Lung Water Increases with Fluid Administration during CPPV after Pulmonary Microembolization

William H. Noble, M.D., F.R.C.P.(C),* and J. Colin Kay, A.I.M.L.T.†

Hypoxemia created by pulmonary microemboli is improved by continuous positive-pressure ventilation (CPPV) but at a cost of reducing cardiac output (Q). In this high pulmonary vascular resistance (PVR), pulmonary edema setting, the authors attempted to increase the Q, which had been reduced by CPPV, with an infusion of dextran. In 14 dogs, 0.125 g/kg of starch microemboli (63–74 μm in diameter) were infused. CPPV at 15 cm H2O then was applied and PaO2 increased from 53 ± 4 to 69 ± 3 mmHg, but Q decreased from 2.9 ± 0.2 to 1.7 ± 0.2 l/min. Seven of these dogs (control group) were monitored for 3 h. In the remaining seven dogs (volume group), dextran 40 was infused until Q returned to pre-CPPV values, and monitoring was continued for 3 h. With return of Q to pre-CPPV levels, indices of tissue oxygenation (O2 transport, PVO2, O2 consumption and metabolic acidosis) were significantly improved. However lung water was increased significantly by the volume infusion, so that at 3 h lung water in the volume group was double the value in the control group. The authors conclude that volume infusion in the face of a high PVR may correct the reduced Q of CPPV and improve tissue oxygenation, but it also may increase pulmonary edema. (Key words: Fluid balance. Heart: cardiac output. Lung: edema; microemboli. Ventilation: continuous positive pressure.)

The adult respiratory distress syndrome (ARDS) is associated with an increase in pulmonary vascular resistance (PVR), pulmonary edema, and arterial hypoxemia. Pulmonary microemboli can create an increased PVR, pulmonary edema, and arterial hypoxemia1 and have been suggested as a cause of ARDS.2 Continuous positive-pressure ventilation (CPPV) is being used to improve the arterial hypoxemia of ARDS, however, we found that CPPV after pulmonary microemboli in dogs improves arterial oxygenation but reduces cardiac output (Q) (unpublished data). The combination of an improved PaO2 and reduced Q resulted in decreased O2 transport to and O2 consumption of tissues and a developing metabolic acidosis. These observations are interesting because they indicate the possibility that patients with a high PVR (ARDS) who require ventilation with high levels of CPPV to improve arterial oxygenation may be improved additionally by increasing cardiac output and therefore oxygen transport and consumption.

It is important to determine whether, in a high PVR setting and with pulmonary edema present (i.e. ARDS), Q can be improved after CPPV by infusing fluid volume intravenously and whether there are any deleterious effects of this increased intravascular volume. The purpose of this study was to determine the effect of infusing intravenous fluid on gas exchange and hemodynamics after the hypoxemia of pulmonary microembolization had been treated with CPPV in dogs.

Methods

Animal Preparation and Measurements

Fourteen mongrel dogs weighing between 16 and 36 kg were studied. Anaesthesia was induced with pentobarbital 30 mg/kg iv and maintained with additional boluses of 50 mg as required. The animals breathed or were ventilated with air throughout the experiment.

The femoral artery and pulmonary artery were catheterized in order to monitor pressure continuously. The left atrium was catheterized from the internal carotid artery to monitor pressure.3 Mean pressures were taken

---

* Professor, Anaesthetist-in-Chief.
† Chief Technician.

Received from the Department of Anaesthesia, St. Michael's Hospital, Toronto, Canada. Accepted for publication May 24, 1984. Funding was provided by the Medical Research Council of Canada. Address reprint requests to Dr. Noble: Department of Anesthesiology, University of Toronto, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario, M5B 1W8, Canada.

---

Abbreviations

- BF = mean arterial blood pressure (mmHg)
- PPA = mean pulmonary artery pressure (mmHg)
- PLA = mean left atrial pressure (mmHg)
- Pmv = pulmonary microvascular pressure (mmHg)
- PVR = pulmonary vascular resistance
- Q = cardiac output (l/min)
- CBV = central blood volume (ml/kg)
- PaO2 = arterial partial pressure of oxygen (mmHg)
- PaCO2 = arterial partial pressure of carbon dioxide (mmHg)
- pH = arterial pH
- PVo2 = mixed venous partial pressure of oxygen (mmHg)
- CaO2 = arterial oxygen content (ml/dl)
- CVO2 = mixed venous oxygen content (ml/dl)
- Qs/Qt = shunt fraction
- VD/Vt = dead space to tidal volume ratio
- O2 CONS = oxygen consumption (ml/min)
- O2 TRANSP = oxygen transport (ml/min)
- O2 ETRV = extravascular thermal volume of lung (l lung water)
- PETW = pulmonary extravascular tissue weight
The animals then were divided into two groups:

1. Control—In seven dogs, while CPPV was applied, measurements were repeated every 30 min for 3 h.

2. Volume—In seven dogs, while CPPV was applied, 10% dextan 40 in normal saline (Rheomacrodex®) was infused until Q was returned to the "embolus value." The volume of dextan infused was 464 ± 24 ml. Measurements were repeated every 30 min for 3 h while CPPV was continued.

At the end of the experiment, the animals were killed with an intravenous injection of KCl and the lungs excised. The extravascular lung water was determined using a gravimetric method to measure pulmonary extravascular tissue weight (PETW). This technique utilizes Hb to determine residual lung blood volume, which is subtracted from total lung weight.

Statistical analysis of the results was carried out using a two-way analysis of variance. Dunnett's and Tukey's test were used for multiple comparisons between means. Comparisons between groups were made using an unpaired t test. P < 0.05 was considered significant. Only significant changes will be discussed. Data are reported as mean ± SEM.

### Results

There were no significant differences between the two groups up to the time dextan 40 was infused. Thirty minutes after emboli, P_{TP} increased from 17 ± 1 to 33 ± 2 mm Hg (P < 0.001); P_{AV} decreased from 82 ± 2 to 53 ± 4 mm Hg (P < 0.001); Q_s/Q increased from 15 ± 2 to 41 ± 4% (P < 0.001); and Q decreased from 3.4 to 0.2 to 2.0 ± 0.2 l/min (P < 0.025). There was a small but significant increase in lung water from
**EFFECT OF FLUID INFUSION DURING CPPV**

### Table 2. Volume Group of Dogs

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Pulmonary Embolism</th>
<th>CPPV</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{ET}$ (mmHg)</td>
<td>17 ± 2</td>
<td>31 ± 3*</td>
<td>34 ± 2</td>
<td>41 ± 3*</td>
<td>41 ± 3</td>
</tr>
<tr>
<td>$P_{TX}$ (mmHg)</td>
<td>5 ± 1</td>
<td>5 ± 1</td>
<td>9 ± 2*</td>
<td>14 ± 1†</td>
<td>13 ± 2†</td>
</tr>
<tr>
<td>$P_{MV}$ (mmHg)</td>
<td>10 ± 1</td>
<td>14 ± 2*</td>
<td>19 ± 2*</td>
<td>25 ± 1†</td>
<td>24 ± 1†</td>
</tr>
<tr>
<td>$B_{F}$ (mmHg)</td>
<td>160 ± 4</td>
<td>138 ± 6*</td>
<td>124 ± 6</td>
<td>144 ± 9</td>
<td>160 ± 3†</td>
</tr>
<tr>
<td>$C_{BV}$ (ml/kg)</td>
<td>18 ± 2</td>
<td>14 ± 1*</td>
<td>13 ± 2</td>
<td>17 ± 2*†</td>
<td>15 ± 2†</td>
</tr>
<tr>
<td>$P_{AO}_{2}$ (mmHg)</td>
<td>82 ± 4</td>
<td>54 ± 5*</td>
<td>71 ± 2*</td>
<td>80 ± 2</td>
<td>72 ± 5</td>
</tr>
<tr>
<td>$P_{A}_{2}$ (mmHg)</td>
<td>41 ± 3</td>
<td>38 ± 3</td>
<td>38 ± 1</td>
<td>38 ± 1</td>
<td>37 ± 1</td>
</tr>
<tr>
<td>$p_H$</td>
<td>7.34 ± 0.02</td>
<td>7.36 ± 0.04</td>
<td>7.31 ± 0.01</td>
<td>7.32 ± 0.01†</td>
<td>7.32 ± 0.02†</td>
</tr>
<tr>
<td>$BE$ (mEq/l)</td>
<td>−4 ± 1</td>
<td>−4 ± 1</td>
<td>−7 ± 1*</td>
<td>−6 ± 1†</td>
<td>−6 ± 1†</td>
</tr>
<tr>
<td>$C_{AO}_{2}$ (ml/dl)</td>
<td>17 ± 1</td>
<td>17 ± 1</td>
<td>19 ± 1</td>
<td>14 ± 1**</td>
<td>14 ± 1†</td>
</tr>
<tr>
<td>$P_{AO}_{2}$ (mmHg)</td>
<td>53 ± 3</td>
<td>36 ± 3*</td>
<td>39 ± 1</td>
<td>46 ± 1**</td>
<td>38 ± 1*</td>
</tr>
<tr>
<td>$C_{PO}_{2}$ (ml/dl)</td>
<td>15 ± 1</td>
<td>13 ± 1</td>
<td>14 ± 1</td>
<td>11 ± 1*</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>$Q_{S}$/Q_{L} (%)</td>
<td>16 ± 3</td>
<td>39 ± 6*</td>
<td>16 ± 2*</td>
<td>15 ± 2</td>
<td>17 ± 4</td>
</tr>
<tr>
<td>$V_{D}$/V_{T} (%)</td>
<td>38 ± 2</td>
<td>62 ± 5*</td>
<td>64 ± 3</td>
<td>58 ± 3</td>
<td>57 ± 4</td>
</tr>
<tr>
<td>$H_{b}$ (g/dl)</td>
<td>13.5 ± 0.6</td>
<td>15.1 ± 0.6*</td>
<td>15.3 ± 0.8</td>
<td>10.9 ± 0.6*†</td>
<td>11.6 ± 0.6†</td>
</tr>
<tr>
<td>$O_{2}$ CONS (ml/min)</td>
<td>127 ± 11</td>
<td>119 ± 11</td>
<td>104 ± 18*</td>
<td>129 ± 12*†</td>
<td>123 ± 14</td>
</tr>
<tr>
<td>$O_{2}$ EXTR (%)</td>
<td>21 ± 2</td>
<td>26 ± 4</td>
<td>34 ± 4*</td>
<td>31 ± 4</td>
<td>36 ± 3</td>
</tr>
</tbody>
</table>

* Significantly different from preceding value (analysis of variance). † Significantly different from control dogs at the same time (unpaired t test).

13.2 ± 3.7 to 16.2 ± 5.1 ml/kg. CPPV at 15 cmH$_2$O after emboli increased Pa$_{O_2}$ from 55 ± 4 to 69 ± 3 mmHg ($P < 0.001$) and reduced Q$_S$/Q$_L$ from 41.4 to $16.2\%$ ($P < 0.001$); but because Q was reduced from $2.9 \pm 0.2$ to $1.7 \pm 0.2$ l/min ($P < 0.001$), O$_2$ transport decreased from $447 \pm 37$ to $310 \pm 35$ ml/min ($P < 0.001$). Other significant changes created by pulmonary emboli and then CPPV 15 cmH$_2$O are reported in tables 1 and 2.

The infusion of dextran 40 immediately increased CBV and $P_{TX}$ (table 2). Dextran restored and maintained Q at the pre-CPPV value (fig. 1). Q was significantly greater after the volume infusion than in the control group. Hb was diluted by dextran 40, and arterial O$_2$ content (Ca$_{O_2}$) was reduced (tables 1 and 2). O$_2$ transport, P$_{O_2}$, and O$_2$ consumption were increased in the volume group. Base excess was less negative and pH less acidic in the volume group (tables 1 and 2).

Lung water (ETV$_L$) was increased significantly immediately by the volume infusion and continued to increase over the remaining hours. By the last determination ETV$_L$ in the volume group was double the value in the control dogs (fig. 2). The ratio of ETV$_L$/PETW was not significantly different between the two groups of dogs. It is greater than one because of thermal equilibrium with airways, pulmonary arteries and veins, the left heart, and a small portion of the inner chest wall, which are not measured by the PETW technique.

**Discussion**

Our results indicate the following: 1) CPPV improves Pa$_{O_2}$ and Q$_S$/Q$_L$, after pulmonary microemboli; 2) CPPV reduces Q in this high PVR setting; 3) the resultant effect of CPPV after pulmonary emboli is to reduce indices of tissue oxygenation (decreased O$_2$ transport and consumption, worsening metabolic acidosis).

![Fig. 1. Cardiac output and oxygen transport in the volume and control groups during the control period (CONT), after emboli (EMB), once CPPV was applied (CPPV), 30 min after treatment was applied (EARLY), and 3 h later (LATE). * indicates a significant difference from the preceding value. † indicates a significant difference from the control group.](image-url)

Downloaded from anesthesiology.pubs.asahq.org by guest on 04/14/2019
controversy over accurate measurement of transmural cardiac pressures during CPPV. In view of this controversy we have not attempted to investigate the cause of the decreased \( \dot{Q} \) after CPPV in this high PVR setting. We have, instead, attempted to return \( \dot{Q} \) to pre-CPPV levels by infusing fluid volume and measured hemodynamic and gas exchange effects of this fluid volume intervention. We were successful in returning \( \dot{Q} \) to pre-CPPV levels (fig. 1) when CBV was returned to control levels and \( P_{\text{LX}} \) was increased by infusing dextran. This is supportive of the large number of studies suggesting CPPV reduces \( \dot{Q} \) by decreasing left ventricular preload. There was a small increase in \( P_{\text{FR}} \); 34 ± 2 to 41 ± 3 mmHg (\( P < 0.025 \)), \( P_{\text{LX}} \) 9 ± 2 to 14 ± 1 mmHg (\( P < 0.05 \)), and \( P_{\text{MV}} \) 19 ± 2 to 25 ± 1 mmHg (\( P < 0.025 \)) (table 2). Hb was diluted by the dextran 40 infused in the volume group, and this reduced \( C_aO_2 \) in these dogs. In spite of this the improved \( \dot{Q} \) in the volume group, increased \( O_2 \) transport (fig. 1), \( O_2 \) consumption, and \( P_{\text{O_2}} \) and reduced the metabolic acidosis (table 2), which was developing in the control dogs (table 1). These criteria of tissue oxygenation indicate the volume-induced increase in \( \dot{Q} \) was beneficial after CPPV and pulmonary microemboli.

However, the volume group of dogs also demonstrated a large increase in lung water (ETV\(_L\)) of 13 ± 2 to 29 ± 5 ml/kg (\( P < 0.001 \)), which was not found in the control group of dogs (ETV\(_L\) 13 ± 1 to 17 ± 2 ml/kg; NS [fig. 2]). It is conceivable that the control group of dogs had lung areas unperfused because of the microemboli and that these lung areas would not be measured by ETV\(_L\). If this were so, ETV\(_L\)/PETW should be reduced in the control group. There was no significant difference between ETV\(_L\)/PETW in the volume and control dogs (fig. 3). Thus, by both measurement techniques (ETV\(_L\) and PETW) we measured a real increase in lung water in the dogs given volume to correct the CPPV reduced \( \dot{Q} \). The cause of the increased lung water in the volume group of dogs must remain conjectural but may relate to higher pulmonary microvascular pressures in these dogs (\( P_{\text{MV}} \) increased from 19 ± 1 to 25 ± 1 mmHg, \( P < 0.025 \), with the infusion of volume). Pulmonary vascular pressures (measured without pleural pressure correction) were increased by the application of CPPV at 15 cmH\(_2\)O (tables 1 and 2), suggesting that transmural pressures were not as high as the absolute pressure would indicate. The volume infusion did not create large increases in pulmonary microvascular pressures (6 mmHg), but in the face of a lung lesion created by pulmonary microemboli (or ARDS in patients) any increase in pulmonary microvascular pressure may produce pulmonary edema. There are suggestions that changes in lung water become more sensitive to even small intravascular pressure changes when capillary per-
meability is increased.24,25 This strongly suggests that the small increase in $P_{\text{ET}}$ (5 mmHg) created by infusing the volume necessary to restore $Q$ resulted in a dramatic increase in lung water.

The fact that lung water increased with the infusion of fluid volume supports previous evidence26,27 that CPPV does not reduce lung water. CPPV does improve $P_{\text{A}}$ and reduces $Q_s/Q_t$ in the face of large increases in lung water.26,27 This presumably accounts for the fact that $P_{\text{A}}$ and $Q_s/Q_t$ remained at control levels after CPPV was applied, even in the volume group of dogs when lung water was increased to alveolar edema levels28 (tables 1 and 2). We would expect (but did not measure) a reduced $P_{\text{A}}$ if CPPV were discontinued in the face of alveolar edema in the volume group of dogs.

The improved cardiac output and indices of tissue oxygenation are certainly desired effects of volume infusion (in a high PVR, pulmonary edema setting). However, they are obtained at a cost of more pulmonary edema. The clinical alternatives available when faced with high PVR, high CPPV, and low $Q$ settings appear to be to reduce CPPV, infuse smaller volumes, and accept smaller increases in $Q$, or improve $Q$ with other techniques than volume infusion or combinations of these. It remains to be seen whether other techniques to improve $Q$ after CPPV, in high PVR settings, can be successful without increasing lung water, e.g., increasing myocardial contractility or decreasing left ventricular afterload.

The authors thank Gary Caskenette and E. Hobbs for their technical assistance and P. Slusarenko for preparing the manuscript.

References


