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Review Article

Helium–oxygen mixture for treatment in upper airway obstruction; a mini-review

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Abstract

In the 1930's Alan Barach introduced helium in combination with oxygen, heliox, to the medical world. He found that helium's physical properties help reduce the work of breathing, reduce airway resistance, and subsequently improve alveolar ventilation in obstructed airways. In the presence of airway narrowing, heliox has the benefits of increasing the tendency to laminar flow (which has lower resistance) and reducing resistance when turbulent flow occurs. Heliox, a helium–oxygen mixture, has since been used sporadically and only scattered reports are found on its use for treatment in patients with upper airway obstruction. The aim of the present review was to search and review the available evidence for its safe and effective clinical use. A total of 20 publications about the use of helium-containing gas mixture for the treatment of upper airway obstruction in adults were found in the search of public domain literature. Most case reports describe short-term beneficial effects, temporarily improving breathing and oxygenation. Authors of the case reports suggest helium–oxygen mixture as an optional bridge, while a more definite treatment takes action. There are, however, no prospective randomized controlled studies and thus there is lack of high-quality proof supporting its safe and efficacious use. In conclusion, the physiochemical properties promoting laminar flow in restricted airways and the sparse but still seemingly positive clinical experience favor the use of helium–oxygen mixture as a symptomatic rescue therapy. The risk for side effects, apart from the reduced oxygen concentration in the inspired gas, seems minor. There is, however, still a lack of evidence to support the general use of oxygen–helium mixture for upper airway compromise due to the sparse information available. Further studies, although not easily designed, are warranted.

Keywords: adults; heliox; helium; upper airway obstruction

1. Introduction

Helium was discovered in the sun in 1868 and is named after Helios, the God of the sun in Greek mythology. Helium, being compound number 2 in the periodic table, has the lowest density of any gas except for hydrogen.[1] Helium is a colorless, odorless and tasteless gas. It is biologically and metabolically inert, poorly soluble, and noncombustible. It is considered safe and nontoxic to humans and is eliminated within a few breaths.[1–3] An equivalent volume of air weighs seven times more than helium (Table 1). Helium also has a different thermal conductivity and if inhaled for a long period of time may cause a change in core temperature, resulting in hypothermia.

In the early 1930's Alan Barach made pioneer studies with helium in combination with oxygen: “heliox”. He hypothesized that when oxygen and helium are mixed in a ratio of 20% to 80%, respectively, the mixture possesses one-third of the density compared to air, with the consequence that a patient could either breathe the mixture with one-third of the working load, or ventilate the lung with three times the volume for the same respiratory effort as used for air.[4] Barach was able to show in experimental setting that helium's physiochemical properties improve the flow of gas in the airway tract by reducing airway resistance. In the presence of airway

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Table 1
Physical properties of pure gases at RTP[2].

	Density (kg/m^3)	Viscosity (μP)	Thermal conductivity (W/m K)
Air	1.184	184.33	0.025
CO_2	1.811	148.71	0.017
Helium	0.166	197.61	0.14
Nitrogen	1.167	177.82	0.126
Oxygen	1.33	205.35	0.026

RTP, Room Temperature and Pressure.

narrowing, heliox has benefits because it increases the tendency to laminar flow (which has lower resistance) and reduces resistance when turbulent flow occurs. This in turn reduces the work of breathing and improves alveolar ventilation and subsequently the concentration of oxygen.[4] Helium gas mixture not only facilitates alveolar ventilation but also decreases the work of breathing in respiratory-distressed patients and thus reduces the amount of CO_2 produced.[1]

Further work on the physiochemical properties was done by Houck et al,[5] investigating the effect of helium concentration in inspired gas on resistance to breathing during experimental upper airway obstruction in healthy volunteers. Obstruction was modelled by the use of a series of four polyvinyl endotracheal tubes, narrowed progressively in their midportions with C clamps. Four helium–oxygen gas mixtures were studied; 0:100, 40:60, 60:40, and 80:20, respectively, with a flow rate of 10 L/min. The main findings were that the effect of helium on reducing resistance and pressure in an obstructed airway was linear and inversely proportional to helium concentration, and further that the reductions in resistance and pressure were larger for the tighter obstructions. Fleming et al[6] confirmed the effects of an 80:20 helium–oxygen gas mixture in an experimental setting. They studied 30 healthy volunteers breathing room air or an 80:20 helium–oxygen mixture through a normal airway and an airway that included a resistor. They found an increase in 1 second forced expiratory volume using a helium–oxygen mixture in a normal airway and that all pulmonary function test scores statistically improved when volunteers inspired helium and oxygen through the restricted airway, demonstrating that helium and oxygen can increase airflow in the presence of an increased airway resistance. Thus, the higher the concentration and the more narrow the airway, the higher the impact of the helium gas. Effects are seen rapidly, and are not dependent on uptake and pharmacological action, directly associated to the physiochemical properties of the gas. Likewise, helium is completely eliminated in a few breaths.[2] Helium *per se* has no curative action but a helium–oxygen gas mixture may "buy time" while awaiting treatment that is aimed at alleviating the obstruction. Since the pioneer work of Barach, helium–oxygen mixtures have been tested for a variety of different causes of respiratory distress. It has been tested in upper airway obstruction due to foreign body, tumor, edema, vocal cord pathology, and croup in children. It has also been described as having a place in the treatment of severe asthma and chronic obstructive pulmonary disease, reducing the work of breathing and thus facilitating the alveolar ventilation and gas exchange. Furthermore, it has been tested during weaning from mechanical ventilation to facilitate breathing in the early extubation phase and particularly in patients showing signs of postextubation croup. Helium–oxygen mixture has been tested in combination with jet-ventilation and has been studied as the carrier gas for nebulization of inhalable drugs—to "carry" the drug further down the airway tract.[1]

The aim of the present review is to provide an update of available literature supporting helium–oxygen gas mixtures as therapy in adult patients with signs and symptoms of upper airway obstruction/distress. Public domain literature from 1935 until the present day, describing the use of helium in patients with primarily upper airway obstructions, is reviewed.

2. Materials and methods

We searched for relevant publications in the electronic database PubMed using the terms "helium" OR "heliox", AND "upper airway obstruction". The inclusion criteria were: (1) English language; (2) humans; (3) adults aged >18 years. A secondary search was performed by retrieving relevant papers and articles from the references of the primary search results (Figure 1).

Due to its high volatility, helium must be administered in very high flow rates (10–15 L/min) in order to guarantee the concentration delivered.[4] Also, the mode of administration is important because a higher concentration of helium in the gas mix achieves a laminar gas flow. Therefore flow rate, gas concentration, and mode of administration have been looked into in more detail in the described cases.

3. Results

From the PubMed search and secondary search we found 14 case reports, two case series, including a total of 15 patients, and four studies starting with Barach and Eckman's[7] 1936 paper "The effects of inhalation of helium mixed with oxygen on the mechanics of respiration".

3.1. Case reports and series

In total there are 29 patients described. The published case reports cover a wide and scattered range of indications, techniques, and conditions related to upper airway obstructions. Information on gas flow, gas composition, and mode of administration is presented in four cases only. Available information is summarized in Table 2.

Positive effects of the administration of helium gas mixture dominate the case reports and series (Table 3), however, the study by Berkenbosch et al[8] did not show consistent benefits, 6/16 showed a positive response. No adverse effects were reported anywhere.

The case reports and the case series are from 1976 to 2012. A total of 26 of 29 patients were treated in North America (Tables 4 and 5).