CONTROL OF INTERMITTENT POSITIVE PRESSURE BREATHING (IPPB) BY EXTRACORPOREAL REMOVAL OF CARBON DIOXIDE

L. GATTINONI, T. KOLOBOW, T. TOMLINSON, D. WHITE AND J. PIERCE

SUMMARY

Five lambs were anaesthetized, paralysed, mechanically ventilated and connected to a membrane “lung” to permit removal of carbon dioxide. When part of the carbon dioxide was removed in this manner, the tidal volume was decreased to keep $P_{acO_2}$ constant. For example, when 70% of carbon dioxide was removed by the membrane lung, total ventilation was reduced by 50%, peak inspiratory pressure was decreased by 45%, and $P_{ao_2}$ was kept constant by increasing the inspired oxygen fraction from 0.21 to 0.27%. The removal of carbon dioxide by a membrane during positive pressure breathing could decrease barotrauma, particularly in poorly compliant lungs. Technically, the extracorporeal removal of carbon dioxide is a relatively simple procedure.

Pulmonary barotrauma may be caused by positive pressure breathing, particularly in poorly compliant lungs. We have shown recently that the rate and tidal volume ($VT$) of the spontaneously breathing lamb is decreased markedly when carbon dioxide is removed from blood by an extracorporeal membrane lung (Kolobow et al., 1977). These results suggest that the volume administered by controlled mechanical ventilation can be decreased similarly and the incidence of barotrauma decreased. For example, if 50% of the carbon dioxide produced were removed by an extracorporeal membrane lung, the alveolar ventilation ($VA$) required for carbon dioxide homeostasis can be decreased by the same fraction.

This study was undertaken in artificially ventilated lambs to show that minute ventilation and airway pressure can be decreased substantially when carbon dioxide is removed by an extracorporeal membrane lung, and basal arterial blood-gas tensions maintained.

METHODS

Five lambs weighing between 11 and 14.5 kg and in which tracheotomy had been performed were anaesthetized with pentobarbitone and paralysed with tubocurarine.

Ventilation was controlled by a modified piston Harvard Ventilator to give a constant inspiratory time of 0.8 s. Expiration was passive to atmosphere. The expired pulmonary gas was collected into a recording spirometer and expired and inspired gases were analysed by a respiratory mass spectrometer (Med. Spect. MMS-8, Scientific Research Instrument Corp., Baltimore). The pressure in the tracheostomy tube (tracheal pressure) was measured using a Statham transducer and recorded. Arterial blood from the subclavian artery was passed through a 1.6-m² silica filler free silicone rubber spiral coiled membrane lung specially designed for the removal of carbon dioxide (CDML) and returned to the external jugular vein at flow rates ranging from 100 to 800 ml min⁻¹. The priming solution was heparinized lactated Ringer’s solution (8 u. ml⁻¹). Continuous anticoagulation was maintained by infusing heparin at 100 u. kg⁻¹ h⁻¹. Arterial blood-gas tensions in the extracorporeal circuit were monitored continuously in line with a second Medical Mass Spectrometer. Arterial blood oxygen saturation before and after the CDML was monitored also with an in-line oximeter (Vurek et al., 1973). Humidified room air (37 °C) was passed through the CDML. The gas compartment was maintained at subatmospheric pressure (40 kPa below atmosphere) and the gas flow was measured by calibrated flowmeters. The gas flow through the CDML ranged between 200 and 4500 ml min⁻¹. The removal of carbon dioxide through the CDML was computed from the gas flow and carbon dioxide concentration of effluent gas, measured by an infra-red carbon dioxide analyser (Beckman Model 315A).

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Blood samples were obtained before and after the CDML and from a Swan–Ganz catheter positioned in the main pulmonary artery (fig. 1). Blood pH, \( P_{O_2} \) and \( P_{CO_2} \) were measured by a Radiometer gas analyser (Mod. PHM 27, Copenhagen, Denmark); the oxygen saturation of haemoglobin was measured using an American Optical Oximeter (10800, Buffalo, N.Y., calibrated for sheep blood); and haemoglobin was measured by Drabkin’s method (Drabkin and Austin, 1932). Using standard equations, we computed total oxygen consumption (\( \dot{V}_{O_2} \)), total carbon dioxide production (\( \dot{V}_{CO_2} \)), respiratory quotient (RQ), CDML oxygen and carbon dioxide exchange, cardiac output (CO), tidal volume (\( V_t \)), respiratory frequency (\( f \)), deadspace fraction (\( \dot{V}_d/\dot{V}_t \)), total ventilation (\( \dot{V}_E \)) and alveolar ventilation (\( \dot{V}_A \)). The ventilatory volumes were expressed at BTPS, and the gas exchange at STPD.

The lambs were ventilated at \( f = 8, 16 \) and 24 b.p.m. with \( V_t \) chosen to give constant baseline \( P_{aCO_2} \) of \( 4.65 \pm 0.13 \) kPa when no carbon dioxide was removed through CDML (zero CDML gas flow). Baseline values were reached when \( P_{aCO_2} \) remained steady as determined by measurements 30 min apart. After baseline conditions had been met, a complete set of measurements was taken and extracorporeal carbon dioxide exchange was started by ventilating CDML with room air. Within \( 30-60 \) s \( P_{aCO_2} \) decreased by \( 0.13-0.26 \) kPa as monitored by the mass spectrometer. \( V_t \) was reduced (\( f \) constant) to return \( P_{aCO_2} \) to the baseline value of \( 4.65 \pm 0.13 \) kPa. The inspired oxygen fraction (\( F_{I_{O_2}} \)) was increased simultaneously to maintain constant baseline arterial blood oxygen saturation. A new set of measurements was taken when \( P_{aCO_2} \) and arterial blood oxygen saturation remained at baseline values (two measurements 30 min apart) with the new ventilator settings. These studies were repeated at the three \( f \) values with different amounts of carbon dioxide removal through CDML (by changing either the gas flow or the blood flow through the CDML).

RESULTS

\( \dot{V}_{O_2} \), \( \dot{V}_{CO_2} \) and CO did not change during the period of extracorporeal carbon dioxide removal when compared with the control period. Blood-gas tensions and alveolar–arterial \( P_{O_2} \) difference were virtually unchanged (table I). There was no change in arterial pH.
TABLE I. Oxygen consumption, total carbon dioxide production (carbon dioxide removed by the natural lung and carbon dioxide removed by CDML), arterial blood-gas tensions, arterial pH and alveolar-arterial oxygen tension gradient during control periods and during the extracorporeal removal of carbon dioxide. Mean values ± SD

<table>
<thead>
<tr>
<th></th>
<th>( V_O (\text{ml kg}^{-1}) )</th>
<th>( \dot{V}_{CO2} (\text{ml kg}^{-1}) )</th>
<th>( PA_O_2 (\text{kPa}) )</th>
<th>( PA_{CO2} (\text{kPa}) )</th>
<th>( pH_A )</th>
<th>( PA_{O2} - PA_{O2} )</th>
<th>( CO (\text{ml kg}^{-1}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4.23</td>
<td>3.06</td>
<td>9.96</td>
<td>4.66</td>
<td>7.30</td>
<td>4.75</td>
<td>203.9</td>
</tr>
<tr>
<td></td>
<td>± 0.86</td>
<td>± 0.35</td>
<td>± 1.26</td>
<td>± 0.13</td>
<td>± 0.077</td>
<td>± 2.79</td>
<td>± 98.5</td>
</tr>
<tr>
<td>Removal of carbon dioxide</td>
<td>4.00</td>
<td>3.30</td>
<td>10.43</td>
<td>4.66</td>
<td>7.29</td>
<td>6.78</td>
<td>239</td>
</tr>
<tr>
<td></td>
<td>± 0.62</td>
<td>± 0.40</td>
<td>± 0.97</td>
<td>± 0.13</td>
<td>± 0.083</td>
<td>± 4.52</td>
<td>± 99</td>
</tr>
</tbody>
</table>

TABLE II. Alveolar ventilation, total ventilation and deadspace fraction during the control periods at different respiratory frequencies. Mean values ± SD

<table>
<thead>
<tr>
<th></th>
<th>( f ) (b.p.m.)</th>
<th>8</th>
<th>16</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>( V_A ) (ml kg(^{-1}))</td>
<td>75.8</td>
<td>73.8</td>
<td>78.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 10.6</td>
<td>± 9.6</td>
<td>± 10.5</td>
<td></td>
</tr>
<tr>
<td>( V_E ) (ml kg(^{-1}))</td>
<td>154</td>
<td>161</td>
<td>188</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 29</td>
<td>± 23</td>
<td>± 34</td>
<td></td>
</tr>
<tr>
<td>( V_D/V_T )</td>
<td>0.49</td>
<td>0.55</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 0.08</td>
<td>± 0.07</td>
<td>± 0.04</td>
<td></td>
</tr>
</tbody>
</table>

FIG. 2. Total ventilation (\( \dot{V}_E \)) as a function of the removal of carbon dioxide through the carbon dioxide membrane lung (CDML) at different respiratory rates (\( f \)) and at constant \( PA_{CO2} \) of 4.66 kPa.

FIG. 3. Peak tracheal pressure as a function of total ventilation.

mean \( V_A \), \( \dot{V}_E \) and \( V_D/V_T \) during control periods as a function of \( f \). During the removal of carbon dioxide, and at constant \( \dot{V}_{CO2} \), \( PA_{CO2} \) and \( pH_A \), \( V_A \) (as per cent of control period) decreased linearly with the increase in the amount of carbon dioxide removed by the CDML. The per cent decrease in \( \dot{V}_E \) (fig. 2) was different at the three values of \( f \), because of the different \( V_D/V_T \) fraction. The airway pressure decreased with the reduction in \( \dot{V}_E \) (fig. 3). The measured \( F_{InO_2} \) required to maintain the saturation of the arterial blood haemoglobin between 90 and 94% during control periods and during the decrease in minute ventilation is shown as a function of RQ (\( \dot{V}_{CO2} \) natural lung/\( \dot{V}_{O2} \)) (fig. 4).

DISCUSSION

For the past 20 yr intermittent positive pressure ventilation has been used in the treatment of respiratory insufficiency. Most of the complications related...
to mechanical ventilator treatment are referred to as "barotrauma" (Kumar et al., 1973; Baeza et al., 1975) and are a result primarily of high peak inspiratory and end-inspiratory pressures when ventilating poorly compliant lungs which have a high airway resistance. The risks of barotrauma are increased with PEEP (Baeza et al., 1975) and haemodynamic impairment as a result of high airway pressures has been observed also (Horton and Cheney, 1975).

Appropriate ventilator settings are determined by the need to eliminate carbon dioxide while maintaining $P_{A\text{CO}_2}$ in the physiological range. We have shown previously that $P_{A\text{CO}_2}$ in awake, spontaneously-breathing lambs remained constant when some carbon dioxide was removed by an extracorporeal CDML. These lambs spontaneously decreased $V_T$ and $f$ to decrease alveolar ventilation. It is apparent that during controlled mechanical ventilation the $V_T$ and $f$ can be modified similarly if part of the carbon dioxide produced is eliminated by CDML. A decrease in $V_T$ in particular can assume practical significance during positive pressure breathing as it can decrease the airway pressure substantially. In preliminary studies in our laboratory, using animals undergoing mechanical ventilation of the lungs and with large pulmonary air leaks, it was possible to stop the air leak permanently when the airway pressure was decreased through a reduction of the $V_T$ and by removing carbon dioxide using CDML. This might also be the case in man.

However, a decrease in alveolar ventilation might impair blood oxygenation by decreasing $P_{A\text{O}_2}$ or by a change in venous admixture. Our experimental data show how $F_{I\text{O}_2}$ must be increased progressively to maintain $P_{A\text{O}_2}$ when the lung value decreases (as more carbon dioxide is removed by CDML) (fig. 4). These results might have been predicted from Riley's equation and are not surprising (Riley et al., 1946). For example, we find that alveolar ventilation can be decreased by 70% of control by a small increase of $F_{I\text{O}_2}$ from 0.21 to 0.27. This increase is not sufficient to cause pulmonary oxygen toxicity, nor will it lead to instability in lung units with a low $V_A/Q$ ratio (Dantzker, Wagner and West, 1975). Despite a decrease in $V_T$ we did not observe significant changes in the alveolar–arterial oxygen tension gradient. These findings are in agreement with Lunn, Mapleson and Chilcoat (1975) who found no change in venous admixture in dogs undergoing mechanical ventilation of the lungs at low $V_T$ and high $f$ with constant $P_{A\text{CO}_2}$. Moreover, it is known also that intermittent sigh can prevent collapse of lung tissue (Bendixen, Hedley-White and Laver, 1963). However, the decrease in pulmonary airway pressure was substantial, being as much as 40% of control.

We believe that the use of CDML during mechanical pulmonary ventilation might decrease or reverse barotrauma without affecting the oxygenation, at a cost of only a marginal increase in $F_{I\text{O}_2}$.

The blood flows required to accomplish carbon dioxide removal (500–1000 ml min$^{-1}$) are between those required for conventional haemodialysis for renal failure (250 ml min$^{-1}$) at the lower end and the higher blood flow required during open heart surgery or extracorporeal respiratory assistance using the membrane lung (3000–5000 ml min$^{-1}$). It appears that the blood required for the removal of carbon dioxide could be obtained through an AV fistula as in haemodialysis. CDML, with its high efficiency of carbon dioxide removal, could be used without blood pumping and might be satisfactory with access to the circulation similar to that used in chronic haemodialysis. Only room air is needed to "ventilate" CDML.

In our opinion, the complexity of the extracorporeal removal of carbon dioxide lies between that of renal haemodialysis and that of extracorporeal oxygenation during open heart surgery or long-term respiratory support with the membrane lung (table III). We
believe that the use of CDML may allow more acceptable ventilator settings in especially difficult clinical situations in man.

REFERENCES


CONTROLE DE LA RESPIRATION SOUS PRESSION POSITIVE INTERMITTENTE (IPPB) PAR L'EXTRACTION EXTRACORPORELLE DU GAZ CARBONIQUE

On a anesthesié, paralysé et ventilé mécaniquement cinq agneaux, puis on les a reliés à une “membrane tenant lieu de poumon” afin de pouvoir extraire le gaz carbonique. Après avoir enlevé de cette manière une partie du gaz carbonique, le volume courant a été diminué de façon à maintenir constant le Pao2. Ainsi après que la “membrane poumon” ait retiré 70% du gaz carbonique, la ventilation totale a été réduite de 50%, la pression inspiratoire de pointe diminuée de 45% et le Pao2 maintenu constant en augmentant la fraction d’oxygène inspirée de 0,21 à 0,27%. L’extraction de gaz carbonique par une “membrane” pendant la respiration sous pression positive pourrait faire diminuer les barotraumatismes, surtout lorsque les poumons ont une mauvaise compliance. Du point de vue technique, l’extraction extracorporelle de gaz carbonique est un procédé relativement simple.

KONTROLLE INTERMITTIERENDER POSITIVER DRUCK-ATMUNG (IPPB) DURCH ENTFERNUNG DES KOHLENDIOXYD VON AUSSEN HER

Fünf Lämmer wurden narkotisiert, paralysiert, mechanisch belüftet und zwecks Entfernung von Kohlendioxid an eine “Membranenlunge” angeschlossen. Nach Entfernung eines Teils des Kohlendioxys wurde die Methämoglobinämie konstant erhalten. Waren also z.B. 70% des Kohlendioxys mittels der Membranenlunge entfernt worden, so wurde die Gesamtblutung um 50% verringert, der Einatmungs-Spitzen- druck wurde um 45% gesenkt, und Pao2 wurde konstant gehalten, indem der eingeatmete Sauerstoff von 0,21 auf 0,27% erhöht wurde. Die Entfernung von Kohlendioxid durch eine Membran während positiver Druckatmung könnte das Barotrauma verringern, besonders in wenig
nachgiebigen Lungen. Rein technisch ist diese Methode der Entfernung von Kohlendioxid ein relativ einfacher Vorgang.

CONTROL DE LA RESPIRACION DE PRESION POSITIVA INTERMITENTE (IPPB) MEDIANTE LA REMOCION EXTRACORPOREA DEL DIOXIDO DE CARBONO

SUMARIO
Se anestesió, paralizó y ventiló mecánicamente a cinco corderos conectados a un “pulmón” de membrana para permitir la remoción del dióxido de carbono. Al extraerse parte del dióxido de carbono de esta forma, el volumen marea disminuyó para mantener constante el $P_{aCO2}$. Por ejemplo, cuando se extrajo un 70% del dióxido de carbono con el pulmón de membrana, la ventilación total se redujo en un 50%, la presión inspiratoria máxima disminuyó en un 45% y el $P_{aO2}$ se mantuvo constante aumentando la porción de oxígeno inspirado de 0,21 a 0,27%. La remoción del dióxido de carbono mediante una membrana durante la respiración de presión positiva pudo disminuir el barotraumatismo, especialmente en pulmones poco elásticos. Técnicamente, la remoción extracorpórea del dióxido de carbono es un procedimiento relativamente sencillo.