Anesthetic Effects on Ventilation in Patients with Chronic Obstructive Pulmonary Disease

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The effects of 1.0 per cent end-tidal halothane–oxygen anesthesia on spontaneous ventilation, ventilatory deadspace, functional residual capacity (FRC), and alveolar–arterial oxygen difference (A-aD\textsubscript{O\textsubscript{2}}) were measured in patients with chronic obstructive pulmonary disease and in normal patients of similar age. Results obtained were compared with values obtained preoperatively from the same patients. The following were measured: 1) ventilation and ventilatory deadspace, breathing room air and breathing 100 per cent oxygen; 2) functional residual capacity (FRC) and alveolar–arterial oxygen tension difference (A-aD\textsubscript{O\textsubscript{2}}); 3) forced expiratory volume in 1 second (FEV\textsubscript{1,0}); 4) ventilatory response to exogenous carbon dioxide. Findings indicated that ventilation is depressed more during halothane anesthesia in patients with emphysema than in normal patients and that the extent of depression is best related to a preoperative measurement of FEV\textsubscript{1,0} (P < 0.001, r = 0.86).

The depression in alveolar ventilation results primarily from a reduction in tidal volume. A-aD\textsubscript{O\textsubscript{2}} and ventilatory deadspace-to-tidal volume ratio are increased and FRC decreased with anesthesia in patients with COPD, but the changes are no greater than those found in normal patients. (Key words: Lung, chronic obstructive pulmonary disease; Oxygen, alveolar–arterial tension difference; Anesthetics, volatile, halothane.)

HALOTHANE-OXYGEN ANESTHESIA depresses spontaneous ventilation in normal subjects,\textsuperscript{1,2} but there is little quantitative information on the respiratory behavior of patients with chronic obstructive pulmonary disease (COPD) under similar circumstances. Numerous factors may interact in COPD to produce carbon dioxide retention during anesthesia with spontaneous ventilation. Abnormal mechanics of ventilation secondary to increased airway resistance may worsen as a result of a decrease in functional residual capacity (FRC).\textsuperscript{3} High inspired oxygen concentrations are known to depress peripheral chemoreceptor drive and ventilation in subjects with carbon dioxide retention, especially when depression of central chemoreceptor drive is accentuated by anesth

The objectives of this study were to determine: 1) the effects of halothane–oxygen anesthesia on alveolar ventilation in patients with COPD; 2) the effects of breathing high oxygen concentrations, changes in physiologic deadspace, and abnormal respiratory mechanics on the depression in alveolar ventilation induced by anesthesia.

Methods

Patients scheduled for elective surgery, excluding thoracic procedures, were studied. Informed consent and protocol were approved by the Human Experimentation Committee of the University of California, San Francisco. On the basis of preoperative clinical and pulmonary function evaluation, subjects were assigned to either the control or the COPD group. Some control patients had slight cough and sputum production compatible with chronic cigarette smoking, but otherwise they were free of clinical respiratory abnormalities.
Patients assigned to the COPD group had the diagnosis of emphysema and had histories and physical examinations compatible with COPD. Additional criteria for assignment to the COPD group included a 1-second forced expiratory volume (FEV₁,₀) less than 70 per cent of predicted, in the sitting position, persisting after inhalation of bronchodilator, and a functional residual capacity (FRC) greater than 120 per cent of predicted. Functional residual capacities with the patients in both sitting and supine positions were determined by a helium-dilution technique. Predicted values were those of Goldman and Becklake. All values were corrected to body temperature and pressure, saturated (BTPS). Subsequent preoperative studies were performed with the patient supine. Following local infiltration analgesia, the radial artery was cannulated. Expired gases were collected in a 10-liter wedge spirometer (Med-Science Electronics, Inc.) through a 25-ml Rudolph nonrebreathing valve and mouthpiece.

The patients breathed through the mouthpiece to accustom themselves to the apparatus. Then, after a short rest, three control measurements of expired minute volume, arterial blood gases, and mixed expired carbon dioxide tension were obtained with the patient breathing room air. To determine the effects of the resistance of the endotracheal tube to be used during anesthesia, the response to breathing through an airway resistor equivalent to a #40 endotracheal tube (0.5 cm H₂O at 0.6 l/sec flow) was observed. Changes in ventilation and Paco₂ after 5 minutes of breathing air with the resistor in circuit were recorded. Minute ventilation, arterial blood gases, pH and mixed expired Pco₂ also were measured after 15 and 30 minutes of breathing humidified oxygen. Arterial blood gases and pH were measured immediately after sampling, using Radiometer electrodes. Mixed expired gas was collected over a 3-minute period during steady-state ventilation and measured with the Pco₂ electrode. Ventilation was judged steady-state by direct measurement and monitoring of end-tidal CO₂ concentration.

Physiologic deadspace-to-tidal volume ratios (Vd/Vt) were calculated following subtraction of the valve deadspace from the physiologic deadspace calculated by the Eng- hoff modification of the Bohr equation. Alveolar-to-arterial oxygen tension differences (A-aD₈₅) were calculated from the values obtained after 15 and 30 minutes of oxygen breathing. Alveolar oxygen tension was calculated by \[ P_{A_o} = P_{I_o} - P_{co}_2 - P_{halothane} \].

The preoperative response to exogenous carbon dioxide administered during oxygen breathing was obtained by addition of sufficient CO₂ to the inspired gas to increase end-tidal Pco₂ by 10 torr as measured by a Beckman LB-1 infrared CO₂ analyzer. Following 9 minutes of this stable elevated Pco₂, we made two simultaneous measurements of minute ventilation and Paco₂ at one-minute intervals. From the averaged control values during breathing of oxygen alone and during breathing of carbon dioxide, a CO₂ response slope was calculated.

On the day of surgery, following atropine premedication, anesthesia was induced with thiopental, 2–3 mg/kg. Succinylcholine, 1 mg/kg, was used to facilitate laryngoscopy, topical laryngeal spray with lidocaine, and endotracheal intubation. Anesthesia was maintained with 1.0 vol per cent end-tidal halothane in oxygen monitored by a Beckman LB-1 halothane analyzer. Ventilation was controlled at a rate of 10/min via a Bennett or Air Shields ventilator with the tidal volume determined by the Radford nomogram. With return of neuromuscular function (indicated by muscle twitch in response to peripheral nerve stimulation), spontaneous ventilation was allowed. The circuit used preoperatively then was utilized for maintenance of anesthesia during the remainder of the study. All measurements except one arterial blood-gas analysis 5 minutes after incision were completed prior to surgical stimulation.

Collections of mixed expired gas, minute ventilation, and arterial blood gases were made 10, 15, and 30 minutes after the return of spontaneous ventilation, except that if Paco₂ rose to above 70 torr, ventilation was controlled for the remainder of the anesthetic period. Physiologic deadspace-to-tidal volume ratios and A-aD₈₅ were calculated from
TABLE 1. Pulmonary Function Data, Subjects Breathing Room Air (Means ± SE)

| Patients' Ages (Years) | P_{Aco_2} (torr) | P_{Aco_2} (torr) | Vital Capacity (% Pred.) | FRC (% Pred.) | FRC × 100 / FVC | FEV_{1.0} % 
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<tbody>
<tr>
<td>Control</td>
<td>58 ± 2</td>
<td>82 ± 4</td>
<td>38 ± 1</td>
<td>103 ± 3</td>
<td>88 ± 4</td>
<td>78 ± 2</td>
</tr>
<tr>
<td>COPD</td>
<td>66 ± 3</td>
<td>74 ± 3</td>
<td>41 ± 5</td>
<td>80 ± 5</td>
<td>130 ± 5</td>
<td>49 ± 4</td>
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Vital capacity and FRC are expressed as percentages of predicted in the sitting position. FEV_{1.0} is expressed as a percentage of forced vital capacity (FVC).

* Significantly different from control.

Values obtained after 15 and 30 minutes of spontaneous ventilation.

Functional residual capacity was measured after 30 minutes of anesthesia with spontaneous ventilation except in patients requiring controlled ventilation. In those cases, subjects were ventilated manually by the spirometer. Sufficient halothane was added to the spirometer to sustain the 1.0 per cent end-tidal concentration. All helium values were corrected for the effect of halothane on the catharometer.

Postoperatively, the tracheas of patients without CO_{2} retention were extubated. Arterial blood gases were sampled and analyzed as soon as the patients became conscious. Subjects requiring controlled ventilation intraoperatively had serial blood gas sampling until P_{Aco_2} became normal during spontaneous ventilation, after which extubation was accomplished.

Statistics

Mean values ± 1 standard error are given. Statistical significance was determined by Student’s t test for paired and unpaired samples. FEV_{1.0} was used as an index of airway obstruction to allow comparison be-

TABLE 2. Effects of Breathing Oxygen on CO_{2} Tension, Tidal Volume, Respiratory Frequency, and V_{E}/V_{T} Ratio Compared with Breathing Air (Means ± SE)

<table>
<thead>
<tr>
<th>P_{Aco_2} (torr)</th>
<th>V_{T} (l)</th>
<th>f (Breaths/Min)</th>
<th>V_{E}/V_{T}</th>
</tr>
</thead>
<tbody>
<tr>
<td>P_{Aco_2} 0.21</td>
<td>F_{O_2} 1.0</td>
<td>F_{O_2} 0.21</td>
<td>F_{O_2} 1.0</td>
</tr>
<tr>
<td>Control</td>
<td>38 ± 1</td>
<td>37 ± 1</td>
<td>0.551</td>
</tr>
<tr>
<td>COPD</td>
<td>41 ± 1.5</td>
<td>42* ± 1</td>
<td>0.548</td>
</tr>
</tbody>
</table>

* Significantly different from control.
† Significantly different from value in own group breathing air.

TABLE 3. Effects of Halothane–Oxygen Anesthesia on Tidal Volume, Respiratory Frequency, and V_{E}/V_{T} Compared with Awake Values Breathing Oxygen (Means ± SE)

<table>
<thead>
<tr>
<th>V_{T} (l)</th>
<th>f (Breaths/Min)</th>
<th>V_{E}/V_{T}</th>
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</thead>
<tbody>
<tr>
<td>Awake</td>
<td>Anesthesia</td>
<td>Awake</td>
</tr>
<tr>
<td>Control</td>
<td>0.535 ± 0.25</td>
<td>0.267†</td>
</tr>
<tr>
<td>COPD</td>
<td>0.521 ± 0.31</td>
<td>0.234†</td>
</tr>
</tbody>
</table>

* Significantly different from control.
† Significantly different from value in own group awake.
between patients. FEV<sub>1.0</sub> was normalized for patient size by division by height in meters. Linear regression analysis gave the line of best fit and correlation coefficients. Hyperbolic regression analysis was performed by use of logarithmic equivalents in the linear regression equation and subsequent plotting of the antilogarithms of the equation obtained. Unless P values are specified, “significantly different” means P < 0.05.

**Results**

Twenty patients, eight controls and 12 with COPD, were studied. Pulmonary function and blood-gas data are shown in table 1. Both groups were normocapnic and normoxic, with no significant difference in these variables. During breathing of air and oxygen V<sub>T</sub>/V<sub>T</sub> ratios were significantly higher in the patients with COPD than in the control group (table 2). During breathing of oxygen, P<sub>aco</sub> was significantly greater in COPD than control patients (table 2). Oxygen breathing also resulted in a significant increase in V<sub>T</sub>/V<sub>T</sub> ratio in patients with COPD but not in the control group (table 2).

Addition of the airway resitance did not produce significant alteration from control values of V<sub>T</sub> or P<sub>aco</sub> for either group.

During anesthesia tidal volume decreased and respiratory frequency increased significantly in both groups. During anesthesia the tidal volume standardized to body size related inversely to P<sub>aco</sub> (fig. 1, r = 0.66, P < 0.01). V<sub>T</sub>/V<sub>T</sub> ratios increased with anesthesia in both groups; they were significantly greater in patients with COPD (table 3). Figure 2 displays the V<sub>T</sub>/V<sub>T</sub> values awake, during breathing of air, and during anesthesia as a function of FEV<sub>1.0</sub>/height (l/m). FEV<sub>1.0</sub> is standardized to body size by division by body height in meters. The slopes of the regression equation do not differ significantly. That is, V<sub>T</sub>/V<sub>T</sub> did not increase more with anesthesia in the COPD patients than in the controls. The ventilatory response to exogenous CO<sub>2</sub> varied inversely with the severity of airway obstruction, that is, the lower the FEV<sub>1.0</sub>, the less the response (fig. 3).

During anesthesia FEV<sub>1.0</sub> related to P<sub>aco</sub> in a hyperbolic fashion; the lower the preoperative FEV<sub>1.0</sub>, the greater the CO<sub>2</sub> retention intraoperatively (fig. 4). Arterial CO<sub>2</sub> tensions exceeded 70 torr in three of the four patients who had FEV<sub>1.0</sub>'s of less than
0.6 l/meter height. The above values were means after 15 and 30 minutes of steady-state anesthesia without surgical stimulation, except in those patients with marked CO₂ retention. Arterial CO₂ tensions were measured at the same anesthetic depth 5 minutes after incision in nine patients. Although mean \( P_{aCO_2} \) decreased approximately 4 torr after incision, the difference was not statistically significant for either group of patients.

Anesthesia increased A-aD\( CO_2 \) significantly (control \( P < 0.003 \); COPD \( P < 0.03 \)), but there was no significant difference between the groups preoperatively, during breathing of oxygen, or during anesthesia (table 4). Similarly, FRC decreased with anesthesia (control \( P < 0.025 \); COPD \( P < 0.05 \)) but there was no significant difference between the two groups.

**Discussion**

The clinical implications to be derived from this study are threefold. The first is that normal blood gases preoperatively, in a patient with COPD, do not preclude significant alveolar hypoventilation intraoperatively, even with "light depths" of anesthesia. Second, depending upon the severity of COPD, controlled or assisted ventilation is mandatory during anesthesia to prevent alveolar hypoventilation. Third, the extent of hypoventilation during anesthesia in patients with COPD correlates best with a simple measurement of airway obstruction, FEV\(_{1.0} \).

The method selected to control anesthetic depth in the present study, maintenance of constant end-tidal halothane concentration, can be criticized. The apparent ventilation/perfusion disparities in subjects with obstructive
tive pulmonary disease probably meant that end-tidal halothane readings reflect a lower “true” alveolar concentration. Thus, patients with COPD were probably studied at a slightly lighter level of anesthesia than were control patients. However, correcting this error would only have increased the alveolar hypoventilation seen in the patients with COPD.

When carbon dioxide production is constant, alveolar ventilation will be reduced by reduction in respiratory frequency or tidal volume or by an increase in ventilatory deadspace. Respiratory frequency increased similarly in both the control patients and those with COPD, and the major factor resulting in alveolar hypoventilation was a decrease in tidal volume (Fig. 1). However, the inverse correlation between tidal volume and $P_{A\text{CO}_2}$ during anesthesia was not close enough ($r = 0.66$) to allow accurate prediction of $P_{A\text{CO}_2}$ from measurement of tidal volume.

Although $V_D/V_T$ increased with anesthesia, the absolute mean values for ventilatory deadspace ($V_D/V_T \times V_T$) decreased in both groups of patients. This reduction agrees with the report by Briscoe et al. of reduction of anatomic deadspace at low tidal volumes. Our value for $V_D/V_T$ in non-anesthetized normal supine subjects is similar to those reported by Raine and Bishop (0.29) and Marshall (0.31). Marshall, however, found that $V_D/V_T$ did not increase with halothane-oxygen anesthesia. This differed from findings in the present study, where $V_D/V_T$ increased from 0.31 to 0.52 under similar anesthetic circumstances. The reason for this difference is not clear. In patients similarly anesthetized, Kain et al. found that $V_D/V_T$ was $0.51 \pm 0.02$ (SE).

$V_D/V_T$ ratios in patients with COPD were significantly higher than those in the control patients, both awake and during anesthesia (Table 3). However, the proportionate increase with anesthesia was not greater in patients with COPD, as the slopes of the $V_D/V_T$ ratio compared with the severity of airway obstruction (Fig. 2) did not differ between the awake and anesthetized states.

FRC decreased and $A-aD_{O_2}$ ($Fi_{O_2} = 1$) increased with anesthesia in both the control patients and those with COPD. It was surprising to us that the magnitudes of these changes were not different in the two groups. The decrease in FRC that occurred with anesthesia may have had more physiologic significance in the patients with COPD. Cheng et al. found that a proportional reduction in FRC caused a greater increase in airway resistance in patients with COPD than in normal subjects. Thus, the decrease in FRC may have increased airway resistance relatively more in patients with COPD than in normal subjects. Additional evidence supporting this thesis is that the three patients whose $P_{A\text{CO}_2}$'s increased to more than 70 torr had marked intercostal retraction not present prior to anesthesia.

The increased hypoventilation associated with halothane anesthesia in patients with emphysema can be attributed to at least three possible causes: 1) increased airway resistance found in emphysematous patients; 2) removal of hypoxic ventilatory drive; 3) reduced central responsiveness to carbon dioxide. The close relationship between alveolar hypoventilation during anesthesia and $FEV_{1.0}$ indicates that altered pulmonary mechanics is an important factor in respiratory depression. As expected, significant hypoventilation did not occur with oxygen breathing. The subjects' $P_{A\text{O}_2}$'s breathing room air were not in the range such that oxygen breathing would suppress ventilation. Oxygen breathing did increase $V_D/V_T$ significantly in patients with COPD, confirming work reported by Lee et al. Our data do not allow us to examine the possible role of central depression of responsiveness to carbon dioxide as a possible mechanism.

<table>
<thead>
<tr>
<th></th>
<th>$A-aD_{O_2}$</th>
<th>FRC Decrease during Anesthesia (Per Cent)</th>
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<tbody>
<tr>
<td></td>
<td>$P_{a\text{O}_2} = 1.0$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Awake</td>
<td>Anesthesia</td>
</tr>
<tr>
<td>Control</td>
<td>132 ± 16</td>
<td>222 ± 27</td>
</tr>
<tr>
<td>COPD</td>
<td>140 ± 16</td>
<td>193 ± 16</td>
</tr>
</tbody>
</table>

Table 4. Effects of Anesthesia on $A-aD_{O_2}$ and FRC Compared with Preoperative Values (Means ± SE)
for alveolar hypoventilation. The existence of an altered central responsiveness to carbon dioxide in patients with emphysema is uncertain. Since apneic thresholds should be relatively independent of pulmonary mechanics, this measurement in patients with emphysema could perhaps be used to answer this question.

References