Heliox for treatment of exacerbations of chronic obstructive pulmonary disease (Review)

Rodrigo GJ, Pollack CV, Rodrigo C, Rowe BH, Walters EH

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[Intervention Review]

Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

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Editorial group: Cochrane Airways Group.
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2009.
Review content assessed as up-to-date: 26 September 2002.

Citation: Rodrigo GJ, Pollack CV, Rodrigo C, Rowe BH, Walters EH. Heliox for treatment of exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2001, Issue 1. Art. No.: CD003571. DOI: 10.1002/14651858.CD003571.

ABSTRACT

Background

Due to its low density properties, helium-oxygen mixtures have the potential to decrease the work of breathing and possibly avoid the need for intubation and mechanical ventilation in patients with respiratory failure.

Objectives

To determine the effect of the addition of helium/oxygen mixtures (heliox) to standard medical care during ventilated and non-ventilated acute exacerbations of COPD.

Search methods

Randomized controlled trials were identified from the Cochrane Airways Review Group asthma Register. Primary authors and experts were contacted. References from included and excluded studies, known reviews and texts were also searched.

Selection criteria

Studies were selected for inclusion if they compared treatment with heliox to placebo (oxygen or air) in randomized controlled trials in adults with an exacerbation of COPD.

Data collection and analysis

Data from all trials were combined using the Review Manager (version 4.1). We planned to perform: 1) random effects weighted mean difference (WMD), with 95% confidence intervals (95% CI), 2) Homogeneity of effect sizes with the Dersimonian and Laird method with $p<0.1$ as the cut point for significance, and 3) sensitivity analysis on different helium-oxygen mixtures (80/20 vs 70/30), and 4) methodological quality (Jadad score >2 vs. <3). An update search conducted in September 2002 identified one further excluded study.

Main results

Four studies, all published between 1997 and 2000 met the inclusion criteria. Two studies compared heliox-oxygen vs. air-oxygen in decompensated COPD patients who were not ventilated. One study was performed in mechanical ventilated patients and one in patients undergoing noninvasive pressure support ventilation (NIPSV). Data could be obtained for only two of the studies. One was a randomized crossover study of 70:30 helium-oxygen vs air-oxygen that involved nineteen patients with acute severe COPD, hospitalized

in an intensive care unit for NIPSV . In the patients receiving heliox, arterial PCO2 fell more; WMD 0.8 kPa (95% CI 0.26, -1.34). The second was a trial involving 47 patients with acute COPD, who presented to an Emergency Department, randomized to receive updraft nebulization of albuterol and ipratropium bromide using 80% helium and 20% oxygen or compressed air as the driving gas. Treatments were administered at 0, 20, 40, and 120 minutes after randomization. There were no significant differences in the change of FEV1 and FVC between the two groups by either the 1 or 2 hours point, although a small improvement in FEF 25-75 was significantly greater in the heliox group than in the air group.

Authors' conclusions

There is currently insufficient evidence to support the use of helium-oxygen mixtures to treat acute exacerbations of COPD in either ventilated or non-ventilated patients. Suitably designed randomised controlled trials with the endpoint being the avoidance of mechanical ventilation may be justified.

PLAIN LANGUAGE SUMMARY

Helium-oxygen mixture for the treatment of exacerbations of chronic obstructive pulmonary disease

Mixtures of helium and oxygen (heliox) may make breathing easier, but there is not enough evidence from trials to show whether these mixtures can relieve attacks of COPD (chronic obstructive pulmonary disease).

BACKGROUND

As early as 1935 helium and oxygen mixtures (heliox) were introduced to the medical community for treatment of airway obstruction (Barach 1935). There was a resurgence in interest in heliox in the 1980's for the treatment of acute asthma. Due to their low density with respect to air, heliox mixtures have the potential to decrease airway resistance and therefore decrease the work of breathing in situations associated with increased airway resistance. Thus, heliox treatment may benefit patients suffering from obstructive lesions of the larynx, trachea, and airways. Additionally, the deposition of inhaled particles in a heliox mixture was shown to be improved, with a greater percentage of particle retention in the lung (Anderson 1993). This suggests that one of the beneficial effects of heliox in situations of reactive airway disease may be the improved deposition of aerosolized bronchodilators.

On the other hand, Hess 1999 concluded that the inhaled mass of albuterol decreased significantly when the nebulizer was powered with heliox rather than air. The authors recommended that the flow to power the nebulizer should be increased when heliox is used. Patients with chronic obstructive pulmonary disease (COPD) have increased resistance to flow due to narrowing of the airways by edema and mucous, and loss of lung collagen, and this increased resistance to flow results in greater work of breathing. It can be expected that breathing a high mixture of helium (>60%) would result in lower resistance to flow, and in a decrease in work of breathing. Research on patients with stable COPD (Swidwa 1985) has demonstrated a decrease in lung hyperinflation (as measured by a fall in functional residual capacity by 15%). This would be expected to place the respiratory muscles at a better mechanical advantage and decrease the work of breathing. Indeed, a significant decline in VCO2 was also noted supporting a reduced work of breathing. Lastly, there was a small but significant fall in the PaCO2. These findings lend support to the therapeutic use of heliox in patients with COPD. Thus, helium-oxygen mixtures have the potential to stabilize patients with acute respiratory failure who might otherwise require intubation and mechanical ventilation. However, little is unknown regarding the use of heliox in treating patients with acute exacerbations of COPD.

OBJECTIVES

The objective of this systematic review was to determine the effect of the addition of heliox to standard medical care during acute COPD exacerbations, as measured by pulmonary function and clinical endpoints.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomized, single or double blind, placebo controlled trials (either parallel group or crossover) were considered for inclusion.

Types of participants

Participants should be adults (>18 years of age) with a clinical diagnosis COPD (according to accepted criteria such as those published by the ATS) experiencing an exacerbation of their COPD, presenting to emergency rooms or other acute care settings. Studies involving patients exclusively with asthma were not included. Studies involving both COPD and asthmatic patients were considered if patients with COPD could be separately analyzed by review the study or through correspondence with the authors. COPD patients requiring mechanical or noninvasive ventilation at presentation were included.

Types of interventions

All patients must have been treated with either helium-oxygen or air-oxygen administered in random order. Study co-interventions such as the use of corticosteroids and other drugs were monitored and would form subgroup comparisons when possible. Also, different helium-oxygen mixtures (80/20, 70/30, 60/40), and duration of heliox administration would be considered in subgroup analysis.

Types of outcome measures

Primary outcomes

The primary outcome measures were changes in peak expiratory flow (PEF; absolute and percent of predicted), forced expiratory volume in the first second (FEV1; absolute and percent of predicted)

Secondary outcomes

Additional outcomes were:
1) Symptom score/symptoms/signs (wheezing, shortness of breath, dyspnea, accessory muscle use)
2) Physiological measures: PaO2, SaO2, tidal volume, minute ventilation, inspiratory time and vital signs
3) Side effects/adverse effects
4) Clinical outcomes: need for mechanical ventilation, admissions to the hospital. The timing of assessment was before, during, and 15-30 minutes after breathing heliox.
Assessments included up to 6 hours of treatment.

Search methods for identification of studies

Electronic searches

A search was carried out using the Cochrane Airways group "COPD RCT" register, derived from a search of EMBASE, MEDLINE, and CINAHL for the years 1966 to 2000. In addition, hand searching of the 20 most productive respiratory care journals was completed and relevant RCTs were added to the register, including those published in languages other than English. Search of this register was completed using the following terms:
(((Emerg* OR acute OR exacerbat*) AND (COPD OR Emphysema OR Chronic bronchitis OR bronchitis OR CAL OR COAD)) AND ((Heliox OR Helium) AND Oxygen))
An advanced search of CENTRAL, the Cochrane Controlled Trials Register was completed using the above search strategy.

Searching other resources

Authors of all studies were contacted to locate other unpublished or "in progress" studies which meet the inclusion criteria. References from included studies and any identified reviews were searched for citations. Also we contacted companies that sell heliox or delivery systems for it.

Data collection and analysis

Selection of studies

1. Titles, abstracts, and citations were independently reviewed by the two reviewers (GJR and CR) to assess potential relevance for full review.
2. From the full text, both reviewers independently assessed studies for inclusion based on the criteria for population, intervention, study design and outcomes.
3. Agreement was measured using kappa statistic values. Any disagreement over inclusion was resolved by a third reviewer (CVP) and consensus.

Data extraction and management

Two reviewers (GJR and CR) would independently extracted data from included trials and enter results into the Cochrane Collaboration software program (Review Manager). Data extraction included the following items:

1. Population: age, gender, number of patients studied, patient demographics, withdrawals
2. Intervention: agent, dose, route of delivery, and duration of therapy
3. Control: concurrent treatments (beta-agonist, ipratropium bromide, corticosteroids, and aminophylline)

4. Outcomes: Pulmonary function measures (FEV1 and PEF), symptom score/symptoms (wheezing, shortness of breath, dyspnea, accessory muscle use), physiological measures (PaO2, SaO2, tidal volume, minute ventilation, inspiratory time and vital signs), side effects/adverse effects, clinical outcomes (need for mechanical ventilation, admissions to the hospital)

5. Design: method of randomization and allocation concealment.

Assessment of risk of bias in included studies

Two reviewers (GJR and CR) assessed the methodological quality of the included trials using two methods. First, using the Cochrane approach to assessment of allocation concealment: 1) Grade A: Adequate concealment; 2) Grade B: Uncertain; 3) Grade C: Clearly inadequate concealment. Second, each study was assessed for validity on a 0-5 scale, by the method of Jadad (Jadad 1995): 1) Was the study described as randomized? (1=yes, 0=no); 2) Was the study described as double-blind? (1=yes, 0=no); 3) Was there a description of withdrawals and drop outs? (1=yes, 0=no); 4) Was the method of randomisation well described and appropriate? (1= yes, 0=no); 5) Was the method of double-blinding well described and appropriate? (1=yes, 0=no); 6) Deduct 1 point if methods of randomisation or blinding were inappropriate. Inter-rater reliability was measured for both quality scales by using kappa statistics.

Assessment of heterogeneity

For pooled effects, heterogeneity would be tested using the Breslow-Day test; with $p<0.1$ considered as statistically significant.

Data synthesis

All included trials would be combined using the Review Manager (version 4.1). For continuous variables the results of individual studies would be calculated as random effects weighted mean difference (WMD) or standardized mean difference (SMD), with 95% Confidence Intervals (CI). All similar studies would be pooled using random effects WMD/SMD and 95% CIs. For dichotomous variables, a random effects relative risk (RR) with 95% CI would be calculated for individual studies. All similar studies would be pooled using random effects RR and 95% CIs.

Sensitivity analysis

Sensitivity analysis would be performed using:

1. Co-interventions with corticosteroids vs. none
2. Different helium-oxygen mixtures (80/20, vs. 70/30 or 60/40)
3. Duration of heliox administration (long vs. short)
4. Methodological quality (concealment Grade A vs. Grades B & C, or Jadad score >2 vs. <3)
5. Random effects vs. fixed effects modelling

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

Three-hundred and forty two articles were identified in this search. Of these, the reviewers selected eighteen papers about the use of heliox-oxygen in airflow obstruction as potentially eligible.

Included studies

We selected four studies (Gerbeaux 1997; Jolliet 1999; Onn 1999; de Boisblanc 2000) published between 1997 and 2000. One study was from France, one from Israel, one from Switzerland, and one from USA. The studies compared heliox-oxygen vs. air-oxygen in decompensated COPD non-ventilated patients, (two studies), in mechanical ventilated patients (one study), and in noninvasive pressure support ventilated patients (one study). Two studies were available in abstract form only, and attempts to contact the authors were unsuccessful so it was not possible to include data from these studies in the meta-analysis (Gerbeaux 1997; Onn 1999). Therefore, we extracted data from two studies (Jolliet 1999; de Boisblanc 2000). An update search conducted in September 2002 identified one excluded study (Gerbeaux 2001).

The Jolliet et al study (Jolliet 1999) was designed to test the hypothesis that, in decompensated COPD, noninvasive pressure support ventilation (NIPSV) using a 70:30 helium:oxygen mixture instead of 70:30 air:oxygen mixture could reduce dyspnea and improve ventilatory variables, gas exchange and haemodynamic tolerance. The study involved 19 severe COPD decompensated patients (FEV1 0.83 L, PCO2 7.3 kPa). The protocol sequence was: 45 min of NIPSV with air:oxygen or helium:oxygen, no ventilation for 45 min, and 45 min of NIPSV with air:oxygen or helium:air. On the other hand, deBoisblanc et al. (de Boisblanc 2000) performed a randomized trial to determine whether the bronchodilator effects of albuterol and ipratropium bromide are greater if updraft nebulization is driven by 80% helium and 20% oxygen than if driven by compressed room air during the treatment of an acute exacerbation of COPD disease. Treatments were given at 0, 20, 40 and 120 minutes after randomization. The study involved 47 COPD decompensated patients (FEV1 40% of predicted), PaCO2 7.3 kPa).

Excluded studies

Nine articles were excluded because they mainly involved acute asthma patients (Shiue 1989 Gluck 1990 Kass 1995; Manthous 1995; Carter 1996; Kudukis 1997; Verbeek 1998; Henderson

1999; Kass 1999); five were excluded due to: 1) no randomized trials on COPD decompensated patients (Diehl 1999; Esquinas 2000; Jaber 2000); 2) helium-oxygen was tested in stable COPD patients (Swidwa 1985); and 3) letter with anecdotal evidence (Polito 1995). See Characteristics of excluded studies.

Risk of bias in included studies

The first manuscript (Jolliet 1999) presented a randomized, crossover design. Its methodological quality was high (Jadad score= 3), but it did not report the use of concealment allocation. On the other hand, the second one (de Boisblanc 2000) showed a randomized design; its methodological quality was low (Jadad= 2), and it did not report concealment allocation. Full manuscripts were not available on two studies (Gerbeaux 1997; Onn 1999), so they were not rated.

Effects of interventions

In Jolliet 1999, air:oxygen and helium:oxygen both decreased respiratory rate and increased tidal volume and minute ventilation. Both gases increased total respiratory cycle time and decreased the inspiratory/total time ratio, the reduction in the latter being significantly greater with helium:oxygen (Change in Ti/Ttot -0.27 (SD 0.1) for helium v. -0.23 (SD 0.07) for air , $p<0.05$). Peak inspiratory flow rate increased more with helium:oxygen. PaO2 increased with both gases, whereas PaCO2, decreased more with helium:oxygen (mean fall in PaCO2 of -7.2 kPa (SD 0.9) with helium v. -6.4 SD 0.8 with air, $p<0.05$). Dyspnea score (Borg scale) decreased more with helium:oxygen than with air:oxygen, (mean change -1.8 points (SD 1.1) on helium and -0.8 points (SD 0.9) on air, $p<0.05$). No clinical outcome data such as duration of non-invasive ventilation, or need for intubation and mechanical ventilation were available

In the second randomized trial (de Boisblanc 2000) there were no significant differences in the change of FEV1 and FVC between the two groups by either the 1 or 2 hours point. However, the small improvement in FEF 25-75 was significantly greater in the heliox group than in the air group (increase with Heliox 15% (95% CI 8% to 21%) and with air 7% (95% CI 4% to 11%), $p=0.05$). The authors concluded that these data do not support the routine use of heliox as a driving gas for nebulization of bronchodilators in acute exacerbations of COPD.

DISCUSSION

To date, we could find only two adequate studies investigating the use of heliox to treat acute exacerbations of airway obstruction due to COPD. These studies included non-ventilated and noninvasively ventilated patients. The data suggest that heliox can improve gas exchange and reduce symptoms in patients receiving non-invasive ventilation for respiratory failure due to exacerbations of COPD, but it has little additional benefit in non-ventilated acute COPD patients.

The improvement in arterial PCO2 was small, but could be sufficient to avoid the need for intubation and mechanical ventilation in some patients. There are, however, no published data to support this conclusion. Suitably designed randomised controlled trials with the endpoint being the avoidance of mechanical ventilation may be justified.

AUTHORS' CONCLUSIONS

Implications for practice

We conclude that currently, there is not enough evidence to support the use of helium-oxygen mixtures to treat acute exacerbations of COPD in either ventilated or non-ventilated patients.

Implications for research

Questions regarding the treatment of acute COPD exacerbations with heliox remain unanswered:

- Larger randomized and controlled studies are needed to clarify its efficacy
- These studies are needed to allow sub-group analyses (severity, clearly defined and based on presenting pulmonary function results and response to initial beta-agonist and/or anticholinergic therapy whenever possible, different helium-oxygen mixtures, and duration of heliox administration).
- Studies are required to examine the effect of heliox with specific co interventions (i.e. corticosteroids and other drugs).
- Future research must concentrate on well defined outcomes which may lead to more informative reviews. More specifically, criteria for discharge and reporting of lung function test data in a systematic fashion would assist in further work.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the assistance of Stephen Milan, Anna Bara, and Jane Dennis of the Cochrane Airways Review Group. We would also like to acknowledge the assistance of the following corresponding authors: Stephen Mette, Laurent Brochard and Jesse B. Hall. Finally, the assistance of Professor Paul Jones (Cochrane Airways Review Group Coordinating Editor) was greatly appreciated.

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Jolliet 1999 *{published data only}*
* Jolliet P, Tassaux D, Thouret JM, Chevrolet JC. Beneficial effects of helium:oxygen versus air:oxygen noninvasive pressure support in patients with decompensated chronic obstructive pulmonary disease. *Critical Care Medicine* 1999; **27**:2422–9.

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Carter ER, Webb CR, Mofitt DR. Evaluation of heliox in children hospitalized with acute severe asthma. *Chest* 1996; **109**:256–61.

Diehl 1999 *{published data only}*
Diehl JL, Mercat A, Guerot E, Michard P, Aissa F, Richard C, et al.Heliox reduces work of breathing during weaning from mechanical ventilation in severe chronic obstructive pulmonary disease (Abstract). *American Journal of Respiratory & Critical Care Medicine* 1999;**159**:A370.

Dorfman unpublished *{published data only}*
Dorfman TA, Burton JH, Jones P, Shipley ER. Inhaled heliox does not benefit emergency department patients with moderate to severe asthma. Unpublished.

Esquinas 2000 *{published data only}*
Esquinas A, Carrillo A, Bano D, Gil J, Jara P, Rodriguez MD, et al.Gas heliox during noninvasive mechanical ventilation in hypercapnic chronic obstructive pulmonary exacerbation (Abstract). *American Journal of Respiratory & Critical Care Medicine* 2000;**161**:A557.

Gerbeaux 2001 *{published data only}*
Gerbeaux P, Gainnier M, Boussuges A, Rakotonirina J, Nelh P, Torro D, et al.Use of heliox in patients with severe exacerbation of chronic obstructive pulmonary disease. *Critical Care Medicine* 2001;**29**(12):2322–4.

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Shiue 1989 *{published data only}*
Shiue ST, Gluck EH. The use of helium-oxygen mixtures in the support of patients with status asthmaticus and respiratory acidosis. *Journal of Asthma* 1989;**26**:177–80.

Swidwa 1985 *{published data only}*
* Swidwa DM, Montenegro HD, Goldman MD, Lutchen KR, Saidel GM. Helium-oxygen breathing in severe chronic obstructive pulmonar disease. *Chest* 1985;**87**:790–5.

Verbeek 1998 *{published data only}*
Verbeek PR, Chopra A. Heliox does not improve FEV1 in acute asthma patients. *Journal of Emergency Medicine* 1998; **16**:545–8.

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Gerbeaux PR, Ledoray V, Boussuges A, Jammes Y, Sainty JM. Breathing heliox during mechanical ventilation: effects in patients with chronic obstructive pulmonar disease (Abstract). *American Journal of Respiratory & Critical Care Medicine* 1997;**155**:A85.

Onn 1999 *{published data only}*
Onn A, Staroselsky A, Mann A, Schwarz Y, Greif J. Usefullness of heliox therapy in COPD exacerbation (Abstract). *American Journal of Respiratory & Critical Care Medicine* 1999;**159**:A811.

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Manthous 1997

Manthous CA, Morgan S, Pohlman A, Hall JB. Heliox in the treatment of airflow obstruction: A critical review of the literature. *Respiratory Care* 1997;**42**:1034–42.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

de Boisblanc 2000

Methods	Design: Prospective, randomized
Participants	Randomized: 50 Eligible: 250 Completed: 47 Majors exclusions: non-availability of one of the investigators or significant co-morbid condition
Interventions	Setting: Emergency Department Interventions: a nebulization of bronchodilators (albuterol and ipratropium bromide) using either 80% helium and 20% oxygen or compressed room air as the driving gas
Outcomes	Outcome: pulmonary function (FEV1, FVC, FEF25-75) as % of predicted
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	Third party randomisation

Jolliet 1999

Methods	Design: Prospective, randomized, crossover. Method of randomization: not stated
Participants	Eligible: 25 Randomized: 20 Completed: 19 Majors exclusions: pneumothorax, severe respiratory failure or haemodynamic instability, with high probability of imminent intubation, hypoxaemia requiring an inspired oxygen fraction >0.3, impaired consciousness. Patients with severe COPD (FEV1=0.83) after initial stabilization
Interventions	Setting:Medical intensive care unit, university tertiary care center. Interventions: Noninvasive pressure support ventilation was administered: 45 min with air:oxygen or helium:oxygen (70:30)
Outcomes	Outcomes included were: dyspnea, respiratory rate, tidal volume, peak inspiratory flow, minute ventilation, inspiratory time, respiratory cycle duration, pH, alveolo-arterial O2 difference, PaO2, PaCO2, systemic arterial pressure, and heart rate
Notes	

Jolliet 1999 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	Information not available

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Carter 1996	Acute asthma patients
Diehl 1999	Abstract. Nonrandomized trial
Dorfman unpublished	Acute asthma patients
Esquinas 2000	Abstract. Nonrandomized trial
Gerbeaux 2001	Retrospective analysis over 18 months
Gluck 1990	Acute asthma patients Nonrandomized trial
Henderson 1999	Acute asthma patients
Jaber 2000	Nonrandomized trial.
Kass 1995	Acute asthma patients Nonrandomized trial
Kass 1999	Acute asthma patients
Kudukis 1997	Acute asthma patients
Manthous 1995	Acute asthma patients Nonrandomized trial
Polito 1995	Letter. Anecdotal evidence
Shiue 1989	Acute asthma patients Nonrandomized trial
Swidwa 1985	Stable COPD patients. Nonrandomized trial.

(*Continued*)

Verbeek 1998	Acute asthma patients Nonrandomized trial

DATA AND ANALYSES

Comparison 1. Nonivasive ventilation using helium -O2 vs air-O2

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dyspnea decrease (Borg scale)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Tidal volume (mL)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Inspiratory/Total time ratio	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 Peak inspiratory flow rate (L/min)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 PaO2 (KPa)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7 PaCO2 (KPa)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8 pH	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9 Heart rate (/min)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 2. Nebulisation of albuterol and ipatropium using Heliox vs Air

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 FEV1 (change in % predicted)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 FEF 25-75 (change in % predicted)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 1 Dyspnea decrease (Borg scale).

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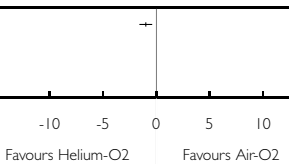
Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 1 Dyspnea decrease (Borg scale)

Study or subgroup	Helium-O2 N	Mean(SD)	Air-O2 N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Jolliet 1999	19	-1.8 (1.1)	19	-0.8 (0.9)		-1.00 [-1.64, -0.36]

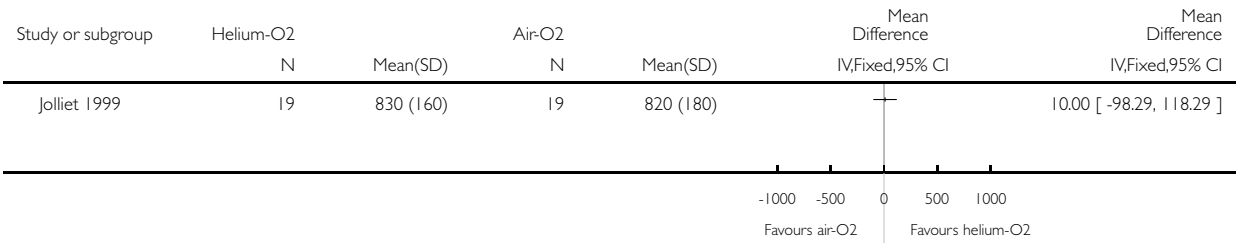


Analysis 1.2. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 2 Tidal volume (mL).

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 2 Tidal volume (mL)

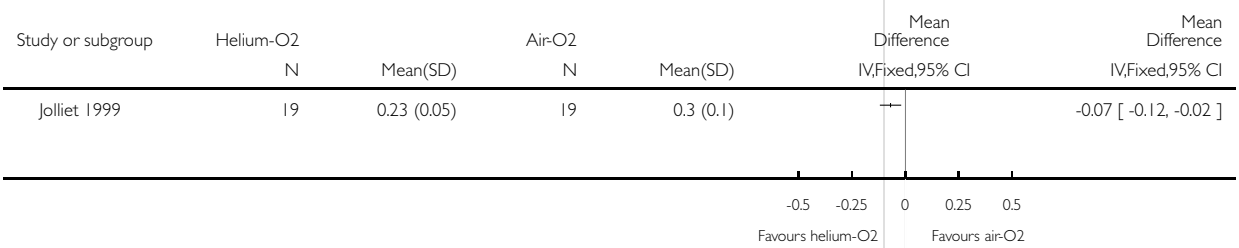


Analysis 1.3. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 3 Inspiratory/Total time ratio.

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 3 Inspiratory/Total time ratio



Analysis 1.4. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 4 Peak inspiratory flow rate (L/min).

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 4 Peak inspiratory flow rate (L/min)

Study or subgroup	Helium-O2 N	Mean(SD)	Air-O2 N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Jolliet 1999	19	110 (20)	19	78 (12)		32.00 [21.51, 42.49]

Analysis 1.5. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 5 PaO2 (KPa).

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 5 PaO2 (KPa)

Study or subgroup	Helium-O2 N	Mean(SD)	Air-O2 N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Jolliet 1999	19	10.2 (2.6)	19	10.5 (2.6)		-0.30 [-1.95, 1.35]

Analysis 1.7. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 7 PaCO2 (KPa).

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 7 PaCO2 (KPa)

Study or subgroup	Helium-O2 N	Mean(SD)	Air-O2 N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Jolliet 1999	19	-7.2 (0.9)	19	-6.4 (0.8)		-0.80 [-1.34, -0.26]

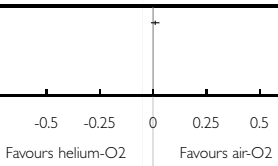
Analysis 1.8. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 8 pH.

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 8 pH

Study or subgroup	Helium-O2 N	Mean(SD)	Air-O2 N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Jolliet 1999	19	7.41 (0.03)	19	7.4 (0.04)		0.01 [-0.01, 0.03]



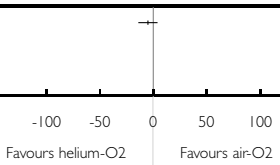
Analysis 1.9. Comparison 1 Nonivasive ventilation using helium -O2 vs air-O2, Outcome 9 Heart rate (/min).

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Nonivasive ventilation using helium -O2 vs air-O2

Outcome: 9 Heart rate (/min)

Study or subgroup	Helium-O2 N	Mean(SD)	Air-O2 N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Jolliet 1999	19	87 (14)	19	92 (14)		-5.00 [-13.90, 3.90]



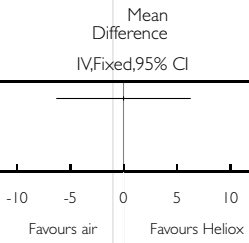
Analysis 2.1. Comparison 2 Nebulisation of albuterol and ipatropium using Heliox vs Air, Outcome 1 FEV1 (change in % predicted).

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 2 Nebulisation of albuterol and ipatropium using Heliox vs Air

Outcome: 1 FEV1 (change in % predicted)

Study or subgroup	Heliox N	Mean(SD)	Air N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
de Boisblanc 2000	23	10 (11)	24	10 (11)		0.0 [-6.29, 6.29]



Analysis 2.2. Comparison 2 Nebulisation of albuterol and ipatropium using Heliox vs Air, Outcome 2 FEF 25-75 (change in % predicted).

Review: Heliox for treatment of exacerbations of chronic obstructive pulmonary disease

Comparison: 2 Nebulisation of albuterol and ipatropium using Heliox vs Air

Outcome: 2 FEF 25-75 (change in % predicted)

Study or subgroup	Heliox N	Mean(SD)	Air N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
de Boisblanc 2000	23	15 (15)	24	7 (9)		8.00 [0.89, 15.11]

FEEDBACK

Quality of the review

Summary

I find it surprising that the Cochrane Library have published a review that concludes that there is insufficient evidence to justify Heliox. If the purpose of the Cochrane library is as stated to synthesise a plethora of articles (so that we do not have to), then why has Rodrigo et al reviewed a subject with only 2 papers and concluded that there is currently not enough data to review!

As to interpretation of the results of the two papers; That Heliox does not alter lung function is not surprising given that Heliox does not treat the underlying obstruction. The fact that PCO2 does fall with the use of Heliox is significant, and I please refer intensivists to Gerbeaux et al Crit Care Med 2001 29:2322-2324 Use of Heliox in patients with severe exacerbations of COPD, before making any decisions on use.

I certify that I have no affiliations with or involvement in any organisation or entity with a direct financial interest in the subject matter of my criticisms.

Contributors

Paul Simpson.

WHAT'S NEW

Last assessed as up-to-date: 26 September 2002.

Date	Event	Description
25 July 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 1, 1999

Review first published: Issue 2, 2000

Date	Event	Description
7 November 2000	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

GR: Protocol initiation and development, assessed search results, data extraction, entry and analysis, interpretation and write-up

CR: Protocol initiation and development, assessed search results, data extraction, entry and analysis, interpretation and write-up

CP: Protocol initiation and development, assessed search results, data extraction, entry and analysis, interpretation and write-up

BR: Protocol initiation and development, assessed search results, data extraction, entry and analysis, interpretation and write-up

EHW: Editorial support throughout

DECLARATIONS OF INTEREST

The authors who have been involved in this review have done so without any known conflicts of interest. They are neither involved with the primary studies nor affiliated with any company that produces heliox.

SOURCES OF SUPPORT

Internal sources

- Departamento de Emergencia Hospital Central de las FF.AA, Uruguay.

External sources

- Garfield Weston Foundation, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Helium [*therapeutic use]; Oxygen [*therapeutic use]; Pulmonary Disease, Chronic Obstructive [*drug therapy]; Randomized Controlled Trials as Topic

MeSH check words

Humans