The Effects of Various Tidal Volumes on Gas Exchange in Pulmonary Edema

S. Carole Burnham, M.D.,* Wayne E. Martin, M.D.,† Frederick W. Cheney, Jr., M.D.‡

Anesthetized dogs were mechanically ventilated using tidal volumes ($V_T$) of 15, 24, 43, and 15 ml/kg with an end-expiratory pressure of 10 cm H$_2$O (continuous positive-pressure ventilation). Pulmonary edema was then induced by injecting oleic acid into the right ventricle and the ventilatory patterns were repeated. Prior to pulmonary edema the only significant finding was that of decreased shunt and cardiac output during CPPV. With pulmonary edema, shunt and $P_{aO_2}$ were significantly improved during ventilation with a $V_T$ of 43 ml/kg and CPPV, compared with ventilation with a $V_T$ of 15 ml/kg. Ventilation with a tidal volume of 24 ml/kg not only failed to improve the shunt and $P_{aO_2}$ seen at a $V_T$ of 15 ml/kg, but also significantly depressed cardiac output. (Key words: Pulmonary edema; Shunt; Mechanical ventilation.)

Several reports$^1$–$^4$ have shown that the pattern of mechanical ventilation can affect the efficiency of pulmonary gas exchange. Uzawa and Ashbaugh$^5$ have shown that dogs with pulmonary edema induced by oleic acid have increased survival times when maintained on intermittent positive-pressure ventilation (IPPV) or continuous positive-pressure ventilation (CPPV), compared with dogs allowed to breathe spontaneously. Dogs treated with CPPV (an end-expiratory pressure of 10 cm H$_2$O was maintained) had higher $P_{aO_2}$ levels than those treated with IPPV (airway pressure returned to ambient pressure at end-expiration). Cheney and Martin$^1$ found that in dogs with pulmonary edema, a tidal volume of 38 ml/kg was as effective in improving $P_{aO_2}$ and reducing shunt as CPPV at a tidal volume of 15 ml/kg with 10 cm H$_2$O end-expiratory pressure. A tidal volume of 38 ml/kg is not attainable with most ventilators available for clinical use in man. This study was done to see whether a tidal volume intermediate between 15 and 38 ml/kg would improve gas exchange in pulmonary edema to the same extent as CPPV at a $V_T$ of 15 ml/kg with 10 cm H$_2$O end-expiratory pressure.

Material and Methods

Thirteen healthy mongrel dogs (body weights 14 to 21 kg, mean 17 kg) were anesthetized with pentobarbital, 30 mg/kg iv, and paralyzed with 40 mg succinylcholine chloride. The trachea of each dog was intubated with a cuffed endotracheal tube. The dog was placed supine and connected to a volume-cycled piston respirator (Harvard Pump) that delivered 100 per cent oxygen at a tidal volume ($V_T$) of 15 ml/kg with an inspiratory:expiratory ratio of 1:1. Succinylcholine and pentobarbital were repeated as needed to maintain paralysis and anesthesia.

Catheters were passed into the aorta via the femoral artery and into the pulmonary artery or right ventricle via the right jugular vein. Appropriate electronic equipment was used to monitor pulmonary arterial or right ventricular pressure, aortic pressure, ECG, and peak airway pressure. Mean airway pressure, obtained by electronic damping of the pressure wave, was recorded from a strain gauge. This

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gauge was connected to a needle placed in the proximal portion of the endotracheal tube. In five dogs mean intrapleural pressure was measured in the same manner from a mushroom catheter placed in the intrapleural space. Cardiac output (Q₄) was measured by the dye-dilution technique utilizing indocyanine green dye. Aortic and pulmonary arterial blood samples were analyzed for PaO₂, PaCO₂, and pH on an Instrumentation Laboratories 113 Blood Gas Analyzer with appropriate corrections for body temperature. PaO₂ values above 150 mm Hg were corrected for temperature with the nomogram of Hedley-Whyte. Oxygen saturation was calculated with the Severinghaus blood-gas calculator, and content was calculated from this plus the measured hemoglobin concentration.

Expired gas volumes were measured in a Collins 9-liter spirometer. The ratio of shunt flow (Qₛ) to cardiac output (Q₄/Qₛ) was determined with values of arterial and venous oxygen content used in the standard mixing equation.

The dogs were ventilated with 100 per cent oxygen throughout the experiment, which lasted three to six hours. Measurements of all variables were made at the end of 20-minute intervals at each of the following patterns of ventilation:

1) IPPV-15: intermittent positive-pressure ventilation, Vₜ = 15 ml/kg.
2) IPPV-24: Vₜ = 24 ml/kg. This tidal volume was calculated by adding the volume (using a 1-liter graduated syringe) needed for static inflation of the dog lung to 10 cm H₂O to the standard 15 ml/kg tidal volume used during IPPV. This Vₜ would then inflate the lungs to the same end-inspiratory volume as during CPPV.
3) IPPV-43: Vₜ = 43 ml/kg. This large tidal volume was achieved by using the maximum volume that could be delivered by the ventilator (730 ml, or a mean of 43 ml/kg).
4) CPPV: Continuous positive-pressure ventilation, Vₜ = 15 ml/kg, with an end-expiratory pressure of 10 cm H₂O. A screw clamp was applied to the expiratory limb of the ventilator tubing until an end-expiratory pressure of 10 cm H₂O was reached. The pressure patterns are illustrated in figure 1.

After measurements of all variables were made (table 1), hemorrhagic pulmonary edema was induced with oleic acid, 0.25 ml/kg injected over a 5-minute period into the right ventricle or pulmonary artery. A saline infusion of 250 ml/hour was maintained during the course of the experiment as partial com-
pensation for fluid loss into the lungs during pulmonary edema.

Following induction of pulmonary edema, the dogs were ventilated initially and terminally with IPPV-15. The sequence of CPPV, IPPV-24, and IPPV-13 was varied randomly in the different dogs but was the same before as after pulmonary edema. Randomization was necessary because of the progressive deterioration of cardiorespiratory function after injection of oleic acid.¹

Respiratory rate was maintained at 15 breaths/min during ventilation of the normal lung. Before pulmonary edema was induced, carbon dioxide was added to the inspired mixture as necessary during IPPV-43 and IPPV-24 to maintain PaCO₂ constant. Carbon dioxide was not added to the inspired mixture after the onset of pulmonary edema. During the final IPPV run during pulmonary edema, the respiratory rate was increased to 19/min because of increasing PaCO₂.

Statistical analysis was carried out with Student's t test for paired data.

**Results**

The results prior to pulmonary edema are summarized in table 1. CPPV decreased cardiac output, while shunt improved compared with the other patterns of ventilation. Systemic blood pressure was essentially constant during each pattern of ventilation prior to induction of pulmonary edema, except for a significant decrease in systolic pressure (P < 0.05) during CPPV compared with IPPV-15.

During pulmonary edema the cardiopulmonary status progressively deteriorated with time. Therefore, we have averaged the initial IPPV-15 and final IPPV-15 values to give a mean value for IPPV-15 (IPPV-15). This deterioration is exemplified by the decrease of mean PaO₂ and mean SaO₂ during IPPV-15 from 62 mm Hg and 70 per cent initially to 29 mm Hg and 40 per cent during the final IPPV-15 run. The apparent discrepancies in arterial oxygen saturation and PaO₂ values seen in table 2 for IPPV-15 and IPPV-24 are due to the shape of the dissociation curve and the averaging of initial and terminal IPPV-15 values.

### Table 1. Mean Values ± 1 SD for 13 Normal Dogs before Pulmonary Edema

<table>
<thead>
<tr>
<th>IPPV-15</th>
<th>IPPV-24</th>
<th>IPPV-43</th>
<th>IPPV-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Arterial Pressure (mm Hg)</td>
<td>72.8 ± 3.0</td>
<td>73.4 ± 3.2</td>
<td>74.2 ± 3.4</td>
</tr>
<tr>
<td>Heart Rate (beats/min)</td>
<td>101 ± 10.9</td>
<td>103 ± 10.9</td>
<td>105 ± 10.9</td>
</tr>
<tr>
<td>Base Excess (mEq/L)</td>
<td>1.4 ± 0.6</td>
<td>1.6 ± 0.7</td>
<td>1.2 ± 0.5</td>
</tr>
<tr>
<td>pH</td>
<td>7.40 ± 0.02</td>
<td>7.39 ± 0.03</td>
<td>7.38 ± 0.02</td>
</tr>
</tbody>
</table>

### Table 2. Mean Values ± 1 SD for Dogs during Pulmonary Edema

<table>
<thead>
<tr>
<th>IPPV-15</th>
<th>IPPV-24</th>
<th>IPPV-43</th>
<th>IPPV-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Arterial Pressure (cm Hg)</td>
<td>50.1 ± 10.3</td>
<td>51.4 ± 10.5</td>
<td>52.7 ± 10.8</td>
</tr>
<tr>
<td>Arterial Oxygen Saturation (%)</td>
<td>84.8 ± 3.4</td>
<td>83.2 ± 3.5</td>
<td>82.6 ± 3.6</td>
</tr>
<tr>
<td>Mean Lung Water (ml/kg)</td>
<td>7.2 ± 1.4</td>
<td>8.4 ± 1.6</td>
<td>9.6 ± 1.8</td>
</tr>
<tr>
<td>Cardiac Output (l/min)</td>
<td>2.6 ± 0.6</td>
<td>2.8 ± 0.7</td>
<td>3.0 ± 0.8</td>
</tr>
</tbody>
</table>

* P < 0.05 compared with IPPV-15. ** P < 0.05 compared with IPPV-24.

¹. IPPV represents the mean of IPPV-15 and IPPV-24 after injection of oleic acid.
TABLE 3. Mean Intrapleural Pressure as
Measured in Five Dogs

<table>
<thead>
<tr>
<th></th>
<th>Control (mm Hg)</th>
<th>Pulmonary Edema (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPPV-15</td>
<td>-4 ± 1</td>
<td>-4.4 ± 1</td>
</tr>
<tr>
<td>IPPV-24</td>
<td>-3 ± 1</td>
<td>-4 ± 1</td>
</tr>
<tr>
<td>IPPV-43</td>
<td>-2 ± 1.2</td>
<td>-2.4 ± 1.5</td>
</tr>
<tr>
<td>CPPV</td>
<td>+0.7 ± 1.35</td>
<td>+0.3 ± 1.65</td>
</tr>
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</table>

With pulmonary edema, cardiac output decreased to less than half that obtained in the control runs. IPPV-43 and CPPV depressed cardiac output, but both improved Qt/Qt and PaO₂ compared with IPPV-15. On the other hand, IPPV-24 also reduced Qt to significantly below IPPV-15, while failing to improve Qt/Qt or PaO₂. The impact of reduction in cardiac output without improvement in PaO₂ with IPPV-24 compared with IPPV-43 and CPPV is illustrated by the SVO₂ of 25 per cent, which is significantly less than the SVO₂'s for the other two patterns. There were no significant changes in blood pressure with any of the patterns of ventilation, except for a significantly lower diastolic pressure with IPPV-43 compared with IPPV-15.

The mean intrapleural pressures recorded in five dogs are shown in table 3. The mean intrapleural pressure after induction of pulmonary edema remained the same as before in each ventilatory pattern.

Mean Hb, which was 14 g/100 ml ± 2 during ventilation of the normal lung, rose to 19 g/100 ml ± 2 during pulmonary edema.

Discussion

The results in the normal anesthetized dog indicate that IPPV with a VT of 15 ml/kg is about as effective as CPPV or higher tidal volumes in maintaining PaO₂ during continuous mechanical ventilation (table 1). There was a significant reduction in Qt/Qt during CPPV compared with the other patterns, but there was no change in PaO₂. The failure of PaO₂ to increase with a decrease in shunt was the result of the reduction in cardiac output with CPPV. This decline in cardiac output was reflected in decreased venous oxygen saturation.

Oleic acid, used to induce pulmonary edema, is a free fatty acid which produces in the dog a clinical and pathologic syndrome similar to the respiratory distress syndrome seen in many following fatty embolism, shock, or trauma to the chest. Pathologic studies have shown that oleic acid injures the alveolar-capillary membrane and leads to edema, congestion, hemorrhage and atelectasis. This sequence of events results in hypoxia owing to shunting of blood past collapsed alveoli. In this respect, also, the oleic-acid model of respiratory failure in the dog resembles the adult respiratory distress syndrome in man.

This study was done with the expectation that during pulmonary edema the higher end-inspiratory lung volume engendered by the tidal volume of 24 ml/kg would improve oxygenation over that seen at a VT of 15 ml/kg. Because calculated end-inspiratory lung volumes were the same with IPPV-24 and CPPV, we expected that the effects of the two patterns of ventilation on gas exchange during pulmonary edema would be similar. Oxygenation with CPPV, however, was far superior (mean PaO₂ = 233 mm Hg ± 187) to that with IPPV-24 (mean PaO₂ = 43 mm Hg ± 11). In fact, compared with IPPV-15, IPPV-24 failed to improve oxygenation and reduce shunt. Although end-inspiratory lung volumes were the same with IPPV-24 and CPPV, with IPPV-24 unstable alveoli must have collapsed during exhalation to ambient pressure. The 10-cm H₂O end-expiratory pressure with CPPV kept these unstable alveoli open at end-expiration, thereby allowing oxygenation of the pulmonary capillary blood. The better oxygenation with IPPV-43 may have resulted from the high tidal volume's inflating of a large number of unstable alveoli, which did not have time to collapse during exhalation to atmospheric pressure. In any event, the results clearly indicate that there is no advantage to increasing tidal volume from 15 to 24 ml/kg for ventilation of the edematous lung.

The significant decrease in cardiac output seen during pulmonary edema may have been due to the oleic acid as well as to hypovolemia. Decreased cardiac outputs have been found in spontaneously-breathing dogs after smaller doses of oleic acid. Although the fluid lost from the circulation into the interstitial areas of the lung and the airways undoubtedly contained colloid, the saline infusion of 250
ml/hour would have partially compensated for this loss. The increased viscosity occurring with the increase in Hb from 14 to 19 g/100 ml would also depress cardiac output.14 Dogs are known to have marked splenic contraction with significant increases in Hb following sympathetic stimulation.15 The hypoxia and hypercarbia observed after onset of pulmonary edema would be an ample source of this sympathetic discharge. Although airway pressures necessary to deliver the same tidal volumes were higher during pulmonary edema, the mean intrapleural pressures before and after injection of oleic acid were about the same during each pattern of ventilation (table 3). Therefore, impedances to venous return were the same during ventilation of normal and edematous lungs.

Although cardiac output decreased during IPPV-43 and CPPV, tissue oxygenation was better than during the other two patterns of ventilation, as reflected in the markedly improved $S\text{O}_2$ (table 2). A decrease in cardiac output in the face of constant oxygen consumption would be expected to decrease $S\text{O}_2$. However, the marked increases in arterial oxygenation brought about by both IPPV-43 and CPPV not only overcame the effect of the decreased cardiac output on $S\text{O}_2$, but caused significant increases in $S\text{O}_2$.

These observations may be important in the treatment of patients with the adult respiratory distress syndrome characterized by low compliance, alveolar collapse, and shunt. The results suggest that moderate increases in tidal volume in a patient who needs continuous mechanical ventilation not only may fail to improve $Pao_2$, but may actually impair tissue oxygenation by decreasing cardiac output. The most efficient ventilatory pattern for clinical use during pulmonary edema or adult respiratory distress syndrome seems to be continuous positive pressure, and this may be essential for adequate oxygenation even with the use of 100 per cent oxygen. CPPV also allows a higher $Pao_2$ with the use of a lower percentage of inspired oxygen than is possible with IPPV, thus reducing the possibility of oxygen toxicity. Whether the tidal volume of 43 ml/kg used in this study may have clinical value would be difficult to ascertain, because such volumes cannot be achieved in most adults with the ventilators presently in clinical use.

References