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RESEARCH LETTERS

Helium-oxygen mixtures and acute severe asthma

To the Editor:

In 1934, Barach first described the use of helium as a therapy for airway obstruction and asthma exacerbations. Its low density and the fact that it is a biologically inert gas, seems to make it ideal for reducing respiratory effort, in children and adults, and decreasing airway resistance. Its key benefit seems to be as temporizing agent while conventional therapies have time to act, since it has no bronchodilator or anti-inflammatory properties.[1]

The authors present a case report of a 28-year-old male, non-smoker, with moderate persistent non-controlled asthma (*G.I.N.A.*), treated only with salbutamol in aerosol as needed.

In May 2008 he was found unconscious by his car. On admission he presented cyanosis, severe respiratory effort with costal and sternal retraction, jugular turgescence, bradycardia (40 bpm) and hypertension (150/80 mmHg). Breath sounds were globally decreased with bilateral wheezing. Arterial blood gas (ABG) evaluation showed severe respiratory acidaemia ($pH = 6.8$), hypercapnia ($pCO_2 = 130$ mmHg) and hypoxaemia ($pO_2 = 62$ mmHg). He was medicated with salbutamol and ipratropium aerosols, intravenous corticosteroids (1 mg/Kg), adrenaline, theophylline, perfusion of salbutamol and 20% magnesium sulphate, with no clinical or gasometric improvement. He was then intubated and started heliox (60:40 mixture), with clinical improvement. Extubation was possible after 24 hours. He remained on intravenous corticosteroids and bronchodilator therapy and started amoxicillin and clavulanic acid for pneumonia, with progressive improvement of clinical status; by day 5 he no longer needed oxygen supplementation. He was discharged from the hospital seven days after admission and was prescribed inhaled corticosteroid and long acting β_2 agonist. He has been asymptomatic ever since, with normal lung function tests.

Applications of helium in respiratory medicine are related to its physical properties. Since it is an inert gas, it does not react with body tissues and it is insoluble in body fluids. Nevertheless, when mixed with oxygen (ie, heliox), the density of helium and its viscosity affect flow through airways.[2] Gas flow in airways may be laminar, turbulent or a combination of both; laminar flow is the most efficient in delivering oxygen to more distal parts of the bronchial tree. Heliox lowers the resistance to gas flow within the airways thereby increasing ventilation by two mechanisms. Most importantly, breathing heliox leads to a reduction in the Reynolds number (i.e. unitless quantity that is proportional to the product of the airway diameter and the velocity and density of the gas, divided by its viscosity), converting turbulent into laminar flow. Secondly, due to its low density, heliox decreases the pressure gradient needed to achieve a given level of turbulent flow, which in theory decreases the respiratory effort.[1] Thirdly, helium's diffusion coefficient allows CO_2 to diffuse more rapidly through heliox than through air or oxygen.[3] In asthma or upper airway obstruction, Heliox use is not intended to treat the obstruction but to decrease airway resistance and respiratory effort until usual treatment options act.[2]

Since the early 1980s, several claims have been made about heliox benefits, namely increasing tidal volume, improving homogeneity of gas distribution and CO_2 elimination, and improving aerosol delivery, as well as its clinical applications in upper airway obstruction, post-extubation stridor, croup, bronchiolitis, chronic obstructive pulmonary disease (COPD) and asthma exacerbations. Although its clinical benefit has not been adequately established in all these applications, there has been increasing investigation over the last two decades.[3]

The success of heliox therapy depends on the methods and devices used. The risks of inadequate administration of heliox include hypothermia (when the gas temperature is $<36^{\circ}C$ and if it is administered for long periods of time), anoxia (by inadvertently administering a oxygen-helium mixtures with a FiO_2 lower than 21%) and delivering a high lung volume, since heliox flows faster than air or oxygen and flow meters designed for the latter give incorrect readings with heliox. Oxygen-helium mixtures are commonly available in concentrations of 80% helium/20% oxygen (80:20 heliox), 70% helium/30% oxygen (70:30 heliox) and 60% helium/40% oxygen (60:40 heliox). When using a flow meter calibrated for air or oxygen, a correction factor must be applied to correct for the different flow rate, namely 1.4 for 60:40 heliox, 1.6 for 70:30 heliox and 80:20 heliox. This should also be taken into account when using heliox as a driving agent for aerosol delivery since too low a flow of heliox may result in inadequate bronchodilator delivery to the patient at a time when aerosol delivery may be critical.[4]

During the last years, β_2 agonist heliox-driven nebulisation has gained wider use in ICU settings and emergency departments, where patients are often seen during severe asthma exacerbations. Heliox physical properties provide the potential benefit of being able to carry aerosols deeper into the distal airways and alveoli during severe airway obstruction, when compared with oxygen or air; this may result in higher deposition at the β_2 agonist site of action in

the distal airways and consequently improved bronchodilation. Heliox aerosol delivery systems also suffer less particle-impaction drug loss within the delivery system, thereby increasing the bronchodilator dose available to the lungs. There may be some limitations to heliox-driven aerosol use; a hypoxic patient may require a higher FiO_2 than the usually 20% or 30% oxygen in the available heliox mixtures. By adding oxygen to the inhaled gas, which increases the FiO_2, the percentage of helium in the mixture decreases, reducing the distal deposition of the bronchodilator; this low helium-oxygen mixture may still benefit the hypoxic patient. Radionuclide studies concluded that heliox was significantly more effective than air in depositing 3.6 μm particles in the alveolar regions, and that this improvement was more pronounced in asthmatic subjects than in healthy subjects[5].

There is still great controversy regarding heliox use in acute asthma. Although Barach first described the use of helium-oxygen mixtures in asthma more than 70 years ago, the use of heliox remains sporadic and undefined. This may be due to the fact that there are no randomised double-blind placebo controlled clinical trials, since a characteristic voice change is induced by breathing helium.[1]

Heliox therapy has shown to quickly improve ventilation in intubated and non-intubated patients with acute severe asthma and respiratory acidosis.[6] In a randomised controlled trial published in 1999, heliox improved airway obstruction and dyspnoea in patients with acute severe asthma.[7] There have also been few case reports, such as this one, in which heliox seems to play an important part in the success of the treatment.[8]

Several reviews have failed to support the administration of heliox in moderate-to-severe acute asthma.[2,9] A recent Cochrane systematic review,[10] including 10 trials and 544 patients, did not support the administration of helium-oxygen mixtures to all patients with acute asthma, stating that heliox has no role in the initial treatment of these patients. However, the authors recognize that new evidence suggests certain beneficial effects in patients with more severe obstruction, although these data should be interpreted with caution.

G.I.N.A. guidelines regarding the management of acute asthma exacerbations also report that heliox use may be considered for patients who do not respond to standard therapy, reflecting the uncertainty regarding the use of heliox.

Despite the lack of concrete evidence, heliox should be considered in hospital protocols for acute asthma treatment (as in Bridgeport Hospital in Connecticut),[1] in a particular set of patients, since there is a small number who do not respond to conventional therapy but still have respiratory muscle reserve.

In conclusion, there is some evidence to support the use of heliox in parallel to conventional therapies in a variety of respiratory diseases (asthma, COPD, croup), although further work is necessary to define its precise role.

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Vocal Cord Dysfunction in a Patient with Schizophrenia

To the Editor:

Vocal cord dysfunction (VCD) is characterized by episodes of involuntary paradoxical movements caused by vocal cord adduction during inspiration, resulting in airflow obstruction. The clinical profile, which is characterized by dyspnoea and wheezing (principally in the cervical region), mimics other respiratory diseases, such as asthma.[1,2]

Patients with asthma can present VCD, which can also be seen, in isolation, in individuals without respiratory disease. Studies conducted in Brazil revealed that the prevalence of VCD in patients with severe asthma was between 15 and 20%.[3] However, VCD is commonly underdiagnosed.