

REVIEW

Use of heliox mechanical ventilation in acute respiratory distress syndrome in adults

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Keywords - ARDS, mechanical ventilation, helium, heliox, intensive care medicine, lung injury, review**Abstract**

Background: In acute respiratory distress syndrome (ARDS) mechanical ventilation is often necessary to manage hypoxia, but mechanical ventilation also induces or aggravates lung injury caused by the respiratory distress. By means of lower volume ventilation and permissive hypercapnia, lung injury is partially prevented; however, other interventions are needed. Helium, in a gas mixture with oxygen (heliox), has a low density and can reduce the flow in narrow airways and allow for lower driving pressures.

Methods: PubMed and EMBASE database were used for a systematic search, using terms referring to ARDS or an acute lung injury condition associated with respiratory failure and the intervention.

Results: In total 576 papers were retrieved, but the majority had to be excluded. This resulted in only five papers of which three described animal models and two described clinical studies. In the animal models, gas exchange was improved by the use of heliox, while also using less invasive ventilation. Clinical studies show a reduction in work of breathing during heliox ventilation, with a concomitant increase in pH and a decrease in PaCO₂ levels compared with oxygen ventilation.

Conclusions: There may be a rationale for heliox ventilation in ARDS as an intervention to improve ventilation and reduce work of breathing, but so far the evidence is very marginal.

Introduction

Acute respiratory distress syndrome (ARDS) is notorious in critically ill patients because of its high mortality rates of up to 60%.^[1,2] Hypoxia and hypercapnia are common features in ARDS. The latter is a result of increased dead space and increased work of breathing, which is due to both obstructed airways with increased airway resistance and an increased need for CO₂ removal.^[3-5] These processes, occurring during ARDS, frequently warrant mechanical ventilation.

Although mechanical ventilation is essential in ARDS, this can also induce or aggravate pulmonary damage. Overstretching of alveoli by application of high tidal volumes or high driving pressures and by repetitive opening and closing of the alveoli can all lead to ventilator-induced lung injury and a proinflammatory state. Furthermore, the inflammatory process and mechanical ventilation probably interact, since a mechanically stressed lung may produce an inflammatory reaction.^[6-8]

It is well recognised that limited tidal volume ventilation of 6 ml/kg is beneficial in ARDS.^[9] Also, the use of even lower tidal volumes resulted in additional protection in ARDS.^[10] In addition to limited tidal volumes, high airway pressures also contribute to lung injury.^[11,12] Even relatively low plateau pressures (26-27 cm H₂O) can generate an inflammatory response in the lung.^[7] Despite recognition that the intensity of mechanical ventilation influences the outcome of ARDS, application of limited tidal volume ventilation and low driving pressures can often not be achieved.^[13] Therefore, adjunctive therapies which allow for less invasive ventilation need to be investigated in ARDS.

Helium is an inert gas with a lower density than air, thus flow of helium through an airway is less turbulent, leading to lower resistance.^[14] As a result, during heliox (helium and oxygen gas mixture) ventilation, lower driving pressures are necessary to distribute oxygen to the distal alveoli to improve oxygenation.^[14,15] Also, the diffusion capacities of CO₂ are increased, resulting in even more improved gas exchange.^[14] Another potential benefit of helium is that it may have anti-inflammatory properties, although more research is necessary.^[16] In day-to-day practice, helium has been used in exacerbations of asthma and chronic obstructive pulmonary disease (COPD) to reduce the work of breathing.^[15,17,18] However, most of these studies were conducted in neonates and children, who have increased airway resistance compared with adults.^[19]

Since limiting intensity of mechanical ventilation is a hot

topic,^[2,7,12] we investigated whether heliox has therapeutic potential in ARDS by reviewing preclinical and clinical studies on the use of heliox in ARDS.

Methods

A systematic search in the PubMed and EMBASE included search terms referring to the condition (“lung injury”; “acute lung injury”; “acute respiratory distress syndrome”; “ARDS, human”; “lung injury”; “ARDS”; “respiratory distress syndrome”; “respiratory failure”; “hypoxia”; “mechanical ventilation”; “artificial respiration”) as well as to the intervention (“Helium”; “Heliox”). Retrieved papers were screened on relevance by the author and another reviewer after reading the abstracts. The reference lists of selected articles were screened for additional relevant papers.

Inclusion criteria for article selection for preclinical studies were use of parameters for animal models of ARDS.^[20] Inclusion criteria for the clinical studies were patient populations that were described as having acute respiratory failure with the need for respiratory support (for studies published prior to existence of ARDS consensus^[21]) or use of the consensus criteria for ARDS.^[21] Titles were limited to the English language.

Results

Of 576 papers retrieved from Medline or EMBASE, 571 articles were excluded based on no use of helium during mechanical ventilation, no original data, or no ARDS/acute lung injury condition associated with respiratory failure, paediatric animal models, or paediatric clinical studies, leaving five papers included and described in detail in this review.

Effect of heliox on lung mechanics and inflammation in animal models

We found three articles describing the effect of heliox on gas exchange in adult ARDS animal models. ARDS was provoked in various manners; a different method was used in each animal model.

In the first rabbit model of ARDS, lung injury was induced by oleic acid instillation.^[22] Animals were ventilated with low bias flow oscillation with a CO₂ scrubber to reduce gas utilisation, creating a modified high-frequency oscillatory ventilation system. Helium concentrations were variable (40-50-60-70%) and balanced with oxygen. All the animals were ventilated in cycles of 20 minutes, where each heliox ventilation cycle was preceded by 20 minutes of ventilation with 40% oxygen and 60% nitrogen. All ventilator settings remained unaltered during the experiment. After each ventilation cycle, blood gases were taken. Their results showed increased CO₂ clearance during helium ventilation compared with nitrogen ventilation. The magnitude of CO₂ clearance correlated with the concentration of helium.

The second study showed a model where ARDS was induced

by saline lavage. The focus of this study was mainly the effect of helium on histopathological and immunohistochemical changes in lung tissue.^[23] Male rats were ventilated in a pressure-controlled mode for one hour with either heliox (50% helium; 50% oxygen) or 100% oxygen. Afterwards, mechanical ventilation continued for two hours with 50% oxygen, before lung tissue was harvested. The severity of pathological features (infiltration of neutrophils, presence of oedema and haemorrhage and hyaline membrane formation) was graded. Heliox ventilation resulted in a reduction of all the pathological features compared with the control group. Also inflammatory parameters (myeloperoxidase and inducible nitric oxide synthase) in lung tissue were reduced due to heliox ventilation. This study therefore suggests a role for heliox in attenuating lung inflammation. Of note, however, the control group in this study showed hyperoxia, which is known to induce inflammation.^[24,25]

The third study provoked ARDS in an adult rat model by using injurious ventilator settings.^[26] With tidal volumes of 15 ml/kg, rats were ventilated with either heliox (50% helium; 50% oxygen) or a standard gas mixture (50% oxygen; 50% air) for four hours. Respiratory rate was adjusted to maintain normocapnia. This study showed significantly reduced minute volume ventilation during heliox ventilation, while maintaining a normal acid-base balance and adequate oxygenation. However, inflammatory parameters (pulmonary protein and inflammatory cytokine levels) were not affected by heliox ventilation.

In conclusion, in animal experiments, heliox improved ventilation in ARDS models. The effects of heliox on inflammation, however, yield contrasting results.^[22,23,26]

Effect of heliox on lung mechanics and gas exchange in clinical studies

Clinical studies of the effect of heliox in adult patients with ARDS are scarce. We found only two articles in the adult patient population.

In mechanically ventilated patients with respiratory failure and hypercapnia, tracheal gas insufflation with either 100% oxygen or 100% helium was investigated.^[27] Tracheal insufflation was administered for 15 minutes at different flows (2-6 l/min). The rationale was to reduce hypercapnia. The results showed a decrease in PaCO₂ levels during heliox ventilation and a decrease in peak inspiratory pressure. The efficiency of tracheal insufflation, calculated by dividing the PaCO₂ change by the change in peak inspiratory pressure, improved with the use of helium.

The other article summarised two case reports of patients with bronchiolitis obliterans syndrome and acute respiratory failure following lung transplantation. In both cases 60% heliox was administered either via bilevel positive airway pressure or high-frequency oscillatory ventilation.^[28] Heliox ventilation clearly improved the respiratory status, by increasing the pH and decreasing the PaCO₂ levels.

Discussion

Safety and future of heliox ventilation

The safety of heliox during mechanical ventilation in patients with acute respiratory failure has rarely been described.^[18] There is extensive experience with heliox in asthma and COPD patients. In these populations, complications have not been reported.^[29-34] Of note, however, safety of heliox in various modes of ventilation has not been studied systematically. The use of a very dense gas such as heliox might exert beneficial effects because it prevents alveolar collapse. Furthermore, the percentage of oxygen within the heliox mixture is a concern when ventilating severely hypoxic ARDS patients. The efficacy of heliox is proportional to the percentage used, which may not allow sufficient FiO₂ in hypoxic patients. Of note, however, adverse outcome in ARDS may be more related to causes other than hypoxaemia, including multiple organ failure and right ventricular failure.

The future of heliox ventilation might be less bright than expected from the physiological benefits. Heliox as a medical gas is expensive and scarce. Also, extracorporeal devices are used more often in the treatment of ARDS. These allow lower respiratory rates by extracorporeal removal of carbon dioxide. In this specific group of patients, heliox may no longer have an additional effect, although the risks of both techniques should be compared.

Maybe, in the future, a combination of the two techniques might be beneficial, since extracorporeal gas exchange might allow to increase the inspiratory helium fraction and hypoxia is treated by the extracorporeal device.

A recent study showed another application of heliox in the post-acute phase in the treatment of ARDS patients.^[35] Breathing a helium-oxygen mixture during weaning from the ventilator reduces carbon dioxide production. Therefore, heliox might facilitate the weaning of ARDS patients from the ventilator, after survival of the acute phase.

Limitations of this review are the small patient numbers, the differences in design of the studies, aetiology of ARDS, the lack of original data and differences in the quality of the papers. All this limits the interpretation of the existing data.

The physiological concept provides a rationale for the use of heliox in ARDS. However, this is without taking into consideration the use of extracorporeal removal of carbon dioxide. Also, ARDS patients are usually in need of high FiO₂ levels and heliox generates a dose-dependent effect. Therefore, nowadays heliox ventilation might not be the first treatment option in acute ARDS. However, its use in a later stage could be promising.

To answer the question as to whether heliox has any potential as a therapy for acute respiratory distress syndrome in adults, more research needs to be conducted.

Conclusion

Although the evidence is very scarce, in these preclinical and clinical studies ventilation and gas exchange is improved with heliox. In adult animal ARDS models, heliox clearly improved ventilation, whereas the effects of heliox on inflammation showed contrasting results. A possible direct anti-inflammatory effect still needs to be investigated. Effects of heliox on the intensity of mechanical ventilation are expected immediately following application of heliox. In line with this, clinical data on ARDS showed direct effects of heliox on short-term outcomes, including applied pressures and gas exchange. However, long-term outcomes have not been investigated.

Disclosures

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