Effects of nutritional management on production performance and rumen fermentation in dairy cows during calving transition

by

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Abstract

Dairy cows usually experience negative energy balance during the calving transition period (3 weeks before to 3 weeks after parturition) due to the rapid increase in nutrient demands for milk production. In order to compensate for the energy deficits, diets rich in highly fermentable carbohydrates are commonly fed to dairy cows after calving. However, the increase in dietary fermentable carbohydrate does not guarantee an increase in energy intake and is likely to decrease rumen pH and increase the risk of sub-acute acidosis (SARA) in dairy cows after calving. The overall objective of this research was to evaluate the effects of nutritional management during the calving transition period on production performance and rumen fermentation in early-lactation dairy cows. The first study (Chapter 2 and 3) evaluated the effects of *Saccharomyces cerevisiae* fermentation product (SCFP) supplementation during the periparturient period on production performance and rumen fermentation of dairy cows fed fresh diets differing in starch content were evaluated. One-hundred seventeen Holstein dairy cows, including 18 ruminally cannulated cows, were fed diets with SCFP (SCFP) or without (CON) from day (d) 28 prior to expected calving date to d 44 after calving. A common basal low-energy diet was fed to all cows during the close-up period. Cows within each treatment (CON or SCFP) were fed either a low-(LS; 22.1% starch) or high-starch (HS; 28.3%) diet during the fresh period (d 1 to 23 after cavling). All cows were fed the HS diets during the post-fresh early lactation period (d 24 to 44 after calving). In Chapter 2, it was found that starch content of fresh diets did not affect dry matter intake (DMI), but LS cows had greater milk yield and tended to lose more body condition during the fresh period compared with HS cows. Supplementation of SCFP transiently increased DMI on d 1 and 5 after calving and increased feed efficiency (3.5% fat-corrected milk yield/DMI) during the post-fresh early lactation period. In Chapter 3, rumen pH data were collected from the eighteen ruminally cannulated cows. Rumen pH was measured over

a 3-d period from d -10 relative to expected calving date and from d -3, 1, 7, and 21 relative to actual calving date. As expected, minimum rumen pH tended to be higher for LS cows than HS cows on d 1 after calving. However, rumen pH was not affected by dietary starch content during the other periods after calving. Supplementation of SCFP tended to increase mean rumen pH on d -3 before calving and tended to increase minimum rumen pH and reduce the duration of pH below 5.8 on d 21 after calving.

Based on the effects of feeding LS diets on increasing rumen pH during the fresh period, I hypothesized that the negative effect of feeding a low-starch close-up diet on increasing the risk of rumen pH depression may occur only during the immediate postpartum period. Therefore, the effects of prepartum dietary starch content on rumen fermentation and responses of dairy cows to grain-induced SARA were evaluated in the second study (Chapter 4). Rumen pH was monitored over a 3-d period from d -10 relative to expected calving date and was measured during the grain challenge. Feeding a low-starch diet (14.0% starch) before calving reduced the duration and area of pH below 5.8 on d -10 before calving compared with a high-starch diet (26.1% starch). Contrary to the hypothesis, feeding a low-starch prepartum diet tended to reduce the duration and area of pH below 5.8 during a grain challenge on d 7, possibly because of reduced inflammation and less rumen epithelial damage as indicated by a lower serum amyloid A concentration. However, rumen pH was not different betwwen treatments during a grain challenge on d 21 after calving. In summary, these findings suggest that 1) feeding low-starch diets during the fresh period can increase milk production of dairy cows fed a low-energy close-up diet and reduce the decrease in rumen pH during the immediate postpartum period, 2) supplementation of SCFP may increase feed intake around calving and feed efficiency in post-transition early lactation period

and can help to reduce the duration of pH below 5.8 by the end of the calving transition, and 3) feeding a high-starch close-up diet may increase the rumen pH depression after calving.

Preface

This thesis consists of two studies. The first study yielded Chapters 2 and 3 and received research ethics approval from the University of Alberta Animal Care and Use Committee for Livestock; project name "Evaluation of nutritional management during calving transition", AUP00001915, June 29, 2016. The second study yielded Chapter 4 and received research ethics approval from the University of Alberta Animal Care and Use Committee for Livestock; project name "Transition cow study", AUP00002342, Aug 11, 2017.

Chapter 2 of this thesis has been submitted as W. Shi, C. E. Knoblock, K. V. Murphy, T. C. Bruinjé, I. Yoon, D. J. Ambrose, and M. Oba. "Effects of Supplementing a *Saccharomyces cerevisiae* Fermentation Product during Periparturient Period on Performance of Dairy Cows Fed Postpartum Diets Differing in Starch Content" to the Journal of Dairy Science". I was responsible for data collection and analysis as well as the manuscript composition. C. E. Knoblock assisted with the sample collection. K. V. Murphy, T. C. Bruinjé, and D. J. Ambrose were responsible for the data collection of reproduction performance and this portion of data was added to Chapter 2 to make one paper. I. Yoon contributed to manuscript edits. M. Oba was the corresponding author and was involved with experimental design, data collection, and manuscript composition.

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List of abbreviations

ADF	Acid detergent fiber
AUC	Area under the curve
BDH1	β-118 Hydroxybutyrate dehydrogenase, isoform 1
BDH2	β-118 Hydroxybutyrate dehydrogenase, isoform 2
BHB	β-hydroxybutyrate
BW	Body weight
BCS	Body condition score
CON	Control
CP	Crude protein
CR	Clearance rate
DA	Displaced abomasum
DIM	Days in Milk
DM	Dry matter
DMI	Dry matter intake
DRA	Downregulated in adenoma
EGFR	Epidermal growth factor receptor
EREG	Epiregulin
FA	Fatty acid
FCM	Fat-corrected milk
GC	Grain challenge
GTT	Glucose tolerance tests
HMGCS1	3-hydroxy-3-methylglutaryl-CoA Synthase 1
HMGCS2	3-hydroxy-3-methylglutaryl-CoA Synthase 2

Hp	Haptoglobin
HS	High-starch
IGF-1	Insulin-like growth factor – 1
IGFBP	Insulin-like growth factor binding protein
LS	Low-starch
LPS	Lipopolysaccharide
MCT1	Monocarboxylate cotransporter, isoform 1
MCT4	Monocarboxylate cotransporter, isoform 4;
MOS	Mannan oligosaccharides
MUN	Milk urea nitrogen
mRNA	Messenger ribonucleic acid
NDF	Netural detergent fiber
NEB	Negative energy balance
NEFA	Non-esterified fatty acids
NFC	Non-fiber carbohydrate
NSC	Nonstructural carbohydrate
OM	Organic matter
PAT	Putative anion transporter
peNDF	Physically effective neutral detergent fiber
PPARα	Peroxisome proliferator-activated receptor α
RPLP0	Ribosomal protein, large P0
SAA	Serum amyloid A
SARA	Sub-acute ruminal acidosis

SCC	Somatic cell counts
SCFP	*Saccharomyces cerevisiae* fermentation product
TGFB1	Transforming growth factor β 1
TGFBR1	Transforming growth factor β receptor 1
TMR	Total mixed ration
VFA	Volatile fatty acid

Chapter 1. Literature review

1.1 Overview of the transition period

As the most critical time period during the life cycle of dairy cattle, the transition period is generally denoted as 3 weeks prior to parturition to 3 weeks after parturition (Grummer, 1995). During this period, dairy cows are faced with great metabolic and physiological challenges in addition to dietary changes (Zaworski et al., 2014). Most metabolic and infectious diseases are likely to occur during this period (Drackley, 1999), and include fatty liver, ketosis, and rumen acidosis. Therefore, a poor transition from late gestation to early lactation can have detrimental effects on cow health, productivity, and reproductive efficiency (Drackley, 1999).

1.1.1 Negative energy balance

1.1.1.1 Definition

As parturition approaches, the nutrient requirements for fetal growth and the initiation of milk production increase while dry matter intake (DMI) often decreases (Ingvartsen and Andersen, 2000). The nutrient demand for conceptus growth increases by about 23% during the last three months of pregnancy (Moe and Tyrrell, 1972). The requirements for glucose, amino acids, and fatty acids are approximately 3, 2, and 5 times greater, respectively, at 4 days postpartum compared with that of at 250 d of gestation (Bell, 1995). The decrease in DMI can occur in late pregnancy and continue into early lactation (Ingvartsen and Andersen, 2000). Bertics et al. (1992) reported that there was a 30% reduction in DMI during the final week prior to calving. More recently, it has been shown that DMI decreased by 32.2% during the final 3 wk of gestation and approximately 89% of this reduction in DMI occurred during the final week prior to parturition (Hayirli et al., 2002). As a result, energy intake from the feed cannot support the drastic increase in the nutrient demands, leading to a state of negative energy balance (NEB) (Drackley, 1999). In an attempt to compensate for the energy deficit

and meet the energy requirements for milk production and maintenance, dairy cows start to mobilize their body reserves, resulting in an increase in plasma concentrations of non-esterified fatty acids (NEFA) and ketone bodies (Herdt, 2000).

1.1.1.2 Major metabolic adaptions in response to NEB

In order to have a successful transition from late gestation to early lactation, dairy cows must undergo metabolic adaptations. The adaptations of glucose metabolism during the calving transition mainly include increased hepatic gluconeogenesis and decreased glucose uptake by peripheral tissues so that glucose can be directed to the mammary gland for milk production (Reynolds et al., 2003; Overton and Waldron, 2004). The amount of glucose available for lactogenesis in the mammary gland determines the milk production of dairy cows (Mepham, 1993). The predominant precursor for gluconeogenesis in dairy cows is propionate, mainly from non-fiber carbohydrate fermentation in the rumen, which accounts for approximately 50 to 60% of hepatic glucose release during the transition period (Herdt, 2000; Reynolds et al., 2003). Other substrates for gluconeogenesis include amino acids from protein breakdown, glycerol from lipolysis, and L-lactate from the Cori cycle (Aschenbach et al., 2010).

The adaptation of lipid metabolism during the transition period involves the mobilization of body fat reserves through lipolysis (Overton and Waldron, 2004). The breakdown of triglyceride from adipose tissue results in the release of NEFA and glycerol, which are bound to serum albumin in the blood. Besides being transferred to the mammary gland for milk fat synthesis, approximately 16 to 23% of NEFA are taken up by the liver (Reynolds et al., 2003) and NEFA can also be used by the skeletal muscle as energy source to reduce the usage of glucose and maintain blood glucose concentration (Herdt, 2000). The uptake of NEFA by the liver is in proportion to their supply

(Andersen et al., 2002). Once taken up by the hepatocytes, NEFA can be oxidized completely to carbon dioxide to provide energy or incompletely to ketone bodies, or re-esterified to triglyceride and exported in the form of very low density lipoproteins (Emery et al., 1992; Bauchart et al., 1996).

1.1.1.3 Health disorders in relation to NEB

In recent times, the intense genetic selection and the improvement in nutritional management have increased milk production of dairy cows (van Kengsel, 2005). However, with the decrease in DMI around partition, the increased milk production potentially exacerbates NEB in early lactation. In addition, dairy cows undergo immunosuppression, environmental stressors associated with on-farm management (i.e. group changes), and diet changes during the transition period (Mulligan and Doherty, 2008), which can further decrease DMI and worsen the NEB. Failure in the adaptation to NEB during the transition period gives rise to the incidence of several metabolic and infectious diseases, most of which occur within the first 2 weeks of lactation (Goff and Horst, 1997; Drackley, 1999; Ingvartsen et al., 2003). When cows experience prolonged periods of NEB, the incidence and severity of diseases increase (Goff, 2006).

Lipid mobilisation in adipose tissue is a natural biological process to support milk production during the transition period in dairy cows that undergo NEB (Mulligan and Doherty, 2008). However, excessive lipid mobilization greatly increases plasma NEFA concentration and results in production of ketone bodies and the accumulation of triglycerides in hepatocytes as the liver has an insufficient capacity to oxidize NEFA or secrete NEFA as lipoproteins (Bauchart et al., 1996; Andersen et al., 2002). Such conditions lead to the development of fatty liver syndrome and ketosis (both clinical and subclinical forms) in dairy cows during the transition period. The occurrence of fatty liver syndrome results in not only damaged liver function and reduced feed intake, but increased incidence of other

health problems (e.g. displaced abomasum and ketosis) and prolonged recovery from those health disorders (Herdt et al., 1988; Emery et al., 1992). It has been reported that the average incidence of subclinical ketosis (BHB concentration of 1.2 to 2.9 mM/L) was 43% and ranged from 26 to 56% in dairy cows within 3 to 16 days after parturition (McArt et al., 2011). Cows with subclinical ketosis are more susceptible to other health problems after parturition, for example, displaced abomasum (DA) and metritis (Duffield et al., 2009), contributing to decreased milk production in early lactation.

Besides the prevalence of fatty liver and ketosis, a series of other metabolic disorders, such as milk fever, DA, and retained placenta can occur in early lactation. In a survey of 61 high-producing herds in the U.S., Jordan and Fourdraine (1993) reported a 7.2% incidence rate of milk fever (range 0 to 44.1%), a 3.3% incidence rate of displaced abomasum (range 0 to 14%), a 3.7% (range 0 to 20%) incidence rate of ketosis, and a 9.0% (range 0 to 22.6%) incidence rate of retained placenta. In addition, Dyk et al. (1995) found that dairy cows with high concentration of NEFA during the last 7 d prior to calving were more susceptible to ketosis, DA, and retained placenta during the periparturient period. More recently, LeBlanc et al. (2004) found that cows with higher serum concentrations of NEFA in the last week before parturition tended to have 77% higher risk of retained placenta.

In addition to metabolic disease, dairy cows are at high risk of infectious diseases, primarily mastitis and metritis, during the first few weeks after parturition (Kimura et al., 2002). The average incidence rate of metritis was 12.8% and ranged from 9 to 66% in dairy cows during the postpartum period (Jordan and Fourdraine,1993). The prevalence of such infectious diseases is probably because dairy cows experience immunosuppression during the periparturient period and have impaired neutrophil function (Mulligan and Doherty, 2008). Although the exact mechanism for

immunosuppression remains unclear, metabolic changes during the transition period may negatively impact the immune function of dairy cows (Nonnecke et al., 2003; Sordillo et al., 2009). Hammon et al. (2006) reported that cows with peripartum NEB, as indicated by high blood NEFA concentration and low DMI had impaired neutrophil function and increased risk of uterine health disorders. Similarly, a greater degree of NEB during the postpartum period is associated with uterine diseases (Galvão et al., 2010).

1.1.2 Insulin resistance

Insulin plays an important role in the physiological adaptation of dairy cows during the transition period (Zachut et al., 2013). As mentioned previously, the glucose requirement of dairy cows increases by 4 fold from late gestation to early lactation due to the growth of fetus and the onset of lactation (Bell, 1995). The metabolic adaptations that support the glucose partitioning to the gravid uterus and the mammary gland include a gradual decline in plasma insulin concentration and establishment of insulin resistance in adipose tissue and skeletal muscle (Bell and Bauman, 1997). Insulin resistance is defined as a state in which the insulin-sensitive tissues have decreased biological response to ordinary levels of insulin (De Koster and Opsomer, 2013). Insulin resistance can be attributed to decreased insulin responsiveness (response of insulin to glucose), decreased insulin sensitivity (response of tissue to insulin), or both (De Koster and Opsomer, 2013; Kawashima et al., 2016). It has been suggested by Bell and Bauman (1997) that the decreased glucose oxidation in peripartal dairy cows implies a decline in glucose uptake by peripheral tissues due to low plasma insulin concentration and possibly reduced tissue sensitivity to insulin.

Insulin resistance prevents the glucose uptake by adipose tissue and skeletal muscle and prioritizes its uptake by the mammary gland to increase milk production. In addition, insulin

resistance also affects the lipolysis and lipogenesis in adipose tissue. In early lactation, insulin resistance favors lipolysis and inhibits lipogenesis (De Koster and Opsomer, 2013), thereby increasing plasma NEFA available for oxidation to provide energy and milk fat synthesis. However, excessive mobilization of fatty acids from adipose tissue during the transition period may predispose dairy cows to metabolic diseases, such as fatty liver and ketosis, and impaired milk production as discussed previously.

Various methods have been developed to measure insulin sensitivity in dairy cow. The gold standard is the hyperinsulinemic euglycemic clamp test (De Koster et al., 2016). However, this method is expensive and laborious. Intravenous glucose tolerance tests (GTT) have been conducted in several studies for the measurement of insulin sensitivity in dairy cows (Holtenius et al., 2003; Chagas et al., 2009; Mann et al., 2016) with the assumption that the disappearance of glucose would be slower in insulin resistant animals (De Koster et al., 2016). The area under the curve (AUC) and the clearance rate (CR) are calculated and greater AUC and lower CR of glucose may indicate decreased insulin sensitivity of peripheral tissues. Several surrogate indices have been proposed to quantify insulin sensitivity in humans and they can be applied in dairy cows as well, including the quantitative insulin sensitivity check index, the revised quantitative insulin sensitivity check index, and the homeostasis model of insulin resistance (Holtenius and Holtenius, 2007; Balogh et al., 2008; De Koster et al., 2016). The calculation of these indices is based on concentrations of glucose, insulin, NEFA, and BHB. However, the use of these indices in dairy cows has not been fully validated yet. Another method for evaluating insulin sensitivity in peripheral tissues in dairy cows is the insulin tolerance test, which is conducted by infusing insulin to the jugular vein and measuring the glucose concentrations in relative to insulin infusion (Kawashima et al., 2016). Dairy cows with a higher

extent of insulin resistance are expected to have a slower rate of decrease in plasma glucose concentration after insulin infusion and extended time to reach the minimum glucose level.

1.2 Sub-acute ruminal acidosis in transition cows

During the transition period, dairy cows often experience NEB because the nutrient requirements for milk production and maintenance cannot meet by the nutrient intake (Drackley, 1999). At the same time, DMI decreases as parturition approaches, reaches a nadir at calving, and does not peak until 8 to 22 wk after calving (Ingvartsen and Andersen, 2000). However, milk yield typically reaches the maximum production level between 5 to 7 wk after calving (Ingvartsen and Andersen, 2000). In order to support milk production and reduce NEB, diets contain highly fermentable carbohydrate are usually fed to dairy cows in early lactation. Given that high forage diets are usually fed in the dry period, the sudden changes in diet composition may predispose dairy cows to risk of ruminal acidosis (Penner et al., 2007).

1.2.1 Definition

Ruminal acidosis is a common digestive disorder in high-producing dairy herds (Duffield et al., 2004). Feeding diets containing a large amount of highly fermentable carbohydrate while being deficient in physically effective fiber rapidly increases volatile fatty acid (VFA) production in the rumen. Once the production rate of VFA exceeds its removal from the rumen, VFA accumulates, rumen pH drops, and rumen acidosis occurs (Allen, 1997). There are two categories of rumen acidosis, acute acidosis and sub-acute rumen acidosis (SARA). Acute rumen acidosis occurs when pH drops below 5.2 and is associated with increased lactic acid production, which can result in a further decrease in rumen pH (Owens et al., 1998).

Unlike acute rumen acidosis, the accumulation of VFA rather than lactic acid is the main cause of SARA (Krause and Oetzel, 2006). In addition, cows affected with SARA often do not

exhibit clear clinical signs (Nocek, 1997). The definition of SARA is based on rumen pH, but the technique and pH threshold used for diagnose SARA vary among studies. Garrett et al. (1999) collected rumen fluid samples by rumenocentesis and used a pH of 5.5 as the threshold for SARA. Plaizier (2004) sampled rumen fluid via a stomach tube at 4 h after feeding and a pH of 6.0 was used as the threshold for SARA. As rumen pH fluctuates considerably within a day (Keunen et al., 2002), rumen fluid samples collected at specific time points during the day may not fully represent the incidence of SARA. An indwelling pH probe or the pH data logger system developed by Penner et al. (2006a) can measure rumen pH continuously for several days, accounting for the high diurnal changes. Beauchemin et al. (2003) measured rumen pH over a 48-h period using pH electrodes and defined a pH of 5.8 as threshold for SARA as the growth and activity of fibrolytic bacteria can be inhibited when pH values below 5.8. In some instances, the duration below the threshold is also included in the definition of SARA, for example, rumen pH below 5.6 for at least 3 h/d (Gozho et al., 2005).

1.2.2 Factors affecting rumen pH

Rumen pH is determined by the balance between the rate of acid production in the rumen and the rate of acid removal from the rumen through absorption, neutralization, and passage to the lower gut (Allen, 1997). When dairy cows consume a large amount of highly fermentable carbohydrates, such as starch and sugar, VFA production increases rapidly and results in the decrease in rumen pH and change in rumen microbial profile (Nocek, 1997). When pH drops below 5.8, the growth and enzymatic activities of fibrolytic microorganisms decrease (Nocek, 1997). As rumen pH continues to drop below 5.2, lactate production increases and further decreases rumen pH as lactate is the strongest acid in the rumen among all organic acids (Nocek, 1997; Owens et al., 1998). When rumen pH reaches 5.0, *Streptococcus bovis* (a major lactate producer) dies off and lactobacilli increases to

produce lactate (Nocek, 1997). As low rumen pH enhances the activity of both pyruvate hydrogenase and lactate dehydrogenase, increasing the conversion of pyruvate to lactate rather than VFA, a severe drop in rumen pH can be irreversible (Owens et al., 1998). Therefore, it is important to prevent the dramatic drop in rumen pH by controlling the fermentability and rate of digestion of the diet and increasing the absorptive capacity of rumen epithelium and the neutralization of VFA.

1.2.2.1 VFA production

Rumen microbial fermentation of organic matter (OM) provides energy for maintenance and growth of rumen microbes and produces VFA, a primary energy source, for the host animal. Total concentration of VFA in the rumen ranges between 60 and 150 mM (Bergman, 1990). Although accumulation of VFA in the rumen decreases rumen pH and leads to SARA, the relationship between rumen pH and total VFA concentration is weak ($r^2 = 0.13$, $P < 0.001$; Allen, 1997). This is because of the dissociation of VFA in the rumen and removal of H^+ from the rumen. Acetate (40-75%), propionate (15-40%), and butyrate (10-20%) are the three predominant VFA produced in the rumen (Bergman, 1990) and the fermentation of 1 mol of glucose can yield 2 mol of acetate, 2 mol of propionate, or 1 mol of butyrate (Bannink et al., 2006).

Numerous nutritional factors can affect the acid production in the rumen, such as carbohydrate fermentability, the rate of carbohydrate digestion (Allen, 1997), passage of rumen digesta to the lower gut (Robinson et al., 1987), as well as microbial efficiency (Sniffen and Robinson, 1987). The extent of carbohydrate fermentation not only depends on feed characteristics, but is affected by the interactions between feed, rumen microbial population, and the animal (Allen, 1997). In order to reduce the risk of SARA immediately after calving and at the same time increase feed intake, the amount of rapidly fermentable carbohydrate fed and its fermentability in the rumen need to be carefully considered.

1.2.2.2 Absorption of VFA through the rumen epithelium

There are two forms of VFA in the rumen, the undissociated form and the dissociated form. Because the VFA are weak acids ($pK_a \leq 4.8$), 90 to 99% of the VFA are in the dissociated form under physiological rumen conditions (Bergman, 1990). Absorption of VFA through the rumen epithelium has been reviewed by Aschenbach et al. (2011). Approximately 50 to 85% of the VFA produced in the rumen is absorbed across the rumen wall through two pathways: passive diffusion and protein-mediated transport (Aschenbach et al., 2011). The protein-mediated transport pathways can be further divided into bicarbonate-dependent and nitrate-sensitive, bicarbonate independent transport, and the former is the main pathway (Penner et al., 2009). The undissociated VFA are absorbed mainly via passive diffusion (Rémond et al., 1996; Gäbel et al., 2002) while the dissociated VFA are absorbed mostly through the protein-mediated transport pathway (Aschenbach et al., 2011). Furthermore, acetate and propionate are more prone to be absorbed through the rumen epithelium via the bicarbonate-dependent transport than passive diffusion, whereas the absorption of butyrate is the opposite (Aschenbach et al., 2009). Once absorbed across the rumen wall, the protonated VFA are dissociated into VFA^- and H^+ in the cytosol of epithelial cells (Aschenbach et al., 2011). The H^+ can be neutralized by HCO_3^-, recycled back to the rumen, or transported to the basolateral space to prevent intracellular acidification (Aschenbach et al., 2011). The VFA^- can be metabolized in the rumen epithelium during absorption from the rumen and transportation to the portal blood (Bergman, 1990). It was estimated that roughly 30%, 50%, and 90% of acetate, propionate, and butyrate, respectively, is metabolized by the rumen epithelium of sheep (Bergman, 1990). Metabolism of butyrate in rumen epithelial cells mainly involves oxidation to carbon dioxide to provide energy and formation of ketone bodies through ketogenesis (Rémond et al., 1995; Bergman, 1990).

Factors that affect the absorption rate of VFA, including type of VFA (Butyrate > Propionate > Acetate), VFA concentration, rumen pH, volume of rumen fluid (Dijkstra et al., 1993), permeability of rumen epithelium and epithelial blood flow (Storm et al., 2012), as well as rumen papillae surface area (Dieho et al., 2017). The adaptation of rumen epithelium to highly fermentable diets has been discussed extensively by Penner et al. (2011), which mainly involves the increase in epithelial surface area and the changes in gene expression associated with VFA transport and metabolism. The VFA can stimulate the proliferation of the rumen papillae, and butyrate has been reported to be the strongest stimulator among the three predominant VFA (Sakata and Tamate, 1978; Penner et al., 2011). Studies have reported increased rumen papillae surface area in dairy cows having higher concentrate allowance after calving (Bannink et al., 2012; Dieho et al., 2016a). It was suggested by Dirksen et al. (1985) that rumen papillae need 6 to 8 weeks to reach maximal increase in response to increased dietary energy density. More recently, Bannink et al. (2008) reported a shorter time period for the maximal increase in rumen papillae surface area, which was 3 to 4 weeks for dairy cows having greater concentrate allowance after parturition compared with 7 to 8 weeks for those that had lower concentrate allowance. Based on those observations, prepartum diets high in energy density are usually fed to dairy cows in the aim to prepare the rumen epithelium and also reduce the NEB. However, increasing energy intake during the dry period did not always stimulate rumen epithelial proliferation prepartum (Rabelo et al., 2001; Reynolds et al., 2004) or postpartum (Reynolds et al., 2004; Dieho et al., 2017). In addition, Penner et al. (2006b) found rumen papillae surface area was not affected by prepartum energy density and reached its maximal increase during the prepartum period.

In addition to the variable effects of dietary energy density on rumen papillae surface area, Dieho et al. (2016b) also found that the increase in papillae surface area occurred without

corresponding increase in VFA absorption rate. The study by Etschmann et al. (2009) suggested that the morphological adaptation of the rumen epithelium may occur at a slower rate than molecular adaptation. However, few studies have investigated the changes in the expression of genes related to epithelial proliferation and VFA transport and metabolism (Steele et al., 2015; Minuti et al., 2015) in transition cows, and the molecular adaptations of the rumen epithelium during the transition period remain largely unknown.

1.2.2.3 VFA removal from the rumen

Neutralization of acids produced in the rumen mainly occurs through saliva secretion, which contains large amounts of bicarbonate (Erdman, 1988). It has been suggested that approximately half of the bicarbonate needed for acid neutralization comes from saliva (Owens et al., 1998) and accounts for around 37% of the proton removal from the rumen (Allen, 1997). The buffering capacity of saliva depends on the amount of saliva produced during eating, ruminating, and resting because its composition is not affected by rate of secretion or diet (Bailey and Balch, 1961). It was reported that the rates of saliva secretion during eating, resting, and ruminating are 0.166 to 0.253 L/min (Cassida and Stokes, 1986; Maekawa et al., 2002a), 0.088 to 0.173 L/min (Cassida and Stokes, 1986; Maekawa et al., 2002b), and 0.272 L/min (Cassida and Stokes, 1986), respectively. Although forage type has no effect on the rate of saliva secretion, it may affect eating time thereby changing the total amount of saliva produced (Beauchemin et al., 2008). Therefore, factors that increase eating and rumination time of animals, such as increased particle size and fiber content of diet, can reduce the risk of SARA by promoting saliva production.

Besides the saliva production, the bicarbonate can also be secreted by the rumen epithelium. As discussed previously, VFA can be absorbed across the rumen wall through bicarbonate dependent transport, which involves the absorption of VFA^- into rumen epithelial cells and the secretion of

HCO_3^- into the rumen (Aschenbach et al., 2011). It is suggested by Aschenbach et al. (2011) that the amount of HCO_3^- secreted by the rumen epithelium into the rumen is equivalent to the amount of HCO_3^- coming from salvia.

In addition to bicarbonate neutralization, the passage of VFA to lower gut provides another way of acid removal. Both VFA and H^+ are water soluble and can pass the rumen mainly with the fluid fraction (Walter and Gutknecht, 1986). Allen (1997) estimated that passage to the lower gut contributes to approximately 15.5% of the total acids removal from the rumen.

1.2.3 Nutritional factors affecting rumen pH

1.2.3.1 Carbohydrate source

Carbohydrates can be classified as nonstructural (NSC or NFC) and structural carbohydrate (NRC, 2001). The NSC are made up of starch, sugar, organic acids, and fructans and starch is the major source of NSC in dairy cow rations; the structural carbohydrates mainly include cellulose, hemicellulose (NRC, 2001). The NSC are found inside the plant cells and generally more digestible and fermented faster than the structural carbohydrates located in plant cell walls (NRC, 2001). Increasing dietary NSC can facilitate milk production by providing more energy; however, SARA may occur when excessive amount of NSC is fed to the animal. It was suggested by Nocek (1997) that the maximum inclusion of NSC should be approximately 30 to 40% of diet DM for lactating dairy cows to avoid acidosis and maintain optimal milk production. In addition to the amount of inclusion, the rate and extent of NSC digestion in the rumen may also affect rumen pH, for example, type of grain and processing method of grain (NRC, 2001). The degradability of starch in common grains ranks oat > wheat > barley > corn (Huntington et al., 2006). Processing of grain can increase starch digestibility by changing the site and extent of digestion (Hale, 1973). This increase in starch

degradability can result in a fast increase in acid production in the rumen which may overwhelm acid removal, leading to SARA (Gonzalez et al., 2012).

Although starch is the main source of NSC fed to dairy cows, many feed ingredients in dairy cow rations contain sugar. Sugars are water-soluble and can be categorized into monosaccharides, such as glucose, fructose, and galactose, and disaccharides, such as lactose, sucrose, and maltose (Oba, 2011). The fermentation of sugar is more rapid than starch in the rumen and the effects of feeding sugars on productivity and rumen fermentation has been discussed in the review by Oba (2011). Feeding high-sugar diets with sugar content to 13% of dietary DM did not decrease rumen pH of lactating dairy cows (DeFrain et al., 2004; Broderick et al., 2008; Gao and Oba, 2016). In addition, providing early lactation dairy cows with more dietary sugar tended to increase rumen pH (Penner and Oba, 2009). Increased DMI was also found for dairy cows fed high-sugar diets in these studies mentioned above (DeFrain et al., 2004; Broderick et al., 2008; Gao and Oba, 2016; Penner and Oba, 2009). The exact reason why dietary addition of sugar did not decrease rumen pH is not fully understood, but it may be associated with increased VFA absorption (Chibisa et al., 2015).

Structural carbohydrates are essential components in dairy cow rations to optimize production and maintain rumen health (NRC, 2001). Besides its slow fermentation in the rumen compared with starch or sugar, dietary fiber can stimulate chewing and thus promote saliva production, increasing the acids neutralization in the rumen (Beauchemin, 1991). While NDF represents the total dietary fiber content, it does not reflect the physical characteristics of the fiber source (Mertens, 1997). Physically effective NDF (peNDF) describes both chemical constituents (NDF content) and particle size (physical characteristics) of the feedstuffs (Zebeli et al., 2012). The Penn State Particle Separator is commonly used to determine the particle size distribution of feeds on-farm (Kononoff er al., 2003). The peNDF content of a diet can be calculated by multiplying the dietary NDF content with the

proportion that retained on the 19 mm and 8 mm sieves (peNDF > 8 mm; Yang and Beauchemin, 2006). Increasing peNDF can stimulate chewing time and reduce the risk of SARA. Dietary peNDF concentration was found to be positively correlated to chewing time and mean rumen pH and increasing peNDF content of low-forage diets through greater NDF content is more effective in preventing SARA compared with increasing forage particle length (Yang and Beauchemin, 2009). It was indicated that increasing dietary forage content increased chewing time and decreased rumen VFA production (Yang and Beauchemin, 2009). In addition, increased particle length had minor effect on chewing activity and the fermentability remained high (Yang and Beauchemin, 2009). In a review by Zebeli et al. (2012), it was suggested that dairy cows rations contain 14.8 to 18% of peNDF (> 8mm) to reduce the risk of SARA, but peDNF (> 8mm) concentration beyond 14.9 % of diet DM may decrease DMI.

1.2.3.2 Sorting behavior

Dairy cows usually sort against long forage particles and preferentially sort for the grain in a TMR (Leonardi and Armentabo, 2003; De Vries et al., 2007). Sorting activity is calculated as the actual intake of feed particles retained on each sieve of the separator divided by the corresponding predicted intake (Lenardi and Armentano, 2003). Values greater than 100% indicate sorting against, equal to 100% indicate no sorting, and less than 100% indicate sorting for. When dairy cows sort for highly fermentable carbohydrates and sort against fiber, SARA may occur due to increased VFA production and reduced buffering capacity in the rumen (Cook et al., 2004; Stone, 2004; De Varies et al., 2007). Gao and Oba (2014) found that dairy cows that are susceptible to SARA sort against long particles to a higher degree than those that are tolerant to SARA. In addition, lactating dairy cows may have higher degrees of sorting against long fiber and for grain when low-forage diets are fed

(DeVries et al., 2007). Therefore, feed sorting may further decrease the rumen pH in early lactation dairy cows that are commonly fed high-concentrate diets and contribute to SARA.

Alternatively, it has been suggested that dairy cows may sort for feed stuffs with higher buffering capacity in an attempt to alleviate the negative effects of low rumen pH (DeVries et al., 2008). Keunen et al. (2002) found that lactating dairy cows experiencing SARA increased their sorting for long alfalfa hay over the alfalfa pellet when given a choice between alfalfa hay and alfalfa pellets. Another two studies showed that dairy cows sorted for long forage particles when rumen pH was below 5.8 (Beauchemin and Yang, 2005; Yang and Beauchemin, 2006).

1.2.4 Prevalence of SARA in early lactation dairy cows

In one field survey of 15 dairy farms in the United States, SARA was detected in 19% of early-lactation dairy cows (Garret et al., 1997). In a German/Dutch study, Kleen (2009) reported that the incidence of SARA was 11% in early-lactation dairy cows. The high prevalence of SARA in early-lactation was probably due to poor microbial adaptation and inadequate surface area of the rumen papillae as suggested by Dirksen et al. (1985). Feeding high grain diets during the dry period may help adapt the rumen papillae and rumen microbial population and therefore reduce the risk of SARA during the postpartum period. However, both Garrett et al. (1997) and Penner et al. (2007) found no effect of dry cow dietary adaptation protocol on the rumen pH in early lactation dairy cows. Furthermore, Penner et al. (2006b) found that the surface area of rumen papillae reached its maximum at 2 wk before parturition. These results suggest that the surface area of rumen papillae may not be the key factor influencing the occurence of SARA after calving. Krause and Oetzel (2006) proposed that the high DMI is an important risk factor for SARA. This may be true for mid-lactation dairy cows fed diets contain highly fermentable carbohydrates, but is not supported by the data from early lactation dairy cows (Penner et al., 2007). The greatest risk of SARA occurred within

the first wk after calving, at the time when the cows had the lowest DMI (Penner et al., 2007). Other researchers proposed that the great risk of developing SARA in early-lactation cows was probably due to the instability in the rumen microbial population (Nocek, 1997) and inadequate absorptive capacity of the rumen papillae (Gäbel et al., 1993). The exact mechanisms dictating the onset of SARA in early lactation are still not clear and requires further investigation.

1.2.5 Consequences of SARA

Economic losses caused by SARA in the U. S. dairy industry have been estimated to be US$500 to US$1 billion per year, with US$1.12 per affected cow per day (Enemark, 2009). These losses from SARA are mainly associated with reduced milk production, reduced milk efficiency, and increased health problems (Krause and Oetzel, 2006).

Decreased or erratic DMI is the most common consequence of SARA in ruminants (Plaizier et al., 2008). The decreased DMI associated with SARA may result from decreased fiber digestibility and increased VFA accumulation and osmolality in the rumen (Allen, 2000). Reduced in situ fiber digestibility and rumen pH during grain-induced SARA has been reported by Plaizier et al. (2001) and Krajcarski-Hunt et al. (2002). This is probably due to a decrease in the number and activity of fibrolytic bacteria because these bacteria are sensitive to the acidic rumen environment and cannot growth at pH below 6.0 (Shi and Weimer, 2002). In addition, inflammation is likely to be induced by SARA, as indicated by increased blood concentrations of acute phase proteins (Gozho et al., 2005; Gozho et al., 2007), and can contribute to the decrease in DMI (Plaizier et al., 2008). As dairy cows often experience NEB during the transition period, the decreased DMI as a result of SARA can further exacerbate the energy balance and negatively impact animal health and production. Therefore, reducing the incidence of SARA during the calving transition should be addressed in the nutritional management of transition cows.

Milk fat depression is another production loss associated with SARA. A field study found that there was a 0.3% reduction in milk fat content with dairy cows that experienced SARA (Stone, 1999). Other researchers also found a reduction in milk fat percentage (Oba and Allen, 2003; Fairfield et al., 2007; Enjalbert er al., 2008), milk fat yield (Krause and Oetzel, 2005), or both (Khafipour et al., 2009) in response to SARA. However, milk fat depression is not a constant consequence of SARA as the decrease in milk fat content was not observed in some studies (Keunen et al., 2002; Luan et al., 2016). Krause and Oetzel (2005) suggested that the short duration of SARA may help explain the inconsistent response in milk fat to SARA. Altered rumen biohydrogenation of fatty acids (FA) has been suggested as the explanation for milk fat depression (Bauman and Griinari, 2001). Milk FA are derived from two sources, half from the de novo synthesis in the mammary gland (mostly short- and medium-chain FA), and another half from circulating FA (long-chain FA) that originated from feed and body fat mobilization (Bauman and Griinari, 2003). When rumen pH drops, the microbial biohydrogenation of dietary unsaturated FA changes and produces unique FA intermediates that can reduce milk fat synthesis (Bauman and Griinari, 2003). This decrease in milk fat tends to be greater for the de novo synthesized FA than the circulating FA, resulting in an increased proportion of long-chain and unsaturated FA and a relatively lower proportion of short- and medium-chain FA (Bauman and Griinari, 2003).

Besides the direct production loss, SARA can reduce herd profitability by compromising dairy cow health. Laminitis, an inflammation of the hoof dermal layer, may occur due to SARA (Nocek, 1997). The exact relationship between laminitis and SARA is not fully understood, but it has been proposed that the consistently low rumen pH during SARA can increase the release of histamine and lipopolysaccharides (LPS) and therefore cause tissue damage, inflammation, and lameness (Nocek, 1997; Plaizier et al., 2008). In addition, the high histamine concentration in the

rumen may induce ruminal epithelial damage (Aschenbach and Gäbel, 2000), reduce the epithelial barrier function, and result in the translocation of rumen bacteria to portal blood and finally liver abscesses (Nocek, 1997; Kleen et al., 2003). The translocation of LPS, an endotoxin released by gram negative bacteria, from the impaired digestive tract into the bloodstream can trigger inflammation responses as indicated by the increased concentrations of acute phase proteins, such as haptoglobin (Hp; Gozho et al., 2005; Khafipoor et al., 2009) and serum amyloid A (SAA; Khafipoor et al., 2009; Gozho et al., 2007).

1.3 Nutritional management during the periparturient period

During the transition period, which is defined as 3 weeks prepartum to 3 weeks postpartum, dairy cows often experience NEB due to the rapid increase in nutrient requirements that cannot meet by the depressed feed intake (Grummer, 1995; Drackely, 1999). Dry matter intake of dairy cows decreases as parturition approaches, reaches a minimum level at calving, and gradually increases to a maximum level between 8 to 22 wk after calving (Ingvartsen and Andersen, 2000). Marquardt et al. (1977) indicated that there was a 25% to 52% decrease in DMI during the final 2 weeks of gestation in dairy cows. Huzzey et al. (2007) found that DMI decreased by approximately 30% in the day before calving. In order to support the growth of the fetus and postpartum milk production, dairy cows start to mobilize their body reserve. However, the excessive fatty acid mobilization from adipose tissues increases plasma NEFA concentration and may lead to a series of metabolic disorders as described in section 1.1.1.3.

Intense genetic selection and improvement in nutritional management have substantially increased milk production of dairy cows (van Kengsel, 2005). From 1980 to 2003, milk production has increased by approximately 2% per year (Eastridge, 2006). With the decrease in DMI around partition, the increased milk production further exacerbates NEB in early lactation. The challenge

faced by the dairy producers for the nutritional management of transition cows is to ensure the cows have a smooth calving transition. To meet this goal, nutritional strategies should aim to minimize the energy deficit and the incidence of health disorders. Increasing energy density of dairy rations to promote energy intake is the common way to offset the energy deficit associated with feed intake (Grummer, 1995). However, this feeding strategy does not guarantee a successful transition from late gestation to early lactation and dairy cows may get overconditioned during the close-up period and go into a more severe NEB in early lactation (Rukkwamsuk et al., 1999). Feeding low-energy diets, also known as controlled-energy diets, has gained popularity in recent decades and studies have shown positive outcomes in dairy cows fed controlled-energy diet, such as increased postpartum DMI (Douglas et al., 2006) and energy balance (Dann et al., 2006). However, dairy cows are at high risk of developing SARA during the first few weeks after calving due to a sudden increase in dietary NFC (Fairfield et al, 2007; Penner et al., 2007). Therefore, prepartum diets containing less, and postpartum diets containing a large amount of highly fermentable carbohydrate may increase the risk of developing SARA in early lactation dairy cows. The nutritional management of transition cows continues to evolve and the following gives a brief summary of some research studies conducted in the past several decades in the field of transition cow nutrition.

1.3.1 Nutritional management during the prepartum period

1.3.1.1 Effects of dietary carbohydrate on production and metabolism

In order to reduce the nutrient deficit resulting from depressed feed intake before calving, increasing energy density of the close-up diet by adding more fermentable carbohydrate has been recommended by NRC (2001). This feeding approach has been proposed to maximize DMI before calving and adapt the rumen microbial population and rumen papillae to the lactation diet (Grummer, 1995). In addition, increasing dietary NFC may promote DMI by reducing physical gut fill (Allen,

2000). In general, it was reported that DMI and energy intake during the prepartum transition period were both positivity correlated with NFC concentration and negatively correlated with NDF content of the diets (Hayirli et al., 2002).

Increasing dietary NFC by adding more grain and reducing fiber content is a common approach to increase dietary energy density and positive results have been reported in some studies (Minor et al., 1998; Vandehaar et al., 1999; Mashek and Beede, 2000). In the study of Minor et al. (1998), for example, cows were fed either a high-energy diet (1.63 Mcal NE_L kg/DM) with 43.8% of NFC and 29.5% of NDF or a low-energy diet (1.34 Mcal NE_L kg/DM) with 23.5% NFC and 48.9% NDF. The difference in NFC content was achieved by changing the amount of cracked corn versus forages. They found that the cows fed the high-energy diet had higher DMI and energy intake compared with those fed the low-energy diet and the former were in positive energy balance, whereas the latter were in NEB during the prepartum transition period. Moverover, plasma NEFA concentration was lower during the week prior to calving in cows a fed high energy diet compared with those fed a low energy diet. Vandehaar et al. (1999) also found that feeding a high energy diet from d 25 prepartum to parturition increased energy intake and tended to reduce plasma NEFA and BHB concentrations during the last 2 wk prepartum compared with those fed a low energy diet. The difference in dietary energy density was accomplished by increasing corn grain and reducing cottonseed hulls and corn silage (Vandehaar et al., 1999). Similar increases in prepartum DMI and decreases in plasma NEFA were reported by Rabelo et al. (2003) for dairy cows fed a high-energy diet (1.70 NE_L kg/DM, 44.6% NFC, 32.2% NDF) compared with those fed a low-energy diet (1.58 NE_L kg/DM, 38.2% NFC, 39.7% NDF). Feeding a high-energy diet also increased prepartum insulin concentration (Rabelo et al., 2003).

Besides increasing dietary starch content, increasing dietary NFC can also be achieved by adding more sugar to the diet, such as sucrose and lactose. Although prepartum plasma glucose concentrations tended to be higher for cows consuming more sucrose, partial replacement of corn grain with sucrose by 2.7 % of diet DM without changing NFC content (approximately 35.2%) in prepartum diet had no effect on DMI, milk production, and plasma NEFA concentration in dairy cows during the periparturient period (Ordway et al., 2002). DeFrain et al (2006) fed transition cows either a corn-based control diet (25.8%) or a diet containing lactose (12.6% starch and 15.8% lactose) with similar dietary NFC content and found that feeding lactose had no effect on prepartum DMI and plasma NEFA concentration. However, DMI from wk 2 to wk 1 decreased in cows fed the control diet but was not observed in cows fed lactose (DeFrain et al., 2006).

Despite the increased DMI before parturition, cows fed a high-energy diet may become overconditioned, which can further exacerbate the NEB (Rukkwamsuk et al., 1999). In addition, feeding a high-energy diet during the prepartum period was associated with increased prepartum insulin concentrations compared with those fed a controlled-energy diet or restricted-fed cows (Holtenius et al., 2003; Douglas et al., 2006; Dann et al., 2006; Janovick et al., 2011). In addition, Holtenius et al. (2003) found that the cows fed a high-energy diet had lower glucose clearance rate during a GTT performed at 3 wk postpartum, suggesting a higher extent of insulin resistance. The higher insulin resistance in overfed cows would further increase lipolysis and inhibit lipogenesis (De Koster and Opsomer, 2013), thereby predisposing dairy cows to metabolic diseases and reducing milk production. Feeding a controlled-energy close-up diet by inclusion of low quality feedstuff (e.g. straw) has shown variable success in studies conducted over the last decades, such as increased postpartum DMI (Douglas et al., 2006) and energy balance (Dann et al., 2006; Hayirli et al., 2011), reduced lipid mobilization postpartum (Douglas et al., 2006; Janovick et al., 2011; Zhang et al., 2015;

Mann et al., 2015), and decreased incidence of subclinical ketosis (Vickers et al., 2013) and episodes of hyperketonemia postpartum (Mann et al., 2015).

1.3.1.2 Effects of dietary carbohydrate on rumen fermentation

Feeding a high-energy diet close-up diet has been proposed to increase rumen epithelial surface area (Dirksen et al., 1985; Grummer, 1995) thereby increasing the absorptive capacity of the rumen and decreasing the risk of SARA after calving. Due to low intake of fermentable carbohydrate, length rumen papillae shorten during the dry period (Dirksen et al., 1985). It has been reported that increasing dietary energy density two weeks before parturition with more grain increases VFA absorption capacity due to increased rumen papillae size (Dirksen et al., 1985). However, increasing energy intake during the dry period does not always stimulate rumen epithelial proliferation prepartum (Rabelo et al., 2001; Reynolds et al., 2004) or postpartum (Reynolds et al., 2004; Dieho et al., 2017). In addition, both Garrett et al. (1997) and Penner et al. (2007) found no effect of dry cow dietary adaptation protocol on the rumen pH in early lactation dairy cows. Feeding a high-energy diet (1.70 Mcal NE_L kg/DM) reduced rumen pH during the prepartum period compared with those fed a low energy diet (1.58 Mcal NE_L kg/DM), but postpartum rumen pH was not affected by prepartum dietary energy density (Rabelo et al., 2003). Furthermore, Penner et al. (2006b) found that the surface area of rumen papillae reached its maximum at 2 wk before parturition. These results indicate that feeding high energy diets by increasing dietary NFC during the prepartum period may not increase VFA absorption capacity of the rumen and reduce the risk of SARA during the postpartum fresh period. This may be related to reduction in DMI as calving approaches which may negatively affect the VFA absorption capacity of the rumen. It has been demonstrated that the rate of VFA absorption decreased after 48 hours of feed withdrawal in sheep fed a hay diet (Gäbel et al., 1993; Gäbel and Aschenbach, 2002). Therefore, maximizing prepartum DMI and minimizing the reduction in DMI

around calving may not only improve the energy balance but may also reduce the severity of SARA in dairy cows after calving.

1.3.2 Nutritional management during the postpartum period

1.3.2.1 Effects of dietary carbohydrate on production and metabolism

During the fresh period, or postpartum transition period, dairy cows are often in negative energy balance due to the rapid increase in milk production and the gradually recovery of feed intake. Increasing dietary carbohydrate content by adding more grain is expected to reduce the extent of negative energy balance and improve performance of dairy cows by increasing energy intake. However, this approach may decrease DMI by increasing propionate flux from the rumen according to hepatic oxidation theory (Allen et al., 2009) that when oxidation of fuels in the liver, such as propionate and NEFA, exceeds the hepatic energy requirements, signals sent to the brain decreases feed intake of the animal. Dairy cows in early lactation are susceptible to SARA (Penner et al., 2007), therefore feeding a high-grain diet may indirectly depress DMI and impair animal health due to SARA (Stone, 2004; Krause and Oetzel, 2006).

However, animal responses to increased postpartum dietary starch content vary among studies. Dieho et al. (2016a) demonstrated that dairy cows produced more milk when they had a lower rate of increase in concentrate allowance (0.25 kg of DM/d) during the postpartum period compared with a faster increase in postpartum concentrate allowance (1.0 kg of DM/d), but DMI was not affected by concentrate treatment. In contrast, Rabelo et al. (2003) found that the cows fed a high-NFC diet (47.2% NFC) had a faster increase in milk production and tended to have greater DMI than those fed a low-NFC diet (41.1% NFC) during the first 20 days after calving. Postpartum plasma concentrations of glucose and insulin were higher and BHB concentration was lower in cows fed a high-NFC diet compared with a low-NFC diet, but NEFA concentration did not differ (Rabelo

et al., 2005). The increase in dietary NFC content was accomplished by adding more ground corn grain (Rabelo et al., 2003; Rabelo et al., 2005). In addition, in the study of McCarthy et al. (2015a), cows fed high-starch diets (26.2% starch) had a faster rate of increase in DMI and milk yield compared with those fed low-starch diets (21.5% starch). Dairy cows fed high-starch diets also had higher plasma concentrations of glucose and insulin and lower plasma concentrations of NEFA and BHB during the fresh period compared with the low-starch group (McCarthy et al., 2015b). Moreover, they found that cows fed high-starch diets had greater insulin resistance, but incidence of health disorders was not affected by dietary starch content during the fresh period.

Partially replacing starch with sugar has been shown to increase DMI (Broderick and Radloff, 2004) and milk production (Gao and Oba, 2016) in studies with mid-lactation dairy cows. Although DeFrain et al. (2006) found no effects of feeding sugar during the transition period on postpartum DMI and milk yield, liver lipid content was lower in transition cows fed a high-sugar diet than the control group. Penner and Oba (2009) fed dairy cows either a high-sugar (8.4%) or a low-sugar diet (4.7%) during the first 4 wk after parturition and observed that cows fed high-sugar diet had greater DMI compared cows fed low-sugar diet but milk yield was not affected by dietary sugar content. However, Ordway et al. (2002) reported that feeding sugar during the transition period had no effect on DMI or milk yield. Some others also reported the lack of effects of feeding sugar on DMI in lactating dairy cows (Penner et al., 2009b; Chibisa et al., 2015). The reason why feeding sugar did not consistently increase DMI or milk yield is not clear, but feeding sugar did not seem to bring harmful effects as summarized by Oba (2011).

1.3.2.2 Effects of dietary carbohydrate on rumen fermentation

As mentioned previously, dairy cows are susceptible to SARA in the postpartum transition period. Increasing dietary fermentable carbohydrate is then hypothesized to reduce rumen pH and

increase the risk of SARA. Rabelo et al. (2003) reported that the cows fed a high-NFC diet during the fresh period had lower ruminal pH compared with those fed a low-NFC diet by the end of the fresh period. Contrarily, rumen pH was not affected by the rate of increase of concentrate allowance in the study by Dieho et al. (2016a). The different response in rumen pH between these two studies may be attributed to the discrepancy in DMI in response to dietary fermentable carbohydrate content. Feeding a high-NFC diet tended to increase postpartum DMI in the study of Rabelo et al. (2003), whereas DMI was not affected by concentrate allowance in the study of Dieho et al. (2016a). Sun and Oba (2014) replaced grain with dried distillers grains with solubles (DDGS) in a dairy cow diet immediately after calving until 12 wk after parturition and measured rumen pH on a weekly basis. They reported that cows fed the DDGS diet did not have increased rumen pH compared with the control group in early-lactation, but the effects of DDGS on rumen pH during the postpartum transition period were not addressed.

A review (Oba, 2011) summarized that partially substituting starch with sugar in ruminant diets did not decrease (DeFrain et al., 2004; Broderick et al. 2008) but even increased (Chamberlain et al., 1993; Heldt et al., 1999) or tended to increase rumen pH (Penner et al., 2009b). Only limited data can be found for the effects of feeding sugar on rumen pH during early-lactation in dairy cows. Penner and Oba (2009) showed that rumen pH tended to be greater in dairy cows fed a high-sugar diet during the first 4 wk after parturition. In order to better understand the effects of replacing starch with sugar in the diet on production and rumen pH in early lactation cows, more research is warranted.

1.4 *Saccharomyces cerevisiae* fermentation product

Saccharomyces cerevisiae is a yeast species commonly used in the dairy industry. There are two kinds of yeast product: active dry yeast and yeast culture. Active dry yeast product must contain

at least 15 billion live yeast cells/g (Poppy et al., 2012) and is expected to influence animal performance through yeast cells that remain alive in the rumen (Newbold et al., 1996). In contrast, *Saccharomyces cerevisiae* fermentation product (SCFP), or yeast culture, is produced through anaerobic yeast fermentation based on *Saccharomyces cerevisiae* strains and affects rumen environment and animal performance independent of live yeast cells (Poppy et al., 2012).

1.4.1 Composition

SCFP consists of *Saccharomyces cerevisiae*, the medium where yeasts are grown (e.g., cereal grain raw ingredients and molasses; Shen et al., 2018), and metabolites produced by yeasts (e.g., enzymes, organic acids, amino acids, and vitamins and minerals; Robison and Erasmus, 2009). The major cell wall components of *Saccharomyces cerevisiae* include mannan oligosaccharides (30-50%), 1,3-β-glucan (30-45%), 1,6-β-glucan (5-10%), and chitin (1.5-6%) (Klis et al., 2006). Of these cell wall components, β-glucan and mannan oligosaccharides extracted from *Saccharomyces cerevisiae* are the ones widely studied.

β-glucans are polysaccharides of glucose and are well-known as biological response modifiers of both cellular and humoral immune system (Novak and Vetvicka, 2008). The immunomodulatory acitivities of β-glucans include modulation of macrophage phagocytosis and stimulation macrophage release of cytokines, such as tumour necrosis factor-α, interleukin-1, interleukin-2, and interleukin-6 (Petravić-Tominac et al., 2010). Binding of β-glucans to specific receptors activates the macrophage and also triggers intracellular activities (Novak and Vetvicka, 2008). In addition, β-glucans may prevent attachment and colonization of pathogents in the gastrointestinal tract by binding to bacteria (Ruiz-Herrera, 2016). It was shown that oral administration of β-glucans promoted intestinal barrier function against pathogenic infection in broiler chickens by increasing the mRNA expression of intestinal tight junction proteins, including

claudin-1 and occluding, and by increasing the number of secretory immunoglobulin A-expressing intestinal cells and the content of secretory immunoglobulin A (Shao et al., 2013). Supplementation of yeast β-glucan at 75 mg/kg feed to pre-weaned calves has reported to increase nutrient digestibility and enhance immunity by increasing serum immunoglobulin G concentration (Tao et al., 2015).

Mannan oligosaccharides (MOS) are polymers of mannose and may block colonization of pathogens in the gastrointestinal tract by providing binding sites for these intestinal pathogens (Heinrichs et al., 2003; Uyeno et al., 2015). The MOS is not digested or absorbed in the small intestine; therefore, certain gram-negative bacteria bound to MOS may exit the intestinal tract without attaching to the epithelium (Spring et al., 2000; Heinrichs et al., 2003). Supplementation of dairy calves with MOS in milk replacer was reported to increase fecal consistency (Heinrichs et al., 2003) and reduce fecal score (Morrison et al., 2010) compared with unsupplemented group. In addition, feeding MOS to beef cows during late lactation through 30 d of lactation tended to limit BCS loss from parturition to the end of the feeding period, but had no effect on passive immunity of calves (Linneen et al., 2014). Supplementation of MOS to dry cows during the last 3 wk before parturition was found to enhance immune response of the cows to rotavirus and tend to promote the subsequent transfer of rotavirus antibodies to calves (Franklin et al., 2005).

1.4.2 Application in dairy industry

Fermentation products of *Saccharomyces cerevisiae* have been widely used as feed additives to modify the rumen environment and promote production performance in ruminants. However, the mechanism of the effects of SCFP is not fully understood. It has been proposed that SCFP contains a mixture of micronutrients (organic acids, amino acids, B vitamins) that can stimulate the growth of cellulolytic bacteria and lactate utilizing bacteria (Callaway and Martin, 1997; Robinson and

Erasmus, 2009), and increase the protozoa count in the rumen (Arakaki et al., 2000; Shen et al., 2018), thereby stabilizing rumen pH. In addition, feeding SCFP increases microbial protein synthesis (Hristov et al., 2010) in dairy cows and reduces methane production in sheep (Mwenya et al., 2004).

Numerous studies have reported the beneficial effects of SCFP supplementation, such as increased DMI (Dann et al., 2000), milk production (Ramsing et al., 2009; Zaworski et al., 2014), and feed efficiency (Schingoethe et al., 2004; Cooke et al., 2007). Dann et al. (2000) also reported that feeding SCFP from d 21 before expected calving date to d 42 after calving increased dietary energy supply during the postpartum period. A meta-analysis by Poppy et al. (2012) showed that SCFP increased 3.5% fat-corrected milk (FCM), energy-corrected milk, and yield of milk fat and protein by 1.61, 1.65, 0.06, and 0.03 kg/d, respectively, in lactating dairy cows. In addition, SCFP increased DMI of dairy cows in early lactation by 0.62 kg/d (< 70 DIM), but reduced DMI in later lactation (> 70 DIM) without decreasing milk production, suggesting that supplementation of SCFP can increase the feed efficiency of dairy cows post-peak lactation. In addition to dairy cows, a meta-analysis evaluating the effects of SCFP supplementation on feedlot performance found that SCFP increased the average daily gain, gain-to-feed ratio, and DMI of beef cattle (Wagner et al., 2016). However, SCFP did not always promote production performance as observed in some studies that feeding SCFP had no effect on DMI or milk yield (Robinson, 1997; Robinson and Garrett, 1999). The inconsistent effects of SCFP supplementation may be associated with the DMI and milk yield of the cows. Previously studies have reported that the effect of various dietary treatments on DMI, digestion, and production of dairy cows is related to pre-trial DMI (Voelker Linton and Allen, 2008) and milk yield (Oba and Allen, 1999) of the animal. For dairy cows fed SCFP from 3 weeks before to 8 weeks after parturition, Erasmus et al. (2005) also found that the DMI responses to SCFP was dependent upon the level of DMI. SCFP supplementation decreased DMI when the cows consumed

less than 23.8 kg of DM per day and increased DMI when the cows consumed more than 23.8 kg/d of DM.

Supplementation of SCFP has also been reported to affect rumen pH in cattle. In a metabolism study with beef heifers, Shen et al. (2018) found that SCFP supplementation increased the minimum rumen pH and reduced the duration of pH below 5.6 by 6 h compared with the control group along with increased rumen and total tract NDF digestibility. However, SCFP supplementation had no effect on rumen pH as observed in some studies with dairy cows (Erasmus et al., 2005; Longuski et al., 2009; Li et al., 2016). Allen and Ying (2012) found that SCFP supplementation reduced the rumen digestion rate of starch for dairy cows with DMI greater than 26 kg/d and increased the rate of starch digestion in the rumen for dairy cows with lower DMI compared with control, suggesting that SCFP may help stabilize the rumen environment when dairy cows consumed large amounts of higher fermentable carbohydrate. Therefore, the variation in the response to SCFP supplementation may be partially attributed to the DMI level of the cows used in the studies.

1.5 Summary

The transition from late gestation to early lactation is a challenging period for dairy cows and also dairy producers. To ensure a smooth calving transition, nutritional management should aim to reduce the extent of NEB and ruminal acidosis after calving. Increasing dietary starch content after calving to promote energy intake is the common way to offset the energy deficit associated with depressed feed intake. However, dairy cows are susceptible to SARA in early lactation and this feeding strategy may increase the risk of developing SARA, especially for dairy cows fed a low energy diet before calving. Fermentation products of *Saccharomyces cerevisiae* have been widely used in diets of dairy cows and it was found recently that SCFP supplementation can reduce the duration of SARA in beef heifers fed a high-starch diet (Shen et al., 2018). However, the interaction

of dietary starch content and SCFP supplementation was not extensively investigated particularly during the fresh period.

Feeding a low energy or controlled-energy diet during the prepartum period has been recommended in order to prevent excess energy intake. However, this feeding approach may also increase the risk of SARA in dairy cows immediately after calving. As time after parturition affects the severity of SARA (Penner et al., 2007), it is not known how long the negative effect of feeding a low energy close-up diet on rumen pH can last after calving.

Therefore, the objectives of this research were to 1) evaluate the effects of starch content of the fresh diet and SCFP supplementation during the periparturient period on production performance and rumen fermentation of dairy cows in early lactation and 2) compare the effects of starch content of the close-up diet on rumen fermentation of dairy cows during calving transition. It was hypothesized that 1) feeding a low-starch fresh diet and supplementing SCFP during the periparturient period would enhance production performance and reduce the risk of SARA in transition dairy cows, 2) the benefits of SCFP supplementation would be greater for dairy cows fed a high-starch diet, and that 3) feeding a low-starch diet during the close-up period would increase the risk of developing SARA during the postpartum period, particularly immediately after calving.

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Chapter 2. Effects of supplementing a *Saccharomyces cerevisiae* fermentation product during periparturient period on performance of dairy cows fed postpartum diets differing in starch content

2.1 Introduction

Dairy cattle often experience negative energy balance during the calving transition period, which is characterized by reduced feed intake and a drastic increase in nutrient demands after the onset of lactation, contributing to high incidence of health problems (Zaworski et al., 2014). Therefore, feeding strategies during the calving transition period should be aimed to maintain feed intake and thus reduce excessive fat mobilization. Increasing starch content of postpartum diets is expected to reduce the extent of negative energy balance and improve performance of dairy cows by increasing energy intake. However, this approach may decrease DMI by increasing propionate flux from the rumen according to hepatic oxidation theory (Allen et al., 2009) and expose dairy cows to a greater risk of SARA (Stone, 2004; Penner et al., 2007). The occurrence of SARA is associated with reduced feed intake and impaired animal health (Stone, 2004; Krause and Oetzel, 2006); therefore, feeding diets high in fermentable carbohydrate during the postpartum transition period may not necessarily improve dairy cow performance.

Fermentation products of *Saccharomyces cerevisiae* (SCFP) have been widely used in diets of dairy cows with the aim to increase production performance and stabilize rumen pH (Erasmus et al., 2005). Several studies have reported such positive effects as increased DMI (Dann et al., 2000) and milk production (Ramsing et al. 2009; Zaworski et al., 2014) when cows were fed SCFP while SCFP supplementation did not affect DMI or milk yield in other studies (Robinson, 1997; Robinson and Garrett, 1999). In a meta-analysis study, Poppy et al. (2012) showed that supplementation of SCFP increased DMI of dairy cows in early lactation (DIM < 70). However, interaction effects

between fermentability of the basal diet and SCFP supplementation on DMI were not addressed. More recently, in a metabolism study with beef heifers, Shen et al. (2018) found that supplementation of a high grain diet (52.8% starch) with SCFP elevated the ruminal minimum pH and reduced the duration of pH < 5.6 by 6 h compared with control heifers along with improved ruminal and total tract NDF digestibility, suggesting that the negative effects of feeding high-starch diet can be attenuated by supplementing SCFP. However, the interaction of dietary starch content and SCFP supplementation were not extensively studied particularly for the immediate postpartum period.

Therefore, the objective of the current study was to evaluate the effects of SCFP supplementation during the periparturient period on DMI, milk production, and apparent total tract nutrient digestibility of dairy cows fed fresh diets varying in starch content. We hypothesized that feeding high-starch diets during the fresh period would negatively affect performance of dairy cows compared with low-starch diets and that supplementing SCFP during the periparturient period would mitigate negative effects of feeding high-starch diets and enhance production performance of dairy cows.

2.2 Materials and Methods

All experimental procedures used in this study were approved by the University of Alberta Animal Care and Use Committee (AUP#1915) and conducted according to the guidelines of the Canadian Council of Animal Care (2009).

2.2.1 Animals, Diets, and Experimental Design

One-hundred seventeen (44 primiparous and 73 multiparous) Holstein dairy cows were assigned to treatment balanced for parity, BCS, BW, and expected calving date (Table 2.7.1). Cows were enrolled into the study at d 28 ± 3 prior to expected calving date and fed diets supplemented

with a *Saccharomyces cerevisiae* fermentation product (SCFP; NutriTek®, Diamond V, Cedar Rapids, IA; n = 59) or without SCFP (CON; n = 58) until d 44 ± 3 after calving. The SCFP was supplemented at 0.173 and 0.095 % of dietary DM in prepartum and postpartum diets, respectively. We intended to provide 19 g/cow/d (as-fed basis) based on expected DMI of the cows (prepartum, 11 kg/cow/d; postpartum, 20 kg/cow/d on DM basis). All cows were fed a common basal controlled-energy diet (1.43 Mcal NE_L/kg DM; 13.8% starch; Table 2.7.2) from d -28 ± 3 relative to expected calving date until parturition (close-up period). Cows within each treatment (CON or SCFP) were fed either a low- (LS) or high-starch diet (HS) for the first 23 ± 3 days after calving (fresh period), and all cows were fed the HS diets from d 24 ± 3 to 44 ± 3 after calving (post-fresh period). The timeline of experimental design was presented in Figure 2.7.1. The starch contents of LS and HS diets were formulated to be 21% and 27% on a DM basis, respectively. Diets were formulated using Dairy NRC (2001) to meet or exceed all nutrient requirements for a 650 kg cow producing 31 kg/d (LS) or 32 kg/d (HS) of milk with 3.8% milk fat and 3.0% milk protein (Table 2.7.2). The LS diets were formulated by decreasing the starch content of HS diets primarily by replacing a portion of the barley grain with beet pulp. Throughout the study, cows were housed individually in tie-stalls and had free access to water. Cows were fed experimental diets once daily at 0730 h and at 105% to 110% of actual feed intake (as-fed basis) of the previous day. Feed was not pushed up as cows were fed using mangers that allow them to have full access to feed throughout the day. Cows, after calving, were milked in their stalls twice daily at 0330 and 1500 h.

2.2.2 Data and Sample Collection

Data and samples were collected on certain day(s) of week (e.g., Tuesday), unless noted otherwise, to facilitate routine management of the dairy operation, and this protocol allowed deviations of up to 3 d from the target sampling day (± 3). The amount of feed offered and refused

was recorded daily for all cows throughout the study. Barley silage samples were collected for three consecutive days weekly and composited to yield one sample per week. Other forage, concentrate, and TMR samples were collected once weekly. The DM concentration of individual feed ingredients was determined weekly in a forced-air oven at 55 ^{o}C for 48 h and diet formulation was adjusted if necessary. Dried samples were ground in a Wiley mill (Thomas-Wiley, Philadelphia, PA) to pass through a 1-mm screen. Ground silage samples were composited monthly, straw and hay samples were composited every two months, and concentrate samples were composited every 4 months.

Milk yield was recorded daily for all cows after calving. Milk samples were collected from all cows once weekly from two consecutive milkings (p.m. and a.m.). Body weight and BCS were determined at the beginning of the study (d -28 ± 3), immediately after calving, at the end of 3 wk (d 23 ± 3) after calving, and at the end of study. Body weight was measured for two consecutive days before feed delivery but after morning milking (after calving). Body condition score was recorded by 3 individuals using a 5-point scale (Wildman et al., 1982). Both BW and BCS data of each measurement point were averaged before statistical analysis and changes in BW and BCS before- and after-calving were calculated. Health status were monitored daily for all cows and recorded throughout the experiment period.

Blood samples were collected from all cows before morning feeding (~ 0700 h) on d -28 ± 3, -10 ± 3, 7 ± 3, 21 ± 3, and 42 ± 3. In addition, d 1 blood samples were collected within 12 h after calving, before cows consumed the postpartum diet. All blood samples were collected via tail blood vessel into Vacutainer tubes containing sodium heparin (Fisher Scientific Company; Nepean, ON, Canada), centrifuged at 4 ^{o}C (3,000 × *g* for 20 min) immediately after collection, and plasma was harvested and stored at -20 ^{o}C until analysis.

A subset of 38 cows was selected after balancing parity, BCS, BW, and expected calving date (Table 2.7.1). For those 38 cows, apparent total tract digestibilities of DM, OM, NDF, and starch were determined on wk 1 and 3 after calving. Fecal grab samples were collected, on d 7 to 9 ± 3 (wk 1) and d 21 to 23 ± 3 (wk 3) after calving, every 9 h for 3-d periods to obtain a representative sample accounting for every 3 h of a 24-h period. Fecal samples were composited for each cow at each sampling period and dried in a forced-air oven for 72 h at 55 °C. Samples of feed ingredients were collected for three consecutive days weekly and composited to yield one sample per week and dried in a forced-air oven at 55 °C for 48 h. Fecal and feed ingredients samples were then ground to pass through a 1-mm screen (Wiley mill, Thomas-Wiley, Philadelphia, PA). Weekly feed ingredient samples were composited by load of feed delivered to the farm (barley silage, n = 9; alfalfa hay, n = 12; concentrates, n = 3 to 6).

2.2.3 Sample Analyses

Milk samples were analyzed for CP, fat, lactose, somatic cell cout (SCC), and milk urea nitrogen (MUN) concentrations by infrared spectroscopy (AOAC International, 2002; method 972.16; MilkoScan 605, Foss North America, Brampton, ON, Canada) at the Alberta Central Milk Testing Laboratory (Edmonton, AB, Canada). The 3.5% FCM was calculated as: 0.432 × milk yield + 16.23 × fat yield, and solids-corrected milk yield (SCM) was calculated as: 12.3 × fat yield + 6.56 × SNF yield – 0.0752 × milk yield (Tyrrell and Reid, 1965).

Plasma glucose concentration was analyzed using a glucose oxidase/peroxidase enzyme (No. P7119; Sigma) and dianisidine dihydrochloride (No. F5803; Sigma). Absorbance was determined with a plate reader (SpectraMax 190; Molecular Devices Crop., Sunnyvale, CA) at the wavelength of 450 nm. Plasma free fatty acid concentration was determined using a commercial kit NEFA HR2; (Wako Chemicals USA, Inc., Richmond, VA). Plasma BHB concentration was measured by the

enzymatic oxidation of BHB to acetoacetate in the presence of 3-hydroxybutyrate dehydrogenase (No. H6501; Roche, Mississauga, Ontario, Canada) followed by determination of NADH production at a wavelength of 340 nm.

Feed and fecal samples were sent to Cumberland Valley Analytical Services (Hagerstown, MD), and analyzed for DM (AOAC International, 2002; method 930.15), OM (AOAC International, 2002; method 942.05), NDF (Van Soest et al., 1991), starch (Hall, 2009), and CP (AOAC International, 2000; method 990.03). Indigestible NDF was determined after 288 h of in situ digestion using a ruminally-cannulated dry cow fed a TMR containing 59.4% triticale silage, 25.5% barley straw, 4.24% rolled barley, 4.24% canola meal, 5.94% barley malt sprouts, and 0.68% minerals and vitamins with 50% dietary NDF content (all on a DM basis) with a method adapted from Huhtanen et al. (1994), and used as an internal marker to estimate fecal output (Cochran et al., 1986).

2.2.4 Statistical Analysis

Statistical analyses were conducted using the Fit Model procedure of JMP 13 and SAS 9.2 (SAS Institute Inc., Cary, NC). Data were analyzed separately for close-up, fresh (d 1 to 23 ± 3), and post-fresh (d 24 to 44 ± 3) periods. Prepartum and postpartum data (both fresh and post-fresh periods) were analyzed using the following model (1) and (2), respectively:

$$Y_{ikl} = \mu + T_i + P_k + W_l + TP_{ik} + TW_{il} + PW_{kl} + e_{ikl}, \quad (1)$$

$$Y_{ijkl} = \mu + T_i + S_j + P_k + W_l + TS_{ij} + TP_{ik} + TW_{il} + SP_{jk} + SW_{jl} + PW_{kl} + TSW_{ijl} + e_{ijkl}, \quad (2)$$

where Y_{ijk} = observations for dependent variables, μ = overall mean, T_i = fixed effect of SCFP supplementation (CON or SCFP), S_j = fixed effects or carryover effects of starch content of fresh diets (LS or HS), P_k = fixed effect of parity (primiparous or multiparous), W_l = fixed effect of week relative to parturition as a repeated measure, TP_{ik} = effect of SCFP and parity interaction, TW_{il} =

effect of SCFP and week interaction, PW_{kl} = effect of parity and week interaction, TS_{ij} = effect of SCFP and starch content interaction, SP_{jk} = effect of starch content and parity interaction, SW_{jl} = effect of starch content and week interaction, TSW_{ijl} = effect of SCFP, starch content, and week interaction, and e_{ijkl} = residuals. Because cows were fed LS or HS fresh diet until d 23 ± 3, and the post-fresh period (wk 4-6) started on a certain day of week (i.e., Friday; allowing a deviation of up to 3 d from the target day relative to calving), wk 1, 2, 3, 4, 5, and 6 were defined as d 1 to 7, d 8 to 14, d 15 to d 23 ± 3, d 24 ± 3 to 30 ± 3, d 31 ± 3 to 37 ± 3, and d 38 ± 3 to 44 ± 3 after calving, respectively.

The repeated measure was used for variables measured over time, such as DMI, milk yield and components, and feed efficiency using the REPEATED statement in the MIXED procedure of SAS. The covariance structure with the smallest Akaike's information criterion was used (Littell et al., 1996). For variables not measured over time, such as BW and BCS changes and plasma metabolites, data were analyzed using JMP 13 and the effect of time relative to parturition and all associated interactions were removed from the model. When an interaction between starch content and SCFP supplementation was detected, comparisons among treatments were conducted using Student's t-test.

For all response variables, significance was declared at $P \leq 0.05$ and tendency was declared at $0.05 < P \leq 0.10$.

2.3 Results

One-hundred-twenty-eight cows had been initially assigned to treatments, but 2 cows that were not fed close-up diets more than 2 weeks due to unexpected early calving and 9 cows that had severe health problems immediately after calving (1 metritis, 1 mastitis, 2 milk fever, 2 fatty liver, and 3 leg injuries; 2 and 7 cows were on CON and SCFP before calving, respectively) were removed

from the study, leaving 117 cows for the statistical analyses. The starch content of fresh diets, calculated from analyses of feed ingredients, was as follows: LS-CON, 21.6% starch; LS-SCFP, 22.5% starch; HS-CON, 27.0% starch; and HS-SCFP, 29.5% starch. Starch content of the HS-SCFP diet was likely overestimated due to sampling error of the concentrate mix stored in a different type of feed bin where access for sampling is difficult.

2.3.1 Animal Responses during the Close-up Period (d -28 ± 3 to parturition)

There were no differences in DMI and BCS change between SCFP and CON group during the close-up period (Table 2.7.3). Energy intake was about 110% of NE_L requirement for both SCFP and CON cows. Initial plasma concentrations of glucose, free fatty acids, and BHB were not different between SCFP and CON cows, and they were not affected by SCFP supplementation on d -10 and d +1 relative to calving (Table 2.7.4).

2.3.2 Animal Responses during the Fresh Period (d 1 to 23 ± 3)

DMI, BW, BCS, and Milk Production. Interactions between dietary starch content and SCFP supplementation were not detected for DMI, BW, BCS, and milk yield (Table 2.7.5). All cows, regardless of treatment, increased DMI during the fresh period (week effect: $P < 0.0001$). Overall DMI and BW change were not affected by starch content of fresh diets, but milk yield was higher (34.1 vs. 32.1 kg/d; $P < 0.05$) and the loss of BCS tended to be greater (-0.42 vs. -0.35 /21d; $P = 0.06$) for cows fed LS than HS diets. In addition, a starch × week interaction was noted for milk yield during the fresh period ($P = 0.04$), suggesting that the cows fed LS diets had a faster increase in milk production. However, yields of milk components, 3.5% FCM, or SCM were not affected by starch content, resulting in similar feed efficiency (3.5% FCM/DMI) between dietary starch treatments. Tendency of interaction between SCFP and day was observed ($P = 0.08$; Figure 2.7.2), and DMI at d 1 (13.0 vs. 11.9 kg/d; $P = 0.02$) and d 5 (15.5 vs. 14.1 kg/d; $P = 0.04$) were greater for SCFP

compared with CON cows. Supplementation of SCFP did not affect overall DMI, BW change, or BCS change during the fresh period. Yields of milk, milk component, 3.5% FCM, or SCM during the fresh period were also not affected by SCFP supplementation.

Interactions between dietary starch content and SCFP supplementation were detected for concentrations of milk fat ($P = 0.03$), total solids ($P = 0.04$), and MUN ($P = 0.02$). Within cows fed CON, feeding LS postpartum diet decreased concentration of milk fat and total solids compared with cows fed HS diet. Supplementation of SCFP increased concentration of total solids compared with CON within cows fed LS postpartum diet. Concentration of MUN was lower for cows fed SCFP than CON when HS diet was fed during the fresh period.

Plasma Metabolites and Health Disorders. No interactions between dietary starch content and SCFP supplementation were detected for plasma concentrations of glucose and BHB on d 7 ± 3 and 21 ± 3 after calving (Table 2.7.6). Interactions of dietary starch content and SCFP supplementation were noted for plasma free fatty acids concentration on both d 7 ± 3 and 21 ± 3 after calving ($P < 0.05$). Cows fed LS diets had higher plasma free fatty acids concentration than HS cows only within CON group. Plasma free fatty acids were lower for SCFP cows compared with CON on d 7 ± 3, but these were observed only for cows fed LS diet. Cows fed LS diets had lower plasma glucose concentrations on d 7 ± 3 (57.3 vs. 60.3 mg/dL; $P = 0.05$) and 21 ± 3 (58.8 vs. 63.9 mg/dL; $P < 0.01$) than those fed HS diets during the fresh period. Plasma BHB concentration was not affected by starch content on d 7 ± 3, but cows fed LS diets had higher plasma BHB than HS cows at d 21 ± 3 (9.95 vs. 8.16 mg/dL; $P = 0.01$). Supplementation of SCFP did not affect plasma glucose on d 7 ± 3 or 21 ± 3 after calving. Supplementation of SCFP had no effect on plasma BHB on both d 7 ± 3 and 21 ± 3. Incidence of health disorders were 27 and 26 cases for LS and HS cows, respectively, and 33 and 20 cases for CON and SCFP cows, respectively (Table 2.7.7).

Digestibility. Interactions between dietary starch content and SCFP supplementation were not detected for any digestibility measurements (Table 2.7.8). There were no starch effect on apparent total tract OM or DM digestibility; however apparent total tract NDF digestibility was greater for LS cows compared to HS cows (40.7 vs. 35.3%; $P = 0.01$) on d 7 sampling period. There was an interaction between dietary starch treatment and parity ($P < 0.01$). Apparent total tract starch digestibility was greater for low-starch diets for multiparous cows on d 7 (98.7 vs. 97.8%; $P = 0.01$) and 21 (98.7 vs. 97.7%; $P < 0.01$), but lower for low-starch diets for primiparous cows on d 7 (98.6 vs. 99.1%; $P = 0.04$) and 21 (98.7 vs. 99.3%; $P = 0.04$). There were no effects of SCFP supplementation on apparent total tract DM, OM, or NDF digestibility.

2.3.3 Animal Responses after the Fresh Period (d 24 ± 3 to 44 ± 3)

DMI and Milk Production. All animals were fed HS diets during the post-fresh period, and effects of dietary starch content described in this section are carry-over effects from the fresh period. Interactions between carry-over effects of starch content of fresh diets and SCFP supplementation were not detected for DMI and milk yield (Table 2.7.9). Overall DMI during the post-fresh period was not affected by starch content of fresh diets, but the cows fed LS fresh diets tended to have higher milk yield (42.2 vs. 40.3 kg/d; $P = 0.09$) than those fed HS diets during the post-fresh period. Yields of milk components during the post-fresh period, however, were not affected by starch content of fresh diets. Although the cows supplemented with SCFP tended to have lower DMI (19.8 vs. 20.6 kg/d; $P = 0.01$) compared with those fed CON, yields of milk, milk components, 3.5% FCM, or SCM was not affected by SCFP supplementation, resulting in increased 3.5 % FCM/DMI (2.27 vs. 2.12; $P < 0.01$). The changes in BW and BCS during the post-fresh period were not affected by starch content of fresh diets or SCFP supplementation. Apparent dietary NE_L density, calculated from energy in actual milk production, maintenance, and energy provided or required by BW change

(Dann et al., 2000), was not affected by starch content, but it was greater for cows fed SCFP than CON (2.07 vs. 1.97 Mcal/kg DMI; $P = 0.05$).

Tendency of interactions between starch content of fresh diets and SCFP supplementation were detected for concentrations of milk fat ($P = 0.08$), total solids ($P = 0.08$), MUN ($P = 0.09$), and SCC ($P = 0.07$) during the post-fresh period. Within cows fed CON, concentrations of milk fat and total solids were lower for cows fed LS postpartum diet compared with cows fed HS diets. Concentration of total solids was greater for SCFP cows compared with CON within cows fed LS postpartum diet. Concentration of MUN was lower for the cows fed SCFP than CON when HS diet was fed during the immediate postpartum period. Within CON group, SCC was lower for LS cows than HS cows. In addition, SCC tended to be lower for SCFP cows versus CON within cows fed HS postpartum diet ($P = 0.07$).

Plasma Metabolites. Interactions of starch content of fresh diets and SCFP supplementation existed for concentrations of plasma free fatty acids ($P < 0.01$) and BHB ($P = 0.03$) on d 42 ± 3. Concentrations of plasma free fatty acids were lower in SCFP cows compared with CON cows, but only for cows fed LS fresh diets. Plasma BHB was also lower in cows that received SCFP supplementation compared with CON cows but the effect was mostly stemming from cows fed the HS fresh diets. Cows fed LS fresh diets tended to have lower plasma glucose than those fed HS fresh diets (62.0 vs. 65.2 mg/dL; $P = 0.06$; Table 2.7.10). Plasma glucose at d 42 ± 3 after calving (66.5 vs. 60.8 mg/dL; $P < 0.01$) was increased in cows that received SCFP supplementation.

2.4 Discussion

2.4.1 Effects of Starch Content of Fresh Diets

In the current study, we found that cows fed LS fresh diets had higher milk yield compared with those fed HS diets during the fresh period. Because the calculated apparent energy density (NE_L)

of LS and HS diets were similar in the current study and DMI was not affected by dietary starch content, it was unlikely that the increased milk production of LS cows resulted from higher energy intake. Cows fed LS diets tended to lose more BCS and had higher concentrations of plasma free fatty acids and BHB during the fresh period compared with HS cows, indicating that the increased milk production of LS cows may be partly supported by mobilization of fatty acids from adipose tissue. However, the increased body fat mobilization of LS cows did not negatively affect the health of dairy cows as suggested by the similar incidence of health disorders for LS and HS cows after calving. In addition, we found an increase in total tract NDF digestibility for the cows fed LS diets. Increased total tract NDF digestibility has been reported in other studies when substituting beet pulp for grain for lactating dairy cows (Voelker and Allen, 2003; Alamouti et al., 2009; Alamouti et al., 2014) and steers (Mojtahedi and Mesgaran, 2011). As fiber generally ferments more slowly and consistently in the rumen compared with starch, energy provided by fiber might have been more favorably partitioned to the mammary gland which is not responsive to insulin for uptake of glucose, whereas the energy from rapid starch fermentation would be taken up to a greater extent by skeletal muscles and adipose tissue that respond to insulin (Oba and Allen, 2000). However, we used beet pulp to replace a portion of barley grain to reduce dietary starch content, and as a result, NFC contents were similar between LS and HS diets. The lack of difference in NFC contents of fresh diets in our study may contribute to the similar 3.5% FCM among treatments.

Contrary to the results of current study, Rabelo et al. (2003) and McCarthy et al. (2015) reported that animal responses to high-starch diets in DMI or milk yield were greater. The discrepancy between their studies (Rabelo et al., 2003; McCarthy et al., 2015) and our study might be explained by differences in close-up diets that animals were fed before calving as proposed by Dann (2016); cows were fed controlled energy close-up diets in our study to reduce postpartum metabolic

complications (Dann et al., 2006; Janovick and Drackley, 2011), but high-starch close-up diets were fed in the previous studies (Rabelo et al., 2003; McCarthy et al., 2015). In the study of Rabelo et al. (2003), even the low-energy close-up diet contained 38.2% NFC, which was far higher than that of our study (25.6% NFC). In the study of McCarthy et al. (2015), starch content of the basal close-up diet was 17.4%, which was 3.6 percentage points higher than the close-up diets used in our study. Considering the effect of NFC fermentation on stimulating the growth of rumen papillae and promoting the adaptation of rumen microbial population to diets high in fermentable carbohydrate, the higher starch content of close-up diets used by those two studies may contribute to the greater animal performance with high-starch fresh diets.

In addition, the greater performance of animals fed high-starch fresh diets for Rabelo et al. (2003) and McCarthy et al. (2015) might be related to possible insulin resistance. Previous studies suggested that cows overfed energy during the dry period had higher prepartum insulin concentrations (Dann et al., 2006; Douglas et al., 2006; Janovick et al., 2011) and exhibited a greater degree of insulin resistance at 3 wk postpartum compared with those fed controlled or restricted diets (Holtenius et al., 2003). Insulin resistance, which was suspected for the studies of Rabelo et al. (2003) and McCarthy et al. (2015), might help cows to partition energy consistently to milk production regardless of fermentability of fresh diets. Contrarily, cows in our study were fed a controlled energy close-up diet, and likely exhibited less insulin resistance during the fresh period compared with cows fed high-energy close-up diets in those studies mentioned above (Rabelo et al., 2003; McCarthy et al., 2015). This may have favored greater glucose uptake by skeletal muscle and adipose tissue, and reduced milk yield particularly when high-starch fresh diets were fed as more energy was provided in a pulsatile manner from starch fermentation. However, low-starch fresh diets provided more energy from fiber, which ferments more slowly in the rumen and provides energy to animals more

consistently, and this may have helped partition relatively more energy to the mammary gland. Interestingly, our observations were consistent with that of Dieho et al. (2016) who fed low energy close-up diets (9% starch on a DM basis) and reported greater milk yield for cows fed less concentrates during the fresh period. However, we did not measure insulin concentration and insulin resistance in our study, and our speculations need to be evaluated in future studies.

2.4.2 Effects of SCFP Supplementation

We had hypothesized that SCFP supplementation would enhance dairy cow performance, and to a greater extent for dairy cows fed a HS diet than those fed a LS diet. However, overall DMI and milk yield during the entire fresh period were not affected by SCFP supplementation, and no interactions were detected between SCFP and dietary starch content. However, we detected a tendency of interaction between SCFP and day during the first 7 days after calving, SCFP treatment transiently increased DMI on d 1 and 5 after calving compared with CON. We speculate that SCFP supplementation helped decrease inflammation and stress around calving increasing DMI immediately after calving. In a companion study (Knoblock et al., 2018), we found that serum haptoglobin concentrations were decreased in SCFP cows on d 7 after calving compared with CON, suggesting reduced inflammation in SCFP cows. In addition, Zaworski et al. (2014) reported SCFP-fed cows had decreased serum cortisol concentration, an indicator of stress and pain associated with various health problems (Gross et al., 2015), on d 1 and 3 after calving compared with CON cows, indicating that SCFP supplementation may reduce stress around calving. In addition, Dann et al. (2000) reported higher DMI in cows fed SCFP than CON during the last 7 days of gestation and a tendency of greater DMI for SCFP cows compared with those fed CON during d 1 to 21 after parturition.

During the post-fresh period, we found that supplementation of SCFP tended to decrease DMI compared with CON diets. However, concentration of plasma glucose was higher and plasma BHB and free fatty acids were lower for SCFP supplemented cows, suggesting that the tendency of lower DMI for cows fed SCFP did not negatively affect the energy status of dairy cows during this period. In addition, yields of milk and 3.5% FCM were not reduced by SCFP supplementation during the post-fresh period. In fact, 3.5% FCM yield was numerically greater for SCFP cows even with the tendency of lower DMI, which contributed to greater feed efficiency for cows fed SCFP. Dann et al. (2000) also reported that feeding SCFP from d 21 before expected calving date to d 42 after calving increased dietary energy supply during the postpartum period. Similar improvements in feed efficiency were reported when SCFP was supplemented to lactating dairy cows (Schingoethe et al., 2004; Cooke et al., 2007). A meta-analysis of the effects of supplementation of SCFP (Diamond V, Cedar Rapids, IA) showed that supplementing SCFP increased DMI by 0.62 kg/d for early lactation dairy cows (< 70 DIM), but decreased DMI by 0.78 kg/d for those in later lactation (> 70 DIM), contributing to increased feed efficiency in combination with greater milk production (Poppy et al., 2012). Previous studies have reported the stimulatory effects of SCFP on the growth of cellulolytic and lactate-utilizing bacteria in the rumen (Harrison et al., 1988; Yoon and Stern, 1996; Callaway and Martin, 1997), which could increase the nutrient and energy availability to the animal. Furthermore, feeding SCFP has shown to increase microbial protein synthesis (Erasmus et al., 1992; Hristov et al., 2010) in dairy cows and reduce methane production in sheep (Mwenya et al., 2004). In the current study, we found that supplementation of SCFP decreased MUN concentration compared with CON within the HS group at both fresh and post-fresh periods. In addition, cows fed SCFP had higher glucose concentration and lower BHB concentration on d 42 ± 3after calving compared with CON cows, suggesting higher energy supply from the diet. Therefore, the increase in

feed efficiency in our study may come from increased energy utilization in the rumen, which is consistent with 5.1% greater apparent diet NE_L density for SCFP treatments. Dann et al. (2000) reported that cows fed SCFP had higher apparent NE_L from feed from d 1 to 42, which was associated with less BW loss in their study. Contrarily, SCFP supplementation did not affect postpartum BW change, but increased feed efficiency in our study. In addition to the greater energy utilization in the rumen of SCFP cows, reduced inflammation for SCFP cows, as reported by Knoblock et al. (2018), may also contribute to the higher feed efficiency for cows fed SCFP compared with CON by decreasing the energy requirement for maintenance.

In general, positive effects of SCFP supplementation were greater during the post-fresh period than the fresh period in the current study, and this might be partly attributed to differences in actual SCFP intake. We intended to provide SCFP at 19 g/d, according to the manufacturer's recommendation, with an assumed DMI of 20 kg/d. However, DMI during the fresh period was lower and averaged 16.6 kg/d, which provided 15.7 g/d of SCFP (17% less than the target amount). This may have contributed to lesser animal responses to SCFP supplementation during the fresh period, and optimum supplementation level of SCFP during the transition period, when DMI is lower, warrants further research.

2.5 Conclusion

For dairy cows fed controlled-energy close-up diets, feeding low-starch diets (22% starch) during the fresh period increased milk production compared with the high-starch diets (28% starch), without affecting DMI but with the tendency of greater BCS loss during the fresh period. The effects of *Saccharomyces cerevisiae* fermentation product supplementation during the periparturient period on feed intake and milk production were not affected by starch content of fresh diets. In addition, supplementation of *Saccharomyces cerevisiae* fermentation product during the periparturient period

did not affect overall DMI during the close-up and fresh periods, but transiently increased DMI on d 1 and 5 after calving and increased feed efficiency during the post-fresh period.

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2.7 Tables and figures

Table 2.7.1. Parity, BW, and BCS of dairy cows at enrollment (d -28 ± 3 relative to expected calving date)[1]

Variable[2]	LS		HS	
	CON	SCFP	CON	SCFP
117 cows				
Parity	2.3	2.3	2.2	2.3
BCS	3.30	3.31	3.24	3.28
BW, kg	653	638	659	653
38 cows				
Parity	2.0	2.0	1.9	1.9
BCS	3.31	3.25	3.35	3.29
BW, kg	639	620	655	632

[1] LS = low-starch fresh diets; HS = high-starch fresh diets; CON = control diet, no *Saccharomyces cerevisiae* fermentation product (SCFP) supplementation; SCFP = SCFP supplemented diet.
[2] The total number of animals used was 117 cows; a subset of 38 cows was used for digestibility measurement.

Table 2.7.2 Ingredient and chemical composition of experimental diets[1]

Item	Prepartum		Postpartum			
	CON	SCFP	LS		HS	
			CON	SCFP	CON	SCFP
Ingredient, % DM						
Barley silage	46.9	46.9	46.5	46.5	46.5	46.5
Alfalfa hay	…	…	2.8	2.8	2.8	2.8
Barley straw	29.1	29.1	…	…	…	…
Corn grain, ground, dry	…	…	12.5	12.5	12.5	12.5
Barley grain, rolled	7.5	7.5	8.9	8.9	18.1	18.1
Beet pulp	…	…	8.3	8.3	…	…
Canola meal	8.2	8.2	10.2	10.2	8.0	8.0
Soybean meal, 44% CP	…	…	3.0	3.0	3.0	3.0
Corn gluten meal	0.5	0.5	0.9	0.9	2.0	2.0
Amino plus	1.8	1.8	2.0	2.0	2.0	2.0
Urea	0.5	0.5	…	…	…	…
F-100, Dairy fat[6]	…	…	1.1	1.1	1.1	1.1
Limestone	0.7	0.7	1.4	1.4	1.6	1.6
Potassium carbonate	…	…	…	…	0.1	0.1
Premix-CON[2]	1.9	…	1.1	…	1.1	…
Premix-SCFP[3]	…	1.9	…	1.1	…	1.1
Rumensin premix[4]	0.8	0.8	0.6	0.6	0.6	0.6
Mineral and vitamin mix[5]	2.1	2.1	0.8	0.8	0.8	0.8
Nutrient content						
%DM	50.2	50.2	50.2	49.9	50.2	50.1
CP, %DM	15.3	15.3	17.3	17.0	17.5	16.9
ADF, %DM	31.6	31.5	20.9	20.3	19.3	19.2
NDF, %DM	49.5	49.4	33.3	32.7	31.7	31.5
Forage NDF, %DM	45.1	45.1	24.0	24.0	24.0	24.0
NFC, %DM	25.6	25.6	39.3	41.3	41.1	42.8
Starch, %DM	13.8	13.9	21.6	22.5	27.0	29.5
Ether extract, %DM	2.5	2.5	3.6	3.6	3.7	3.7
NE_L, Mcal/kg DM	1.43	1.43	1.60	1.62	1.63	1.64
DCAD, mEq/kg	26.0	25.0	192	164	170	138
NE_L allowable milk, kg/d	…	…	31.5	31.5	32.1	32.1
MP allowable milk, kg/d	…	…	32.7	32.7	32.7	32.7

[1] CON = control diet, no SCFP supplementation, Premix-CON was used in the diet; SCFP = SCFP supplemented diet, Premix-SCFP was used in the diet; LS = low-starch diets; HS = high-starch diets.

[2] Contained 99.0% of dry ground corn grain and 1.0% of canola oil, providing 0 g/d of SCFP.

[3] Contained 91.1% of dry ground corn grain, 7.9% of SCFP, and 1.0% of canola oil, providing 19 g/cow/d of SCFP (as-fed basis) based on expected dry matter intake of cows (11 kg/cow/d before calving; 20 kg/cow/d after calving).

[4] Contained 1.2% of Rumensin, 97.5% of dry ground barley grain, and 1.3% of canola oil.

[5] Contained 11.0% Ca, 2.78% Na, 14.2% Cl, 11.8% Mg, 7.68% S, 16.2 mg/kg of Mn, 4.88 mg/kg of I, 1,212 kIU/kg of vitamin A, 121 kIU/kg of vitamin D, and 4,040 IU/kg of vitamin E for close-up diet; contained 0.71% Ca, 24.3% Na, 39.4% Cl, 13.0% Mg, 0.13% S, 2,427 mg/kg of Cu, 4,244 mg/kg of Mn, 174 mg/kg of Co, 4,583 mg/kg of Zn, 10.0 mg/kg of Se, 85.0 mg/kg of I, 543 kIU/kg of vitamin A, 155 kIU/kg of vitamin D, and 5,118 IU/kg of vitamin E for postpartum diets.

[6]F-100 Dairy Fat (Pro-Ag, Winnipeg, MB).

Table 2.7.3 Effects of a *Saccharomyces cerevisiae* fermentation product (SCFP) supplementation on DMI and BCS change during the prepartum period

Variable	CON[1]	SCFP[2]	SE	*P*-value
DMI, kg/d	11.0	11.2	0.26	0.61
BCS change, /21d	-0.02	-0.03	0.03	0.68
Energy intake[4], %	113	114	3.01	0.83

[1] CON = control diet, no SCFP supplementation.
[2] SCFP = SCFP supplemented diet.
[3] Body condition score used for calculation were measured at the time of enrolment (d -28 ± 3) and immediately after calving (d 1 ± 1).
[4] Percentage of NE_L requirement; calculated according to Dann et al. (2006).

Table 2.7.4 Effects of a *Saccharomyces cerevisiae* fermentation product (SCFP) supplementation on plasma metabolite concentrations on d -28, -10, and +1[1] relative to calving

Variable	CON[2]	SCFP[3]	SE	*P*-value
d -28				
Glucose, mg/dL	70.2	67.9	1.25	0.20
Free fatty acids, µEq/L	169	169	13.9	0.98
BHB[4], mg/dL	7.41	7.15	0.20	0.36
d -10				
Glucose, mg/dL	66.9	68.3	1.73	0.59
Free fatty acids, µEq/L	272	241	21.3	0.30
BHB, mg/dL	7.23	6.87	0.23	0.26
d +1				
Glucose, mg/dL	87.8	87.7	3.81	1.00
Free fatty acids, µEq/L	373	396	29.4	0.59
BHB, mg/dL	8.91	8.49	0.27	0.29

[1] d +1 blood samples were collected within 12 h after calving and before postpartum diets were fed.
[2] CON = control diet, no SCFP supplementation.
[3] SCFP = SCFP supplemented diet.
[4] BHB = β-hydroxybutyrate

Table 2.7.5 Effects of starch content of fresh diets (ST) and supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) on DMI, BW and BCS changes, and milk yield and composition of dairy cows during the fresh period (d 1 to 23 ± 3 after calving)

Variable	LS1		HS2			*P-value*		
	CON[3]	SCFP[4]	CON[3]	SCFP[4]	SE	ST	SCFP	ST*SCFP
DMI, kg/d	16.2	17.2	16.4	16.5	0.48	0.58	0.23	0.36
Initial BW[5], kg	627	627	629	637	11.9	0.58	0.72	0.75
BW change, kg/d	-2.20	-2.44	-1.86	-2.27	0.32	0.44	0.32	0.79
Initial BCS[5]	3.26	3.27	3.24	3.24	0.06	0.60	0.94	0.96
BCS change, /21d	-0.43	-0.41	-0.32	-0.37	0.04	0.06	0.71	0.31
Yield, kg/d								
Milk[6]	34.4	33.8	31.1	33.0	1.03	0.05	0.54	0.24
Fat	1.48	1.61	1.53	1.53	0.05	0.73	0.22	0.21
CP	1.19	1.22	1.13	1.19	0.04	0.17	0.22	0.74
Lactose	1.71	1.70	1.58	1.67	0.05	0.12	0.49	0.36
Total solids	4.78	4.95	4.60	4.76	0.14	0.19	0.25	0.99
3.5% FCM	40.5	42.6	40.0	40.6	1.22	0.31	0.26	0.56
Solids-corrected milk	37.0	38.8	36.3	37.3	1.10	0.30	0.21	0.68
3.5% FCM/DMI	2.54	2.50	2.52	2.50	0.08	0.85	0.72	0.93
Milk composition								
Fat, %	3.99[a]	4.30[ab]	4.44[b]	4.24[ab]	0.11	0.09	0.65	0.03
CP, %	3.15	3.24	3.26	3.26	0.04	0.15	0.30	0.30
Lactose, %	4.50	4.49	4.51	4.54	0.02	0.23	0.85	0.40
Total solids, %	12.7[a]	13.1[b]	13.3[b]	13.1[b]	0.14	0.05	0.41	0.04
MUN[9], mg/dL	13.2[ab]	13.8[ab]	14.0[b]	12.8[a]	0.39	0.80	0.37	0.02
SCC[9], 10^3 cells/mL	80.5	95.8	187	95.4	60.1	0.38	0.53	0.38
Apparent dietary NE_L[7]								
Mcal/d	26.0	27.7	27.4	26.4	1.43	0.99	0.81	0.35
Mcal/kg DMI	1.58	1.57	1.66	1.60	0.08	0.52	0.65	0.74
NE_L balance[8], Mcal/d	-10.7	-10.5	-9.07	-10.6	1.37	0.57	0.64	0.51

[a,b] Means in the same row with different superscripts differ significantly ($P < 0.05$) when an interaction of main treatment effect was observed.
[1] LS = low-starch fresh diets.
[2] HS = high-starch fresh diets.
[3] CON = control diet, no SCFP supplementation.
[4] SCFP = SCFP supplemented diet.
[5] Body weight and BCS were measured immediately after calving.
[6] Week × ST; $P = 0.04$.
[7] Calculated according to Dann et al. (2000).
[8] Apparent dietary NE_L (Mcal/d) minus NE_L required for milk output and maintenance (Mcal/d). The NE_L required for milk and maintenance were calculated according to Dann et al. (2000).
[9] MUN = milk urea nitrogen; SCC = somatic cell counts

Table 2.7.6 Effects of starch content of fresh diets (ST) and supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) on plasma metabolite concentrations on d 7 ± 3 and 21 ± 3 after calving

Variable	LS[1]		HS[2]		SE	*P*-value		
	CON[3]	SCFP[4]	CON[3]	SCFP[4]		ST	SCFP	ST*SCFP
d 7								
Glucose, mg/dL	58.5	56.2	61.0	59.6	1.52	0.05	0.23	0.75
Free fatty acids, µEq/L	568[a]	423[b]	386[b]	463[ab]	50.7	0.16	0.50	0.03
BHB[5], mg/dL	9.34	8.44	9.23	8.51	0.64	0.98	0.20	0.90
d 21								
Glucose, mg/dL	58.2	59.4	64.6	63.2	1.61	< 0.01	0.96	0.43
Free fatty acids, µEq/L	416[a]	331[ab]	274[b]	368[ab]	43.6	0.23	0.91	0.04
BHB, mg/dL	9.66	10.2	8.30	8.02	0.73	0.01	0.83	0.54

[a,b] Means in the same row with different superscripts differ significantly ($P < 0.05$) when an interaction of main treatment effect was observed.
[1] LS = low-starch fresh diets.
[2] HS = high-starch fresh diets.
[3] CON = control diet, no SCFP supplementation.
[4] SCFP = SCFP supplemented diet.
[5] BHB = β-hydroxybutyrate.

Table 2.7.7 Incidence of health disorders during d 1 to 44 ± 3 after calving[1]

Item	LS[2]		HS[3]	
	CON[4]	SCFP[5]	CON	SCFP
Subclinical ketosis[6]	7	2	5	3
Displaced abomasum	3	1	2	0
Metritis	2	3	1	2
Retain placenta	3	0	4	5
Mastitis	3	1	1	0
Hypocalcaemia	1	0	0	3
Foot problem	1	3	1	1
Edema	1	0	0	0
Liver abscess	0	1	0	0
Total cases of health disorders	21	11	14	14

[1]There were 53 cases of health disorders during wk 1 to 3, and 7 cases of health problems during wk 4 to 6. The number of health problems 20, 7, 13, and 13 during wk 1 to 3, and was 1, 4, 1, and 1 during wk 4 to 6, respectively for LS-CON, LS-SCFP, HS-CON, and HS-SCFP.
[2] LS = low-starch fresh diets.
[3] HS = high-starch fresh diets.
[4] CON = control diet, no SCFP supplementation.
[5] SCFP = SCFP supplemented diet.
[6] defined as administration of propylene glycol according to farm protocol.

Table 2.7.8 Effects of starch content of fresh diets (ST) and supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) on apparent total tract DM, OM, NDF, and starch[1] digestibility on d 7 ± 3 and 21 ± 3 after calving

Variable	LS[2]		HS[3]			*P*-value		
	CON[4]	SCFP[5]	CON[4]	SCFP[5]	SE	ST	SCFP	ST*SCFP
d +7								
DM	65.2	64.8	63.7	65.3	1.21	0.66	0.61	0.40
OM	67.4	66.9	65.7	67.4	1.16	0.61	0.62	0.37
NDF	41.9	39.4	33.7	36.8	2.06	0.01	0.89	0.18
Starch (primiparous)	98.4	98.9	99.0	99.1	0.18	0.04	0.13	0.24
Starch (multiparous)	98.8	98.5	97.3	98.3	0.32	0.01	0.35	0.06
d +21								
DM	65.3	64.4	64.8	65.5	1.39	0.83	0.96	0.57
OM	66.9	66.6	66.6	67.5	1.28	0.81	0.82	0.61
NDF	40.2	38.9	36.4	37.8	2.25	0.27	0.97	0.55
Starch (primiparous)	98.8	98.5	99.2	99.4	0.26	0.04	0.78	0.31
Starch (multiparous)	98.9	98.6	97.4	97.9	0.31	< 0.01	0.71	0.19

[1] Interaction between dietary starch treatment and parity ($P < 0.01$).
[2] LS = low-starch fresh diets.
[3] HS = high-starch fresh diets.
[4] CON = control diet, no SCFP supplementation.
[5] SCFP = SCFP supplemented diet.

Table 2.7.9 Effects of supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) and carryover effects of starch content of fresh diets (ST) on DMI, BW and BCS changes, milk yield and composition during the post-fresh period (d 24 ± 3 to 44 ± 3 after calving)

Variable	LS[1]		HS[2]			*P*-value		
	CON[3]	SCFP[4]	CON[3]	SCFP[4]	SE	ST	SCFP	ST*SCFP
DMI, kg/d	20.7	19.9	20.6	19.8	0.47	0.77	0.10	0.98
Initial BW[5], kg	576	578	585	588	9.94	0.33	0.78	0.94
BW change, kg/d	0.48	0.61	0.32	0.32	0.28	0.42	0.82	0.82
Initial BCS[5]	2.79	2.83	2.88	2.83	0.06	0.39	0.95	0.44
BCS change, /21d	-0.18	-0.13	-0.15	-0.11	0.03	0.48	0.16	0.77
Yield, kg/d								
Milk	42.6	41.9	39.4	41.2	1.13	0.09	0.59	0.26
Fat	1.56	1.66	1.60	1.63	0.05	0.91	0.21	0.46
CP	1.21	1.24	1.18	1.24	0.03	0.64	0.23	0.64
Lactose	1.98	1.95	1.87	1.96	0.06	0.34	0.53	0.28
Total solids	5.16	5.27	5.05	5.24	0.13	0.63	0.26	0.78
3.5% FCM	43.8	45.2	43.4	44.6	1.17	0.69	0.25	0.94
SCM	39.6	40.9	39.3	40.5	1.04	0.77	0.22	0.96
3.5% FCM/DMI	2.12	2.29	2.14	2.26	0.05	0.91	< 0.01	0.61
Milk composition								
Fat, %	3.74[a]	4.00[ab]	4.05[b]	3.95[ab]	0.10	0.19	0.41	0.08
CP, %	2.86	2.95	2.95	2.96	0.04	0.15	0.17	0.27
Lactose, %	4.65	4.63	4.64	4.65	0.02	0.92	0.86	0.63
Total solids, %	12.2[a]	12.6[b]	12.6[b]	12.5[b]	0.13	0.09	0.26	0.08
MUN[8], mg/dL	3.74[a]	4.00[ab]	4.05[b]	3.95[ab]	0.10	0.19	0.41	0.08
SCC[8], 10^3 cells/mL	37.4[a]	88.3[ab]	164[b]	55.5[ab]	42.8	0.28	0.50	0.07
Apparent dietary NE_L[6]								
Mcal/d	40.7	40.8	39.8	40.8	1.16	0.71	0.65	0.68
Mcal/kg DMI	1.98	2.07	1.96	2.07	0.05	0.84	0.05	0.86
NE_L balance[7], Mcal/d	2.35	1.36	1.60	1.55	0.74	0.75	0.56	0.59

[a,b] Means in the same row with different superscripts differ significantly ($P < 0.05$) when an interaction of main treatment effect was observed.

[1] LS = low-starch fresh diets.

[2] HS = high-starch fresh diets.

[3] CON = control diet, no SCFP supplementation.

[4] SCFP = SCFP supplemented diet.

[5] Body weight and BCS were measured on d 23 and 24 ± 3 before morning feeding.

[6] Calculated according to Dann et al. (2000).

[7] Apparent dietary NE_L (Mcal/d) minus NE_L required for milk output and maintenance (Mcal/d). The NE_L required for milk and maintenance were calculated according to Dann et al. (2000).

[8] MUN = milk urea nitrogen; SCC = somatic cell counts.

Table 2.7.10 Effects of supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) and carryover effects of starch content of fresh diets (ST) on plasma metabolite concentrations on d +42 after calving

Variable	LS[1]		HS[2]		SE	*P*-value		
	CON[3]	SCFP[4]	CON[3]	SCFP[4]		ST	SCFP	ST*SCFP
Glucose, mg/dL	59.0	65.0	62.6	67.9	1.72	0.06	< 0.001	0.84
Free fatty aicds, μEq/L	360[a]	207[b]	250[ab]	345[a]	39.7	0.73	0.47	< 0.01
BHB[5], mg/dL	8.43[ab]	8.57[ab]	10.1[a]	7.55[b]	0.61	0.59	0.05	0.03

[a,b] Means in the same row with different superscripts differ significantly ($P < 0.05$) when an interaction of main treatment effect was observed.
[1] LS = low-starch fresh diets.
[2] HS = high-starch fresh diets.
[3] CON = control diet, no SCFP supplementation.
[4] SCFP = SCFP supplemented diet.
[5] BHB = β-hydroxybutyrate

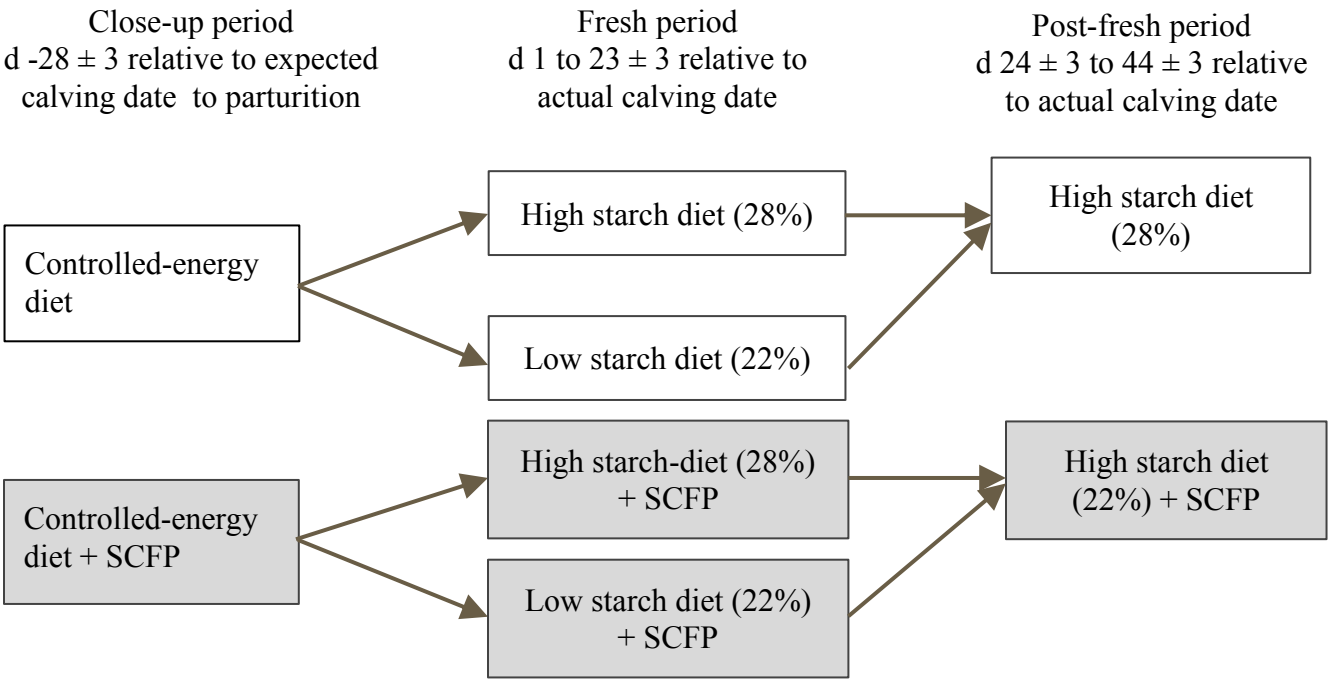

Figure 2.7.1 Timeline of experimental design

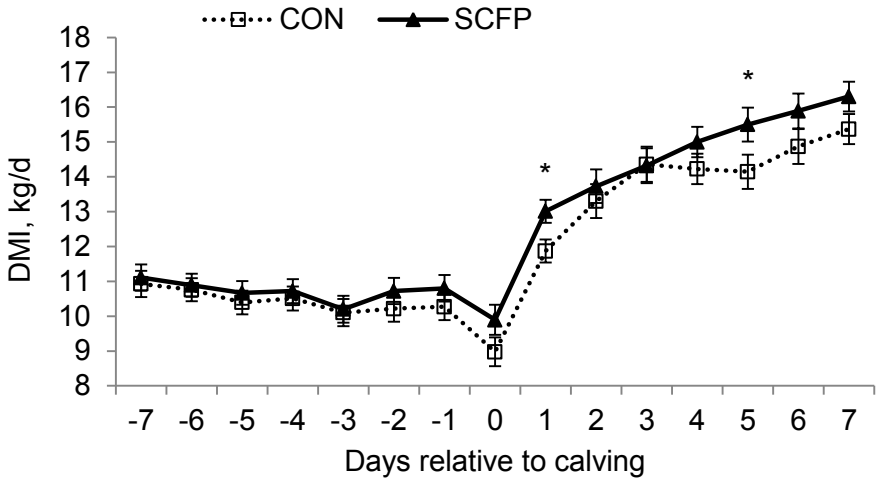

Figure 2.7.2 Daily DMI of cows with *Saccharomyces cerevisiae fermentation product (SCFP) supplementation* or without (CON) fed either a low or high-starch diet after calving. The *P*-values for SCFP, day, and their interaction during d -7 to 0 relative to parturition were 0.44, < 0.01, and 0.82, respectively. No interaction was observed for starch content × SCFP ($P = 0.47$) and starch content × day ($P = 0.15$) during d 1 to 7 after calving. The *P*-values for SCFP, day, and their interaction during d 1 to 7 after calving were 0.10, < 0.01, and 0.08, respectively. Data were analyzed individually for each time point using student's T-test. Effects of SCFP on DMI was significant ($P < 0.05$) on d 1 and 5 after calving as indicated by *. Data are shown as least square means ± standard error.

Chapter 3. Effects of supplementing a *Saccharomyces cerevisiae* fermentation product during the transition period on rumen fermentation of dairy cows fed postpartum diets differing in starch content

3.1 Introduction

Dairy cows often experience negative energy balance in early lactation because the energy intake lags behind the sudden increase in nutrient demands for milk production (Esposito et al., 2014). High-starch diets are usually fed to early-lactation dairy cows to reduce the energy deficit. However, the large increase in dietary fermentable carbohydrates during the calving transition decreases rumen pH and further increases the risk of SARA (Penner et al., 2007). The occurrence of SARA is associated with reduced DMI, production losses, and impaired animal health (Stone, 2004; Krause and Oetzel, 2006) and thus may exacerbate the negative energy balance. Therefore, reducing the duration and severity of SARA should be taken into account for the nutritional management of dairy cows during the calving transition besides increasing their energy intake. Reducing dietary starch content by replacing grain with non-forage fiber sources has shown positive effects on rumen fermentation of dairy cows without impairing production performance, such as a tendency of higher rumen pH (Zhang et al., 2010) and lower pH range (Voelker and Allen, 2003a,b). However, these studies were conducted using dairy cows post-peak lactation; less is known about the effects of feeding a low-starch diet on rumen fermentation of dairy cows during the fresh period, which warrants further investigation.

Saccharomyces cerevisiae fermentation products (SCFP) have been widely used in dairy cow rations as rumen fermentation modifiers to increase production performance and stabilize rumen environment (Erasmus et al., 2005). Previous studies have documented the beneficial effects of SCFP on rumen fermentation, probably through stimulating the growth of cellulolytic (Harrison et al., 1988;

Zhu et al., 2017) and lactate-utilizing bacteria (Callaway and Martin, 1997), fungi (Mao et al., 2013; Zhu et al., 2017), and protozoa (Arakaki et al., 2000; Shen et al., 2018), contributing to greater fiber digestion, lower lactate concentration, and increased microbial protein synthesis (Hristov et al., 2010). In addition, it has been reported recently that supplementation of SCFP to beef heifers fed a high-grain diet (52.8% starch) increased the minimum ruminal pH and reduced the duration of pH < 5.6 by 6 h compared with control heifers along with increased ruminal and total tract NDF digestibility (Shen et al., 2018), indicating that supplementation of SCFP can reduce the drop in rumen pH induced by feeding a high-starch diet. However, the interaction effects of dietary starch content and SCFP supplementation on rumen fermentation were not extensively studied, particularly for the immediate postpartum period.

Therefore, the objective of the current study was to investigate the effects of SCFP supplementation during the calving transition period on rumen pH, VFA profile, and the expression of genes in rumen epithelium in dairy cows fed fresh diets differing in starch content. We hypothesized that feeding a low-starch diet during the fresh period and supplementing SCFP during the transition period would reduce the decrease in rumen pH after calving, and that the benefits of SCFP supplementation would be greater for dairy cows fed a high-starch diet.

3.2 Materials and Methods

All experimental procedures used in this study were approved by the University of Alberta Animal Care and Use Committee: Livestock (AUP#1915) and conducted according to the guidelines of the Canadian Council of Animal Care (2009). Two companion papers (Shi et al., 2018; Knoblock et al., 2019) reported the effects of starch content and SCFP on production performance and immune function.

3.2.1 Animals, Diets, and Experimental Design

Eighteen multiparous ruminally cannulated Holstein cows, as a subset of 117 dairy cows used in the companion paper (Shi et al., 2018), were assigned to treatments after balancing BCS, BW, and expected calving date. Complete details of experimental design and animal management were described in the companion paper. Animal enrollment and data and sample collection were conducted on certain day(s) of week to facilitate routine management of the dairy operation, and this protocol allowed deviations of up to 3 d from the target date (± 3). Briefly, cows were enrolled into the study at 28 ± 3 prior to expected calving date and fed diets supplemented with a *Saccharomyces cerevisiae* fermentation product (SCFP; NutriTek®, Diamond V, Cedar Rapids, IA; n = 9) or without SCFP (CON; n = 9) until d 23 ± 3 after calving. The SCFP was supplemented at 0.173 and 0.095 % of dietary DM in pre- and postpartum diets, respectively, to meet the target inclusion rate of 19 g/cow/d (as-fed basis) based on expected DMI of the cows (prepartum, 11 kg/cow/d; postpartum, 20 kg/cow/d on DM basis). All cows were fed a common basal controlled-energy diet before calving. Cows within each treatment (CON or SCFP) were fed either a low- (LS) or high-starch diet (HS) after calving. Diet ingredients and nutrient composition is shown in Table 3.6.1. Details of feed sampling and analysis have been reported in Shi et al. (2018).

3.2.2 Rumen pH and Rumen Fermentation

Rumen pH data were recorded every 30 s continuously for 72 h in the ventral sac during five sampling periods, including d −10 to −8 ± 3 relative to expected calving date and d -3 to -1, 1 to 3, 7 to 9 ± 3, and 21 to 23 ± 3 relative to actual calving date using the pH measurement system developed by Penner et al. (2006). Daily minimum, mean, and maximum rumen pH, and duration and area below rumen pH 5.8, as well as acidosis index (area of pH below 5.8/DMI) were calculated for each cow during each period.

Rumen fluid samples were collected every 9 h over a 72-h period on d −10 to −8 ± 3, 7 to 9 ± 3, and 21 to 23 ± 3. Briefly, samples were collected from cranial dorsal, cranial ventral, central, caudal dorsal, and caudal ventral sacs, then combined and strained through a perforated material (Peetex, pore size = 355μm; Sefar Canada Inc., Scarborough, Canada). Samples were centrifuged at 4°C at 3,000 × *g* for 20 min immediately after collection and stored at −20 °C until analysis. Eight rumen fluid samples taken from each period were composited to form one sample for each cow. Gas chromatography was used to determine rumen fluid VFA profile as described by Khorasani et al. (1996).

3.2.3 Rumen Papillae Collection

Rumen papillae samples were collected before morning feeding on d -10 ± 3 and 21 ± 3. Approximately 30 adjacent papillae were biopsied from the ventral sac of the rumen and rinsed with ice-cold PBS (pH 7.4) to remove adherent rumen content. After washing, samples were placed into RNAlater (Cat. No. AM7020, Thermo Fisher Scientific, Waltham, Massachusetts, USA) and stored at -80 °C until RNA extraction.

3.2.4 RNA Extraction and Reverse Transcription

Rumen papillae samples were cut into small pieces and homogenized with TRIzol Reagent (ThermoFisher, Waltham, Massachusetts, USA) and beads (CK-14 Precelleys® lysine kit) using a Precylleys® 24 homogenizer (Bertin Technologies, Montigny, France) with two cycles of 30 s at 6200 rpm and 10 s pause between cycles. Following homogenization, chloroform was added to remove DNA and high salt solution (1.2M NaAc, 0.8M NaCl) was added to precipitate RNA. Then, the RNA pellet was solubilized in nuclease-free water and incubated with 3M NaAc and 100% ethanol overnight at -20°C. The RNA was then centrifuged to form a pellet, washed with 75% ethanol, and dissolved in nuclease-free water. The concentration of RNA was measured at

absorbance 260 nm and 280 nm using a ND-1000 spectrophotometer (NanoDrop Technologies, Wilmington, USA). The absorbance ratio (260:280) of all the samples was between 1.96 and 2.08, suggesting high RNA purity. Single strand cDNA was synthesized using the iScript™ Reverse Transcription Supermix (Bio-Rad, Montreal, Quebec, Canada). Samples of cDNA were diluted 20 × using nuclease-free water and stored at -80 °C until use.

3.2.5 Quantitative Real-Time PCR

Prior to quantitative real-time PCR (qRT-PCR), primers were tested to ensure the presence of desired genes (Table 3.6.2) in all samples. The qRT-PCR was then conducted to measure the relative expression of genes of interest with the StepOnePlus Real-Time PCR system (Applied Biosystems by Life Technologies, Foster City, CA, USA) using the Fast SYBR Green kits. The reactions were performed according to the following conditions: 20 s at 50°C, 40 cycles of 3 s at 95°C and 30 s at 60 or 63°C. All samples were run in triplicate.

Three house-keeping genes were used in this study, including β-actin (ACTB), glyceraldehyde-3-phosphate dehygrogenase (GADPH), and ribosomal protein large, P0 (RPLP0). The relative changes in gene expression were calculated using the $2^{-\Delta\Delta C}{}_T$ method (Livak and Schmittgen, 2001). One cow in the LS-SCFP group with the lowest mean rumen pH during the d -10 sampling period was chosen as the calibrator. The ΔC_T was calculated as the difference between the average C_T for each cow and gene and the corresponding geometric mean of 3 house-keeping genes. The $\Delta\Delta C_T$ for each cow and gene was then calculated by subtracting ΔC_T of the calibrator from the ΔC_T.

3.2.6 Statistical Analysis

Statistical analyses were conducted using the Fit Model procedure of JMP 13 (SAS Institute Inc., Cary, NC). Prepartum and postpartum data were analyzed using the following model (1) and (2),

respectively:

$$Y_i = \mu + T_i + e_i, \quad (1)$$

$$Y_{ij} = \mu + T_i + S_j + TS_{ij} + e_{ij}, \quad (2)$$

where Y_{ij} = observations for dependent variables, μ = overall mean, T_i = fixed effect of SCFP supplementation (CON or SCFP), S_j = fixed effects of starch content of fresh diets (LS or HS), TS_{ij} = interaction effects of SCFP with starch content of fresh diets, and e_{ij} = residuals.

Significance was declared at $P \leq 0.05$ and tendency was declared at $0.05 < P \leq 0.10$.

3.3 Results

3.3.1 Rumen pH and VFA Profile

Before calving, DMI was not affected by SCFP supplementation during the pH measurement period (Tables 3.6.3 and 3.6.4). During the d −10 sampling period, no differences were observed in minimum, mean, and maximum rumen pH between SCFP and CON group, as well as duration and area of rumen pH below 5.8. Total VFA concentration and molar proportions of butyrate and propionate were not different between SCFP and CON group, but molar proportion of acetate tended to be greater for SCFP cows than CON ($P = 0.10$). During the d -3 sampling period, minimum rumen pH was not affected by SCFP supplementation, but mean and maximum rumen pH tended to be higher for SCFP group than CON ($P = 0.09$ and 0.08, respectively). The duration and area of rumen pH below 5.8 did not differ between SCFP and CON groups.

After calving, no interactions were observed for SCFP supplementation and dietary starch content for variables of interest and DMI was not affected by SCFP supplementation or starch content (Table 3.6.5, 3.6.6, and 3.6.7). During both d 1 and d 7 sampling period, SCFP supplementation had no effects on minimum, mean, and maximum rumen pH, as well as duration and area of rumen pH below 5.8. Total VFA concentration and VFA profiles were not different

between SCFP and CON during d 7 sampling period. During the d 21 sampling period, minimum rumen pH tended to be higher (5.64 vs. 5.44; $P = 0.07$) and duration of pH below 5.8 tended to be lower (116 vs. 323 min/d; $P = 0.10$) for the cows fed SCFP than CON. However, there were no differences in mean and maximum rumen pH and area of rumen pH below 5.8 between SCFP and CON group. Total VFA concentration tended to be lower (149 vs. 166 mM; $P = 0.09$) for SCFP group than CON, whereas VFA profiles were not affected by SCFP supplementation.

Dietary starch content had no effect on mean, maximum rumen pH, and duration and area of rumen pH below 5.8 during the d 1 sampling period, but minimum ruminal pH tended to be higher for LS than HS cows (5.63 vs. 5.41; $P = 0.09$). During the d 7 sampling period, only maximum rumen pH was affected by dietary starch content and was lower for LS cows compared with those fed HS diet (6.69 vs. 6.89; $P = 0.04$). Total VFA and VFA profiles were not affected by dietary starch content. During the d 21 sampling period, none of the rumen pH parameters was affected by starch content. Total VFA concentration was not different between LS and HS group. However, molar proportion of acetate tended to be higher (60.6 vs. 58.2 mol/100mol; $P = 0.08$) and molar proportion of propionate tended to be lower (23.1 vs. 25.2 mol/100mol; $P = 0.10$) for the cows fed LS compared with HS group, resulting in a tendency of higher acetate to propionate ratio (2.65 vs. 2.34; $P = 0.07$) for the cows fed LS diet than HS.

3.3.2 Rumen Epithelium Gene Expression

Before calving, the relative mRNA abundance of genes encoding for VFA transporters and epithelial cell VFA metabolism were not different between SCFP and CON groups (Table 3.6.8). In addition, among the genes encoding for rumen epithelium growth, the relative mRNA abundance of transforming growth factor β family (TGFB1) and its receptor (TGFBR1), epidermal growth factor receptor (EGFR), and epiregulin (EREG) did not differ between SCFP and CON cows. However,

among those insulin-like growth factor binding proteins (IGFBP), the relative mRNA abundance of IGFBP6 was higher for the cows fed SCFP compared with CON, whereas the relative mRNA abundance of IGFBP2, IGFBP3, and IGFBP5 were not different between SCFP and CON group.

After calving, the interaction effects of SCFP supplementation and dietary starch content was only observed for the expression of 3-hydroxybutyrate dehydrogenase, type 2 (BDH2; Table 3.6.9). The majority of the genes evaluated in this study were not affected by SCFP supplementation, but the relative mRNA abundance of putative anion transporter, isoform 1 (PAT1) was lower for SCFP compared with CON (1.12 vs. 2.27; $P = 0.01$). Dietary starch content had no effect on the expression of the genes evaluated in this study.

3.4 Discussion

3.4.1 Effects of SCFP Supplementation

In the current study, we found that SCFP supplementation tended to increase molar proportion of acetate and mean ruminal rumen pH during the d -10 and d -3 sampling period, respectively. These may indicate increased fiber digestion as previous studies have shown that SCFP supplementation increased the growth and activity of certain fiber-digestion bacteria (Harrison et al., 1988; Callaway and Martin, 1997). More recently, it has been reported that there was a liner increase in the population of certain cellulolytic bacteria in response to an increasing amount of SCFP in mid-lactation dairy cows fed low-quality forage (Zhu et al., 2017). In addition to the changes in rumen fermentation, increased mRNA abundance of IGFBP6 was observed for SCFP supplemented cows. As a member of the IGFBP family, IGFBP6 binds insulin-like growth factor (IGF)-2 preferentially over IGF-1 and inhibits IGF-2 actions including proliferation, differentiation, and survival of many cell types (Bach, 2016). It has been reported that the expression of IGFBP6 was downregulated during high-grain feeding (Steele et al., 2011) and was upregulated with increased NDF to starch

ratio (Ma et al., 2017), suggesting that the expression of IGFBP6 may be related to the dietary NDF content. However, NDF content were similar between SCFP and CON diet in our study, therefore, the greater mRNA abundance of IGFBP6 for SCFP group may be related to the tendency of higher molar proportion of acetate.

Besides its stimulatory effect on the growth of cellulolytic bacteria, supplementation of SCFP has been reported to facilitate the growth of lactic acid utilizing bacteria (Callaway and Martin, 1997) and increase the protozoa count in the rumen (Arakaki et al., 2000; Shen et al., 2018), contributing to a more stable rumen environment. In this study, we hypothesized that supplementation of SCFP can reduce the drop in rumen pH associated with the sudden change in diet composition after calving, and to a greater extent for dairy cows fed a high-starch fresh diet compared with those fed a low-starch fresh diet. However, we did not observe any interactions between SCFP supplementation and starch content of fresh diet on rumen pH and VFA profiles. Furthermore, supplementation of SCFP had no effect on rumen pH immediately after calving during d 1 and d 7 sampling period. The beneficial effects of feeding SCFP on rumen pH were only observed by the end of the calving transition, as indicated by the tendency of higher minimum rumen pH and shorter duration of rumen pH below 5.8 during the d 21 sampling period. Similarly, in our companion study (Shi et al., 2018), the positive effects of SCFP supplementation were greater during the post-fresh early lactation period (d 24 ± 3 to d 44 ± 3) than the fresh period (d 1 to 23 ± 3). For example, the increase in feed efficiency was observed for the dairy cows in SCFP group during the post-fresh early lactation period, but not during the fresh period. The discrepancy in rumen pH in response to SCFP supplementation may be also related to the differences in actual SCFP intake. The postpartum diets in our study were formulated based on an expected DMI of 20 kg/d and to provide SCFP at 19 g/d (as-fed) according to the manufacturer's recommendation. However, the actual SCFP intake,

calculated from the average DMI during d 1 (13.4 kg/d) and d 7 (17.2 kg/d), was 12.7 g/d and 16.3 g/d, respectively. This was 33% and 14% less than the target amount, respectively; therefore, the unexpected lower SCFP intake during the immediate postpartum period may account for the differences in rumen pH in response to SCFP supplementation during different sampling period.

It has been reported previously that supplementation of SCFP increased ruminal protozoal concentrations in steers (Arakaki et al., 2000) and beef heifers (Shen et al., 2018). Rumen protozoa have been proposed to prevent the drop in rumen pH by engulfing starch granules and reducing the starch degradation by amylolytic bacteria (Williams and Coleman, 1997), contributing to the lower rate of VFA production. Therefore, we speculated that the decreased duration of pH below 5.8 associated with SCFP supplementation may be related to an increase in ruminal protozoa count for SCFP cows compared with CON. In addition, β-glucan and mannan oligosaccharides (MOS), as the main cell wall components of *Saccharomyces cerevisiae*, may increase rumen epithelium health by preventing the colonization of pathogens (Ruiz-Herrera, 2016; Heinrich et al., 2003). Supplementing MOS to sheep fed a high grain-based diet has been reported to increase rumen pH and reduce plasma concentration of lipopolysaccharides (Diaz et al., 2018). Therefore, it is likely that SCFP cows had less rumen epithelial damage compared with CON cows, contributing to greater VFA absorption and less VFA accumulatation in the rumen. Besides rumen pH, we also observed a tendency of lower total VFA concentration and lower mRNA abundance of PAT1 for the cows in SCFP group compared with CON. The PAT1 is a transporter protein that involves in the bicarbonate-dependent transport pathway, which transports dissociated VFA into rumen epithelial cells and move bicarbonate ions back to the ruminal lumen (Conner et al., 2010). It has been reported that incubation of rumen epithelial cells isolated from goats with VFA in vitro increased the mRNA expression of PAT1, but decreasing the pH of the incubation medium had no effect on PAT1 expression (Yan et al.,

2014). This suggested that the lower mRNA abundance of PAT1 for the cows fed SCFP may be associated with the tendency of lower total VFA concentration compared with CON group.

3.4.2 Effects of Starch Content during the Fresh Period (d 1 to 23 ± 3)

In several studies, the rapid change from a high-forage diet to a high-grain diet decreased rumen pH and induced SARA in Holstein dairy cows immediately after switching the diet (Steele et al., 2010; Li et al., 2012; AlZahal et al., 2014). Therefore, it was expected that the change from a controlled-energy close-up diet with 29% (DM basis) inclusion of straw to fresh diets that contained large amount of grain would largely reduce rumen pH immediately after parturition. In our study, rumen pH decreased and the duration and area of rumen pH below 5.8 increased by approximately 24-fold and 27-fold, respectively, immediately after calving as observed during the d 1 sampling period compared with that of during the d -3 sampling period. Similar changes in rumen pH around parturition have been reported by Penner et al. (2007), in which rumen pH decreased substantially immediately after calving during d 1 to 5. As rumen pH decreases with excessive amounts of NFC, we hypothesized that feeding a LS diet during the fresh period would reduce the drop in rumen pH compared with feeding a HS diet.

As expected, feeding LS diets showed beneficial effects on rumen pH as observed during the d 1 sampling period that the cows fed LS diets tended to have higher minimal ruminal pH compared with those fed HS diets. Although duration and area of pH below 5.8 were not different between the LS and HS groups, high variation existed among animals as indicated by the high SE. The substantial variation accounted for approximately 44% and 66% of the mean for duration and area of pH below, respectively, which probably masked any treatment differences (Penner et al., 2007). The increase in rumen pH associated with feeding a LS diet was also observed in other studies for dairy cows post-peak lactation, such as a tendency of higher minimum rumen pH (Zhang et al., 2010) and a tendency

of reduced pH range (Voelker and Allen, 2003). However, dietary starch content had no effect on rumen pH during both the d 7 and 21sampling periods. In contrast to our results, Rabelo et al. (2003) reported that the cows fed a high-NFC diet during the fresh period had lower ruminal pH compared with those fed a low-NFC diet by the end of the fresh period. The decreased rumen pH in their study may be a result of a tendency of greater DMI for the cows fed high-NFC diet compared with those fed low-NFC diet during the fresh period (d 1 to 20), whereas DMI was not affected by starch content in our study. In addition, rumen fluid samples were only taken once in the study of Rabelo et al. (2003) at 5 to 6 after feeding for pH measurement, therefore the rumen pH data in their study were not fully representative of the changes in rumen fermentation.

We speculated that the lack of difference in rumen pH in response to different dietary starch content during the d 7 and 21 sampling periods may be associated with the rapid adaptation of rumen epithelium in dairy cows fed the HS diets, which allows a faster absorption of VFA from the rumen. The absorption rate of VFA has been shown to be affected by rumen papillae surface area (Melo et al., 2013) and VFA are commonly considered as the stimulatory factor of the proliferation of the rumen epithelium (Bannink et al., 2012). Studies have reported that increasing the energy intake of dairy cows increased the absorptive surface of rumen epithelium (Melo et al., 2013). More recently, Dieho et al. (2016) found that rumen papillae respond to a rapid increase in concentrate allowance after calving by increasing growth rate, resulting in increased rumen papillae surface area. Similar to our results, total VFA concentration and rumen pH were not affected by the rate of increase of concentrate allowance in the study by Dieho et al. (2016). Therefore, it is likely that the cows fed HS diets in our study had greater rumen epithelial surface area compared with those fed LS diets, contributing to higher VFA absorption in HS cows and preventing the drop in rumen pH from additional starch fermentation. Besides this, the high variation within individual animals as

mentioned previously may also contribute to the lack of response during the d 7 and 21 sampling period.

In addition to the rumen pH during the d 21 sampling period, the expression of genes encoding for rumen epithelial growth, VFA transporters, and VFA metabolism were also not affected by dietary starch content. We noticed that in studies where differential expression of genes involved in the IGF-axis (Steele et al., 2011; Steele et al., 2012) and VFA absorption (Yan et al., 2014) were observed, there were larges differences in dietary starch or NFC content. The difference in dietary starch content between the high-forage and high-grain diet was 34% (DM basis) in the study of Steele et al. (2011), and was 11% (DM basis) in the study of steele et al. (2012). In addition, the difference in dietary NFC content was 16% in the study of (Yan et al., 2014). However, the difference in starch content between LS and HS diets was approximately 6%, which was lower than those studies mentioned above. Therefore, the lack of response in expression of genes evaluated in our study may be partially attributed to the relatively lower difference in dietary starch content.

3.5 Conclusion

The sudden change in diet composition around calving decreases rumen pH immediately after calving. Both SCFP supplementation and reducing dietary starch content showed beneficial effects on rumen pH. Supplementation of SCFP during the calving transition may reduce the duration of SARA by the end of the calving transition and feeding a low-starch diet during the fresh period may help increase rumen pH immediately after parturition.

3.6 References

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3.7 Tables

Table 3.7.1 Ingredient and chemical composition of experimental diets[1]

Item	Prepartum		Postpartum			
	CON	SCFP	LS		HS	
			CON	SCFP	CON	SCFP
Ingredient, % DM						
Barley silage	46.9	46.9	46.5	46.5	46.5	46.5
Alfalfa hay	…	…	2.8	2.8	2.8	2.8
Barley straw	29.1	29.1	…	…	…	…
Corn grain, ground, dry	…	…	12.5	12.5	12.5	12.5
Barley grain, rolled	7.5	7.5	8.9	8.9	18.1	18.1
Beet pulp	…	…	8.3	8.3	…	…
Canola meal	8.2	8.2	10.2	10.2	8.0	8.0
Soybean meal, 44% CP	…	…	3.0	3.0	3.0	3.0
Corn gluten meal	0.5	0.5	0.9	0.9	2.0	2.0
Amino plus	1.8	1.8	2.0	2.0	2.0	2.0
Urea	0.5	0.5	…	…	…	…
F-100, Dairy fat[6]	…	…	1.1	1.1	1.1	1.1
Limestone	0.7	0.7	1.4	1.4	1.6	1.6
Potassium carbonate	…	…	…	…	0.1	0.1
Premix-CON[2]	1.9	…	1.1	…	1.1	…
Premix-SCFP[3]	…	1.9	…	1.1	…	1.1
Rumensin premix[4]	0.8	0.8	0.6	0.6	0.6	0.6
Mineral and vitamin mix[5]	2.1	2.1	0.8	0.8	0.8	0.8
Nutrient content						
%DM	50.2	50.2	50.2	49.9	50.2	50.1
CP, %DM	15.3	15.3	17.3	17.0	17.5	16.9
ADF, %DM	31.6	31.5	20.9	20.3	19.3	19.2
NDF, %DM	49.5	49.4	33.3	32.7	31.7	31.5
Forage NDF, %DM	45.1	45.1	24.0	24.0	24.0	24.0
NFC, %DM	25.6	25.6	39.3	41.3	41.1	42.8
Starch, %DM	13.8	13.9	21.6	22.5	27.0	29.5
Ether extract, %DM	2.5	2.5	3.6	3.6	3.7	3.7
NE_L, Mcal/kg DM[6]	1.43	1.43	1.60	1.62	1.63	1.64
DCAD, mEq/kg	26.0	25.0	192	164	170	138
NE_L allowable milk, kg/d[6]	…	…	31.5	31.5	32.1	32.1
MP allowable milk, kg/d[6]	…	…	32.7	32.7	32.7	32.7

[1] Adapted from Shi et al. (2018). CON = control diet, no *Saccharomyces cerevisiae* fermentation product supplementation, Premix-CON was used in the diet; SCFP = *Saccharomyces cerevisiae*

fermentation product supplemented diet, Premix-SCFP was used in the diet; LS = low-starch diets; HS = high-starch diets.

[2] Contained 99.0% of dry ground corn grain and 1.0% of canola oil, providing 0 g/d of SCFP.

[3] Contained 91.1% of dry ground corn grain, 7.9% of SCFP, and 1.0% of canola oil, providing 19 g/cow/d of SCFP (as-fed basis) based on expected dry matter intake of cows (11 kg/cow/d before calving; 20 kg/cow/d after calving).

[4] Contained 1.2% of Rumensin, 97.5% of dry ground barley grain, and 1.3% of canola oil.

[5] Contained 11.0% Ca, 2.78% Na, 14.2% Cl, 11.8% Mg, 7.68% S, 16.2 mg/kg of Mn, 4.88 mg/kg of I, 1,212 kIU/kg of vitamin A, 121 kIU/kg of vitamin D, and 4,040 IU/kg of vitamin E for close-up diet; contained 0.71% Ca, 24.3% Na, 39.4% Cl, 13.0% Mg, 0.13% S, 2,427 mg/kg of Cu, 4,244 mg/kg of Mn, 174 mg/kg of Co, 4,583 mg/kg of Zn, 10.0 mg/kg of Se, 85.0 mg/kg of I, 543 kIU/kg of vitamin A, 155 kIU/kg of vitamin D, and 5,118 IU/kg of vitamin E for postpartum diets.

[6] F-100 Dairy Fat (Pro-Ag, Winnipeg, MB).

Table 3.7.2 Gene name and primer sequences for quantitative real-time PCR analysis

Gene name	Gene ID	Primer	Annealing temperature	Source
Insulin-like growth factor binding protein 2 (IGFBP2)	AF074854	F:GCATGGCCTGTACAACCTCAA R:TCCCGGTGTTAGGGTTCACA	63	Rhoads et al., 2008
Insulin-like growth factor binding protein 3 (IGFBP3)	NM_001075549	F: GCGACAAGAAGGGCTTTTACAA R: TATCCACACACCAGCAGAAACC	60	Steele et al., 2015
Insulin-like growth factor binding protein 5 (IGFBP5)	BC102850	F: CTACAAGAGAAAGCAGTGCAAACC R: TCCACGCACCAGCAGATG	60	Steele et al., 2015
Insulin-like growth factor binding protein 6 (IGFBP6)	NM_001105613	F: CGCAGAGACCAACAGAGGAACT R: GGGACCCATCTCAGTGTCTTG	63	Steele et al., 2012
Transforming growth factor beta 1 (TGFB1)	NM_177497	F: TGAGCCAGAGGCGGACTACT R: TGCCGTATTCCACCATTAGCA	63	Steele et al., 2015
Transforming growth factor beta 1 receptor (TGFB1R)	NM_174621.2	F: CAGAGTGGGAACAAAAAGGTACATG R: CATTGCATAGATGTCAGCACGTT	60	Minuti et al., 2015;
Epidermal growth factor receptor (EGFR)	NM_001037319.1	F: TGAAAAACAGTGCAAGGCCG R: ACGACTGAAGTTCTGGCAGG	60	Steele et al., 2015
Epiregulin (EREG)	NM_001075549	F: GCGACAAGAAGGGCTTTTACAA R: TATCCACACACCAGCAGAAACC	60	Steele et al., 2015
Monocarboxylate cotransporter, isoform 1 (MCT1)	NM_001037319	F: AACACTGTGCAGGAACTTTACTTTTC R: TGCCAGCGGTCGTCTCTTAT	60	Dieho et al., 2016
Monocarboxylic acid transporter 4, (MCT4)	NM_001109980	F: GACCGAGCGGCAGCAG R: GTCCTGACAGAGGCTGTTCC	63	Dias et al., 2018
Downregulated in adenoma (DRA)	NM_001083676	F: CCTAGCAGGCAGACTTTCCA R: GCGATCAACTCCTGATTGCC	60	Dieho et al., 2016
Putative anion transporter, isoform 1 (PAT1)	NM_001076852	F: TACCACAGGGCCTTGCCTAT R: CTGCCCACCATCACAGACAT	60	Dieho et al., 2016
Peroxisome proliferator-activated receptor a (PPARa)	NM_001034036	F: GGATGTCCCATAACGCGATT R: GGTCATGCTCACACGTAAGGATT	60	Dieho et al., 2016
3-Hydroxybutyrate dehydrogenase, type 1 (BDH1)	NM_001034600	F: GCAAAAGGCCGCGTTGTTA R: GTCAGAGAAAGCCTCCACCC	60	Dieho et al., 2016
3-Hydroxybutyrate	NM_001034488	F: TGGCTCAGAAATCTGGCAAC	60	Dieho et al., 2016

dehydrogenase, type 2 (BDH2)		R: AACTGTTCCTGGACACACACA		
3-Hydroxy-3-methylglutaryl-CoA synthase 1 (HMGCS-1)	NM_001206578	F: CAGCTCTTTGAGGAGTCTGGG R: GGCATACCGTCCATCCCAAG	60	Dieho et al., 2016
3-Hydroxy-3-methylglutaryl-CoA synthase 2 (HMGCS-2)	NM_001045883	F: GCAACACTGACATTGAGGGC R: ACCAGTGCATAGCGACCATC	60	Dieho et al., 2016
Bibosomal protein large, P0 (RPLP0)	AF013214	F: CAACCCTGAAGTGCTTGACAT R: AGGCAGATGGATCAGCCA	60	Robinson et al., 2007
Glyceraldehyde-3-phosphate dehydrogenase (GAPDH)	AF022183	F: GGCGTGAACCACGAGAAGTATAA R: CCCTCCACGATGCCAAAGT	60	Robinson et al., 2007
β-Actin (ACTB)	AF191490	F: CTAGGCACCAGGGCGTAATG R: CCACACGGAGCTCGTTGTAG	60	Malmuthuge et al., 2013

Table 3.7.3 Effects of a *Saccharomyces cerevisiae* fermentation product (SCFP) supplementation on rumen fermentation during d -10 to -8 ± 3 before calving

Variable	CON[1]	SCFP[2]	SE	*P*-value
DMI, kg/d	12.3	11.2	0.78	0.32
Rumen pH				
Nadir	5.99	6.08	0.10	0.53
Mean	6.50	6.54	0.07	0.73
Maximum	6.95	6.99	0.04	0.55
Duration pH <5.8, min/d	20.1	56.3	46.1	0.59
Area pH <5.8, pH × min/d	2.79	17.8	14.6	0.48
Acidosis index, pH × min/kg	0.27	2.78	2.29	0.45
Rumen VFA				
Total VFA, mM	136	133	5.67	0.64
Acetate, mol/100 mol	64.9	66.1	0.45	0.10
Propionate, mol/100 mol	21.7	20.6	0.76	0.33
Butyrate, mol/100 mol	9.14	8.98	0.31	0.72
Isobutyrate, mol/100 mol	1.12	1.10	0.02	0.63
Valerate, mol/100 mol	1.24	1.26	0.07	0.85
Isovalerate, mol/100 mol	1.48	1.53	0.16	0.81
Caproate, mol/100 mol	0.37	0.40	0.07	0.76
Acetate:propionate	3.02	3.22	0.12	0.24

[1] CON = control diet, no SCFP supplementation
[2] SCFP = SCFP supplemented diet

Table 3.7.4 Effects of a *Saccharomyces Cerevisiae* fermentation product (SCFP) supplementation on rumen fermentation during d -3 to -1 before calving

Variable	CON[1]	SCFP[2]	SE	*P*-value
DMI, kg/d	11.5	10.4	0.90	0.43
Rumen pH				
Nadir	6.03	6.18	0.09	0.22
Mean	6.49	6.64	0.06	0.09
Maximum	6.97	7.12	0.05	0.08
Duration pH <5.8, min/d	22.1	13.3	14.0	0.67
Area pH <5.8, pH × min/d	2.18	4.66	3.44	0.62
Acidosis index, pH × min/kg	0.27	0.66	0.49	0.58

[1] CON = control diet, no SCFP supplementation
[2] SCFP = SCFP supplemented diet

Table 3.7.5 Effects of starch content of fresh diets (ST) and supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) on rumen fermentation during d 1 to 3 after calving

Variable	LS[1]		HS[2]			*P*-value		
	CON[3]	SCFP[4]	CON	SCFP	SE	ST	SCFP	ST*SCFP
DMI, kg/d	12.0	12.9	15.4	13.1	1.98	0.39	0.73	0.43
Rumen pH								
Nadir	5.68	5.58	5.44	5.37	0.12	0.09	0.47	0.92
Mean	6.15	6.05	5.96	5.89	0.14	0.25	0.56	0.94
Maximum	6.69	6.66	6.56	6.47	0.13	0.23	0.66	0.84
Duration pH <5.8, min/d	291	437	452	575	195	0.46	0.51	0.96
Area pH <5.8, pH × min/d	40.5	68.9	133	131	58.5	0.21	0.83	0.80
Acidosis index, pH × min/kg	4.84	4.69	13.1	10.8	6.19	0.27	0.85	0.86

[1] LS = low-starch fresh diets.
[2] HS = high-starch fresh diets.
[3] CON = control diet, no SCFP supplementation.
[4] SCFP = SCFP supplemented diet.

Table 3.7.6 Effects of starch content of fresh diets (ST) and supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) on rumen fermentation during d 7 to 9 ± 3 after calving

Variable	LS[1]		HS[2]			*P*-value		
	CON[3]	SCFP[4]	CON	SCFP	SE	ST	SCFP	ST*SCFP
No. of animal	4	5	5	4				
DMI, kg/d	15.4	18.6	17.3	17.3	2.03	0.90	0.45	0.43
Rumen pH								
Nadir	5.61	5.50	5.62	5.69	0.12	0.41	0.87	0.45
Mean	6.14	6.09	6.23	6.24	0.10	0.26	0.82	0.81
Maximum	6.67	6.71	7.00	6.77	0.09	0.04	0.29	0.14
Duration pH <5.8, min/d	157	282	226	69.1	115	0.54	0.89	0.24
Area pH <5.8, pH × min/d	18.2	50.5	86.2	11.8	43.8	0.74	0.64	0.24
Acidosis index, pH × min/kg	1.60	2.43	7.24	0.60	3.67	0.61	0.44	0.33
Rumen VFA								
Total VFA, mM	157	154	140	145	10.4	0.23	0.91	0.68
Acetate, mol/100 mol	59.5	57.8	55.7	57.1	1.40	0.12	0.93	0.30
Propionate, mol/100 mol	24.8	26.5	27.8	25.9	1.46	0.43	0.91	0.24
Butyrate, mol/100 mol	10.5	11.3	11.6	11.8	0.47	0.12	0.29	0.50
Isobutyrate, mol/100 mol	0.91	0.82	0.96	0.99	0.05	0.04	0.59	0.24
Valerate, mol/100 mol	1.80	1.63	1.85	1.86	0.09	0.16	0.40	0.39
Isovalerate, mol/100 mol	1.77	1.52	1.67	1.79	0.21	0.69	0.77	0.40
Caproate, mol/100 mol	0.72[a]	0.39[b]	0.44[ab]	0.65[ab]	0.10	0.92	0.57	0.02
Acetate:propionate	2.40	2.23	2.03	2.24	0.16	0.29	0.87	0.26

[1] LS = low-starch fresh diets.
[2] HS = high-starch fresh diets.
[3] CON = control diet, no SCFP supplementation.
[4] SCFP = SCFP supplemented diet.

Table 3.7.7 Effects of starch content of fresh diets (ST) and supplementation of a *Saccharomyces cerevisiae* fermentation product (SCFP) on rumen fermentation during d 21 to 23 ± 3 after calving

Variable	LS[1]		HS[2]			*P*-value		
	CON[3]	SCFP[4]	CON	SCFP	SE	ST	SCFP	ST*SCFP
No. of animal	4	5	5	4				
DMI, kg/d	21.8	20.8	20.0	20.1	1.73	0.49	0.82	0.76
Rumen pH								
Nadir	5.41	5.58	5.47	5.70	0.10	0.40	0.07	0.77
Mean	6.00	6.21	6.13	6.25	0.10	0.38	0.11	0.67
Maximum	6.53	6.75	6.77	6.72	0.08	0.20	0.26	0.11
Duration pH <5.8, min/d	372	184	274	48.1	119	0.34	0.10	0.88
Area pH <5.8, pH × min/d	87.1	37.4	56.7	9.90	33.1	0.40	0.17	0.97
Acidosis index, pH × min/kg	4.46	1.67	3.07	0.47	1.74	0.47	0.14	0.96
Rumen VFA								
Total VFA, mM	164	155	169	142	9.72	0.67	0.09	0.38
Acetate, mol/100 mol	60.1	61.2	57.4	59.0	1.28	0.08	0.31	0.87
Propionate, mol/100 mol	23.5	22.7	26.4	24.0	1.20	0.10	0.19	0.53
Butyrate, mol/100 mol	11.3	10.9	10.9	11.2	0.45	0.92	0.87	0.45
Isobutyrate, mol/100 mol	0.89	0.98	0.95	1.06	0.06	0.27	0.12	0.85
Valerate, mol/100 mol	1.72	1.86	1.77	1.86	0.20	0.88	0.59	0.91
Isovalerate, mol/100 mol	1.70	1.88	2.06	2.11	0.17	0.11	0.50	0.71
Caproate, mol/100 mol	0.77	0.54	0.46	0.78	0.12	0.75	0.70	0.04
Acetate:propionate	2.57	2.73	2.21	2.48	0.16	0.07	0.19	0.73

[1] LS = low-starch fresh diets.
[2] HS = high-starch fresh diets.
[3] CON = control diet, no SCFP supplementation.
[4] SCFP = SCFP supplemented diet.

Table 3.7.8 Relative mRNA abundance of rumen epithelial genes for dairy cows fed prepartum diet with (SCFP) or without (CON) supplementation of a *Saccharomyces cerevisiae* fermentation product

Gene[3]	CON[1]	SCFP[2]	SE	*P*
Rumen epithelial growth and differentiation				
IGFBP2	1.52	3.49	0.95	0.17
IGFBP3	0.47	0.62	0.13	0.46
IGFBP5	0.83	0.75	0.17	0.75
IGFBP6	0.69	1.10	0.09	0.01
TGFB1	1.02	1.12	0.11	0.55
TGFB1R	0.91	0.82	0.12	0.59
EGFR	1.37	1.63	0.57	0.75
EREG	62.9	83.0	21.7	0.53
VFA transporter				
MCT1	1.28	1.10	0.33	0.70
MCT4	1.99	1.77	0.30	0.62
PAT1	1.73	1.64	0.35	0.86
DRA	0.89	1.07	0.27	0.66
VFA metabolism				
PPARα	1.34	1.39	0.34	0.91
BDH1	1.05	0.86	1.35	0.33
BDH2	0.63	0.66	0.14	0.87
HMGCS1	0.77	1.15	0.28	0.37
HMGCS2	1.60	0.83	0.33	0.12

[1] CON = control diet, no SCFP supplementation.
[2] SCFP = SCFP supplemented diet.
[3]IGFBP2 = IGF-binding protein 2; IGFBP3 = IGF-binding protein 3; IGFBP5 = IGF-binding protein 5; IGFBP6 = IGF-binding protein 6; TGFB1 = transforming growth factor β 1; TGFBR1 = transforming growth factor β receptor 1; EGFR = epidermal growth factor receptor; EREG = epiregulin; MCT1 = monocarboxylate cotransporter, isoform 1; MCT4 = monocarboxylate cotransporter, isoform 4; PAT1 = putative anion transporter, isoform 1; DRA = downregulated in adenoma; PPARα: peroxisome proliferator-activated receptor α; BDH1 = β-118 Hydroxybutyrate dehydrogenase, isoform 1; BDH2 = β-118 Hydroxybutyrate dehydrogenase, isoform 2; HMGCS1 = 3-hydroxy-3-methylglutaryl-CoA Synthase 1; HMGCS2 = 3-hydroxy-3-methylglutaryl-CoA Synthase 2.

Table 3.7.9 Relative mRNA abundance of rumen epithelial genes for dairy cows fed low-starch (LS) or high-starch (HS) fresh diet with (SCFP) or without (CON) supplementation of a *Saccharomyces cerevisiae* fermentation product

Gene[5]	LS[1]		HS[2]		SE	*P*-value		
	CON[3]	SCFP[4]	CON	SCFP		ST	SCFP	ST*SCFP
Rumen epithelial growth and differentiation								
IGFBP2	3.87	3.52	3.57	3.26	1.33	0.84	0.81	0.99
IGFBP3	0.22	0.45	0.27	0.41	0.16	0.98	0.24	0.79
IGFBP5	0.55	0.69	0.29	0.67	0.18	0.47	0.17	0.54
IGFBP6	0.69	0.96	1.16	1.13	0.32	0.34	0.72	0.64
TGFB1	1.10	1.10	1.25	1.52	0.34	0.42	0.70	0.71
TGFB1R	0.73	0.69	1.42	0.78	0.27	0.17	0.22	0.27
EGFR	0.91	1.14	2.08	1.20	0.39	0.14	0.42	0.18
EREG	33.1	55.8	39.2	61.1	22.3	0.79	0.32	0.99
VFA transporter								
MCT1	1.31	1.12	1.01	0.94	0.42	0.58	0.76	0.90
MCT4	1.15	1.29	1.34	1.90	0.41	0.35	0.41	0.62
PAT1	2.70	1.15	1.85	1.08	0.41	0.28	0.01	0.35
DRA	1.23	0.89	1.03	1.28	0.29	0.74	0.89	0.32
VFA metabolism								
PPARα	1.42	1.45	1.94	1.29	0.41	0.67	0.46	0.42
BDH1	1.15	0.89	0.79	1.00	0.17	0.81	0.45	0.36
BDH2	0.88	0.60	0.34	0.85	0.18	0.42	0.54	0.05
HMGCS1	0.85	0.85	1.14	0.80	0.28	0.67	0.55	0.56
HMGCS2	1.31	1.09	1.51	1.39	0.32	0.45	0.61	0.88

[1] LS = low-starch fresh diets.
[2] HS = high-starch fresh diets.
[3] CON = control diet, no SCFP supplementation.
[4] SCFP = SCFP supplemented diet.
[5]IGFBP2 = IGF-binding protein 2; IGFBP3 = IGF-binding protein 3; IGFBP5 = IGF-binding protein 5; IGFBP6 = IGF-binding protein 6; TGFB1 = transforming growth factor β 1; TGFBR1 = transforming growth factor β receptor 1; EGFR = epidermal growth factor receptor; EREG = epiregulin; MCT1 = monocarboxylate cotransporter, isoform 1; MCT4 = monocarboxylatecotransporter, isoform 4; PAT1 = putative anion transporter, isoform 1; DRA = downregulated in adenoma; PPARα: peroxisome proliferator-activated receptor α; BDH1 = β-118 Hydroxybutyrate dehydrogenase, isoform 1; BDH2 = β-118 Hydroxybutyrate dehydrogenase, isoform 2; HMGCS1 = 3-hydroxy-3-methylglutaryl-CoA Synthase 1; HMGCS2 = 3-hydroxy-3-methylglutaryl-CoA Synthase 2.

Chapter 4. Effects of prepartum dietary starch content on rumen fermentation of dairy cows during the transition period

4.1 Introduction

During the transition from late gestation to early lactation, the rapid increase in nutrient demands for fetal growth and the onset of lactation cannot meet by the energy intake from feed, resulting in a state of negative energy balance (NEB) (Drackley, 1999). Excessive NEB and massive mobilization of body fat reserve exert detrimental effects on the health, productivity, and reproduction performance of dairy cows (van Knegsel et al., 2005; Chapinal et al., 2012). Increasing energy density of the close-up diet with more fermentable carbohydrates has been traditionally recommended by NRC (2001). In addition, feeding a high-energy diet during the prepartum transition period may help dairy cows adapt rumen microbes and papillae to lactation diet (Grummer, 1995). However, dairy cows may get overconditioned due to excessive energy intake, leading to depressed appetite and more severe NEB after calving (Rukkwamsuk et al., 1999). Moreover, excessive energy intake in late gestation may increase insulin resistance (Holtenius et al., 2003), thereby increasing blood free fatty acids concentration due to increased lipolysis (De Koster and Opsomer, 2013). The elevated concentration of blood free fatty acids and their uptake by the liver may result in the development of metabolic (e.g. fatty liver and ketosis) and infectious diseases (e.g. mastitis and metritis; Adewuyi et al., 2006).

In order to prevent excess energy intake during the dry period, a low-energy or controlled-energy diet is currently recommended. Feeding a controlled-energy diet during the dry period has been shown to increase postpartum DMI (Douglas et al., 2006) and energy balance (Dann et al., 2006; Hayirli et al., 2011), reduce lipid mobilization postpartum (Douglas et al., 2006; Janovick et al., 2011; Zhang et al., 2015; Mann et al., 2015), and decrease the incidence of

subclinical ketosis (Vickers et al., 2013) and the episodes of hyperketonemia postpartum (Mann et al., 2015). However, dairy cows have a high risk of ruminal acidosis after calving (Penner et al., 2007) and a sudden shift from a controlled-energy dry cow diet to a high-concentrate lactating diet predisposes dairy cows to sub-acute ruminal acidosis (SARA), which can adversely affect feed intake and animal health (Krause and Oetzel, 2006). The incidence of SARA is often determined by measuring rumen pH at specific time points relative to feeding or over a certain period. Evaluating the response of dairy cows to grain-induced SARA provides an alternative way of accessing the susceptibility of cows to SARA. Therefore, the objective of the current study was to compare the effects of prepartum dietary starch content on rumen fermentation and responses of dairy cows to grain-induced SARA. We hypothesized that restricting prepartum energy density by decreasing dietary starch content would reduce lipid mobilization and increase the risk of SARA during the postpartum period.

4.2 Materials and Methods

All experimental procedures used in this study were approved by the University of Alberta Animal Care and Use Committee: Livestock (AUP#2342) and conducted according to the guidelines of the Canadian Council of Animal Care (2009).

4.2.1Animals, Diets, and Experimental Design

Eighteen multiparous Holstein dairy cows fitted with ruminal cannulas were assigned to treatment balanced for parity, BCS, BW, and expected calving date. Cows were enrolled into the study at d 28 ± 3 prior to expected calving date and fed either a low-starch (LS) or high-starch (HS) diets until parturition (Table 4.7.1). All cows received the same fresh cow ration until d 21 ± 2 after parturition (Table 4.7.1). The fresh diet was formulated using Dairy NRC (2001) to meet or exceed all nutrient requirements for a 650 kg cow producing 32.4 kg/d of milk with 3.8%

milk fat and 3.0% milk protein. A grain challenge was performed on d 7 ± 2 and 21 ± 2 at 1000 h by dosing 7 kg (as-fed basis) of finely ground barley and wheat grain (1:1) into the rumen through the rumen cannula. Before the grain challenge, cows were fasted for 12 hours. On the day of challenge, grain was mixed with rumen contents until no obvious dry mixture was observed within 10 minutes before dosing. Then, the mixture was put back into the rumen of the cow through the rumen cannula. Cows had no access to TMR until 6 hours after grain challenge at 1600 h.

Throughout the study, cows were housed in individual tie-stalls and had free access to water. Cows were fed experimental TMR once daily at 0800 h and at 105 to 110% of actual feed intake (as-fed basis) of the previous day. The weight of feed offered and refused was recorded on a daily basis for all cows. Cows, after calving, were milked in their stalls twice daily at 0330 and 1500 h. Milk yield was recorded daily for all cows after calving.

4.2.2 BW and BCS

Body weight and BCS were determined at the beginning of the study (d -28 ± 3), immediately after calving, at the end of the study (d 21 ± 2). Body weight was measured consecutively for two days before feed delivery but after morning milking (after calving). Body condition score was recorded by 2 individuals using a 5-point scale (Wildman et al., 1982). Both BW and BCS data of each measurement point were averaged before statistical analysis and changes in BW and BCS before- and after-calving were calculated.

4.2.3 Feed sampling and analysis

Forages, concentrate, and TMR samples were collected once weekly. Barley grain and wheat grain were stored separately in bags so samples were collected from each bag (8 bags each) and composited to yield two samples for each of them. Feed samples were dried in a forced-air

oven at 55 ℃ for 48 h to determine the DM content and diet formulation was adjusted if necessary. Dried samples were ground in a Wiley mill (Thomas-Wiley, Philadelphia, PA) to pass through a 1-mm screen. Ground samples were composited monthly. Feed samples were sent to Cumberland Valley Analytical Services (Hagerstown, MD), and analyzed for and analyzed for DM (AOAC International, 2002; method 930.15), OM (AOAC International, 2002; method 942.05), NDF (Van Soest et al., 1991), starch (Hall, 2009), and CP (AOAC International, 2000; method 990.03).

4.2.4 Blood Sampling and Analysis

Plasma and serum samples were collected from all cows via the tail blood vessel before morning feeding (~ 0700 h) on d -28 ± 3, -10 ± 3, 3 ± 1, and 20 ± 2 (the day before d 21 grain challenge) relative to expected (prepartum) or actual calving date (postpartum). On the day of the grain challenge, jugular catheters were placed one hour before the grain challenge (0900 h) for blood collection. The catheters and extenders were flushed with 2 ml of heparinized saline (2% solution) before and after sample collection. Plasma samples were collected at 0, 30, 60, 90, 120, 150, 180, 210, 240, 300, 360 min relative to grain challenge and serum samples were collected at 0 and 360 min relative to grain challenge. All plasma samples were collected into Vacutainer tubes containing sodium heparin (Fisher Scientific Company; Nepean, ON, Canada) and centrifuged at 4 ^{o}C (3,000 × *g* for 20 min) immediately after collection. Serum samples were collected into Vacutainer tubes containing no anticoagulant (Fisher Scientific Company; Nepean, ON, Canada) and left in room temperature for 1 h before centrifugation. Blood samples were stored at -20 ^{o}C until further analysis.

Concentrations of glucose, free fatty acids, BHB, and insulin were determined for all plasma samples. For those collected not during grain challenge, plasma concentrations of

glucagon-like peptide(GLP)-1 and GLP-2 were also measured. Plasma glucose concentration was analyzed using a glucose oxidase/peroxidase enzyme (No. P7119; Sigma) and dianisidine dihydrochloride (No. F5803; Sigma). Absorbance was determined with a plate reader (SpectraMax 190; Molecular Devices Crop., Sunnyvale, CA) at the wavelength of 450 nm. Plasma free fatty acid concentration was determined using a commercial kit NEFA HR2; (Wako Chemicals USA, Inc., Richmond, VA). Plasma BHB concentration was measured by the enzymatic oxidation of BHB to acetoacetate in the presence of 3-hydroxybutyrate dehydrogenase (No. H6501; Roche, Mississauga, Ontario, Canada) followed by determination of NADH production at a wavelength of 340 nm. Plasma concentrations of insulin, GLP-1, and GLP-2 were measured according to the method described by Inabu et al. (2017).

For serum samples taken on d -28, -10, 3, and 21 relative to calving, insulin-like growth factor-1 (IGF-1) concentrations were analyzed at Prairie Diagnostic Services (University of Saskatchewan, Saskatoon, SK, Canada) using a solid-phase, enzyme-labeled chemiluminescent immunometric assay (Immulite 1000 analyzer, Siemens, Oakville, ON, Canada). For serum samples taken during the grain challenge, haptoglobin (Hp; PHASE Haptoglobin Assay, Catalog No. TP 801) and serum amyloid A (SAA; Multispecies SAA ELISA kit, Catalog No. TP 802) concentrations were measured.

4.2.5 Rumen pH and VFA Profile

Rumen pH was measured using the pH measurement system developed by Penner et al. (2006a). Before calving, rumen pH data were recorded every 30 s continuously for 72 h in the ventral sac from d −10 to −8 ± 3 relative to expected calving date. Rumen fluid samples were collected concurrently every 9 h over a 3-d period. Briefly, samples were collected from cranial dorsal, cranial ventral, central, caudal dorsal, and caudal ventral sacs, then combined and strained

through a perforated material (Peetex, pore size = 355μm; Sefar Canada Inc., Scarborough, Canada). Samples were centrifuged at 4°C at 3,000 × *g* for 20 min immediately after collection and stored at −20 °C until analysis. Rumen fluid samples were composited to form one sample for each cow immediately before analysis. After calving, rumen pH data were measured on d 1 to 5, the day before grain challenge, and during grain challenge. Rumen fluid samples were collected at 0, 3, and 6 h relative to the grain challenge. Minimum, mean, and maximum rumen pH, and duration and area below rumen pH 5.8 were calculated for each cow. Rumen fluid VFA profile was determined by gas chromatography as described by Khorasani et al. (1996).

4.2.6 Calculations and Statistical Analysis

For plasma insulin during the grain challenge, data of maximum concentration (Cmax), the change from baseline to maximum concentration (delta change), and time to reach maximum concentration (Tmax) were organized and calculated. For plasma free fatty acids during the grain challenge, rate of change from baseline level to the end of grain challenge (360 min) was calculated. The net incremental area under the curve (AUC) during the grain challenge for insulin and free fatty acids were calculated using the trapezoidal rule.

Statistical analyses were conducted using the FIT Model procedure of JMP 14 and SAS 9.2 (SAS Institute Inc., Cary, NC). Repeated measure was used for variables measured overtime, such as DMI, milk yield, and blood parameters and VFA profiles during grain challenge, using the PROC MIXED procedure in SAS. Four covariance structure (compound symmetry, heterogeneous compound symmetry, first-order autoregressive, and unstructured) were tested and the one with the lowest Akaike's information criterion was selected. Data were analyzed using the flowing model:

$$Y_{il} = \mu + S_i + T_j + ST_{ij} + e_{ij},$$

where Y_{ij} is the observations for dependent variables, μ is overall mean, S_i is the fixed effect or carryover effects of prepartum starch content (LS or HS), T_i is the fixed effect of time relative to parturition (week) or grain challenge (hour) as the repeated measure, ST_{ij} is the interaction between starch content and time, and e_{ij} is the error term. Covariate was used for insulin and GLP-2 using their respective concentration at d -28.

For variables not measured over time, such as BW and BCS changes, rumen pH, and blood parameters at individual time points relative to parturition and grain challenge, data were analyzed using JMP 14 and the fixed effect of time and its interactions with prepartum starch content were removed from the model. For rumen pH during the grain challenge on d 7, basal rumen pH (-1 h to 0 relative to grain challenge) was used as a covariate. Significance was declared at $P \leq 0.05$ and tendency was declared at $0.05 < P \leq 0.10$.

4.3 Results

The starch content and energy density of pre- and postpartum diets, calculated from analyses of feed ingredients, were as follows: LS, 14.0% starch, 1.54 NE_L Mcal/kg DM; HS, 26.1% starch, 1.63 NE_L Mcal/kg DM; postpartum diet, 25.1% starch, 1.62 NE_L Mcal/kg DM (Table 4.7.1). The starch content of the grain mixture used for the grain challenge was 58.7% on DM basis.

4.3.1 DMI, BW and BCS, and Milk Yield

Prepartum DMI tended to be lower for the cows fed LS than those fed HS when expressed as actual intake ($P = 0.07$) and as a percentage of BW ($P = 0.08$; Table 4.7.2) . Regardless of treatments, all cows reduced DMI as calving approached ($P < 0.01$). Initial BW and BCS were not different between the LS and HS groups and dietary starch content had no effect on the changes in BW and BCS during the prepartum period. Energy intake expressed as

percentage of NE_L requirement was higher for the LS cows compared with the HS cows (P = 0.02; Table 4.7.2). In addition, prepartum dietary starch content had no carry-over effects on DMI and milk yield during the postpartum transition period (Table 4.7.3). The BW and BCS at calving and changes in BW and BCS during the postpartum transition period were not different between LS and HS group.

4.3.2 Blood Metabolites and Hormones

Plasma glucose concentration was lower for the cows in LS group compared with those in HS group on d -10 (P = 0.05; Table 4.7.4) relative to expected calving date, whereas concentrations of plasma free fatty acids and BHB were not different between those two groups. Concentrations of plasma insulin, GLP-1, and GLP-2, and serum IGF-1 were not affected by dietary starch content on d -10 before calving.

After calving, no differences were observed in concentrations of plasma glucose nor free fatty acids between LS and HS cows on both d 3 and d 21. Plasma BHB concentration was lower for the cows in LS group compared to those in HS group on d 3 (P = 0.05), but was not different between treatment groups on d 21. Concentrations of plasma insulin and GLP-2, and serum IGF-1 were not different between LS and HS cows on both d 3 and d 21 after calving. Plasma GLP-1 concentration was higher for the cows in LS group than those in HS group on d 3 (P = 0.04), but no difference was found between those two groups on d 21 after calving.

4.3.3 Prepartum Rumen pH and VFA Profiles

Minimum (P < 0.01), mean (P = 0.01), and maximum rumen pH (P = 0.01) were higher for LS cows compared with HS cows during the d -10 sampling period (Table 4.7.5). In addition, the cows fed LS prepartum diet had shorter duration of rumen pH below 5.8 (P = 0.02) and less area of rumen pH below 5.8 (P = 0.03) compared with those fed HS diet. Moreover, the acidosis

index ($P = 0.03$) was smaller for LS cows than HS cows. Total VFA concentration ($P = 0.10$) and molar proportion of butyrate ($P = 0.09$) tended to be lower and molar proportion of acetate was higher ($P = 0.05$) for LS than HS group, but molar proportion of propionate was not affected by dietary starch content.

4.3.4 Grain Challenge

Rumen pH and VFA Profiles. Regardless of treatment groups, the grain challenge conducted on both d 7 ($P < 0.0001$; Table 4.7.6) and d 21 ($P < 0.0001$; Table 4.7.7) after calving reduced mean rumen pH compared with the basal mean rumen pH measured during 1 h before grain challenge. The basal mean rumen pH was higher for LS cows than HS cows on d 7 ($P = 0.02$) and contributed to the tendency of higher mean rumen pH in LS cows during the grain challenge ($P = 0.09$). Unlike basal rumen pH on d 7, no difference was observed for basal mean rumen pH on d 21 before the grain challenge.

After accounting for the confounding effects from basal rumen pH, minimum, mean, and maximum rumen pH were not different between LS and HS cows during the grain challenge on d 7 after calving (Table 4.7.6). However, duration and area of rumen pH below 5.8 tended to be lower for LS than HS group on d 7 during grain challenge ($P = 0.07$ and 0.08, respectively). During the grain challenge on d 21, minimum, mean, and maximum, as well as duration and area of rumen pH below 5.8 were not different between LS and HS cows (Table 4.7.7). Total VFA concentration and molar proportions of acetate, propionate, and butyrate were not affected by prepartum starch content and its interaction with time (hour) relative to grain challenge during both d 7 and 21 grain challenge.

Hp and SAA. There was a tendency for an interaction between prepartum dietary starch content with time (hour) relative to grain challenge on serum Hp concentration during the grain

challenge on d 7 after calving ($P = 0.10$; Table 4.7.6). No interaction was detected in serum SAA concentration between prepartum dietary starch content and time, but the cows in LS group tended to have lower serum SAA than those in HS group at both 0 ($P = 0.06$) and 6 h ($P = 0.09$) relative to grain challenge on d 7 after calving. However, neither serum Hp or SAA concentration was affected by prepartum dietary treatment or its interaction with time during the grain challenge on d 21 after calving (Table 4.7.7).

Blood metabolites and insulin. There were no interactions between prepartum dietary treatment with time (min) relative to grain challenge on concentrations of glucose, insulin, free fatty acids, and BHB (Figure 4.7.10) on d 7 during the grain challenge. Regardless of treatment group, plasma concentrations of glucose and BHB was stable over the 6 h grain challenge period, but insulin concentration increased by 65% ($P < 0.01$) and free fatty acids concentration decreased by 76.7% ($P < 0.01$) by the end of grain challenge on d 7 after calving. No differences were observed for plasma concentrations of glucose, free fatty acids, and BHB between LS and HS cows, but insulin concentration tended to be lower for the cows in LS group than those in HS group (1.09 vs. 1.40 ng/mL; $P = 0.09$) over the 6 h grain challenge period. Specifically, the cows in the LS group tended to have lower insulin concentration at 30 min (0.78 vs. 1.13 ng/mL; $P = 0.07$) and 60 min (0.88 vs. 1.11 ng/mL; $P = 0.10$) after dosing grain into the rumen compared with those in the HS group. Furthermore, Cmax, Tmax, and delta change, as well as AUC at 360 min for insulin did not differ between LS and HS cows (Table 4.7.8). For plasma free fatty acids, Cmin, Tmin, the ratio of delta change to Tmin, and AUC at 360 min, as well as the ratio of $AUC_{\text{free fatty acids}}$ to AUC_{insulin} at 360 min were not different between LS and HS groups.

During the grain challenge on d 21, interactions between prepartum dietary treatment and time (min) relative to grain challenge were detected for plasma glucose ($P = 0.04$) and insulin (P

< 0.01) (Figure 4.7.11). The cows in LS group tended to have lower glucose concentration at 60 min (57.1 vs. 62.8 mg/dL; $P = 0.07$), 90 min (55.9 Vs. 61.6 mg/dL; $P = 0.08$), 120 min (55.4 vs. 61.6 mg/dL; $P = 0.06$), and 210 min (54.7 vs. 61.5 mg/dL; $P = 0.08$) relative to grain dosing compared with those in HS group. Insulin concentration also tended to be lower for the LS group than the HS group at 180 min (1.20 vs. 1.70 ng/mL; $P = 0.08$) and 240 min (1.39 vs. 1.94 ng/mL; $P = 0.06$) relative to grain dosing. Regardless of treatment groups, plasma free fatty acids decreased ($P = 0.02$) and BHB concentration increased ($P < 0.01$) during the grain challenge. Overall plasma free fatty acids concentration during the grain challenge on d 21 after calving was not affected by prepartum treatment, however, the cows in LS group had higher plasma free fatty acids concentration at 360 min relative to grain dosing (123 vs. 75.6 μEq/L; $P = 0.04$). No differences in Cmax, Tmax, and delta change, as well as AUC at 360 min for insulin were found between the cows in the LS and HS groups (Table 4.7.9). The minimum concentration of plasma free fatty acids tended to be lower for HS cows compared with LS cows ($P = 0.08$) , whereas Tmin, the ratio of delta change to Tmin, and AUC at 360 min, as well as the ratio of $AUC_{\text{free fatty acids}}$ to AUC_{insulin} at 360 min were not different between LS and HS group.

4.4 Discussion

4.4.1 Production Performance and Blood Parameters

We hypothesized that restricting prepartum energy density by reducing the dietary starch content might provide beneficial effects on postpartum production performance. However, we found that postpartum DMI and milk yield were not affected by prepartum dietary starch content, whereas prepartum DMI tended to be lower for the cows fed LS diet. In this study, dietary starch content was reduced mainly by replacing barley grain with straw, therefore, the tendency of lower DMI for the cows in LS group may be associated with the higher NDF content of LS diet

by increasing physical fill in the rumen (Oba and Allen, 1999a). Similar responses to prepartum dietary energy diet during both pre- and postpartum periods have been reported by other researchers (Rabelo et al., 2003; Dann et al., 2006; Mann et al., 2015).

Plasma glucose concentration on d -10 before calving was lower for LS cows than HS cows, which was consistent with some previous studies (Janovick et al., 2011; Mann et al., 2016). This is because of the lower availability of hepatic gluconeogenesis precursor, propionate, in cows fed the LS diet compared with those fed the HS diet. The increase in glucose was not accompanied by the increase in GLP-1, which is secreted by the enteroendocrine L-cells within the gut in response to luminal nutrients (Hansen et al., 2004) and is involved in glucose homeostasis and potentially the regulation of DMI (Relling and Reynolds, 2007). This is supported by the study of Relling and Reynolds (2008) that GLP-1 concentration was not affected by abomasal infusion of starch in lactating dairy cows. However, it is not clear why LS cows had greater GLP-1 concentration on d 3 after calving compared with HS cows even though plasma glucose did not differ between treatments.

Although feeding the LS diet tended to limit prepartum DMI, plasma concentrations of free fatty acids and BHB on d -10 and the changes in prepartum BCS and BW were not different between the LS and HS groups, indicating that lipid mobilization were not affected by dietary starch content during the prepartum period. However, several studies reported increased plasma free fatty acids in the feed-restricted cows or cows fed a low-energy diet ad libitum, indicating higher lipid mobilization during the prepartum period compared with over-fed cows (Holtenius et al., 2003; Rabelo et al., 2005; Dann et al., 2006; Janovick et al., 2011). This discrepancy in lipid mobilization between those studies and our experiment may be the result of differences in plasma insulin concentration in response to prepartum plane of nutrition. In those studies

(Holtenius et al., 2003; Rabelo et al., 2005; Dann et al., 2006; Janovick et al., 2011), plasma insulin concentration was lower for the cows fed a low-energy diet or feed-restricted cows than over-fed cows, while plasma insulin concentration did not differ between the LS and HS groups in our study. The decreased plasma insulin concentration facilitates lipolysis, therefore, cows fed a low-energy diet or restricted-fed during the prepartum period had increased plasma free fatty acids concentrations in those above-mentioned studies.

We hypothesized that feeding the LS diet during the prepartum period would reduce lipid mobilization after calving. However, plasma free fatty acids concentrations on both d 3 and 21 after calving were not different between the LS and HS cows. This may be associated with the lack of difference in postpartum DMI and plasma insulin concentration between the HS and LS cows. A similar lack of treatment effects on postpartum free fatty acids concentrations was observed in the study of Dann et al. (2006). In contrast, both Mann et al. (2016) and Janovick et al. (2011) observed reduced plasma concentrations of free fatty acids during the postpartum period in cows fed prepartum a low-energy diet compared with those fed a prepartum high-energy diet. In the study of Mann et al. (2016), cows fed a low-energy prepartum diet had lower plasma free fatty acids on d 4 after calving and this may have resulted from a greater insulin concentration compared with those in the high-energy group. In this study, we did not observe any differences in plasma insulin concentration between the LS and HS cows after calving; therefore, the difference in lipid mobilization during the postpartum period between the study of Mann et al. (2016) and our study may be attributed to the different response in insulin concentration to prepartum plane of nutrition. However, this speculation fails to explain the difference in postpartum lipid mobilization between the study of Janovick et al. (2011) and our study because plasma insulin concentration during the postpartum period was not affected by

prepartum plane of nutrition in the study of Janovick et al. (2011). We noticed that in the companion paper, Janovick et al. (2010) reported that the cows fed a low-energy diet maintained DMI during the prepartum period while the over-fed cows had decreased DMI as calving approached. Although plasma free fatty acids concentration during the prepartum period was greater for cows fed a low-energy diet than the over-fed cows, it became the opposite at parturition that cows fed the low-energy diet tended to have lower plasma free fatty acids than over-fed cows (Janovick et al., 2011). In our study, DMI declined as calving approached for all cows, regardless of treatments. Therefore, the different pattern in DMI close to parturition may help explain the difference in postpartum lipid mobilization between Janovick et al. (2011) and our study.

4.4.2 Prepartum Rumen Fermentation

As expected, the cows in the LS group had higher rumen pH during the prepartum period due to the lower amount of dietary fermentable carbohydrate compared with those in the HS group. However, we found that the acidosis index was also lower for the cows in the LS group, indicating that those cows were less susceptible to SARA under normalized DMI compared with those in the HS group. In agreement with our study, Rabelo et al (2003) reported a tendency of greater rumen pH for the cows fed low energy diet compared with those fed high energy diet.

Supplying more highly fermentable carbohydrates in the diet facilitated the rumen epithelial proliferation (Bannink et al., 2008), therefore feeding the LS diet prepartum was supposed to have less stimulatory effects on the growth of rumen papillae compared with feeding the HS diet prepartum. However, rumen epithelial growth may not have been different between LS and HS cows in our study as indicated by the similar prepartum plasma concentrations of IGF-1 and GLP-2 between treatment groups. It has been reported in an *in vitro* study that IGF-1

could stimulate the growth of rumen epithelial cells (Baldwin, 1999). In addition, feeding a high-energy diet to young goats increased rumen papillae proliferation along with increased plasma IGF-1 concentrations (Shen et al., 2004). Glucagon-like peptide-2 is a hormone produced by enteroendocrine L-cells within the gut (Relling and Reynolds, 2008) that stimulates the intestinal growth and blood flow in nonruminants and may promote epithelial growth in ruminants (Taylor-Edwards et al., 2011). Therefore, the lack of difference in IGF-1 and GLP-2 concentrations in ours study may suggest that dietary starch content during the prepartum period may not affect rumen epithelial growth.

4.4.3 Grain challenge

Grain challenges on both d 7 and 21 after calving successfully induced a drop in rumen pH. We hypothesized that the cows in the LS group may experience a greater depression of rumen pH compared with those in the HS group during postpartum grain challenges. However, we found that cows in the LS group tended to have shorter duration of pH below 5.8 and less area of pH below 5.8 during the grain challenge on d 7 after calving. We speculated that the tendency of decreased duration and severity of SARA in LS cows may be associated with reduced inflammation and less rumen wall damage as indicated by the lower serum SAA concentration at 0 h relative to grain challenge. Serum amyloid A and Hp are quantitative biomarkers that increase rapidly in response to infection and inflammation and in most cases, SAA is a more sensitive indicator than Hp (Paulina and Tadeusz, 2011). Increased concentration of SAA has been reported during SARA (Gozho et al., 2005; Gozho et al., 2007; Khafipoor et al, 2006), possibly due to the translocation of LPS into blood as a result of rumen epithelial damage and intercellular junction erosion as observed in sheep (Liu et al., 2013) and dairy cows (Steele et al., 2009) fed high-grain diets. The cows in the LS group had lower duration and severity of

SARA compared with cows in the HS group during the prepartum period, therefore, it is likely that the cows in HS group had impaired rumen epithelium, which increased their susceptibility to SARA during grain challenge.

Unlike the response to the grain challenge on d 7 after calving, rumen pH and serum SAA and Hp concentrations in response to the grain challenge on d 21 after calving were not different between the LS and HS groups. It is possible that during the grain challenge on d 7 or the adaptation to the fresh diet, the starch content of which was similar to the prepartum HS diet, the cows in the LS group had impaired rumen epithelium to an extent similar to those in HS group, resulting in reduced VFA absorption in LS cows. To think in another way, the lack of treatment difference in response to grain challenge on d 21 may suggest that cows may reach maximal rumen epithelial surface area after switching to a lactating diet high in fermentable carbohydrate within 3 weeks after parturition. However, previous research indicated that the time required for maximal increases for ruminal epithelial surface area was approximately 6 to 8 weeks after an increase in dietary energy density (Dirksen et al., 1985) or shorter around 3 to 4 weeks after parturition (Bannink et al., 2008). Therefore, the time needed for maximal increase in rumen epithelial surface area after parturition warrants further investigation.

We hypothesized that feeding a LS prepartum diet may reduce insulin resistance in dairy cows after calving compared with feeding a HS prepartum diet. In contrast to our hypothesis, we did not detect any differences in AUC at 360 min for both plasma insulin and free fatty acids between the LS and HS groups during the grain challenge on d 7, suggesting that the extent of insulin resistance may not be different between LS and HS cows on d 7 after calving. During the grain challenge on d 21, we found that the minimum plasma free fatty acids concentration tended to be greater for LS cows than those in the HS group even though mean and maximum insulin

concentration were not different beween treatment groups. However, we noticed that at 240 min after dosing grain into the rumen, which was close to the time that cows reached the minimum plasma free fatty acids concentration, plasma insulin concentration tended to be lower for LS cows compared with HS cows. This may explain why LS cows had a smaller decrease in plasma free fatty acids concentration compared with HS cows during the grain challenge on d 21. In addition, the delta change and AUC at 360 min for plasma free fatty acids were not different between treatment groups. Therefore, the extent of insulin resistance may also not be different between LS and HS cows on d 21 after calving.

Previous studies used the glucose tolerance test (GTT) to investigate the effects of prepartum plane of nurtion on insulin resistance of dairy cows after calving (Mann et al., 2016; Holtenius et al., 2003). In agreement with our study, Mann et al. (2016) reported that prepartum plane of nutrition did not affect glucose tolerance as evaluated with GTT on d 4 and 21 after calving. However, reduced insulin resistance in dairy cows fed a low plane of nutrition during the prepartum period has been reported by Holtenius et al. (2003) that the clearance of glucose following the glucose tolerance test (GTT) performed at 3 wk postpartum was 20% greater in cows fed a low-energy diet than those fed a high-energy diet. Since only a few studies evaluated the insulin resistance in dairy cows fed different prepartum plane of nutrition, such discrepancies in insulin resistance warrants further research.

4.5 Conclusion

Prepartum dietary starch content may not affect lipid mobilization during both pre- and postpartum period. However, feeding a low-starch diet may reduce the risk of SARA before calving and may not increase the risk of developing SARA after calving. Furthemore, prepartum dietary starch content may not effect on insulin resistance on d 7 and 21 after calving.

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4.7 Tables and figures

Table 4.7.1 Ingredient and chemical composition of experimental diets[1]

Item	Prepartum		Postpartum
	LS	HS	
Ingredient, % DM			
Barley silage	56.9	56.6	39.9
Straw	23.6	4.4	…
Barley grain	…	22.1	14.3
Corn grain	…	…	11.8
Corn gluten meal	…	…	2.4
Soybean meal	…	…	1.9
Canola meal	6.6	1.8	8.1
Malt sprouts	7.0	7.0	2.4
Soy hulls	0.9	2.6	11.4
Distillers' grains with solubes	…	…	2.9
Amino plus	…	…	0.6
Urea	0.5	0.5	0.3
Mill run	1.8	1.7	…
Oil	0.4	0.4	0.8
Limestone	1.1	1.8	1.7
Magnesium sulfate	0.3	0.1	…
Sodium bicarbonate	…	…	0.7
Potassium carbonate	…	…	0.1
Mineral and vitamin mix[2]	1.0	1.0	0.7
Nutrient content			
%DM	42.8 ± 5.34	42.1 ± 4.44	50.4 ± 4.69
CP, %DM	15.0 ± 1.40	14.6 ± 1.04	17.9 ± 0.39
ADF, %DM	31.5 ± 2.23	23.3 ± 2.15	22.0 ± 2.15
NDF, %DM	47.7 ± 2.20	37.8 ± 2.46	33.8 ± 2.54
Starch, %DM	14.0 ± 3.92	26.1 ± 4.14	25.1 ± 2.91
NFC, %DM	28.1 ± 4.07	39.4 ± 4.25	39.5 ± 4.38
NE_L, Mcal/kg DM	1.54 ± 0.03	1.63 ± 0.02	1.62 ± 0.05
DCAD, mEq/kg	30	28	…
NE_L allowable milk, kg/d	…	…	32.4
MP allowable milk, kg/d	…	…	34.6

[1] LS = low-starch diet; HS = high-starch diet.

2Contained 21.0% Ca, 33.0% Cl, 7.11% Na, 7.29% S, 3,964 kIU of vitamin A, 397 kIU of vitamin D, and 1,3216 kIU of vitamin E for LS diet; contained 13.5% Ca, 25.0% Cl, 6.29% Na, 4.15% S, 2,2014 kIU of vitamin A, 2,201 kIU of vitamin D, and 7, 3380 kIU of vitamin E for HS diet; contained 6.85% Ca, 5.12% P, 18.8% Mg, 20.1% Cl, 0.02% K, 13.0% Na, 0.63% S, 91.8

mg/kg of Co, 4,407 mg/kg of Cu, 208 mg/kg of I, 8,037 mg/kg of Mn, 13.2 mg/kg of Se, 6,630 mg/kg of Zn, 1,998 kIU of vitamin A, 201 kIU of vitamin D, and 6, 643 kIU of vitamin E for postpartum diet.

Table 4.7.2 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on DMI and changes of BW and BCS before parturition

Variable	Prepartum diet		SE	*P*-value		
	LS	HS		TRT[1]	WK[2]	TRT*WK
DMI[3], kg/d	10.7	12.8	0.74	0.07	0.004	0.98
DMI[3], % BW	1.54	1.81	0.10	0.08		
Energy intake[4], %	116	150	9.24	0.02		
Initial BW[5], kg	706	710	29.4	0.92		
BW change, kg/d	-2.66	-1.96	0.59	0.41		
Initial BCS[6]	3.08	3.07	0.11	0.93		
BCS change, /21d	-0.30	-0.18	0.08	0.29		

[1]Effects of prepartum dietary starch content (LS vs. HS).
[2]Effects of week relative to parturition.
[3]DMI during the prepartum transition period (wk -3 to -1).
[4]Percentage of NE_L requirement; calculated according to Dann et al. (2006).
[5]Body weight measured at the beginning of the study (d -28 ± 3).
[6]Body condition score measured at the beginning of the study (d -28 ± 3).

Table 4.7.3 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on DMI, milk yield, and changes of BW and BCS during the fresh period (wk 1 to 3 after calving)

Varible	Prepartum diet		SE	*P*-value		
	LS	HS		TRT[1]	WK[2]	TRT*WK
DMI, kg/d	17.5	16.6	0.80	0.40	<0.0001	0.50
DMI, % BW	2.81	2.54	0.16	0.24		
Milk yield, kg/d	38.1	37.7	1.48	0.84	<0.0001	0.31
BW at calving, kg	643	667	25.8	0.52		
BW change, kg/d	-1.05	-2.10	0.63	0.26		
BCS at calving	2.72	2.88	0.13	0.41		
BCS change, /21d	-0.26	-0.21	0.09	0.73		

[1] Effects of prepartum dietary starch content (LS vs. HS).
[2] Effects of week relative to parturition.

Table 4.7.4 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on concentrations of blood metabolites and hormones during the transition period

Variable[4]	Prepartum diets		SE	*P*-value
	LS	HS		TRT[1]
d -10[2]				
Glucose, mg/dL	65.7	71.7	2.00	0.05
Free fatty acids, µEq/L	266	286	61.6	0.82
BHB, mg/dL	5.49	6.40	0.41	0.13
Insulin, ng/mL	1.30	1.54	0.18	0.43
IGF-1, ng/mL	87.8	88.9	7.77	0.92
GLP-1, ng/mL	0.12	0.10	0.01	0.21
GLP-2, ng/mL	0.40	0.40	0.06	0.93
d 3[3]				
Glucose, mg/dL	58.6	59.9	2.29	0.70
Free fatty acids, µEq/L	465	513	104	0.75
BHB, mg/dL	7.12	8.49	0.47	0.05
Insulin, ng/mL	1.15	1.13	0.17	0.93
IGF-1, ng/mL	33.5	42.7	5.75	0.28
GLP-1, ng/mL	0.25	0.16	0.03	0.04
GLP-2, ng/mL	0.30	0.37	0.04	0.29
d 21[3]				
Glucose, mg/dL	57.4	60.5	2.38	0.37
Free fatty acids, µEq/L	271	391	95.1	0.39
BHB, mg/dL	8.48	7.56	0.94	0.50
Insulin, ng/mL	1.60	1.49	0.20	0.73
IGF-1, ng/mL	50.8	50.9	4.98	0.99
GLP-1, ng/mL	0.31	0.27	0.04	0.43
GLP-2, ng/mL	0.44	0.46	0.05	0.87

[1] Effects of prepartum dietary starch content (LS vs. HS).
[2] Relative to expected calving date.
[3] Relative to actual calving date.
[4] Serum sample was used for IGF-1 analysis; plasma samples was used for analysis of all other variables. BHB = β-hydroxybutyrate; IGF-1 = insulin-like growth factor 1; GLP-1,2 = glucagon-like peptide 1, 2.

Table 4.7.5 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on rumen pH and VFA profiles during d -10 to -8 ± 3 relative to expected calving date

Variable	LS	HS	SE	*P*-value
No. of animal[1]	8	5		
DMI, kg/d	11.1	13.1	0.79	0.11
Rumen pH				
Nadir	5.87	5.45	0.09	< 0.01
Mean	6.42	6.11	0.08	0.01
Maximum	6.99	6.75	0.05	0.01
Duration pH <5.8, min/d	49.2	369	80.8	0.02
Area pH <5.8, pH × min/d	5.20	85.1	21.8	0.03
Acidosis index, pH × min/kg	0.64	6.18	1.54	0.03
Rumen VFA				
Total VFA, mM	63.1	69.1	2.37	0.10
Acetate, mol/100 mol	65.5	63.3	0.52	0.05
Propionate, mol/100 mol	21.3	20.8	0.46	0.45
Butyrate, mol/100 mol	8.98	10.7	0.65	0.09
Isobutyrate, mol/100 mol	0.87	0.90	0.04	0.65
Valerate, mol/100 mol	1.27	1.59	0.06	0.005
Isovalerate, mol/100 mol	1.60	1.94	0.12	0.07
Caproate, mol/100 mol	0.44	0.72	0.07	0.02
Acetate:propionate	3.08	3.05	0.07	0.75

[1] Rumen pH data were not available from 1 cow in LS group and 4 cows in HS group due to early calving.

Table 4.7.6 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on rumen pH, VFA profiles, and serum concentrations of haptoglobin (Hp) and serum amyloid A (SAA) during the grain challenge (6-h period) on d 7 after calving

Variable	Prepartum diets		SE	*P*-value		
	LS	HS		TRT[1]	Hour[2]	TRT*Hour
Mean rumen pH				0.03	<0.0001	0.44
Mean basal[3]	6.57	6.15	0.12	0.02		
Mean GC[4]	6.15	5.84	0.13	0.09		
Rumen pH over 6-h period						
Nadir[5]	5.48	5.42	0.13	0.77		
Mean[5]	6.00	5.99	0.10	0.96		
Maximum[5]	6.57	6.61	0.06	0.64		
Duration pH < 5.8, min/6h	75.7	177	36.4	0.07		
Area pH < 5.8, pH × min/6h	20.3	67.8	18.3	0.08		
Rumen VFA						
Total VFA, mM				0.27	<0.0001	0.69
0 h	45.8	56.9	6.39	0.23		
3 h	81	90.3	6.39	0.31		
6 h	89.7	91.1	6.39	0.88		
Acetate, mol/100mol				0.37	<0.0001	0.77
0 h	59.3	61.1	1.87	0.5		
3 h	53.3	55.2	1.87	0.48		
6 h	51.7	54.7	1.87	0.27		
Propionate, mol/100mol				0.36	<0.0001	0.51
0 h	25.2	23.6	1.79	0.53		
3 h	30	27.1	2.18	0.37		
6 h	31.4	27	2.89	0.30		
Butyrate, , mol/100mol				0.23	0.007	0.62
0 h	10.2	10.8	0.73	0.6		
3 h	11.6	12.9	0.59	0.13		
6 h	11.9	13.9	1.11	0.24		
Hp, mg/mL				0.32	0.98	0.10
0 h	0.17	0.31	0.07	0.17		
6 h	0.21	0.27	0.08	0.57		
SAA, µg/mL				0.07	0.81	0.24
0 h	23.8	56.0	11.5	0.06		
6 h	26.4	54.3	10.9	0.09		

[1] Effects of prepartum dietary starch content (LS vs. HS).
[2] Effects of hour relative to grain challenge.
[3] Basal mean rumen pH calculated from data measured during 1 h before grain challenge.
[4] Mean rumen pH calculated from data measured during grain challenge (GC) over a 6-h period.
[3] Covariate (rumen pH measured over 60 min before grain challenge) was used for the minimum, mean, and maximum rumen pH during grain challenge, respectively.

Table 4.7.7 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on rumen pH, VFA profiles, and serum concentrations of haptoglobin (Hp) and serum amyloid A (SAA) during the grain challenge (6-h period) on d 21 after calving

Variable	Prepartum diets		SE	*P*-value		
	LS	HS		TRT[1]	Hour[2]	TRT*Hour
Mean rumen pH				0.63	<0.0001	0.57
Mean basal[3]	6.63	6.60	0.14	0.88		
Mean GC[4]	6.23	6.11	0.10	0.40		
Rumen pH over 6-h period						
Nadir	5.72	5.49	0.13	0.23		
Mean	6.23	6.11	0.10	0.40		
Maximum	6.83	6.77	0.13	0.76		
Duration pH < 5.8, min/6h	58.9	92.2	25.6	0.37		
Area pH < 5.8, pH × min/6h	15.5	20.2	7.44	0.66		
Rumen VFA						
Total VFA, mM				0.19	<0.0001	0.60
0 h	50.5	56.2	3.29	0.24		
3 h	92.9	105.3	6.14	0.17		
6 h	87.0	95.7	6.81	0.38		
Acetate, mol/100mol				0.34	<0.0001	0.51
0 h	63.1	62.2	1.09	0.58		
3 h	57.5	55.5	1.34	0.30		
6 h	57.3	54.8	1.75	0.33		
Propionate, mol/100mol				0.33	3E-04	0.39
0 h	20.0	21.7	1.09	0.28		
3 h	22.1	24.5	1.4	0.25		
6 h	20.8	22.5	1.68	0.51		
Butyrate, , mol/100mol				0.79	<0.0001	0.61
0 h	10.7	10.6	0.64	0.89		
3 h	14.1	14.2	1.19	0.96		
6 h	15.6	16.8	1.44	0.57		
Hp, mg/mL				0.88	0.67	0.26
0 h	0.18	0.15	0.06	0.73		
6 h	0.16	0.22	0.09	0.62		
SAA, µg/mL				0.77	0.95	0.27
0 h	57.2	45.2	17.1	0.06		
6 h	52.5	50.6	16.5	0.09		

[1] Effects of prepartum dietary starch content (LS vs. HS).
[2] Effects of hour relative to grain challenge.
[3] Basal mean rumen pH calculated from data measured during 1 h before grain challenge.
[4] Mean rumen pH calculated from data measured during grain challenge over a 6-h period.

Table 4.7.8 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on plasma insulin and free fatty acids during the grain challenge on d 7 after calving

Item	Prepartum diet		SE	*P*-value
	LS	HS		
Insulin[1]				
Cmax (ng/mL)	1.54	1.96	0.3	0.34
Tmax (min)	217	263	31.1	0.31
delta (ng/mL)	0.68	0.92	0.23	0.46
AUC (ng/mL × 360 min)	416	542	77.8	0.27
Free fatty acids[2]				
Cmin (μEq/L)	184	134	28.9	0.24
Tmin (min)	283	277	26.2	0.86
delta (μEq/L)	-755	-672	104	0.58
delta/Tmin (μEq/L*min^{-1})	-3.14	-2.52	0.57	0.45
AUC (mEq/L × 360 min)	139	112	17.9	0.31
$AUC_{free\ fatty\ acids}/AUC_{insulin}$ (μEq/ng)[3]	248	252	65.6	0.32

[1]Cmax = maximum concentration; Tmax = time to reach maximum concentration; delta = the change from baseline to maximum concentration; AUC = area under the concentration-time curve.
[2] Cmin = minimum concentration; Tmin = time to reach minimum concentration; delta = the change from baseline to minimum concentration; AUC = area under the concentration-time curve.
[3] Calculated as AUC for plasma free fatty acids at 360 min divided by AUC for plasma insulin at 360 min.

Table 4.7.9 Effects of feeding a low-starch (LS) or high-starch (HS) diet prepartum on plasma insulin and free fatty acids during the grain challenge on d 21 after calving

Item	Prepartum diet		SE	*P*-value
	LS	HS		
Insulin[1]				
Cmax (ng/mL)	1.76	2.21	0.20	0.13
Tmax (min)	230	243	24.9	0.71
delta (ng/mL)	0.71	1.12	0.18	0.13
AUC (ng/mL × 360 min)	485	561	40.8	0.21
Free fatty acids[2]				
Cmin (μEq/L)	102	76.2	9.89	0.08
Tmin (min)	250	297	28.4	0.26
delta (μEq/L)	-314	-392	46.0	0.25
delta/Tmin (μEq/L*min^{-1})	-1.24	-1.38	0.14	0.51
AUC (mEq/L × 360 min) [2]	68.3	61.2	7.09	0.49
$AUC_{free\ fatty\ acids}/AUC_{insulin}$ (μEq/ng)[3]	111	151	25.8	0.29

[1]Cmax = maximum concentration; Tmax = time to reach maximum concentration; delta = the change from baseline to maximum concentration; AUC = area under the concentration-time curve.
[2] Cmin = minimum concentration; Tmin = time to reach minimum concentration; delta = the change from baseline to minimum concentration; AUC = area under the concentration-time curve.
[3] Calculated as AUC for plasma free fatty acids at 360 min divided by AUC for plasma insulin at 360 min.

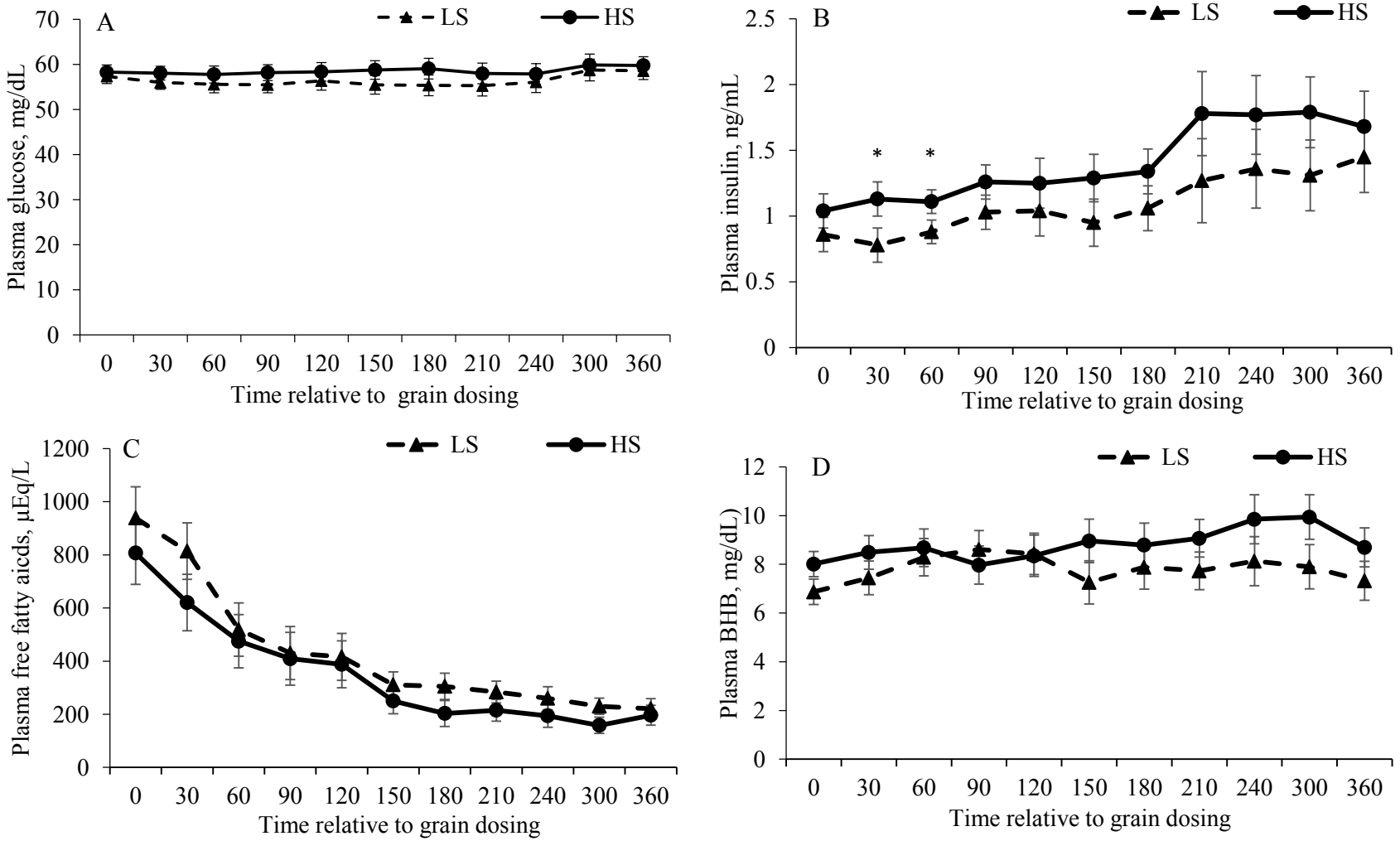

Figure 4.7.1 Plasma concentrations of glucose (A), insulin (B), free fatty acids (C), and BHB (D) during a grain challenge on d 7 in dairy cows fed a prepartum low-starch (LS) or high-starch (HS) diet. Data are presented as LSM ± SE. A: treatment, $P = 0.38$; time, $P = 0.26$; treatment × time, $P = 0.64$. B: treatment, $P = 0.09$; time, $P < 0.0001$; treatment × time, $P = 0.94$. C: treatment, $P = 0.31$; time, $P = 0.002$; treatment × time, $P = 0.74$. D: treatment, $P = 0.30$; time, $P = 0.52$; treatment × time, $P = 0.34$. Data were analyzed individually for each time points and * indicates $0.05 < P < 0.10$.

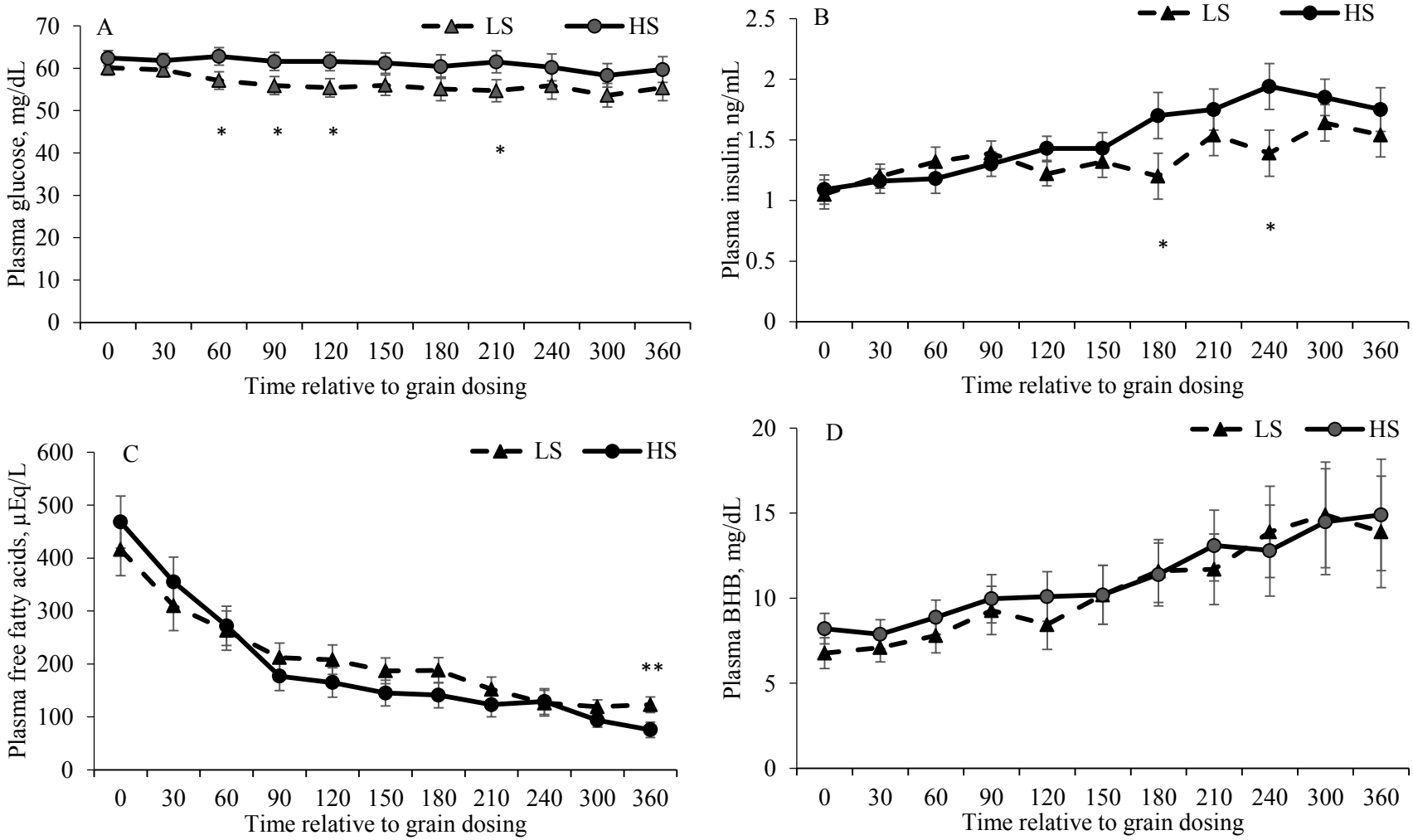

Figure 4.7.2 Plasma concentrations of glucose (A), insulin (B), free fatty acids (C), and BHB (D) during a grain challenge on d 21 in dairy cows fed a prepartum low-starch (LS) or high-starch (HS) diet. Data are presented as LSM ± SE. A: treatment, $P = 0.14$; time, $P = 0.03$; treatment × time, $P = 0.04$. B: treatment, $P = 0.34$; time, $P < 0.0001$; treatment × time, $P < 0.01$. C: treatment, $P = 0.64$; time, $P = 0.02$; treatment × time, $P = 0.39$. D: treatment, $P = 0.81$; time, $P < 0.0001$; treatment × time, $P = 1.00$. Data were analyzed individually for each time points and * indicates $0.05 < P < 0.10$ and ** indicates $P < 0.05$.

Chapter 5. General discussion

5.1 Summary and industry implications

Transition cow nutritional management is of great importance for the production and health of cows and the profitability of dairy operations. Numerous studies have investigated the effects of prepartum plane of nutrition, but little is known about the nutritional management for fresh cows. Chapter 2 and 3 evaluated the effects of peripartum SCFP supplementation and starch content of fresh diets on production and rumen fermentation of dairy cows in early lactation. A basal controlled-energy diet was fed during the prepartum period. In general, only few interactions were found for SCFP and dietary starch content for variables of interest in Chapter 2 and 3. Supplementation of SCFP, as shown in Chapter 2, had no effect on prepartum DMI, but transiently increased DMI on d 1 and 5 after calving compared with CON. This may attribute to reduced inflammation as indicated by lower serum haptoglobin concentration in SCFO cows than CON cows on d 7 after calving (Knoblock et al., 2018). As cell wall components of SCFP, β-glucan modulates both cellular and humoral immunity (Novak and Vetvicka, 2008) and mannan oligosaccharides binds to pathogens to prevent their colonization in gastrointestinal tract (Heinrichs et al., 2003). In addition, supplementation of β-glucan (Tao et al., 2015) and mannan oligosaccharides (Morrison et al., 2010; Linneen et al., 2014) has shown positive effects on immune function in ruminants. Therefore, it is likely that the β-glucan and mannan oligosaccharides components in SCFP reduced inflammation and increased DMI in dairy cows after calving. During the post-fresh early lactation period, SCFP cows had greater feed efficiency, as indicated by a tendency of lower DMI and similar 3.5% FCM compared with CON cows. Changes in BW and BCS were not affected by SCFP supplementation.

In Chapter 3, it was found that SCFP tended to increase molar proportion of acetate and mean rumen pH during d -10 and -3 sampling period, respectively, which may have resulted from increased fiber digestion as SCFP have been reported to increase the growth of cellulolytic bacteria (Callaway and Martin, 1997). After calving, SCFP supplementation tended to increase minimum rumen pH and reduce the duration of pH below 5.8 during d 21 sampling period, but SCFP had no effect on rumen pH during d 1 and 7 sampling period. Although SCFP supplementation increased DMI only on d 1 and 5 after calving and had no effect on rumen pH during d 1 and 7 sampling period, it cannot be neglect that the actual SCFP take during the fresh period was lower than the target amount recommended by manufacture as explained in Chapter 2. Therefore, it is reasonable to speculate that SCFP supplementation can exert greater positive effects on production and rumen fermentation of fresh cows if SCFP consumption reached the target amount. In summary, my studies showed the potential of supplementing SCFP to transition cows to promote DMI immediately after calving when dairy cows experience tremendous physiological changes, and to post-fresh early lactation dairy cows to reduce the duration of rumen pH depression.

As for the effects of dietary starch content, Chapter 2 showed that feeding LS diets increased milk production during the fresh period compared with HS diets, without affecting DMI. Although LS cows tended to lose more body condition during the fresh period, this did not lead to negative effects on the health of LS cows. In accordance with previous studies (Penner et al., 2007; Fairfield et al., 2007), dairy cows in our study were in great risk of SARA immediately after calving regardless of treatment group, as observed in Chapter 3. Feeding LS diets showed positive effects on rumen pH such that minimum rumen pH tended to be higher for LS cows than HS cows during the d 1 sampling period. However, dietary starch content had no effect on rumen

pH during the d 7 and 21 sampling period. In addition, the expression of genes encoding for rumen epithelial growth, VFA transporters, and VFA metabolism did not differ between LS and HS cows on d 21.

Fresh diets should be formulated to accelerate the increase in DMI and reduce the decrease in rumen pH that results from the sudden increase in diet fermentability after parturition. In Chapter 2 and 3, LS diets and HS diets had similar energy content and the results of these two chapters suggested that LS fresh diets (22% starch) can be fed to dairy cows that have consumed a controlled-energy close-up diet. Based on my results, however, it is worth noting that dairy cows may lose more body condition when LS diets are fed compared with HS diets during the fresh period. Therefore, the change in body condition score during the fresh period and incidence of health disorders in early lactation dairy cows should be closely monitored as increased fatty acids mobilization from adipose tissue is associated with greater incidence of health disorders, decreased DMI and milk production, and impaired reproduction efficiency (Drackley, 1999; Adewuyi et al., 2006). In addition, the average BCS of all cows used in Chapter 2 was 3.25. For skinny cows with low BCS at calving, feeding LS diets may not be a good choice compared with HS diets considering of the tendency of higher body condition loss observed for LS cows in my study. It is also worth noting that the energy contents were similar between the LS and HS diets used in Chapter 2 and 3; therefore, when a LS diet that contains less energy than a HS diet was fed to skinny cows during the fresh period, it may further worse the body condition of fresh cows compared with feeding a HS diet.

Chapter 4 investigated the effects of prepartum dietary starch content on rumen fermentation and plasma metabolites and hormones during the transition period. In addition, grain challenges were conducted on d 7 and 21 after calving to evaluate the extent of adaptation

of the rumen. Feeding the LS diet reduced duration and area of rumen pH below 5.8 during d -10 sampling period. Surprisingly, cows fed the LS prepartum diet tended to have lower duration and area of rumen pH below 5.8 during a grain challenge on d 7 compared with HS cows. This is probably due to reduced inflammation and less rumen wall damage in the LS cows as indicated by lower serum SAA concentration at 0 h relative to grain challenge. Rumen pH during a grain challenge on d 21 after calving was not different between the LS and HS cows. In summary, feeding a HS diet containing 26% of starch (DM basis) during the prepartum period is not desirable based on the results of my study because it showed no beneficial effects on postpartum rumen pH. Instead, feeding a HS diet can increase duration of rumen pH below 5.8 and might impair the rumen epithelium. Therefore, dairy operations should at least avoid feeding close-up diets with high starch content, for example 26% of starch.

5.2 Limitations and future studies

Dairy cows are fed TMR in commercial farm settings, therefore SCFP was provided to dairy cows through TMR in Chapter 2 and 3. I intended to provide SCFP at 19 g/d, according to the manufacturer's recommendation, based on the expected DMI of 20 kg/d postpartum. However, cows consumed less than expected during the fresh period in Chapter 2, which was 16.6 kg/d on average, leading to lower intake of SCFP (15.7 g/d) than the target level. Additionally, cows did not have expected DMI until the end of the fresh period in Chapter 3. As more positive effects of SCFP supplementation were observed before calving and by the end of the fresh period, but not between these two periods, such as rumen pH and postpartum feed efficiency, it was speculated that such variation in animal response may possibly be attributed to the differences in actual SCFP intake. Because of the lower SCFP intake than the manufacturer's recommendation, it is not known whether increasing the SCFP intake of dairy cows can result in

more beneficial effects on production and rumen fermentation, such as greater DMI during the fresh period (Dann et al., 2000) and reduced risk of SARA in dairy cows fed HS diet (Shen et al., 2008). To address this, future studies could use various dosages of SCFP (e.g. 2-fold, 3-fold greater than the recommended level) and then evaluate the effects of the supplemention level of SCFP on production and rumen fermentation in transition dairy cows.

In Chapter 2, feeding low-starch fresh diets enhanced milk production of dairy cows fed controlled-energy diets during the close-up period. In contrast, dairy cows were fed high-starch close-up diets in the study of McCarthy et al. (2015a) and Rabelo et al. (2003) and showed positive effects on production performance when high-starch diets were fed after calving. This may suggest that the response of dairy cows to the dietary starch content of fresh diet is affected by that of close-up diet as proposed by Dann et al. (2016). However, it is not known how large the difference in dietary starch content between the close-up diet and fresh diet could be, without inducing negative effects on performance of dairy cows after parturition. To confirm this speculation and find out the upper limit of the difference in starch content between the close-up diet and fresh diet, future studies with various starch contents of both pre- and post-partum diets are needed.

In Chapter 3, the difference in rumen pH between the LS cows and HS cows was only observed during d 1 sampling period but not during d 7 or d 21 sampling period. Moreover, dietary starch content of fresh diets had no difference in expression of genes encoding for rumen epithelial growth, VFA transporters, and VFA metabolism. It is not known if such results are related to increased rumen papillae surface area or increased VFA absorption in LS cows compared with HS cows. In Chapter 4, cows fed a high-starch close-up diet had longerduration of rumen pH below 5.8 than cows fed a low-starch close-up diet during a grain challenge on d 7

calving. However, no difference in rumen pH between treatment groups was observed during a grain challenge on d 21 after calving. It is unknown if cows in both group reached maximal rumen epithelial surface area before the grain challenge on d 21. Therefore, future studies should address the effects of starch content on rumen epithelial surface area and VFA absorption during the calving transition.

5.3 Conclusions

The findings from this thesis suggest that for dairy cows fed a controlled-energy close-up diet, feeding LS diets during the fresh period can increase milk production without affecting DMI compared with feeding HS diets. In addition, feeding LS fresh diets may increase the rumen pH immediately after calving. However, cows fed LS fresh diets may lose more body condition than cows fed HS fresh diets. Supplementation of SCFP during the periparturient period may help increase DMI transiently after calving, reduce the duration of pH below 5.8 by the end of fresh period, and increase the feed efficiency during the post-fresh early lactation period.

For dairy cows during the close-up period, feeding a HS diet during the close-up period may increase duration of rumen pH below 5.8 and might impair the rumen epithelium compared with feeding a LS diet.

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