 18 years of age, Cobb angles of 10 to 45°, and with or without a brace. Exclusion criteria were having undergone any torso or lower limb surgery.

Participants were imaged using a 3D US imager with location tracking during single sessions in a natural standing position within a stabilizing frame and four prone positions: natural, passively supported, with active Schroth corrections, and active Schroth corrections with psoas activation. A Schroth therapist guided exercises. Participants were scanned from C7 to L5 and images analysed using custom software. With training, a novice rater digitized the center of the laminae for each vertebra to extract the lateral thoracic and lumbar curve angles in each position. Differences between positions were compared using a repeated measures ANOVA with Sidak post-hoc comparison.

Results:

A total of 85 thoracic and 85 lumbar curves were identified from seventeen female participants (n=17) with a mean age of 15±3 years. Schroth curve types included: 4CP (n=14), 4C (n=2), and 3CP (n=1). Thoracic curve angles in standing (10±5°) were not significantly different than prone or prone with any Schroth corrections added. Lumbar curve angles in standing (13±8°) were significantly reduced (p<0.05) in prone passively supported (5±9°), Schroth corrected (3±7°), and Schroth corrected with psoas activation (5±9°). In comparison to standing, median lumbar curve angle decreases of 74% and 43% were found in the prone Schroth corrected and the prone Schroth corrected with psoas activation positions, respectively.

Conclusion:

Prone Schroth PSSE's provide immediate correction for lumbar curves but without significant effect on thoracic curves in individuals with AIS. Future research will compare other Schroth PSSE positions to inform clinical practice and determine if immediate in-exercise correction predicts long-term outcome.

The Power of Partnership

Introduction:

Adult Scoliosis (AS) is the most common spine deformity in adult population. Back pain is the main symptom that leads patients to seek medical consultation. Stabilization exercise has been reported to be effective in reducing back pain. The literature has not been reviewed to examine the effects of such exercises on back pain in adult with scoliosis.

Objectives: To evaluate the effect of the stabilization exercise on back pain and quality of life in adult with scoliosis.

Study design:

A systematic review.

Search method:

We conducted a systematic search in the following databases from inception up to March 9, 2017: Medline (OVID), CINAHL (EBSCO), Embase (OVID), SportDiscus (EBSCO) and Cochrane Central Register of Controlled Trials (CENTRAL).

Selection criteria:

Randomized controlled trials (RCTs), prospective controlled clinical trials, and retrospective controlled studies that compare core stabilization exercise to placebo, no treatment or any other type of treatment. Participants had to be diagnosed with AS and be 18 years of age or more. Studies with participants presenting any torso or lower extremity surgery, any injection in the last six months, any comorbidity that could affect the spine, red flags signs or with a history of spine trauma were excluded.

Results:

We found 908 articles, resulting in 630 articles after excluding duplicates. After screening the titles and abstracts, only 105 articles were included for full-text screening. A total of 98 full-text articles could be retrieved and after screening, only one article fit the selection criteria and was included in this review. The main reasons for exclusion were study design and patient population. The included study presented a low risk of bias for all criteria except blinding. Authors also did not report if the timing of assessments was similar between groups.

Conclusion:

Stabilization exercise, as reported in the included study, is shown to be effective in reducing back pain and improving quality of life in adults with scoliosis. However, this review highlights the paucity of literature examining the effect of exercise on back pain in adult with scoliosis and strongly suggests that further experimental research is needed.

The Power of Partnership

Abstract #:   159
Presenter: Kim-Cuong Nguyen
Supervisor: Lawrence Le
Title: Utrasonography versus CBCT for evaluating the alveolar bone level: A systematic review
Authors: Kim-Cuong Nguyen, Camila Pachêco-Pereira, Neelambar Kaipatur, June Cheung, Paul Major, Lawrence Le
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Background and Objective: The periodontium is a complex tooth-supporting structure consisting of four main components: the alveolar bone, cementum, gingiva, and periodontal ligament. Alveolar bone is the portion of the jawbone that holds the teeth in the mouth. Periodontitis or inflammation of the gingiva may result in bone loss and subsequent loss of teeth, if left untreated. Research has shown an association between periodontal disease and other diseases such as diabetes, cardiovascular, osteoporosis, and respiratory illness. Pregnant women are particularly vulnerable to periodontal disease due to hormonal changes during pregnancy. Research has also found that women with periodontal disease are at higher risk for delivering pre-term, low-birth-weight infants. The level of the facial alveolar bone is an important parameter for the diagnosis of periodontal disease. The current methods to evaluate the facial alveolar bone in human include flap elevation and cone-beam computed tomography (CBCT). However, these methods are either invasive or expose the subject to ionizing radiation. Therefore, medical ultrasound, which is non-invasive and free from ionizing radiation, has been investigated as an alternative imaging technique for alveolar bone. In order to assess the validity and reliability of medical ultrasound for evaluating the alveolar bone level in compared to CBCT, a systematic review was conducted.

Study Design: Seven databases were searched (PubMed, Embase, CINAHL, the Cochrane Library, LILACS, MEDLINE, and Web of Science) up to March 31, 2017. Studies addressing examination of alveolar bone level via CBCT and ultrasound were selected. There was no language restriction in database searches. Risk of bias under Cochrane guidelines was used as a methodological quality assessment tool.

Results: All the four included studies were *ex vitro* studies that used porcine or human cadaver samples. The alveolar bone level was measured by the distance from the alveolar bone crest to certain landmarks such as cemento-enamel junction or gingival margin. The risk of bias was found as low. The mean difference between ultrasonography and CBCT was from 0.07 mm to 0.68 mm, equivalent to 1.6% - 8.8%.

Conclusions: There is currently limited evidence to support a strong conclusion about the use of ultrasonography as compared to CBCT for the examination of alveolar bone level. Further studies comparing medical ultrasound to gold standard methods would be necessary to help validate the accuracy of this diagnostic technique in periodontal imaging.

The Power of Partnership

Abstract #:   160
Presenter: Tho Tran
Supervisor: Lawrence Le
Title: On the relationship between ultrasonic indicators and the gold standard bone mineral density for diagnosing Osteoporosis
Authors: Tho N.H.T. Tran, Phuong-Thuy T. Nguyen, Mauricio D. Sacchi, Jacob J. Jaremko, Lawrence H. Le
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Tho N.H.T. Tran[1], Phuong-Thuy T. Nguyen[1], Mauricio D. Sacchi[2], Jacob L. Jaremko[1], Lawrence H. Le[1,2]

[1]Department of Radiology and Diagnostic Imaging, University of Alberta

[2]Department of Physics, University of Alberta

Introduction: Osteoporosis is a skeletal disease characterized by low bone mass, deterioration of bone tissue, and cortical thinning, leading to high risk of fracture. Currently, dual energy X-ray absorptiometry (DXA), which relies on ionizing radiation to measure bone mineral density (BMD), is the gold standard for osteoporosis assessment. However, bone strength is not determined by bone mass only but also mechanical properties. This leads to studies for alternative osteoporosis diagnostic modalities which can reach a complete quantitative assessment of bone quality. Ultrasound has several advantages mainly due to its lack of ionizing radiation and its sensitivity to the mechanical elasticity of bone tissues. Recent preliminary studies using axial transmission technique, which uses a set of transducers positioned linearly along the bone axis, have shown that quantitative ultrasound is a valid modality for cortical bone quality assessment. The objectives of this study are to extract the ultrasonic velocity and attenuation information from the human tibia datasets and to correlate the ultrasonic indicators with DXA-BMD.

Methods: The ultrasonic data were collected at a Medical Imaging Consultant (MIC) clinic in Edmonton. A TomoScan Focus LT[TM] phased array ultrasound system (Olympus NDT Inc., Canada) was used for the data acquisition. Consents were obtained from the recruited volunteers, who had bone densitometry examinations. For each subject, ultrasonic data from the left midshaft tibia was acquired and analyzed.

Results: Data from 20 subjects aged 50 to 80 years were used for this pilot study. For each dataset, the transit times and amplitudes of the first detectable signals at the receiving probes were measured. The midtibial ultrasonic velocity and attenuation coefficient could then be estimated by linear regression. The cortical speed of sound was found to increase while cortical attenuation decreases with BMD, i.e. they are sensitive to osteoporosis-related changes in bone. This may be due to the cortex trabecularization leading to cortical thinning and increasing intra-cortical porosity.

Conclusions: The findings provide confidence to analyze the remaining subjects' data and to further examine the correlation between ultrasonic parameters and bone health. This will lead to a novel application of ultrasonic inspection technique in osteoporosis-related cortical thinning assessment and fracture risk prediction.

The Power of Partnership

Introduction: Measuring quality-of-life (QOL) for adolescents with idiopathic scoliosis (AIS), a lateral spine curvature, is recommended by research guidelines. Existing QOL instruments for scoliosis present limitations. The ISYQOL, developed in Italy, was shown to be appropriate in determining QOL for patients with AIS treated non-surgically. Our objective was to develop an English version of the questionnaire and compare its internal consistency and validity to other self-appearance questionnaires.

Methods: The Italian SYQOL was translated to English by consensus of four team members and reviewed by three Italian developers for compatibility with the original version. Thirty-nine consecutive volunteer females with scoliosis and over 10 years old were recruited from the Stollery Children's Hospital and surgeons' offices and asked to complete the English SYQOL, Scoliosis Research Society-22 (SRS-22), Spinal Appearance Questionnaire (SAQ), Body Image Disturbance Questionnaire for Scoliosis (BIDQS), and Trunk Anterior Asymmetry Scoliosis Questionnaire (TAASQ). These self-appearance questionnaires were completed using REDCAP prior to physician consult. Adequate internal consistency was determined using Cronbach alpha (over 0.7) and adequate validity was determined by Pearson correlation coefficient (over 0.5) between convergent constructs in SPSS.

Results: The mean age of the 43 participants was 17 ± 2yrs. Eighteen patients were under observation, thirteen received exercise treatment, nine had bracing, one received pain medication, and one considered surgery. All internal consistency estimates (Cronbach α) were over the 0.70 threshold (range 0.7 to 0.96) except the SAQ Shoulder (0.66), SRS22 function (0.59), and all TAASQ Breast subscores (0.00). The convergent validity of the translated SYQOL Spine Health score calculated in all participants was supported by Pearson correlation coefficients larger than 0.5 with all SRS-22 scores, BIDQS scores, all TAASQ scores unrelated to the breast, and with SAQ General, Curve, Waist, Shoulders, Kyphosis, Chest, Appearance, and Expectations. The validity of SYQOL Total score was also supported in participants with a brace by correlation coefficients over 0.5 for all SRS-22 scores, BIDQS scores, all TAASQ scores unrelated to the breast and with the SAQ General, Curve, Waist, and Expectations scores.

Conclusions: The English version of the ISYQOL shows good internal consistency and construct validity when compared to other self-appearance questionnaires. Its development, based on patient opinion and usage of Rasch scaling, supports that it may be more appropriate for measuring quality-of-life in patients with AIS treated non-surgically. To confirm that this questionnaire would be suitable for clinical use, we need to assess test-retest reliability, ceiling effects, and responsiveness.

The Power of Partnership

Abstract #:	162
Presenter:	Kelsea Drall
Supervisor:	Anita Kozyrskyj
Title:	Lack of postnatal multivitamin supplementation may be a risk factor for maternal postpartum depression
Authors:	Kelsea Drall, Justin Mahoney, Liane J Kang, Allan B Becker, Piushkumar J Mandhane, Stuart E Turvey, Padmaja Subbarao, Malcolm R Sears, James A Scott, Anita L Kozyrskyj
Affiliations:	University of Alberta
Research Activity:	Maternal and Infant Healthy Development

INTRODUCTION:

Generally, postpartum depression (PPD) affects around 13% of mothers. Depressive episodes not only reduce the mother's quality of life, but are linked to poor health outcomes in children including wheeze, obesity and atopic diseases. A precipitating factor for PPD may be the depletion of vitamin stores during pregnancy and breastfeeding. Reduced micronutrient intake, particularly B-group vitamins, vitamin D and iron, has previously been correlated with maternal PPD. In this study, we investigated the association between postnatal multivitamin use and PPD in Canadian mothers.

METHODS:

We identified 2,871 mothers with complete data from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. Mothers in this sample reported regular (2 or more days per week) postnatal vitamin, supplement and/or medication use during the first 3 months after childbirth. Additionally, mothers were asked to record depressive symptoms on scored-scales at 6 months and 1 year postpartum. Depressive symptoms were ascertained using the validated Centre for Epidemiologic Studies Depression Scale (CES-D). Chi-square analysis revealed the statistical relationship between PPD and multivitamin use.

RESULTS:

Of the 2,871 mothers, 43.1% reported regularly taking a multivitamin. The control group (remaining 56.9%) was comprised of those who consumed non-multivitamin supplements and/or medications. Of those mothers taking multivitamins, 18.7% experienced clinically significant depression (a score of 16 or greater on the CES-D scale) 6 months or 1 year after childbirth. The proportion of mothers who experienced depression was 1.5 times greater in the control compared to the multivitamin supplemented group ($p = 0.069$).

CONCLUSIONS:

Mothers who do not regularly take multivitamins appear to have a greater incidence of PPD compared to those taking multivitamin supplements. The evidence supporting this finding however, is inconclusive in this study and controversial in the literature. Confounding variables will be identified and assessed in future analyses. Further investigation could reveal a relationship between multivitamin use and PPD and ultimately improve outcomes for new mothers and their children.

The Power of Partnership

Abstract #:   163
Presenter: Marihan Lansing
Supervisor: Justine Turner
Title: Plasma Citrulline does not identify intestinal adaptation in neonatal piglet models of short bowel syndrome
Authors: Marihan Lansing, Pamela Wizzard, Celeste Lavallee, David W. Liam, Mitsuru Muto, Patrick N. Nation, Paul B. Pancharz, Ronald O. Ball,
                   Paul W. Wales, Justine M. Turner
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Premature infants are at risk of intestinal failure, most often due to necrotizing enterocolitis and short bowel syndrome (SBS). Parenteral nutrition (PN) is essential for these infants, however, is complicated by sepsis and liver disease and is costly. Therefore, early enteral autonomy, through intestinal adaptation, is critical. Currently, there are no direct in vivo methods to measure adaptation in babies on PN. Plasma citrulline (CIT) is a proposed biomarker for adaptation, due to its correlation with intestinal length. Our aim was to evaluate the utility of CIT relative to the histological gold standard measure of adaptation, jejunal villus length. We evaluated two SBS anatomical subtypes: a mid-intestinal resection with jejunoileal anastomosis, and a distal resection of the ileum and ileocecal valve, which in our experience exhibits minimal adaptation.

Methods: Neonatal piglets (2-4d) were randomly allocated to either: 75% mid small intestinal resection (jejunoileal/JI, n= 5), 75% distal small intestinal resection (jejunocolic/JC, n=9), or sham control (n=8). A jugular catheter was inserted for PN and a gastric tube for trophic enteral nutrition. At laparotomy day 7, small intestine length and weight were measured, followed by jejunal tissue collection for blinded histopathological assessment of villus height and crypt depth. Baseline and terminal plasma CIT were measured using DC/LC-MS. Statistical analysis included independent t tests, one-way ANOVA, and linear regression.

Results: Amongst all piglets, mean CIT declined from baseline; sham (-42 %), JI (-64%) and JC (-58%). Day 7 CIT correlated with intestinal length ($R2=0.34$; $p=0.003$) and mucosal mass ($R2=0.34$; $p=0.003$). For SBS piglets alone, CIT did not correlate with intestinal length ($p=0.7$), mucosal mass ($p=0.8$) or jejunal villus height ($p= 0.9$). JI compared to JC piglets demonstrated an increase in small intestinal length (+18.3 vs -15.9cm; $p<0.001$) and greater mucosal mass (187.2 vs 153.5mg/cm; $p=0.03$). However, CIT did not differ between the SBS groups (729.0 vs 785.9 pM; $p=0.6$).

Conclusion: In neonatal piglets' plasma citrulline levels correlate with large differences in small intestinal length, and hence 'identify' SBS. However, citrulline did not discriminate between JI and JC surgical anatomy and failed to identify adaptive changes that were occurring in JI animals. Therefore, in this preclinical model of SBS, citrulline was not a useful biomarker of intestinal adaptation.

The Power of Partnership

Background: Current methods evaluating food marketing to children often study only a single marketing channel or type. As the World Health Organization urges the removal of unhealthy food marketing in children's settings, measurement methods that comprehensively explore the nature and extent of food marketing within a setting from multiple marketing channels and types may be needed. This study aimed to develop a novel theoretically grounded settings-based audit tool that could reliably and validly measure the exposure and power of food and beverage marketing to children in recreational sport settings.

Methods: The Food and beverage Marketing Assessment Tool for Settings (FoodMATS) was developed and pilot tested in five public recreation and sport facilities (sites) and subsequently used in 51 sites across Canada for a cross-sectional analysis of food marketing. In all sites, raters recorded the count of food or beverage marketing instances, presence of child-targeted, and sports-related marketing techniques, and the physical size of the marketing instance. Inter-rater reliability was tested for agreement using pilot data between raters using percent agreement, Cohen's kappa (κ) and intra-class correlations (ICC). Marketing instances were classified by unhealthfulness after data collection. Each site was scored using an algorithm that represented the theoretical impact of the marketing environment on food preferences, purchases, and consumption. Higher FoodMATS scores represented sites with higher exposure and more powerful (unhealthy, child-targeted, sports-related, large) food marketing. Construct validity of the scoring algorithm was tested through Pearson's correlations between FoodMATS scores and facility sponsorship dollars, and (2) prediction of unhealthy food sales from FoodMATS scoes via sequential multiple regression.

Results: Inter-rater reliability was very good or excellent (κ=0.88-1.00, $p<0.001$; ICC=0.97, $p<0.001$). There was a strong positive correlation between FoodMATS scores and food sponsorship dollars, after controlling for facility size ($r=0.86$, $p<0.001$). The FoodMATS score explained 14% of the variability in "Least Healthy" concession food sales ($p=0.012$) and 24% of the variability total "Least Healthy" food sales ($p=0.003$), but did not predict unhealthy vending sales.

Conclusions: FoodMATS has high inter-rater reliability and construct validity. FoodMATS scores were strongly correlated with food sponsorship and predicted "Least Healthy" sales. As the first validated tool, the FoodMATS presents a novel opportunity to comprehensively track change in food marketing environments and may be valuable in monitoring the impact of regulatory interventions. With the forthcoming restrictions on marketing to children in Canada, the FoodMATS may prove to be a fundamental ingredient in designing and monitoring effective regulatory interventions.

The Power of Partnership

Abstract #:   165
Presenter: Kaiyuan Yang
Supervisor: Benjamin Willing
Title: The impact of early-life antibiotics on pancreatic islet development
Authors: Kaiyuan Yang, Janelle Fouhse, Erinn Mills, Catherine Chan, Benjamin Willing
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Antibiotic-induced alterations in gut microbiota, may greatly affect host metabolism, especially during postnatal period. Epidemiological studies have associated antibiotic usage during the first months of life with greater risk of metabolic diseases later in life. Experimental research has identified the role of gut microbiota in mediating this effect. Using a piglet model, we demonstrated that early life amoxicillin treatment led to a transient change in microbes that was associated with reduced glucose tolerance well after antibiotic withdrawal. Nonetheless, it remains to be elucidated how host postnatal development is affected by an antibiotic-altered microbiota. Therefore, the aim of the present study is to characterize the developmental changes in islets induced by postnatal antibiotic-exposure in a well-established piglet model.

Methods

Neonatal piglets (N=7/group) received amoxicillin (ANTI, 30mg/kg/day) or placebo (CON) from post-natal day (PND) 0-14. Blood and pancreases were collected at PND 7, 14, 49 to assess GLP-1/insulin/glucose levels, beta-cell area, islet function and relevant gene expression.

Results

At PND7, ANTI pigs had elevated active GLP-1 concentrations in plasma, although no changes in plasma insulin or glucose were observed. In isolated islets from PND7 ANTI pigs, there was upregulated gene expression of GLP1 receptor, syntaxin-1a (important for insulin exocytosis), enzymes for insulin/glucagon processing and proglucagon, but not insulin. Islet insulin secretion upon glucose stimulation was not different from CON at PND7.

At the end of the antibiotic treatment (PND14), ANTI pigs had greater beta-cell area and their islets secreted more insulin with glucose-stimulation even though the changes in gene expression mentioned above disappeared; however, expression of genes important to beta-cell development and function (PDX1 and IGF2) were decreased as well as transporters for glucose and short-chain fatty acids.

At PND49, ANTI pigs had reduced beta-cell area, and their islets had similar insulin secretion with glucose-stimulation compared with CON, but a decrease in islet insulin content, indicating a reduction in beta-cell function. Meanwhile, ANTI showed increased plasma insulin concentrations but no change in blood glucose, which is an indication of insulin resistance compared to CON.

Conclusion

Pancreatic islets appeared to be expanding more rapidly in response to antibiotic treatment, however might not be functionally intact as indicated by reduction in pdx-1. Postnatal antibiotic exposure altered the development of islet/beta-cells, which may have a crucial impact on host metabolic health later in life.

The Power of Partnership

Introduction: Crohn Disease (CD) is an inflammatory bowel disease that can have detrimental effects on the growth and quality of life of pediatric patients. A concrete cause of CD is yet to be determined and no cure exists. Exclusive enteral nutrition (EEN) has been shown to be as effective as steroids in management, without the negative side effects, but can be challenging to adhere to. Based on work in mice, we hypothesized that previous diet can help predict response to EEN therapy in pediatric CD, which would enable clinicians to predict patient response to EEN and stratify treatment at diagnosis.

Methods: Data from Food Frequency Questionnaires (FFQ) collected by the Edmonton Pediatric IBD Clinic (EPIC) was used to assess dietary intake from the year before diagnosis. Each FFQ line was categorized to a food group and the percentage a food group contributed to an individual's diet was calculated in excel. Four dietary patterns were determined, and patients were divided into quintiles and halves according to percent intake of each food group. Patient data on course of disease and treatment was prospectively collected by EPIC and used to determine time points on EEN therapy, in order to define response to EEN and more long-term clinical outcomes. Response to EEN was measured by failure (defined as requiring additional, unplanned medication); change in physician global assessment; and PCDAI score.

Results: Ninety-six IBD patients were included; 34 with CD on EEN. A previous diet high in sugar-based carbohydrates was found to increase risk of failure on EEN($p=0.0093$). A high fruits and vegetables diet had a trend towards increased likelihood of success ($p=0.0583$). Diet high in processed meats increased short term response to therapy ($p=0.0397$), when response was measured using PCDAI scores.

Conclusions: This pilot project has shown variation in response to EEN associated with previous diet, indicating that aspects of diet before diagnosis may be able to predict response to EEN. A high intake of processed meats in previous diet may be associated with an initial response to therapy due to a more drastic change in diet and nutrition. Further research with a larger population size will be beneficial to confirm results. Other dietary approaches are being tested, which may have similar predictors of response.

The Power of Partnership

Justin J Mahoney[1*], Sarah L Bridgman[1], D.S. Guttman, A.B. Becker, P.J. Mandhane, S.E. Turvery, P. Subbarao, M.R. Sears, J.A. Scott, A. L. Kozyrskyj[1,2]

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INTRODUCTION

The objective of this analysis is to investigate the factors that influence increased propylene glycol levels in faecal samples of infants at 3 to 4 months. Initially, a pilot study of 17 infants enrolled in the **Canadian Healthy Infant Longitudinal Development (CHILD)** general population cohort was conducted. Metabolic profiling of faecal samples taken at a mean age of 14.8 weeks was conducted using **nuclear magnetic resonance (NMR). S**ignificant differences in several metabolites, including propylene glycol, was observed between breastfed and non-breastfed infants. Much higher levels of propylene glycol were observed in breastfed infants.

METHODS

This study involved 237 infants, 87 of whom breastfed exclusively, 92 partially and 58 of whom did not breastfeed at all. Infants were selected from 3 sites including Winnipeg, Edmonton and Vancouver and were a subset of the general cohort of the Canadian Healthy Infant Longitudinal Development (CHILD) Study. Metabolic profiling of infant stool samples collected at ages ranging from 3 – 4 months was conducted using nuclear magnetic resonance (NMR). Subsequently, propylene glycol levels were analyzed. Wilcoxon signed-rank test and Kruskal Wallis tests to compare propylene glycol distributions between groups.

RESULTS

Propylene glycol levels of exclusively breastfed infants had a mean of 697uM and median of 322uM; partially breastfed had a mean of 479uM and median of 114uM; non-breastfed infants had a mean of 128uM and median of 35uM. By recursive partitioning of data to generate a regression tree, using *Breastfeeding Status, Maternal Medication* and *Infant Medication* to predict *Propylene glycol*, the 237 individuals were placed into 1 of 5 groups according to propylene glycol level.

CONCLUSION

Propylene glycol levels from groups 1 through 5 are as follows: 122uM (n=57), 271uM (n=82), 551uM (n=79), 2248uM (n=8), 1953uM (n=11). Statistical tests pending.

The Power of Partnership

Abstract #:   168
Presenter: Ane Sofie Kokkvoll
Supervisor:
Title: Long-term outcomes in treating childhood obesity: Three-year results from the Finnmark Activity School study - a randomized controlled trial
Authors: Ane Sofie Kokkvoll, Sameline Grimsgaard, Lars Bo Andersen, Trond Flagstad, Inger Njolstad
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Many efficacy and effectiveness trials that applied lifestyle and behavioral interventions for treating childhood obesity have reported reductions in weight-related outcomes; however, evidence of long term sustainability and health improvements is less clear. The objective of this study was to compare changes in weight-related outcomes and cardiometabolic risk factors across two intervention groups (single-family care *versus* multi-family care), one-year after families completed the intervention.

Method: Children (aged 6-12 with severe overweight or obesity) from the two northernmost counties in Norway were randomised to either single-family intervention (n=49) or multiple-family intervention (n=48) in a parallel design. The single-family intervention included counselling by a paediatric nurse, paediatric consultant physician and nutritionist at the hospital, follow-up care was provided in the community by a public health nurse (10.5 hours of contact-time). The multiple-family intervention included group based meetings with other families, support from a multidisciplinary team at the hospital, weekly physical activity sessions in their communities and a 3-day family camp (119 hours of contact time). The trial started in April 2009 with a two-year intervention phase followed by one-year follow-up. Primary outcome assessors were blinded to group assignment. Changes in BMI and BMI standard deviation score (SDS; primary outcomes) and cardio metabolic risk factors (waist circumference, blood pressure and laboratory data; secondary outcomes) were analysed using linear mixed models.

Results: Over the three-year study period, BMI increased by 3.0 kg/m² in children from single-family group and by 2.1 kg/m² in children from the multiple-family group; no between group differences were detected, (p= 0.1). BMI SDS decreased -0.13 units in the single-family group and -0.24 in the multiple-family group, (p=0.15). HDL-C decreased by -0.17 mmol/ L in the single-family group and increased by 0.01 mmol/L in the multiple-family group, (p< 0.01). Insulin increased by 72 pmol/L in the single-family group and decreased by -44 pmol/L in the multiple family group, (p=0.04). When data from both intervention groups were pooled we found decreases in total cholesterol (-0.57 mmol/L; p<0.001), LDL-C (-0.52 mmol/L; p< 0.001) and BMI SDS (-0.19 units; p< 0.001). Retention was 81 % and 64% at two- and three-year follow-up, respectively.

Conclusion: No between-group differences in BMI or BMI SDS were detected at three years follow-up. Between-groups differences in children's HDL-C and insulin were observed in favor of the multiple family group. Pooled data from both intervention groups showed significant improvements in BMI SDS, total cholesterol and LDL cholesterol.

The Power of Partnership

Abstract #:   169
Presenter: Lisa Shulman
Supervisor: Yan Yuan
Title: Extending functional principal component analysis to model weight gain and fat mass accretion during pregnancy
Authors: Lisa Shulman, Linglong Kong, Yan Yuan
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction

Normal physiological adaptations favour weight gain and fat accretion during pregnancy to support fetal growth, followed by postpartum weight loss and fat mobilization to meet increased maternal energy demands during lactation. It is well-known that the risk of poor maternal and fetal health outcomes increases when women gain either too little or too much weight during pregnancy. Previous study has used the functional principal component analysis (FPCA) approach and successfully estimated individual weight trajectories in pregnant women. However, it ignored women's pre-pregnancy body mass index (BMI). In this study, we address the limitations by extending FPCA to incorporate additional BMI category-specific principal components. We then use this new method to estimate individual weight and fat trajectories during pregnancy and early postpartum.

Methods

Weight and fat mass data during pregnancy and early postpartum were collected from a large cohort (n = 1649) of pregnant and postpartum women. Longitudinal weight measurements were irregularly spaced and obtained from multiple data sources. Longitudinal total body fat mass were derived from skinfold thickness measurements at standard anatomical sites at different time points.

Results

Trajectory modeling of gestational weight and fat accretion indicates that our new method results in a significant improvement in explaining the weight and fat mass variation. Furthermore, our approach successfully captures differences in GWG patterns among different pre-pregnancy BMI categories: in particular, we find that the weight trajectories for women with pre-pregnancy obesity are more gradually rising than those for women with lower pre-pregnancy BMI.

Conclusions

We present an extension of the FPCA method that provides a better fit to individual gestational weight and fat gain trajectories than the original FPCA approach. Our results highlight the differences in body composition changes between pre-pregnancy BMI categories.

The Power of Partnership

Abstract #:   170
Presenter: Nadia Browne
Supervisor: Geoff Ball
Title: The readiness and motivation interview (RMI-Family) for families managing pediatric obesity: Preliminary findings
Authors: Nadia E Browne, Josie Geller, Nicholas Spence, Kathleen O'Connor, Suja Srikameswaran, Joanna Zelichowska, Josephine Ho, Rebecca Gokiert, Valerie Carson, Nicole Gehring, Heidi Virtanen, Cheyanne Hinkley, Louise C Mâsse, Katherine M Morrison, Jennifer L Kuk, Nicholas L Holt, Geoff DC Ball
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: To assess motivational factors in youth with obesity and their parents[1] before initiating pediatric weight management, we developed a structured interview – *The Readiness and Motivation Interview for Families – RMI-Family*. We piloted the RMI-Family to (*i*) determine the feasibility and acceptability of the *RMI-Family* and (*ii*) describe preliminary findings.

Methods: From November 2016 to June 2017, we recruited and enrolled youth aged 13-17 years with obesity (body mass index [BMI] ≥95th percentile) and their parents from two tertiary-level, multidisciplinary pediatric weight management clinics in Edmonton and Calgary. The RMI-Family, which was administered by interviewers who were trained in motivational interviewing techniques, was completed (independently) at two time points by youth-parent dyads. Interview questions probed motivational constructs known to be relevant in previous work for youth and parents regarding changes to diet and physical activity habits in youth. Using the RMI-Family interview, youth rated their perceptions of *importance* and *difficulty* regarding change; parents rated their perceptions of *importance*, *influence* and *confidence* regarding their youth making change. Sociodemographic, anthropometric, lifestyle habits, and psychosocial functioning data were also measured. Feasibility and acceptability of the RMI-Family were determined by the number of families enrolled and recruited, and oral feedback after each interview.

Result: Youth (n=4 girls; n=2 boys) were 15.8±1.1 years old and most (n=5) met the criteria for severe obesity (BMI ≥99th percentile). Parents (n=6) were mainly biological parents (n=5), female (n=4), and had average household incomes ≥$70,000 (n=5). At time 1, based on data from the RMI-Family, youth rated greatest *importance* to changing their sleep habits and lowest *difficulty* to reducing their intake of treat foods. Parents reported greatest *importance* to changing their youth screen time, sleep, and overeating as well as having greatest *influence* and *confidence* in reducing the intake of treat foods for their youth. At time 2, youth ratings remained largely unchanged, while parents rated having greatest *influence* on and *confidence* in changing emotional eating for their youth. Feasibility was low for the RMI-Family (n=6/110; 5%), but the tool was acceptable to measure motivation among families.

Conclusions: Our preliminary data suggest that the RMI-Family interview was an acceptable tool to measure motivation among youth with obesity and their parents. The 'full' study is designed to extend these findings, which will include assessing the psychometric properties of the RMI-Family and examine its utility in predicting clinical outcomes in this population.

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[1] Adults who self-identified as the youth's primary caregiver are referred to as 'parents'.

Abstract #:   171
Presenter: Tianna Clarke
Supervisor: Robin Clugston
Title: Sex as a biological variable: Comparing vitamin A status in male and female BALB/c mice
Authors: Tianna Clarke, Niranjanaa Shenoy, Robin Clugston
Affiliations: University of Alberta
Research Activity: Maternal and Infant Healthy Development

Introduction: In the past, research has been conducted without consideration of sex as a variable, although it has been shown to be imperative to many disciplines. When failing to consider the sex of a sample being studied, valuable information may be lost or misinterpreted. Organisations providing research funds have been stressing this factor because samples coming from the female sex in the past have been underrepresented, and as a result, there have been significant consequences in the interpretation of the data. For example, clinical trials with various drugs have shown complications due to incompatibility with the female population. The Clugston lab has a strong focus on the role of vitamin A and its contribution to health and disease. Thus, a richer understanding of the way in which sex impacts vitamin A status in male and female BALB/c mice could provide beneficial information for the future translational research.

Methods and Results: To comprehend the differences within the vitamin A metabolic pathway between the two sexes, various genes were examined using qPCR. Of those genes, CRBP1 (Cellular retinol binding protein 1) and RXRα (Retinoid X receptor α) were found to be statistically significant between the males and females. High-pressure liquid chromatography (HPLC) was also used to quantify the retinoid content in multiple tissues, including mouse lung, liver and plasma. This HPLC data showed no significant variation in the vitamin A status between the sexes.

Conclusion: Our data indicate that in the context of vitamin A status, there appears to be no notable difference between male and female BALB/c mice. However, the significance of sex as a biological variable should be further investigated within the research of other disciplines.

The Power of Partnership

Introduction: Nuclear acid modifications is related to the development of T2DM. Fat mass- and obesity-associated (FTO) protein, an RNA demethylase, has been associated with T2DM and obesity. Here, we investigated the RNA methylation in T2DM patients and a T2DM animal model.

Materials and Methods: Whole blood samples (WBSs) from T2DM patients (n=88) and healthy individuals (n=92) as well as T2DMSprague-Dawley (T2DMSD) rats were collected. The liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS) method was performed to detect the N6-methyladenosine (m6A) content in RNA from the WBSs. RT-qPCR was used to examine the mRNA levels of FTO, alkB homolog 5 (ALKBH5), methyltransferase-like-3 (METTL3), -like-14 (METTL14) and Wilms tumor-1-associated protein (WTAP) genes. We screened for 4 FTO single-nucleotide polymorphisms (SNPs).

Results: In T2DM, the m6A content in the RNA from T2DM was lower compared to controls ($P=2.6 \times 10\text{-}24$). Similar results were seen in T2DMSD-rats ($P=0.001$). FTO mRNA was higher in T2DM than the controls ($P=0.0007$). We found no difference in the distributions of the four SNPs. METTL3, METTL14 and WTAP mRNAs were higher in T2DM than controls. METTL3 and METTL14 mRNAs only were also higher in T2DMSD-rats ($P<0.001$). METTL14 mRNA level was negatively correlated with m6A contents ($r=-0.258$, $P=0.001$).

Conclusions: M6A can characterize T2DM and the increase of FTO could be responsible for the reduction of m6A in T2DM. FTO mRNA may be a novel potential biomarker of T2DM and METTL14 seems to play a central role in the methyltransferase complex.

The Power of Partnership

Introduction: 10% of newborns require help to initiate effective breathing immediately after birth. Respiratory support in the form of positive-pressure ventilation (PPV) delivers an adequate tidal volume to facilitate lung aeration and gas exchange for these infants. The effectiveness of PPV is currently assessed by monitoring heart rate and oxygen saturations; however these parameters only indirectly evaluate gas exchange. Recently, the use of exhaled carbon dioxide (ECO_2) has been described as a potential indicator for lung aeration, and thus might be helpful to guide respiratory support in the delivery room (DR). We aimed to assess how mask leak and airway obstruction affects ECO_2 measurements during respiratory support in the DR.

Methods: Deliveries of 100 premature infants (<33 weeks of gestation) needing PPV were attended by the research team. A flow sensor was placed between the T-Piece and the ventilation device to record various respiratory parameters (e.g. tidal volume, mask leak, airway obstruction). A breath-to-breath analysis was performed to assess tidal volume, airway pressures, gas flow, and ECO_2 on breaths delivered by PPV. Mask leak and airway obstruction were extrapolated from these values.

Results: Measured ECO_2 will be correlated to mask leak and airway obstruction for each infant, and statistical analysis will be performed to determine the presence of associations between these parameters.

Conclusion: We hope that the results of this study will shed light on the use of ECO_2 as an assessment tool for mask leak and airway obstruction during PPV and whether its use as part of respiratory support in the DR will be beneficial to neonatal resuscitation.

The Power of Partnership

INTRODUCTION: International guidelines provide conflicting recommendations on how to use bronchodilators to manage childhood acute wheezing conditions in the emergency department (ED), and there is variation within and among countries in how these conditions are managed. This may be reflective of uncertainty about the evidence.

METHODS: This overview of systematic reviews (SRs) aimed to synthesize, appraise, and present all SR evidence on the efficacy and safety of inhaled short-acting bronchodilators compared to any appropriate comparator to treat asthma and wheeze exacerbations in children 0-18 years presenting to the ED. Short-acting bronchodilators included short-acting beta-agonists (SABA), short-acting anticholinergics (SAAC), and magnesium sulphate, and could be administered intermittently or continuously via metered-dose inhaler or nebuliser. Searching, SR selection, data extraction and analysis, and quality assessments were conducted using methods recommended by The Cochrane Collaboration.

RESULTS: Thirteen SRs containing 56 relevant trials and 5526 patients were included. Using metered-dose inhaler with spacer compared to nebuliser to deliver SABA reduced hospital admission in younger children (< 3 years) by 44% (RR: 0.56; 95% CI: 0.38 to 0.82) and ED length of stay in older children (> 3 years) by 33 minutes (MD: -33.48; 95% CI: -44.32 to -23.65). Compared to SABA alone, SABA+SAAC reduced hospital admission in older children by 27% (RR: 0.73; 95% CI: 0.63 to 0.85). Compared to SAAC alone, SABA+SAAC reduced hospital admission in older children by 74% (RR: 0.26; 95% CI: 0.07 to 0.92). Continuous compared to intermittent nebulization, addition of magnesium sulfate to SABA, and levosalbutamol compared to salbutamol did not reduce risk of hospital admission and/or ED length of stay in older children.

CONCLUSIONS: This comprehensive synthesis of extensive SR evidence provides a solid base for guideline recommendations. Results demonstrate the efficacy of SABA delivered by metered-dose inhaler as first-line therapy for younger and older children. SAAC should be added to SABA for older children in severe cases. Continuous nebulization, addition of magnesium sulfate to SABA, and levosalbutamol compared to salbutamol cannot be recommended in routine practice.

The Power of Partnership

Introduction: Breathing is most vulnerable to apneas and other disturbances during sleep in both humans and rodents, especially in the newborn period. We recently demonstrated in adult rats that, in contrast to the atonia typical of skeletal muscles during rapid eye movement (REM) sleep, the normally passive expiratory muscles become active, and their activity is associated with stabilization of breathing and increased ventilation.

Methods: In this study we investigated the relationship between respiration and expiratory muscles recruitment across sleep states during the first two weeks of rat postnatal development. We instrumented rats with EMG electrodes in neck and abdominal muscles while sleep states (active and quiet sleep) were classified based on nuchal muscle tone and overt behavior inside a whole-body plethysmograph.

Results: Our results indicate that breathing was most irregular in active sleep and that rats displayed frequent recruitment of expiratory muscle activity, which occurred in both active and quiet sleep states. While the occurrence of active expiration in quiet sleep did not affect ventilation and its frequency decreased with age, the recruitment of expiratory muscles during active sleep was present across development and it was associated with a reduction in respiratory variability and an increase in ventilation.

Our results further demonstrate that the onset of abdominal recruitment in active sleep across development is associated with respiratory stabilization and potentiation of ventilation. We conclude that the occurrence of active expiration is a common feature of respiration in the postnatal period and it significantly contributes to ventilation, in particular in active sleep.

The Power of Partnership

Introduction

Congenital central hypoventilation syndrome (CCHS) is a genetic disorder that is caused by the mutation of the paired-like homeobox 2b (PHOX2B) gene, a transcription factor that is important for neural development of several classes of neurons in the brainstem. This mutation in turn causes the inability to maintain proper ventilation of the lungs (and thus blood) during sleep, and in the most dramatic cases, even during wakefulness. There is no effective cure for the disease and the only possible treatment is mechanical ventilation or diaphragm pacing. In addition, common respiratory stimulants have proven ineffective. Some observations in patients affected by CCHS have indicated that the use of the contraceptive drug Desogestrel, a potent progestin, improved their ventilatory function.

Methods

To further investigate our hypothesis that etonogestrel (the active metabolite of desogestrel) may interact with progesterone receptors and stimulate progesterone receptors expressing neurons to improve ventilatory output, adult female rats were implanted with varying sizes of etonogestrel implants to deliver the progestin chronically over a four-week period. They were then tested weekly in a whole-body plethysmograph to determine respiratory parameters (frequency, tidal volume, and minute ventilation) during normal conditions and during respiratory challenges.

Results
Across all trials no increase in ventilation baseline conditions or hypoxic (low $\%O_2$) and hypercapnic (high $\%CO_2$) responsiveness, compared to control groups, was found.

Conclusion

In summary, we determined that Etonogestrel at blood serum concentrations approximating levels found in patients taking contraceptive drugs (~200pg/ml) failed to elicit an increase in ventilatory output in normal, hypoxic and hypercapnic conditions in a healthy animal model. Estrogen supplementation has been observed to upregulate progesterone receptors numbers various tissues, which may then allow an increased sensitivity to both endogenous and exogenous progestins. Further experimentation is currently ongoing using estrogens to upregulate progesterone receptors in rats in combination with chronic progestin administration, which could potentate the effects of etonogesrel on ventilation.

The Power of Partnership

Abstract #:   177
Presenter: Telford Yeung
Supervisor: Israel Amirav
Title: Evaluating caregiver management of asthma exacerbation at home
Authors: Telford Yeung, Israel Amirav, Chris Ewing, Michelle Balcom, Janny Kwan
Affiliations: University of Alberta
Research Activity: Children's Health and Well-Being

Introduction: Effective management of asthma at home requires asthma education from a health professional along with written plans for asthma exacerbations. Nevertheless, a large number of asthma exacerbations continue to result in emergency department visits or hospital admissions. Several studies suggest that caregivers may lack the knowledge, the skills, or the confidence to provide care for their child during an asthma exacerbation. The objective of this study was to determine the proportion of caregivers who appropriately manage their child's acute asthma at home as per the 2014 Global Initiative for Asthma (GINA) guidelines and to identify factors that may be associated with deviations from these guidelines.

Methods: We recruited caregivers of children with asthma using a paper-based questionnaire in a single-center outpatient asthma clinic. 108 caregivers of children aged 3 to 17 years with a physician made diagnosis of asthma were included. We used the z test of proportions and Student's t-test ($\alpha = 0.05$) to assess caregiver management of asthma and caregiver use of written asthma action plans (AAP).

Results: A substantial (up to 52%) proportion of caregivers incorrectly treated their child's asthma exacerbation in a home setting. However, this was not associated with a difference in the number of ER visits (0.8 ± 1.2 versus 0.8 ± 1.2, $p = 0.87$) or hospital visits (0.1 ± 0.3 versus 0.1 ± 0.4, $p = 0.89$) between these two groups in the past year. Among the 65% of caregivers who used an AAP, we did observe a significantly greater number of ER visits (1.1 ± 1.3 versus 0.5 ± 0.9, $p < 0.05$) and hospitalizations (0.2 ± 0.4 versus 0.0 ± 0.0, $p = 0.03$) when compared to no AAP use. Scores for asthma knowledge and confidence in management were not significantly different regardless of proper asthma management and AAP use.

Conclusion: Parents of children with asthma in Canada may still lack education about proper home management of asthma exacerbations. Surprisingly, we found a higher number of ER visits and hospitalizations in those using an AAP compared to those who did not use an AAP. These data suggest that the role of AAP needs to be revisited. Meanwhile, routine assessment and review by a healthcare professional is essential in reinforcing recommended behaviours for home asthma management.

The Power of Partnership

Breast cancer is the most common cancer amongst women in Canada. 10 – 20 % of patients receiving the present standard treatment regime for early stage breast cancers, breast-conserving surgery with radiation therapy, develop local recurrence. Some patients develop metastatic spread associated with a high lethality rate. The underlying cause is likely the failed eradication of tumour initiating cells or cancer stem cells (CSCs). CSCs show characteristically high plasticity and unfortunately often also increased radioresistance compared to the bulk of the cancer cells. Radiosensitizers, drugs that increase ionizing radiation (IR)-induced tumour cell killing, promise to improve the efficacy of RT. ATR and Wee1 inhibitors have been found to radiosensitize (bulk) cancer cells and now are in phase I/II clinical trials.

Following ionizing radiation (IR), DNA damage is signalled by two apical kinases of partially overlapping pathways, ATR and ATM. Of the two, especially ATR activity is often upregulated in cancer stem cells. We hypothesize that: *ATR signalling is fundamental for the observed enhanced radioresistance of breast cancer stem cells (BCSCs) and responsible for breast cancers being refractory to radiation therapy.*

Our data suggests that *in vitro* inhibition of ATR radiosensitizes the BCSC population. Further, our preclinical findings indicate that ATR inhibition shows tumour-selective synthetic lethality with inhibition of the checkpoint kinase Wee1. The orthotopic breast tumour bearing mice which received combined treatment of the ATR and Wee1 inhibitor showed synergistic killing of tumour cells leading to tumour shrinkage to impalpable levels and suppression of metastasis. As a result, this treatment regime considerably increased overall survival. We are currently expanding our animal studies and will determine the mechanisms underlying synergism between inhibition of ATR and Wee1.

The Power of Partnership

Abstract #:   179
Presenter: Huachen Chen
Supervisor: Yangxin Fu
Title: Transcription factor ZIC2 regulates tumorigenic phenotypes in epithelial ovarian cancer
Authors: Huachen Chen, Krista Vincent, Zhihua Xu, Lynne-Marie Postovit, Yangxin Fu
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Objectives

Most epithelial ovarian cancers (EOCs) are diagnosed at advanced stages. Current therapies are ineffective against advanced EOCs due to the recurrence of disease and acquired chemoresistance driven by tumor initiating cells (or cancer stem cells, CSCs). Transcription factor ZIC2 has been recognized as an important factor regulating self-renewal of CSCs. This project aims to study the relation between transcription factor ZIC2 and the tumorigenic phenotypes in EOC.

Methods

Correlation between ZIC2 expression and survival of EOC patients was analyzed using The Cancer Genome Atlas (TCGA) dataset. ZIC2 and Oct4 (a major pluripotency factor) expression was examined in a panel of established EOC cell lines at the mRNA and protein level. ZIC2 knockout models established by CRISPR/cas9 were subjected to Western Blot and quantitative (q)RT-PCR analysis for OCT4 and *ALDH1A1* (a commonly used marker for ovarian CSCs) expression. ALDEFLUOR^{TM} assay was used to determine the CSC population in EOC cells. Clonogenic assay, soft agar assay, and sphere formation assay were carried out to test the biological function of ZIC2 in EOC. The effect of ZIC2 overexpression on ALDH1A1, PROM1, NANOG and SOX2 mRNA expression was determined by qRT-PCR.

Results

The TCGA database analysis indicates that higher ZIC2 mRNA expression is associated with shorter survival of EOC patients. ZIC2 expression is strongly correlated with pluripotency factor Oct4 expression at both mRNA and protein levels in the panel of EOC cell lines. CRISPR knockout of ZIC2 in the ZIC2-positive EOC cell lines results in decreased growth, colony formation, and sphere formation (an *in vitro* assay to assess the self-renewal ability), as well as decreased expressions of stem cell-associated genes, such as Oct4 and *ALDH1A1*. Furthermore, ZIC2 knockout dramatically decreased ALDH1^{+} population in EOC cells compared to the parental cells. Overexpression of ZIC2 increased the expression of stem cells associated genes (ALDH1A1, PROM1, NANOG, and SOX2) in EOC cells.

Conclusions

Our *in vitro* work indicates that ZIC2 plays an important role in regulating tumorigenic phenotypes in EOC.

The Power of Partnership

Introduction

The role of healthcare providers in breaking the silence of women who experience Intimate Partner Violence (IPV) is significant. In order to provide best possible care to these women, it is necessary to understand how multiple factors act in an integrated manner to reinforce silencing surrounding IPV. Thus, the study aimed to use a socio-ecological model to examine the factors influencing silencing of women who experience IPV. Comprehensive understanding of the interactional pattern of the factors influencing silencing of women who experience IPV and their relation to the healthcare system must be understood to initiate more effective interaction between healthcare providers and women.

Methods

The study will follow integrative review methodology. Eight databases namely PyschInfo, CINAHL, Medline, PubMed, Sociological Abstract, Scopus, Web of Science and Gender Abstract were searched. Different combinations of the keywords like partner, family, domestic, spouse, wife, marital, husband, women, abuse, violence, batter, assault, beat, non-disclosure, secret, and silent were used. Hand search, reference search and expert network consultation will be performed to extract the important articles. Grey literatures will also be included. Inclusion and exclusion criteria will be used to screen the articles. The data extraction tables obtained from National Institute of Health and Care Excellence (NICE) will be modified and used to extract the data. NVivo 11.0 will be used to do the coding.

Results

The search revealed 2217 articles. The findings will be categorized according to the country where the study was conducted. Then, they will be further arranged into continents (Asia, Africa, South America, North America, Europe, and Australia). The socio ecological framework will form the basis for coding the findings. Grey literatures will be integrated in the findings section with each theme from the socio-ecological framework (interpersonal factors, intrapersonal factors, institutional, public policy and communal factors). The discussion section will focus on how healthcare providers can incorporate the findings into providing the best possible care to women who experience IPV.

Conclusion

The study will identify and add clarity to how factors operating at various levels of influence increase silencing, which interact in an integrated manner to shape women's responses to violence. The study will also prompt the healthcare providers to develop an insight to their potential contribution to women's reluctance to disclose IPV, as well as their significant role in helping women at different point of times in their life journey.

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Problem

Unsafe abortion remains a neglected public health issue in Pakistan, even though thousands of women each year suffer, and sometimes die, from its consequences. Current evidence shows that the average Pakistani woman will have one abortion in her lifetime. Abortion is legal in Pakistan to save the woman's life or to provide "necessary treatment," however; safe abortion and post abortion care services are often inaccessible due to lack of knowledge, stigmatization, and lack of women friendly services.

Purpose

The purpose of this project was to sensitize young nurses/midwives and doctors (Age 18 to 32 years) who are providing abortion services to visualize abortion through a gender lens and in turn motivate them to provide more ethical and women-centered care.

Methodology

To meet the stated objectives, two full days advocacy program was provided in one community setting in Karachi, Pakistan in 2015. The program targeted 20 young health care providers of various medical institutes to build participants' capacity and commitment to take action for safe abortion. Purposeful sampling technique was used to select participants. The workshop included several teaching learning strategies like small group discussions, power point presentations, videos, reflections, role pay, etc.

A knowledge and attitudes based pre-and post-test survey was conducted followed up by in-depth interviews with participants who agreed to meet at their work place within 3 months of the advocacy program. In-depth interviews from participants revealed changes in attitude about abortion stigma and increased awareness in providing more sensitive care to women seeking abortion.

Results and Discussion

The study involved fifty (n=20) health care providers who participated in the workshop. The participants' age was M = 23.85, SD = 3.15 years on average. Among the participants (n=5, 25%) were midwives, (n=1, 5%) were physicians while majority (n=14, 70%) of the participants were nurses. Overall statistically significant gain was observed for all the knowledge questions (80%).

Participants showed high level of satisfaction from the training and stated their views that abortion care is not yet a fully integrated or accepted part of midwifery and nursing.

Conclusion

Complications from unsafe abortions cause a serious global threat to women's health and lives. Therefore, advocacy to raise awareness on abortion and making it legal can prevent women from seeking unsafe abortions. Also, adding the topic of gender, rights and safe abortion in nursing, midwifery and medical education curriculum will make a difference in health care workers attitude.

The Power of Partnership

Abstract #:   182
Presenter: Guanmin Meng
Supervisor: David Brindley
Title: An inflammatory response involving increased autotaxin production in human adipose tissue after radiotherapy: Implications for breast cancer treatment
Authors: Guanmin Meng, Xiaoyun Tang, Zelei Yang, Matthew Benesch, Denise Hemmings, Todd McMullen, David Brindley
Affiliations:
Research Activity: Lifelong Women's Health

Introduction: Our group developed a new paradigm for understanding breast tumor progression and treatment in which adipose tissue adjacent to breast tumors becomes inflamed by inflammatory cytokines from the tumor. This stimulates autotaxin (ATX) secretion from adipocytes, whereas breast cancer cells produce insignificant ATX. Lysophosphatidate (LPA) produced by autotaxin promotes a vicious cycle of inflammation by stimulating the secretion of more inflammatory mediators, which increases further ATX production. This LPA-induced inflammation promotes tumor growth, metastasis and resistance to chemotherapy. LPA signaling also protects cells from radiation-induced cell death. Neo-adjuvant or post-adjuvant radiation treatment for breast cancer patients normally involves irradiating the whole breast with 25 fractions of ~2 Gy. We hypothesized that irradiation-induced damage to breast adipose tissue will increase the secretion of ATX and other inflammatory mediators that should protect residual cancer cells against further fractions of radiotherapy.

Methods and Results: Cultured rat abdominal adipose tissue and human breast and neck adipose tissue were exposed to 0.25 to 5 Gy of g-radiation. This increased mRNA concentrations for ATX, cyclooxygenase-2, IL-1b, Il-6, IL-10, TNFa and $LPA_{1/2}$ receptors. There was also increased secretion of ATX and 14 inflammatory mediators from human adipose tissue. Blocking signaling downstream of radiation-induced damage by inhibiting the activities of NFkB, cyclooxygenase-2, poly[ADP-ribose]polymerase-1(PARP-1) or ataxia telangiectasia and Rad3-related protein(ATR) prevented the inflammatory responses to g-radiation. Furthermore, higher ATX activity and levels of IL-2, CXCL5 and TNFα, together with lower levels of anti-inflammatory adiponectin, were detected in the plasma of mice where only part of the breast adipose tissue was irradiated with 7.5 Gy.

Conclusions: Radiation-induced damage of breast adipose tissue establishes a comprehensive inflammatory response, which involves increased signaling by LPA, COX-2 and other inflammatory mediators. We will now test if blocking this inflammatory response with an ATX inhibitor will increase the efficacy of focused radiotherapy in destroying breast tumors.

The Power of Partnership

Abstract #:   183
Presenter: Alexandra Malley
Supervisor: Sue Ross
Title: An environmental study to guide the design of a therapeutic walking program for menopausal women
Authors: Alexandra Malley, Beate Sydora, Sue Ross, Tami Shandro
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction

Walking represents a low cost, simple exercise with proven health and environmental benefits, and has the potential to be incorporated into almost every able-bodied person's schedule and lifestyle. The Mature Women's Health Research group at the University of Alberta aims to design a study to investigate whether a walking exercise program will improve quality of life in women seeking help at Edmonton's menopause clinics, with moderate to severe menopause symptoms. An important part of this study, and the focus of this particular project, was an environmental scan to support the design of a suitable walking exercise regime in Edmonton that would engage women in a walking program year round.

Methods

For the environmental scan, we conducted explorative research, gathering information on existing walking groups and walking events in Edmonton using online resources, community contacts, and word of mouth. Information included history and success of the walking program, program details such as walking trails outdoors (tracks in the city or River Valley) and indoors (mall walking, indoor facilities), walking frequencies, and participant characteristics. Data was collected in excel and analyzed descriptively.

Results

We identified a variety of groups and organizations that engage in regular, year round walking exercises and primarily include women in the age of menopause transition. All initiatives claim recurrent return of participants. Routes were mostly variable and could range from 8 to 32 km or last about 90 minutes. Main reason for participation was quoted as social interaction and staying fit.

Conclusion

Our results will assist in our goal of designing a walking program in the Edmonton area that would provide year-round walking opportunities and would be attractive for women to start and maintain a walking habit. This program ultimately has the potential of generating a meaningful and sustainable impact on health outcomes for these women.

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Introduction : Triple negative breast cancer (TNBC) is a subtype of breast cancer with poor prognosis and high death rate. Tumor suppressor PTEN plays an important role in cell proliferation and cell migration through negatively regulation of the PI3K/Akt pathway. PTEN is down-regulated by microRNAs in multiple cancers. However, very little microRNAs were reported to directly targeting PTEN in TNBC.

Methods: In this study, predicted PTEN targeting microRNAs were screened by immunoblotting and luciferase reporter assay. The expression of miR #14 was determined by TaqMan microRNA assay. We performed clonogenic assay, cell cycle assay and scratch wound assay to examine the oncogenic role of miR #14.

Results: We found and demonstrated that microRNA #14 (miR #14) directly targeted to PTEN mRNA 3'UTR and inhibited PTEN protein level in TNBC cells. The miR #14 overexpressed in TNBC cell lines compared to normal breast cell line MCF-10A. The miR #14 promoted cell proliferation and cell cycle progress in TNBC cells in a PTEN-dependent manner. Suppression of miR #14 overexpression impaired the oncogenic effect of miR #14 on cell proliferation and cell migration.

Conclusion: This study identified a novel microRNA (miR #14) overexpressed in TNBC cells and its oncogenic role through repressing PTEN, which provided new insight on down-regulation of PTEN and potential therapeutic target in TNBC.

Keywords: miR #14, PTEN, triple negative breast cancer

The Power of Partnership

Abstract #:   185
Presenter: Timothy Fu
Supervisor: Hasan Uludag
Title: The effect of TRAIL transfection on breast cancer cell viability
Authors: Timothy Fu
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction:

Current breast cancer treatments, including chemotherapy, radiation, and surgery, carry severe side effects or limitations. TNF-related apoptosis-inducing ligand (TRAIL) is a protein known to stimulate apoptosis in cancer cells and TRAIL-induced apoptosis can be a potential therapeutic approach for cancer. The objective of this study is to optimize the transfection efficiency of TRAIL cDNA into human embryonic kidney (HEK) 293T cells and eventually into immune cells, and to determine the therapeutic effect of transfected TRAIL in breast cancer cells.

Methods:

To optimize transfection conditions of pEGFP-TRAIL into HEK 293T, we used different polymer carriers (linear polyethylenimine (PEI) and modified PEI), different carrier/plasmid weight ratios, and the addition of organic solvents for transfection. Transfection efficiency was determined by EGFP fluorescence intensity measured using a fluorescence microplate reader. Supernatant from transfected HEK 293T cell cultures was collected and added to cultured breast cancer cell line MDA-MB-231. The effect of TRAIL in the supernatant on cell viability was measured by MTT assay. Breast cancer cell lines MDA-MB-231 and SUM146 cells were also transfected with pEGFP-TRAIL, and the effect of expressed TRAIL on cell viability was measured by MTT assay.

Results:

With linear PEI as the carrier, the addition of dimethyl sulfoxide (DMSO) and a carrier/plasmid weight ratio of 2.5 resulted in improved transfection efficiency of pEGFP-TRAIL into HEK 293T as determined by EGFP fluorescence intensity. The addition of supernatant collected from HEK 293T cells transfected with pEGFP-TRAIL to breast cancer cells slightly but consistently decreased cell viability. Transfection of pEGFP-TRAIL into breast cancer SUM146 cells using linear PEI with a carrier/plasmid weight ratio of 2.5 resulted in an approximate 15% decrease in cell viability. A polymer library screening showed that transfection with pEGFP-TRAIL using two polymers (PEI1.2-tLA4 and PEI1.2-tαLA6) resulted in the largest (40-50%) decrease in cell viability in MDA-MB-231 cells, suggesting that these two polymers were the most effective in transfection.

Conclusion:

Improved transfection efficiency of pEGFP-TRAIL was achieved by combination of various transfection conditions. Both the addition of conditioned medium collected from HEK 293T cells transfected with pEGFP-TRAIL and direct transfection of pEGFP-TRAIL resulted in decreases in cell viability in breast cancer cells. Future studies involve further optimization of transfection efficiency of pEGFP-TRAIL into immune cells.

The Power of Partnership

Abstract #:   186
Presenter: Min Hsuan Wu
Supervisor: Armin Gamper
Title: The regulation of transcription factor Sox2 via genotoxic stress and hypoxia
Authors: Min Hsuan Wu, Amirali Bukhari
Affiliations: University of Alberta
Research Activity: Lifelong Women's Health

Introduction: Within a tumour, only a subset of cells called **C**ancer **S**tem **C**ells (**CSC**s) can form neoplasms. CSCs, like normal tissue stem cells, are characterized by high cellular plasticity. One transcription factor crucial for the establishment of plasticity is **S**ex-determining region Y b**ox** protein **2** (**Sox2**). Upregulation promotes tumour progression in certain tissues, and its activity has been associated with CSC maintenance in breast cancer.

Recent studies suggest that some DNA damaging therapies may trigger dedifferentiation and an increase in CSCs. Hypoxic conditions can promote both stemness and radioresistance, and upregulate Sox2 levels. As DNA damage and hypoxia have been reported to regulate cancer cell plasticity, we hypothesize that **DNA damage signalling can regulate Sox2 levels and activity, and hypoxia can modulate this regulation. The resulting alteration in Sox2 has important consequences for the establishment/maintenance of CSCs, resulting in adverse outcome for genotoxic therapies.** I hope to gain insight into mechanisms underlying Sox2 regulation, and establish whether DNA damage and hypoxia-induced changes in Sox2 activity affect cancer cell plasticity.

Methods/Results:

Aim 1: *Sox2 levels and activity after DNA damage and hypoxia.* Sox2 protein is depleted in cancer cells after exposure to ionizing radiation (IR). Because exogenous Sox2 expressed by a viral promoter shows similar depletion kinetics, regulation seems to be at the post-transcriptional level. Treatment with an inhibitor of the DNA damage signaling kinase, ATM, inhibited damage-induced down regulation of Sox2, highlighting a link between DNA damage signalling and Sox2 regulation. Measuring Sox2 activity by FACS using a reporter cell line, I observed that IR and hypoxia synergistically activate Sox2.

Aim 2: *Sox2 interacting proteins following DNA damage and hypoxia.* BirAR118G is a mutant biotin ligase that attaches biotin to nearby lysines, allowing the use of proximity-dependent biotin identification (BioID) to identify transient interaction partners of Sox2. Tagging with the FLAG peptide allows for identification of stable interaction partners by immunoprecipitation. I have established cell lines expressing BirAR118G fused to Sox2. By comparing hits from unperturbed cells to cells treated with DNA damage and/or hypoxia, we can obtain important information on Sox2 regulation based on its interacting partners.

Conclusion: My preliminary data show depletion of Sox2 protein following IR and induction of its activity with IR and hypoxia. We intend to study the specific upstream signalling pathways regulating Sox2 protein levels following genotoxic stress and hypoxia as well as the control mechanisms of its transcriptional activity.

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Notes

DISCLAIMER:
While the abstracts have been slightly modified for consistency, each abstract has been predominantly printed exactly as originally submitted.

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