

Clinical Observations

Using helium-oxygen mixtures in the management of acute upper airway obstruction

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Resistance to the flow of gas within the tracheobronchial tree results from convective acceleration and friction.¹ Convective acceleration is the increase in the linear velocity of fluid molecules in a system of flow in which the cross-sectional area is decreasing. Frictional resistance may be either turbulent or laminar depending on the nature of the flow. Since resistance associated with these factors is density-dependent, breathing a less dense gas should decrease flow resistance and, consequently, reduce respiratory work. An obstruction in the upper airway causes a resistance to flow that is primarily convective and turbulent and therefore susceptible to modulation through a change in gas density.

Barach² introduced the use of helium-oxygen mixtures in respiratory medicine and advocated it in the management of obstructive conditions of the trachea, larynx and bronchi, as well as asthma, emphysema, bronchiectasis and pulmonary fibrosis. The use of these mixtures fell from favour as a therapeutic tool partly because the response in patients who had asthma and emphysema was unpredictable. Barnett³ pointed out that the different responses might result from differences in the nature and loci of the obstructing lesions. In dogs the increase in work produced by partially clamping the trachea was effectively

reduced when the animals breathed a mixture of helium and oxygen; however, when smaller airways were constricted by histamine infusion into the inferior vena cava the increase in elastic and nonelastic work was not affected by the use of helium. Later investigators used helium mixtures to identify the site of airflow obstruction.^{4,5} The successful use of these mixtures in patient management was reported only rarely, though, after the initial publication. Recently, however, Pingleton and coworkers⁶ used a helium-oxygen mixture during fiberoptic bronchoscopy in patients who were being mechanically ventilated through an endotracheal tube, and Lu and colleagues⁷ reported improvement in a patient with left main stem bronchial obstruction who was given helium and oxygen.

We report our clinical experience with the use of helium-oxygen mixtures in the management of acute upper airway obstruction, together with the experimental demonstration of changing flow rates and studies carried out on a single healthy subject.

Experimental study

Methods and materials

A Venturi orifice was constructed to approximate the smallest opening in an obstructed airway that we had seen by roentgenography in one of our patients.⁸ The diameter of the opening was 4.76 mm. Gases of different densities were formed by adding oxygen to a mixture of 80% helium and 20% oxygen or by using either 100% oxygen or air. The oxygen concentration in the final

mixture was determined with an OM-11 oxygen analyser (Beckman Instruments, Schiller Park, Illinois). Each gas mixture in turn was passed through the Venturi orifice from a Tissot spirometer (Warren E. Collins Inc., Braintree, Massachusetts) at increasing flow rates. The flow rate was calculated from the volume-time curve of the spirometer, and the pressure drop across the Venturi orifice was determined with a DP 45 pressure transducer (Validyne Instruments, Northridge, California). The signals were displayed on a multichannel recorder (Electronics for Medicine, Inc., White Plains, New York).

The work of breathing was determined in one subject, who sat in a variable-volume plethysmograph breathing either air or a helium-oxygen mixture (80%/20%) through the Venturi tube. An esophageal balloon was placed in the lower third of the esophagus to produce esophageal pressure, and static pressure-volume curves were determined before each respiratory maneuver.⁹ The subject then breathed through the Venturi tube at frequencies of 24 and 36 breaths/min while being paced with a metronome. A target tidal volume of approximately 1 litre was visually displayed to the subject on an oscilloscope. All signals were displayed on a multichannel recorder. In addition, phase-corrected pressure and volume signals were displayed on a 7046 A x-y recorder (Hewlett-Packard Corporation, Waltham, Mass.). Subsequently the appropriate areas of the pressure-volume curves were integrated to calculate the total mechanical work.¹⁰

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Results

From the flow rates and gas densities observed (Fig. 1) we calculated that the flow was inversely related to the square root of the density for a given driving pressure. This meant that at any given flow rate the driving pressure dropped as the density of the gas decreased. Also, the advantage of the helium in a mixture was progressively lost as the concentration of oxygen increased. The divergence of the family of curves at low densities showed that there was a greater increase in absolute flow for a given increase in driving pressure with lower gas densities than with higher ones.

The total mechanical work involved in breathing first air and then a helium-oxygen mixture (80%/20%) through the Venturi tube was calculated by integrating the areas of the dynamic pressure-volume curves (Table I). No difference was seen in the static pressure-volume curves determined while the subject was breathing either air or the helium-oxygen mixture. Breathing the mixture at 24 and 36 breaths/min was associated with 36% and 31% decreases in total mechanical work, respectively, from the work of breathing air.

Clinical application

We used helium-oxygen mixtures during the period 1976 through 1980 to treat 10 patients who were in respiratory distress from an upper airway obstruction. All had been admitted to the intensive care unit, where they received constant nursing care, continuous electrocardiographic monitoring and, in most cases, frequent blood gas analysis by means of an indwelling arterial line.

When needed, the helium-oxygen mixture was supplied at a concentration of 80%/20% from a tank that was connected to a humidifier (Puritan Bennet Corporation, Kansas City, Missouri). The humidifier was set at 100% gas delivery to minimize the entrainment of air into the system. The tank's flow rate was set at 10 to 15 l/min; higher rates would have exhausted the contents of a large tank in less than 3 hours. To change the proportions of the gases we connected an additional source of

oxygen to the humidifier and adjusted the flow rate until a portable oxygen analyser showed the desired concentration at the mask outlet.

There were three classes of upper airway obstruction among our 10 patients: 4 had respiratory distress following the removal of an endotracheal tube, 3 had an obstruction associated with radiation therapy, and in 3 patients the cause was a primary tumour. The value of giving a helium-oxygen mixture is illustrated by a case history from each of the three groups.

Case 1: Obstruction following removal of an endotracheal tube

Shortly after admission to hospital because of a multiple drug overdose, a 23-year-old woman became unable to draw air into her lungs, and respiration stopped. We inserted an endotracheal tube and began mechanical ventilation. Five days later, while she was breathing through a T-piece at a fractional intake of oxygen ($F_{I}O_2$) of 0.3, analysis of arterial blood showed a pH of 7.48, a carbon dioxide tension ($P_{a}CO_2$) of 31 mm Hg and an oxygen tension pressure ($P_{a}O_2$) of 109 mm Hg.

The patient complained of a sore throat and shortness of breath after we had removed the endotracheal tube. Racemic epinephrine steroids were administered, but her respiratory effort increased, and tachypnea and stridor developed. We then gave her a helium-oxygen mixture (60%/40%), and after 1½ hours the blood gas values were: pH 7.29, $P_{a}CO_2$ 54 mm Hg and $P_{a}O_2$ 86 mm Hg. The proportion of helium in the mixture was increased to 80%, and 5 hours after the tube was removed the blood gas values were: pH 7.41, $P_{a}CO_2$ 33 mm Hg and $P_{a}O_2$ 63 mm Hg. The woman breathed the helium-oxygen mixture for another 24 hours and had no further difficulty.

Case 2: Obstruction secondary to radiation therapy

An 80-year-old woman underwent radiation therapy for a squamous cell carcinoma of the upper esophagus that had directly invaded the trachea. Initially clinical assessment showed only normal respiratory findings, but after 5 days of radiotherapy she was in respiratory distress, had difficulty in clearing secretions and showed inspiratory

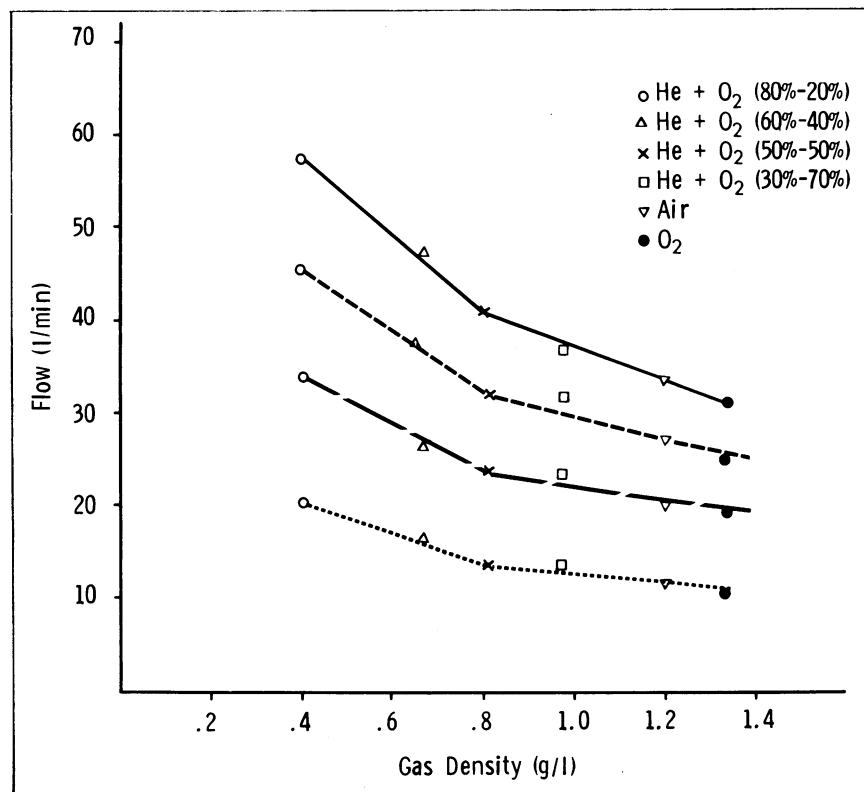


FIG. 1—Relation between flow (l/min) and gas density (g/l) across a Venturi orifice 4.76 mm in diameter with helium, oxygen and air. In descending order of curves, driving pressures were 7, 5, 3 and 1 cm H₂O.

stridor with intercostal indrawing. Laryngoscopy revealed a one-third narrowing of the tracheal lumen by tumour tissue. Arterial blood gas values when the patient was breathing room air were: pH 7.26, PaCO₂ 44 mm Hg and PaO₂ 47 mm Hg. Steroids were administered intravenously, and supplemental oxygen was given by mask at an F_IO₂ of 0.7. A follow-up analysis of arterial blood gases showed the following: pH 7.38, PaCO₂ 41 mm Hg and PaO₂ 65 mm Hg. The woman's respiratory rate continued to increase, though, reaching 60 breaths/min. A helium-oxygen mixture was substituted for the oxygen and her clinical condition improved within a few minutes. One hour later, when she was breathing a 70%/30% helium-oxygen mixture, the arterial blood gas values were: pH 7.47, PaCO₂ 31 mm Hg and PaO₂ 89 mm Hg. Two days later she was discharged from the intensive care unit without further need of supplemental oxygen.

Case 3: Primary tumour obstruction

After 2 weeks of progressively worsening shortness of breath associated with stridor, a 67-year-old man presented at the hospital. He had a known carcinoma of the left lung that had been treated with radiation 14 months earlier; the lung had been completely collapsed. A roentgenogram of the chest now showed no changes from the previous year. He was tachypneic and sweating. Despite inhalation therapy with salbutamol and racemic epinephrine the arterial blood gas values while he was breathing air at an F_IO₂ of 0.28 were: pH 7.35, PaCO₂ 52 mm Hg and PaO₂ 61 mm Hg. A helium-oxygen mixture (70%/30%) was given, and 1½ hours later the

blood gas values were: pH 7.43, PaCO₂ 45 mm Hg and PaO₂ 73 mm Hg. The patient was visibly more comfortable and his respiratory rate fell from 40 to 24 breaths/min. We continued treatment with the helium-oxygen mixture and performed bronchoscopy with a rigid instrument. This examination revealed a tumour mass extending across the carina from the totally obstructed left main stem bronchus to partially obstruct the right as well. Bronchoscopic removal of the intraluminal tumour relieved the man's symptoms. He was discharged 8 days later, after radiotherapy.

Discussion

In our one normal subject breathing through an orifice 4.76 mm in diameter we demonstrated a one-third decrease in respiratory work on switching from air to a helium-oxygen mixture. This is similar to the 33% mean reduction in nonelastic work seen in Barnett's experiments with dogs whose tracheas were partially clamped.³ Roussos and Macklem¹¹ have shown that healthy subjects can maintain ventilation with an inspiratory load equal to 40% of the maximal transdiaphragmatic pressure. Beyond this critical load the diaphragm will fatigue and fail, the time before failure being a curvilinear function of the load. A decrease in work such as we have demonstrated with helium could reduce resistance loading to below this critical level, thus preventing diaphragmatic fatigue and respiratory failure. Even a reduction in respiratory work to a value that just exceeds the critical load should significantly prolong the time before respiratory failure.

Among the 10 patients we treated

The Royal College of Physicians and Surgeons of Canada

Examinations

The written examinations of the Royal College are held in September each year. Applicants wishing to sit the examinations should note the following:

1. Every applicant for admission to the examinations must submit an application for assessment of training.

2. Applicants in training in Canada should apply for preliminary assessment of training at least one year before they expect to sit the examinations, that is not later than September 1st of the preceding year.

Applicants who have had training outside Canada should submit their initial application for assessment at least 18 months before they expect to sit the examinations, that is by March 1st of the preceding year.

Only applicants whose assessment of credentials is complete will be accepted to sit the examinations.

3. Applicants who desire to sit an examination, having complied with the above requirement of preliminary assessment of training, must notify the College in writing of their intent before February 1st of the year of the examination. Upon receipt of this notice of intent, the evaluation of the applicant's performance during training will be added to the previously completed assessment of credentials. Each applicant will then receive notification as to eligibility.

Those accepted as candidates will receive an examination application form to be completed and returned to the College.

4. The following documents may be obtained from the College office.

- (a) Application forms for assessment of training.
- (b) General information booklet on training requirements and examinations.
- (c) Specific requirements for training and regulations relating to the examinations in each specialty. Please indicate the specialty or specialties you are interested in.
- (d) Listing of specialty training programs in Canada accredited by the College.

5. Address all enquiries to:

Office of Training and Evaluation
**THE ROYAL COLLEGE OF
 PHYSICIANS AND SURGEONS
 OF CANADA**
 74 Stanley
 Ottawa, Canada K1M 1P4
 Tel. (613) 746-8177

Table 1—Total mechanical work of breathing through a Venturi orifice 4.76 mm in diameter, calculated from dynamic pressure-volume curves*

Respiratory frequency (breaths/min)	Total mechanical work (kgf-m/min)		
	Breathing air	Breathing helium-oxygen (80% / 20%)	Decrease in work,† %
24	1.51	0.96	36
36	2.88	2.00	31

*Measured tidal volume, 1.5 l.

†Calculated thus: $\frac{\text{work (air)} - \text{work (helium-oxygen)}}{\text{work (air)}} \times 100.$

with helium-oxygen mixtures 9 benefited substantially. In the seven patients whose respiratory distress was associated with the removal of an endotracheal tube or radiation therapy in the area of the trachea the use of helium allowed recovery without recourse to intubation or tracheostomy. In two of the three patients with an obstruction caused by a primary tumour the use of the helium-oxygen mixture improved their breathing and gave us additional time to assess the obstruction and the patient's general condition before we operated. In the third, therapy with helium was unsuccessful because the redundant tissue of the glottis caused either a high-grade obstruction or intermittent complete blockage of the airway.

When helium-oxygen mixtures are used in the management of respiratory distress the gas of lowest density (the one with the highest possible helium concentration) should be chosen. This is because there is an exponential increase in flow through a constricted orifice at a given pressure gradient as the density of the gas is reduced, and because a given increase in the driving pressure has a greater effect on flow at low gas densities. The latter point is apparent from Fig. 1, where it can be seen that the flow of a helium-oxygen mixture (80%/20%) rises from 20 to 57 l/min as the driving pressure changes from 1 to 7 cm H₂O. The same increase in driving pressure applied to air raises the flow from 12 to 33 l/min, an increase of only 21 l/min. While aiming for the easing of respiratory work with a high helium concentration, a balance will have to be established that takes into account the need of a greater F_IO₂ to deal with hypoxemia.

If the administration of a helium-oxygen mixture is successful, the clinical improvement in respiratory effort will be evident within minutes. The clinical signs of respiratory effort, such as increased rate and depth of respiration, indrawing of intercostal muscles and use of the accessory muscles of ventilation, can be monitored to assess improvement. When the respiratory workload has led to hypoventilation and hypercapnia, the PaCO₂ may fall as alveolar ventilation increases. The im-

provement in hypoxemia may be smaller, though, for it depends less on overall ventilation than on regional maldistribution of ventilation that may be due to pre-existing lung disease or retention of secretions associated with the obstruction.

The definitive treatment of an upper airway obstruction is still endotracheal intubation or tracheostomy. If these are difficult to perform in a particular instance, the use of a helium-oxygen mixture may provide a useful adjunct to therapy in the intensive care unit. Its efficacy can be determined in minutes, and, if the obstruction is transient and reversible, the mixture's use may obviate the need for surgery. In other cases it may transform an emergency operation at the bedside into an urgent elective procedure in the operating room, with better results and fewer complications.

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Brief prescribing information

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Action

Iron is utilized chiefly in the synthesis of hemoglobin, myoglobin and certain respiratory enzymes; unless it is supplied in appropriate amounts, the maturation of the red cells is retarded and the numbers discharged from the bone marrow into the general circulation are reduced.

Folic acid exerts important effects on hemopoiesis. It is essential in the synthesis of the cell's nucleoproteins. The reactions in which folic acid participates are important in the synthesis of DNA. As a consequence, deficiency of folic acid leads to damage in those tissues in which DNA synthesis and turnover are rapid. This includes the hematopoietic tissues, the mucosa of the gastrointestinal tract, and the developing embryo.

The controlled-release base of Slow-Fe folic tablets is specially formulated to release the tablet's contents evenly over an average period of two hours, the optimum time for maximum effective absorption. Furthermore, high concentrations of iron during the tablet's passage through the stomach and upper small intestine are avoided thus minimizing the incidence of gastrointestinal side effects.

Indications and clinical uses

Prophylaxis of iron and folic acid deficiencies and treatment of megaloblastic anemia, during pregnancy, puerperium and lactation.

Contraindications

Hemochromatosis, hemosiderosis and hemolytic anemia.

Warnings

Keep out of reach of children.

Precautions

The use of folic acid in the treatment of pernicious (Addisonian) anemia, in which vitamin B₁₂ is deficient, may return the peripheral blood picture to normal while neurological manifestations remain progressive.

Oral iron preparations may aggravate existing peptic ulcer, regional enteritis and ulcerative colitis.

Iron, when given with tetracyclines, binds in equimolecular ratio thus lowering the absorption of tetracyclines.

Adverse reactions

Nausea, diarrhea, constipation, vomiting, dizziness, abdominal pain, skin rash, headache.

Symptoms and treatment of overdose

Signs of toxicity from folic acid have not been observed even with doses several times higher than the usual therapeutic levels.

Ingestion by infants and young children of doses of ferrous sulfate in excess of 2 gm may cause death and ingestion of 1 mg could be considered toxic. Iron poisoning is rare in adults. Therapy should be instituted immediately.

Symptoms: The clinical effects of ingesting toxic doses of iron occur in four phases. The first phase begins with abdominal pain, nausea, and vomiting, about 30 to 60 minutes after ingestion. Irritability, pallor, and drowsiness appear, along with frequent black or bloody diarrhea.

Symptoms of acidosis and cardiovascular collapse may become prominent; coma and death ensue within 4 to 6 hours in about 20% of children taking large doses of iron. The second phase consists of a period of improvement, with subsidence of the initial symptoms spontaneously or in response to treatment. This period, lasting 8 to 16 hours, may herald the onset of progressive improvement. Often, however, it is followed by the third phase of progressive cardiovascular collapse, convulsions, coma, and a high mortality about 24 hours after ingestion. Finally, a fourth phase of gastrointestinal obstruction from scarring of the stomach or small intestine may occur weeks or months after the initial episode of iron intoxication.

Treatment should be instituted by giving milk immediately and vomiting induced. Eggs and milk should then be fed (to form iron protein complexes) until it is possible to perform gastric lavage. Gastric lavage with a 1% solution of sodium bicarbonate, to convert the iron to a less soluble form, should be administered within the first hour after ingestion of iron. An enema is administered to remove iron from the lower bowel. If an iron-chelating agent such as Desferal is available, it should be utilized. Peripheral vascular clots should be combatted including early replacement of body fluids and electrolytes. Additional measures include use of oxygen and vasopressor substances to help combat shock. The use of barbiturates or paraldehyde may be required to control convulsions.

In combating iron toxicity of children, the most important measure is its prevention. This can be accomplished by warning mothers to keep iron preparations out of reach of children, who are usually attracted by the sugar coating of pills that look like candy, and the use of "childproof" closures. Tests have shown that the coloured tablets are more attractive to children and likely to prove a greater temptation.

Dosage and administration

Prophylaxis: One tablet daily throughout pregnancy, puerperium and lactation. To be swallowed whole at any time of the day regardless of meal times.

Treatment of megaloblastic anemia: During pregnancy, puerperium and lactation; and in multiple pregnancy: two tablets, in a single dose, should be swallowed daily.

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Reference

- Course in Drug Therapy Sponsored by McGill University Department of Pharmacology and Therapeutics March 31 and April 1, 1977.

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