Ventilatory Reserve in the Dog during Partial Curarization

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In dogs respiratory workloads were increased by partial airway obstruction or strapping the chest and by addition of a mechanical deadspace of 200 ml. The ventilatory responses and bloodgas values were within normal ranges during the respiratory challenge. When partial curarization was induced, ventilatory reserve diminished; with the addition of deadspace and either airway obstruction or decreased compliance induced by strapping respiratory arrest occurred when the dogs breathed room air. When the dogs breathed 100 per cent oxygen, respiratory arrest did not occur in response to the same respiratory challenges. It is suggested that hypoxia plays a role in initiating postoperative respiratory failure following anesthesia produced with neuromuscular blockers.

The muscles of breathing in man and other animals under normal conditions are considerably less sensitive to neuromuscular blocking agents than the muscles of the neck and extremities. Depolarizing neuromuscular blockers seem to "spare" respiration in man to the same degree as do nondepolarizing agents, the muscles participating in inspiration being influenced to the same degree as those participating in active expiration. The difference in sensitivity to neuromuscular blockers among various muscle groups in the body may be caused by differences in muscle blood flow, differences in innervation, or qualities inherent in the muscle fibers.

The work of breathing is small, and requires only 1 to 2 per cent of the total oxygen consumption. Work increases, however, with increase in ventilation, decrease in thoracic compliance, and increase in airway resistance. Under such circumstances the energy expended for breathing can require as much as 40 per cent of the total oxygen consumption.

In this study respiratory workload was increased in the dog in order to evaluate the respiratory response in the presence of partial curarization. The information gained may help to elucidate postoperative respiratory insufficiency following anesthesia produced with neuromuscular blockers.

Methods

Twelve mongrel dogs weighing between 12 and 27 kg (average 17.4 kg) were anesthetized with thiopental sodium (Thiopental) (400–600 mg) injected intravenously. A tracheostomy was established and airway pressure measured in the tracheostomy tube. A femoral artery was cannulated for blood pressure measurement and sampling of arterial blood gases. A femoral vein was cannulated for injection of thiopental, and the jugular vein was cannulated for infusion of d-tubocurarine chloride. Airway pressure and blood pressure were measured with Sanborn transducers (Model 267B) and recorded on a Sanborn Polyvisco recorder (Model 350). The sciatic nerve was isolated and severed cephalad to the point of application of two copper-plated electrodes, and stimulated with supramaximal stimuli at a rate of 1/sec from a Grass Stimulator (Model S4). Responses registered as isometric tension of the tibial muscle via a Walton Brodie strain gauge arch sewn onto the muscle, were recorded on the Sanborn recorder.

Paco2 was measured with a Severinghaus electrode, pH and Pao2 by means of Radiometer electrodes at 37 C. Results were corrected for changes in body temperature.

The dogs breathed room air unless otherwise stated. Ventilation was measured with a Wright respirometer. Deadspace was increased by attachment to the tracheostomy of
a tube 3.5 cm in diameter, with a capacity of 200 ml, which produced an average increase in $V_D$ of 11.8 ml/kg.

Airway obstruction was produced by introduction into the breathing circuit of a cylinder 41 mm long with an internal diameter of 4 mm. This resulted in negative inspiratory pressures of 14–17 mm Hg and positive expiratory pressures of 10–14 mm Hg. Compliance was decreased 40–50 per cent by application to the chest of an elastic tape corset, 15 cm wide. The corset was tightened until peak airway pressure for a given tidal volume had doubled during brief ventilation with a constant-volume piston pump (Harvard Apparatus Co.).

$\alpha$-tubocurarine was infused by means of a constant-infusion pump at a rate that maintained a constant level of curarization, as indicated by the magnitude of the tibial muscle twitch.

Two series of experiments were performed. In six dogs, deadspace, then airway obstruction, and finally deadspace and airway obstruction combined, were applied. Each increase in respiratory workload was maintained for ten minutes before measurements were made. A steady level of curarization, as indicated by a reduction of the tibial twitch tension to 50–60 per cent of the original tension, was then induced. Again, respiration was challenged, first with deadspace, then with obstruction, and finally with deadspace plus obstruction, for periods of ten minutes each, and measurements were repeated.

In six other dogs essentially the same experiment was performed, the only variation being that instead of obstruction of the airway compliance was decreased. Measurements were again made after ten minutes, before and during curarization.

**Results**

*Arterial blood gas* values were essentially constant during the control noncurarized runs in both series, indicating that the added respiratory workload was surmountable.

In the first series of six dogs with obstructed airways the mean degree of curarization was reflected by a 58 to 63 per cent reduction of tibial twitch tension. After curarization was induced, unchallenged ventilation was almost identical to the initial ventilation (fig. 1), but when either obstruction or deadspace was added, there was a definite decrease in respiratory response, as judged by total ventilation and by $P_{A_{O_2}}$, $P_{A_{CO_2}}$ and pH (table 1). When the combination of deadspace and airway obstruction was imposed during curarization, all six dogs continued to breathe for two to three minutes, but with slowly decreasing airway pressure (fig. 2) (further evidence of decreased ventilation) until breathing eventually stopped. At the time of respiratory arrest $P_{A_{O_2}}$ was 26 ± 7 mm Hg, $P_{A_{CO_2}}$ 85 ± 7 mm Hg, pH 7.15 ± 0.2. The lungs were ven-
tilated for approximately half a minute with 100 per cent oxygen, which restored spontaneous breathing. The combination of deadspace and airway obstruction was imposed again while the dogs were breathing 100 per cent oxygen. Although the level of curarization was still the same, the dogs breathing 100 per cent O₂ were able to overcome the respiratory challenge. Blood samples taken 45 to 90 minutes after the addition of oxygen disclosed \( \text{Pao}_2 = 203 \pm 89 \text{ mm Hg, PaCO}_2 = 148 \pm 66 \text{ mm Hg, and pH } 6.79 \pm 0.2. \) Two dogs, each exposed for a second time to room air while breathing against airway obstruction and deadspace, again had respiratory arrest and were again resuscitated successfully by ventilation with oxygen.

Respiratory rates decreased during airway obstruction in both the noncurarized and the curarized state.

In the second series of dogs decreased compliance was substituted for airway obstruction (fig. 3). Ventilation was unchanged from the initial value and gas exchange was near normal at a mean level of curarization of 51 per cent. A decrease in compliance alone did not change these values, whereas the combination of decreased compliance and increased deadspace produced respiratory arrest in four dogs within five minutes, and in the remaining two after 12 and 30 minutes, respectively (table 2). After respiratory arrest the lungs were ventilated artificially for 30–60 seconds with oxygen. When spontaneous respiratory movements reappeared, ventilation comparable to the control value was maintained as long as the inspired oxygen concentration was 100 per cent. In these dogs respiratory arrest was induced a second time by changing the inspired gas to room air. At the first respiratory arrest the average \( \text{Pao}_2 \) was 26 mm Hg, average \( \text{PaCO}_2 \) 85 mm Hg, and average \( \text{pH}_{\text{a}} \) 7.15. The values after 30 to 90 minutes of breathing oxygen were \( \text{Pao}_2 \) 205 mm Hg, \( \text{PaCO}_2 \) 133 mm Hg, \( \text{pH}_{\text{a}} \) 6.97.

In both groups circulatory responses were unremarkable until respiratory arrest impeded, at which time arterial blood pressure suddenly increased 30 to 40 mm Hg and pulse pressure widened.
VENTILATORY RESERVE DURING PARTIAL CURARIZATION

Fig. 2. Respiratory response to increased deadspace and airway resistance. Continuous recording illustrating the apnea which occurs as a result of the respiratory challenge. In column 5, oxygenation permits the resumption of spontaneous breathing. Airway pressure provides an indirect measure of the ventilatory activity.

Discussion

This investigation has demonstrated that resting ventilation may be adequate during partial curarization. If, however, an additional workload is placed upon the respiratory muscles, in the form of obstruction of the airway, increase in mechanical deadspace, or restriction of chest expansion, a diminished ventilatory reserve becomes evident. This is not unexpected, since a considerable proportion of motor units of the respiratory muscles is affected under these circumstances.

Severe arterial hypoxemia (Pao₂ about 25 mm Hg) seems to be the decisive factor in causing the respiratory arrest, since the accompanying respiratory acidosis continued and increased to a new steady state after reoxygenation and resumption of spontaneous breathing. Nicol and Campbell suggested that the lowest tolerable Pao₂ is in the order of 20 mm Hg, for brief periods only. Although it is possible that cessation of respiration under these circumstances was caused by hypoxic failure of the respiratory center, it is not the most acceptable explanation since in similar studies of hypoxia spontaneous respiration has been preserved for considerably longer periods than those observed here.

Fig. 3. Respiratory response to increase in deadspace (Vₐ), decrease in compliance (C), and increased deadspace + decreased compliance in six dogs, breathing atmospheric air unless stated otherwise.
Table 2. Results (Mean ± SD) in Six Dogs, Minute Ventilation Challenged by Decrease in Compliance, before and after Curarization

<table>
<thead>
<tr>
<th></th>
<th>Initial Value</th>
<th>200-ml Develve V0 Challenge</th>
<th>Decrease in Compliance (V0 Challenge)</th>
<th>Vp + C</th>
<th>Value after Curarization</th>
<th>200-ml Develve V0 Challenge</th>
<th>Decrease in Compliance (V0 Challenge)</th>
<th>Vp + C</th>
<th>Vp + C + O2</th>
<th>O2</th>
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<tbody>
<tr>
<td><strong>Minute Ventilation (V0/kg)</strong></td>
<td>0.36 ± 0.07</td>
<td>1.25 ± 0.51</td>
<td>0.48 ± 0.18</td>
<td>1.14 ± 0.48</td>
<td>0.35 ± 0.17</td>
<td>0.88 ± 0.35</td>
<td>0.52 ± 0.33</td>
<td>0</td>
<td>0.47 ± 0.35</td>
<td>0</td>
</tr>
<tr>
<td><strong>Respiratory rate (l)</strong></td>
<td>31 ± 12</td>
<td>41 ± 15</td>
<td>43 ± 22</td>
<td>38 ± 15</td>
<td>37 ± 25</td>
<td>55 ± 33</td>
<td>44 ± 26</td>
<td>0</td>
<td>20 ± 17</td>
<td>0</td>
</tr>
<tr>
<td><strong>Pao2 (mm Hg)</strong></td>
<td>96 ± 9</td>
<td>94 ± 14</td>
<td>93 ± 10</td>
<td>80 ± 15</td>
<td>81 ± 12</td>
<td>40 ± 21</td>
<td>82 ± 10</td>
<td>26 ± 7</td>
<td>205 ± 67</td>
<td>20 ± 11</td>
</tr>
<tr>
<td><strong>Paco2 (mm Hg)</strong></td>
<td>42 ± 9</td>
<td>40 ± 11</td>
<td>30 ± 7</td>
<td>50 ± 10</td>
<td>40 ± 14</td>
<td>72 ± 21</td>
<td>48 ± 14</td>
<td>85 ± 7</td>
<td>133 ± 35</td>
<td>139 ± 20</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>7.38 ± 0.01</td>
<td>7.34 ± 0.07</td>
<td>7.30 ± 0.01</td>
<td>7.35 ± 0.05</td>
<td>7.22 ± 0.08</td>
<td>7.34 ± 0.07</td>
<td>7.15 ± 0.12</td>
<td>0.97 ± 0.12</td>
<td>0.95 ± 0.04</td>
<td></td>
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<tr>
<td><strong>Twitch tension (% of control value)</strong></td>
<td>51 ± 11</td>
<td>50 ± 13</td>
<td>55 ± 13</td>
<td>53 ± 11</td>
<td>43 ± 9</td>
<td></td>
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It could be that the point of failure was in the respiratory muscles themselves. The respiratory muscles, being the most vulnerable to asphyxia is a respiratory stimulant initially, and the phrenic nerve is the supranumerary, to which the paralyzed phrenic nerve was anastomosed. It may be that muscular contraction becomes impossible, but in the dog, muscular contraction becomes impossible. This may be an increase in the compliance, but without failure, and loss of life, leading to an increased load, and increased load in a relatively rapid fall. The other values for Pao2 during breathing of oxygen indicate that a combination of breathing of oxygen and increased load in a successive increase in various circumstances and the experimental circumstances. The blood pressure tolerated the phrenic nerve is the supranumerary, to which the paralyzed phrenic nerve was anastomosed.
oxygen tension in the immediate postoperative period this complication may be avoided.

References
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16. Henningson P, Johansen SH: The respiratory response to severe airway obstruction at low oxygen tensions (To be published.)
23. Foldes FF: Factors which alter the effects of muscle relaxants. ANESTHESIOLOGY 20: 464, 1959

Drugs

PROPANIDID Anesthesia was induced with propanidid (5 to 7 mg/kg body weight) and maintained with methoxyflurane in 450 patients. Propanidid is a non-barbiturate which is rapidly broken down into inactive metabolites and, therefore, does not influence the postoperative period. Induction was smooth and rapid and blood pressure and pulse rate remained remarkably stable, even in hypertensive patients. (Schulte-Steinberg, O.: Induction of Methoxyflurane Anesthesia with Propanidid, Der Anaesthesist 18: 334 (Oct.) 1969.)