Helium-Oxygen in the Postextubation Period Decreases Inspiratory Effort

SAMIR JABER, ANNALISA CARLUCCI, MOHAMED BOUSSARSAR, REDOUANE FODIL, JÉRÔME PIGEOT, SALVATORE MAGGIORE, ALAIN HARF, DANIEL ISABEY, and LAURENT BROCHARD

Service de Réanimation Médicale, Hôpital Henri Mondor, AP-HP, Université Paris 12 and INSERM U492, Créteil, France

After tracheal extubation, upper and total airway resistances may frequently be increased resulting in an increase in inspiratory effort to breathe. We tested whether breathing a helium-oxygen mixture (HeO_2) would reduce inspiratory effort in the period after extubation. Eighteen consecutive patients with no chronic obstructive pulmonary disease who had received mechanical ventilation (> 48 h) were successively studied immediately after extubation (N_2O_2), 15 min after breathing HeO_2, and after return to N_2O_2. Effort to breathe, assessed by the transdiaphragmatic pressure swings (ΔPdi) and the pressure-time index of the diaphragm (PTI), comfort, and gas exchange, were the main end points. The mean reduction of the transdiaphragmatic pressure under HeO_2 was 19 ± 5%. All but three patients presented a decrease in transdiaphragmatic pressure under HeO_2, ranging from − 4 to − 55%, and a significant reduction in ΔPdi was observed between HeO_2 and N_2O_2 (10.2 ± 0.7 versus 8.6 ± 1.1 versus 10.0 ± 0.8 cm H_2O for the three consecutive periods; $p < 0.05$). PTI also differed significantly between HeO_2 and N_2O_2 (197 ± 19 versus 166 ± 22 versus 201 ± 23 cm H_2O/s/min for the three periods; $p < 0.05$). Breathing HeO_2 significantly improved comfort, whereas gas exchange was not modified. We conclude that the use of HeO_2 in the immediate postextubation period decreases inspiratory effort and improves comfort.

Keywords: Helium-oxygen; exutbation; weaning; work of breathing

After endotracheal extubation, upper and total airway resistances may frequently be increased, resulting in high inspiratory effort to breathe. A few patients, ranging from 5 to 16%, develop postextubation airway obstruction and frank respiratory distress (1–3). In addition, a substantial number of patients develop inspiratory distress after extubation, leading to reintubation (4, 5). In these patients an increase in upper airway and total inspiratory resistance may also participate to this respiratory distress.

Helium-oxygen (HeO_2) mixture has a low density and a high kinematic viscosity, allowing for a reduction in airway resistance. Some studies showed that it could have beneficial effects in the treatment of upper airway obstruction (6). Previous studies have demonstrated that breathing a helium-oxygen mixture reduces dyspnea and improves gas exchange in nonintubated patients with severe exacerbation of chronic obstructive lung disease (7) or asthma (8). Recently, helium-oxygen breathing was shown to improve pH, Pa_{CO_2} and inspiratory effort in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD), and these beneficial effects were enhanced by combining noninvasive pressure support ventilation with helium-oxygen (9). The use of helium-oxygen in the postextubation period where the upper and total airway resistances may be increased, could also decrease patient's effort to breathe in this situation.

The aim of this study was to evaluate the short-term effects of HeO_2 inhalation on gas exchange, comfort, and respiratory effort in the postextubation period. Inspiratory effort and gas exchange were also evaluated before extubation when patients were spontaneously breathing through their endotracheal tube. The effect of helium-oxygen (HeO_2) was compared with the measurements obtained with the usual air-oxygen mixture (N_2O_2) Because we previously assessed the effect of HeO_2 in patients with COPD (9), these patients were not included in the present study.

METHODS

The institutional review board for human subjects of Henri Mondor Hospital (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale) approved the experimental protocol. Written informed consent was obtained from each patient.

Patients

Eighteen consecutive patients who had been intubated for at least 48 h in the unit, were studied immediately after endotracheal extubation. Patients with COPD were not included. The study was performed over 5 mo in 1998.

Protocol

Patients were fully conscious and sitting in their bed at 60 degrees from horizontal. Their position was kept constant throughout the study. The esophageal-gastric catheter for measurements of effort was inserted before the beginning of the spontaneous breathing trial. During the spontaneous breathing trial, the endotracheal tube was connected to a T-piece providing humidification and oxygen. The first measurements were obtained at the end of the spontaneous breathing trial.

Two gas mixtures were tested after extubation: N_2O_2 and HeO_2. The same FI_{O_2} (25 to 40%) was adjusted in each patient to maintain $Sa_{O_2} > 92\%$ and was kept constant with the two gas mixtures. N_2O_2 was studied twice: N_2O_2-1 was the period immediately after extubation; the following period used HeO_2, and a new period of N_2O_2-2 ensued. Each period lasted for 15 min.

To make sure that the only alteration was due to the gas mixture, the three conditions after endotracheal extubation were delivered with the same experimental apparatus, and the two studied gas mixtures (N_2O_2 and HeO_2) were delivered in a similar fashion in terms of patient's equipment. The patients were not informed about the nature of the inhaled gas mixture. However, some patients were able to detect HeO_2 if they happened to speak ("Donald Duck" voice).

Experimental Apparatus

Medical gas administration. The medical gases were administered through a nonrebreathing face mask, in order to reduce the amount of external air entrained on inspiration, which could result in diluting helium concentration. The HeO_2 mixture composed of 22% oxygen and 78% helium was provided by a high-pressure source (cylinder of 4 bar-compressed gas; Air Liquide Medical, Bonneuil S/Marne, France).

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Correspondence and requests for reprints should be addressed to Pr L. Brochard, Réanimation Médicale, Hôpital Henri Mondor, 94000 Créteil, France. E-mail: laurent.brochard@hmn.ap-hop-paris.fr

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The gas was depressurized through a specific pressure regulator (HBS 315-8 No. 20 305) which was connected by plastic tubing to a tight-fitting face mask (HeO_2 flow between 6 and 12 L/min). A second part of T connector was connected to the wall oxygen supply, permitting O_2 enrichment of the gas mixture and the desired $F_{I_{O_2}}$ as described below (oxygen flow between 1 and 5 L/min). To ensure that the reservoir bag of the rebreathing mask had similar degree of filling when the patient was breathing N_2O_2, and to maintain the same $F_{I_{O_2}}$, the plastic tubing was connected to the wall air supply and the airflow was adjusted to provide the desired $F_{I_{O_2}}$ as described below.

The $F_{I_{O_2}}$ was maintained constant throughout the study and below 40% (beyond such a Heproportion, the physical properties of the HeO_2 mixture become comparable to an N_2O_2 mixture).

Measurements. Measurements were performed before extubation at the end of a 2-h T-piece trial, 10 to 15 min after extubation when patients breathed N_2O_2 (N_2O_2-1), after 15 min of HeO_2 breathing, and after 15 min of N_2O_2 (N_2O_2-2). Data were recorded during a 2-min period in each studied condition once a stable breathing pattern was observed.

Esophageal (Pes) and gastric (Pga) pressures were measured using a double balloon catheter (Marquat, Boissy Saint Léger, France). This catheter was inserted through the nose after the application of topical anesthesia and advanced until the distal balloon was in the stomach and the proximal balloon was in the middle portion of the esophagus. Each balloon, filled with 1 ml of air, was connected to a differential pressure transducer (MP45, ± 100 cm H_2O; Validyne, Northridge, CA). Appropriate placement of the esophageal balloon was assessed with the usual method (10). Adequate placement of the gastric balloon was ascertained by gentle manual pressure on the patient's abdomen to observe fluctuations in Pga, as well as by asking the patient to swallow and verifying that the sharp increase in Pes caused by esophageal contraction was not observed on the Pga tracing (11). Transdiaphragmatic pressure (Pdi) was obtained by subtracting the Pes signal from the Pga signal. Pressure signals were digitized at 128 Hz and sampled using an analog-to-digital converter system (MP100; Biopac Systems, Santa Barbara, CA). Flow measurement was not performed because using a pneumotachograph at the mouth would have considerably modified the breathing pattern of the patients by adding equipment dead space, inspiratory resistance, and altering the route of breathing. Because we were expecting moderate changes in effort to breathe and because we wanted to be as close as possible to the clinical situation, we decided against having any measurement of flow.

The $F_{I_{O_2}}$ was measured with an oxygen analyzer (Miniox I; MSA, Pittsburg, PA).

Dyspnea. Changes in comfort with each gas mixture were evaluated by a simple questionnaire when going from N_2O_2-1 to HeO_2, then when switching from HeO_2 to N_2O_2-2, as follows: +2: large improvement, +1: moderate improvement, 0: no change, −1: moderate worsening, −2: major worsening.

A catheter was inserted in a radial artery to allow arterial blood gas analysis at the end of each tested period. Blood gases were measured using an ABL 520 analyzer (Radiometer, Copenhagen, Denmark). Standard three-lead monitoring electrodes continuously monitored heart rate (HR) and rhythm. Systolic (SBP) and diastolic (DBP) arterial blood pressure were continuously monitored through the radial artery catheter signal. Oxygen saturation (Sa_{O_2}) was continuously monitored by pulse oxymetry.

Data Analysis and Assessment of Patient's Effort

The patient's inspiratory effort was evaluated by pressure indexes: the esophageal (Pes) and transdiaphragmatic pressures swings (ΔPdi), and the transdiaphragmatic pressure-time product (PTP). These calculations are independent of flow and volume signals. The pressure-time product is calculated as the integral of pressure over time during the phase of inspiratory muscular effort. The pressure-time product per breath for the diaphragm (PTPdi/breath) was obtained by measuring the area under the Pdi signal from the onset of its positive deflection to its return baseline (12). After elimination of artefactual cycles corresponding to cough, and esophageal spasms, 10 to 20 successive breaths were used to compute average values. The average PTPdi/breath (cm H_2O/s) was multiplied by respiratory frequency to obtain the PTPdi/min (cm H_2O/s/min).

Statistical Analysis

Data are given as mean ± SD. The measurements obtained during the four different conditions of the study were compared, the patients serving as their own controls. Two-way repeated measure analysis of variance (ANOVA) was used to test whether the different conditions had significant effects on the different variables, with Fisher's least statistical difference test being used for two-by-two comparisons when appropriate. A paired chi-square test was used to compare the comfort changes with each gas mixture. A p value below 0.05 was considered as the limit of significance.

RESULTS

Patients

The characteristics of the eighteen patients enrolled in this study are listed in Table 1 (13). All patients were studied in the immediate postextubation period. All 18 patients tolerated well HeO_2 breathing. The mean $F_{I_{O_2}}$ was 33 ± 2 %. Two patients (Patients 4 and 17) were reintubated in the following 48 h.

Respiratory Rate, Gas Exchange, and Hemodynamics

Respiratory rate and blood gas and hemodynamic parameter values are given in Table 2. All patients but one had a pH value above 7.37, and all had a Pa_{CO_2} value below 46 mm Hg. Respiratory rate and blood gas and hemodynamic parameters values did not significantly differ among the four study conditions.

Effort to Breathe

The transdiaphragmatic pressure swings and the pressure time product were similar before and after extubation (p = NS).

After extubation, all indexes of respiratory effort decreased with HeO_2 as compared with N_2O_2, whereas no difference existed between N_2O_2-1 and N_2O_2-2. The significant decrease in the transdiaphragmatic pressure-time product observed with HeO_2 (197 ± 19 for N_2O_2-1 versus 166 ± 22 for HeO_2 versus 201 ± 23 cm H_2O/s/min for N_2O_2-2; $p < 0.05$) is illustrated in Figure 1. Individual values for ΔPdi (in cm H_2O) are presented in Figure 2. The mean reduction of the transdiaphragmatic pressure under HeO_2 was 1.5 ± 0.6 cm H_2O or 19 ± 5%. All but three patients presented a decrease in ΔPdi with HeO_2, ranging from −0.2 to −3.9 cm H_2O or −4 to −55%, and a significant reduction in ΔPdi was observed between HeO_2 and N_2O_2 (10.2 ± 0.7 for N_2O_2-1 versus 8.6 ± 1.1 for HeO_2 versus 10.0 ± 0.8 cm H_2O for N_2O_2-2; $p < 0.05$). An experimental record from one patient (Patient 5) illustrates that swings in Pes, Pga, and Pdi were smaller in HeO_2 than in N_2O_2 (Figure 3).

Comfort to Breathe

Individual values for comfort scale obtained when patient were switched from N_2O_2-1 to HeO_2 and from HeO_2 to N_2O_2-2 are presented in Figure 4 for 16 subjects (in two subjects the information could not be obtained). Breathing helium-oxygen mixture improved comfort to breathe ($p < 0.001$).

DISCUSSION

Abnormalities of the upper airway and including the glottis could participate to contribute a high degree of inspiratory mechanical loads experienced by some patients in the period after extubation, and contribute to postextubation respiratory distress. The present study is the first evaluation of the effects of a helium-oxygen mixture (HeO_2) on inspiratory effort, blood gases, and comfort to breathe in the immediate postex-

TABLE 1. CHARACTERISTICS OF THE PATIENTS

Patient No.	Age (*yr*)	Sex (*M/F*)	SAPS II	Underlying Disease	Etiology of Respiratory Failure	ETT ID (*mm*)	Duration of Mechanical Ventilation (*d*)
1	86	M	66		Hemorrhagic and septic shock	8.0	20
2	75	F	56		Bacterial pneumonia, ARDS	7.5	25
3	37	F	68		Coma, drug overdose	7.5	24
4	61	M	82	Renal transplantation	Cardiogenic and septic shock	7.5	12
5	75	M	44		Cardiac surgery (endocarditis)	8.0	2
6	59	M	55		Coma, meningoencephalitis	8.0	11
7	53	M	32	Ischemic cardiopathy	Bacterial pneumonia	8.0	8
8	45	F	37	Sickle cell disease	Abdominal surgery	7.0	2
9	54	M	18	Ischemic cardiopathy	Cardiac surgery	8.0	2
10	79	M	41	Ischemic cardiopathy	Cardiac surgery	7.5	12
11	30	M	31	Surgery for aortic dissection	Cardiogenic pulmonary edema	8.0	2
12	60	F	54	Ischemic cardiopathy	Cardiogenic pulmonary edema	8.0	12
13	46	M	23		Cardiac surgery (endocarditis)	7.5	2
14	65	M	75	Immunodeficiency	Septic shock	8.0	14
15	55	F	69	Ischemic cardiopathy	Cardiac surgery	7.5	17
16	29	M	17	Guillain Barré syndrome	Bacterial pneumonia	8.0	9
17	53	F	29		Surgery, cellulitis	8.0	20
18	73	F	88		Septic shock and ARDS	7.5	17
Mean	58	11M/7F	49				12
SD	16		22				8

Definition of abbreviations: SAPS II = Simplified Acute Physiology Score II (12); ETT ID = endotracheal tube internal diameter; ARDS = acute respiratory distress syndrome.

tubation period, in non-COPD patients who had been intubated at least for 48 h. The results obtained demonstrate that using HeO_2 instead of N_2O_2 can reduce the inspiratory effort and improve comfort after tracheal extubation.

The use of HeO_2 mixture in adults (14–17) and in children (18–22) with upper airway obstruction has been reported in several anecdotal series and a few studies, and it has become one of the more accepted indications for HeO_2 use (6). Although its effect was shown mainly through observational studies, the fact that the immediate improvement obtained with HeO_2 breathing was reversed when it was discontinued even briefly, suggested an independent beneficial effect of the gas related to its physical properties. Barach (14) first reported the use of HeO_2 mixture in the treatment of both upper and lower airway obstruction. Skrinskas and colleagues (17) reported their experience with HeO_2 treatment in a series of 10 patients with acute upper airway obstruction. Four developed respiratory distress after the removal of an endotracheal tube, three had an obstruction associated with radiation therapy, and in three patients the cause was a primary tumor. Except in a case of intermittent complete blockade of the airway, the use of HeO_2 improved the patients, allowing the avoidance of intubation and/or creating time to prepare the patients for a surgical procedure. Duncan (18) reported a pediatric experience in seven patients with upper airway obstruction caused by viral or postintubation severe croup, in whom artificial airways were avoided by the use of HeO_2. In a double-blind, randomized, controlled, crossover trial, Kemper and coworkers (21) reported a 38% reduction in respiratory distress score with HeO_2 breathing compared with N_2O_2 in 13 children with burns and other trauma with postextubation stridor. These results are comparable to those of the study of Rodeberg and coworkers (22) who reported the successful use of HeO_2 in the treatment of postextubation stridor in six of eight pediatric patients with burns, who were unresponsive to racemic epinephrine.

In the present study, both the effort to breathe and the comfort were improved with HeO_2. All but three patients (Patients 2, 3, and 7) presented a decrease in transdiaphragmatic pressure measured under HeO_2 from a range of −4 to −55%. Patient 3, who presented an increase in transdiaphragmatic pressure with helium-oxygen (16.6 to 19.5 cm H_2O), had an esotracheal fistula diagnosed subsequently, and the modification of the gas mixture did not modify the comfort scale. The two other patients (Patients 2, 7) presented either a moderate improvement in comfort with HeO_2 or no change after return to N_2O_2. The two patients (Patients 4 and 17) who were reintubated in the following 48 h, presented a 31 and 17% reduction

TABLE 2. ARTERIAL BLOOD GASES AND HEMODYNAMIC PARAMETERS DURING THE FOUR STUDY CONDITIONS*

	T-piece	N_2O_2 (*before*)	Helium-Oxygen	N_2O_2 (*after*)	Statistics
RR, breaths/min	29.7 ± 8.6	28.9 ± 9.1	28.0 ± 8.5	29.0 ± 8.7	NS
pH	7.42 ± 0.05	7.42 ± 0.06	7.42 ± 0.06	7.43 ± 0.06	NS
Pa_{CO_2}, mmHg	37 ± 6	38 ± 6	38 ± 6	38 ± 5	NS
Pa_{O_2} mmHg	97 ± 30	88 ± 29	84 ± 21	91 ± 31	NS
FI_{O_2}, %	33 ± 5	34 ± 4	33 ± 4	33 ± 9	NS
HR, beats/min	104 ± 19	105 ± 21	104 ± 20	104 ± 19	NS
SBP, mmHg	133 ± 26	137 ± 22	129 ± 24	129 ± 23	NS
DBP, mmHg	65 ± 10	69 ± 13	64 ± 12	66 ± 11	NS

Definitions of abbreviations: RR = respiratory rate; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; NS = nonsignificant.

* Values are means ± SD.

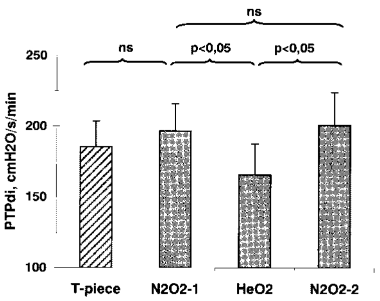

Figure 1. Mean values (± SEM) of the transdiaphragmatic pressure-time index (PTPdi) during the four consecutive periods of the study: at the end of the spontaneous breathing trial before extubation (T-piece), then after extubation successively during N_2O_2, HeO_2, and N_2O_2 breathing again.

in transdiaphragmatic pressure with helium-oxygen, and moderate and large improvement in comfort with HeO_2.

Our study has presented some limitations. First, some patients could discern which gas they were receiving, which could bias the patients' assessment of their degree of dyspnea. Second, the investigators were not blinded to the gas being delivered.

Some studies (23, 24) reported an increase in the work of breathing after extubation, and the investigators suggested a role of the supraglottic airway in explaining the increase of work of breathing noticed after extubation. Straus and coworkers (25) reported no significant difference in inspiratory effort before and after removal of the endotracheal tube in successfully extubated patients, and these results are confirmed by the present study. Straus and coworkers also recorded the longitudinal area profile of the upper airway after extubation with the acoustic reflection technique used by Louis and coworkers (26) and found that in all but one patient, the narrowest part of the airway was the glottis. The glottis area was found to be smaller than normal, supporting the idea that mild inflammation of the glottis is probably a frequent phenomenon in this situation. This phenomenon may explain in part the beneficial effect of helium-oxygen breathing mixture in the present study. The density of the tested HeO_2 mixture used ($F_{I_{O_2}} = 0.33$) was about two times smaller than the density of air. This reduced density (ρ), together with the almost negligible increase in the dynamic viscosity (μ) of HeO_2 as compared with air ($\leq 10\%$), results in an increase in kinematic viscosity ν ($= \mu/\rho$) and in a decrease in the Reynolds number (Re). This reduction in Reynolds number is responsible for less turbulent and more laminar flow, and less airway resistance. These improvements lead to the decrease in the inspiratory effort.

No patient with COPD was included in the present study because the effect of HeO_2 in these patients has been previously studied (9). The observed improvement of inspiratory effort and comfort obtained in the studied patients could have been strongly reinforced by including patients with COPD who do have a reduction in breathing effort with HeO_2. In a previous study assessing the effect of HeO_2 in patients with COPD (9), three of the 10 patients were studied during an episode of mild-to-moderate respiratory distress after extubation. The use of HeO_2 in these three patients, similar to that in the other patients with COPD and respiratory distress, permitted a significant reduction in inspiratory effort and an improvement in gas exchange, with either HeO_2 alone in spontaneous ventilation or when combining noninvasive ventilation with HeO_2.

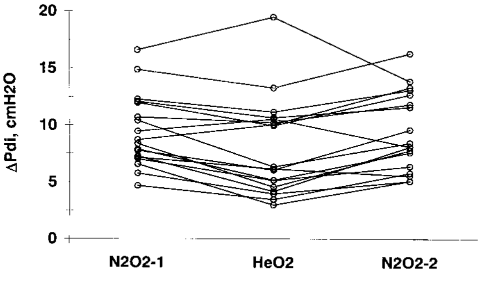

Figure 2. Individual values of the transdiaphragmatic pressure swings (ΔPdi) measured during the three periods after extubation: N_2O_2-1, He-O_2, and N_2O_2-2.

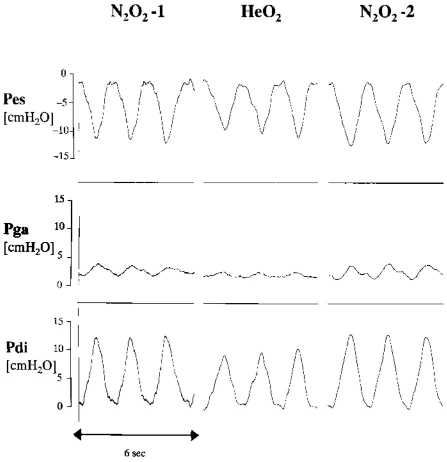

Figure 3. Tracings of esophageal, gastric, and transdiaphragmatic pressures over time in one patient (Patient 5) during the three periods after extubation (N_2O_2-1, He-O_2, and N_2O_2-2). These tracings illustrate the reduction in breathing effort obtained with the helium-oxygen mixture.

In the present study, flow measurements were not performed in order to evaluate inspiratory effort in real conditions, without additional work load induced by the pneumotachograph and equipment, and without altering the route of breathing. Several studies (7, 9, 27), however, have already demonstrated that substituting HeO_2 for N_2O_2 does not significantly modify breathing pattern parameters. The lack of significant alterations in respiratory rate and gas exchange observed in the study is in accordance with these results.

Using HeO_2 mixture alone or in association with noninvasive ventilation could be proposed in patients who develop acute respiratory failure in the postextubation period, and es-

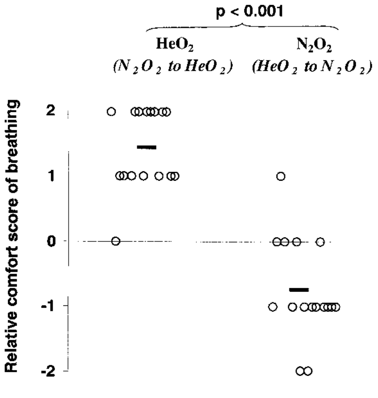

Figure 4. Individual values of the relative comfort scale observed when switching from N_2O_2-1 to HeO_2 (*left*) and from HeO_2 to N_2O_2-2 (*right*).

pecially if upper airway obstruction is part of the pathophysiology of the decompensation. Although the majority of patients who develop postextubation stridor do not require intubation and there is not yet a randomized control trial showing that noninvasive ventilation is benefited after extubation, the present results suggest that, in some cases, HeO_2 could be an interesting additional therapy, allowing clinical improvement and giving time to usual therapy to work such as epinephrine inhalation and corticosteroid. Helium is an inert gas, almost insoluble in tissues and nonreactive with biologic membranes, and not associated with any toxic effects. This unloading effect could facilitate the period after extubation in selected patients who develop respiratory distress shortly after extubation and may avoid reintubation in some cases. Further studies are needed to better define its therapeutic role.

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