The effect of passive hyperventilation on intraventricular pressure in the dog

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The effectiveness of passive hyperventilation in reducing intracranial pressure was studied in mongrel dogs by varying the levels of end-tidal pCO₂ and airway pressure, and comparing the positive-negative and positive-atmospheric pressure. It has been shown that there is a point beyond which reduction of pCO₂ does not affect cerebral blood flow. The present study demonstrates that another limiting factor is the degree of positive or negative airway pressure. Positive airway pressure impedes venous drainage, thereby increasing intracranial pressure. This increase could only partly be offset by applying negative expiratory airway pressure, since it was found that excessive negative airway pressure (greater than static recoil pressure of the lung) may trap air in alveoli. An optimal range of positive and negative airway pressures is defined.

Key Words: hyperventilation, positive-atmospheric pressure, positive-negative pressure, pCO₂, intracranial pressure

Passive hyperventilation is widely used in neuroanesthesia as a means of reducing intracranial pressure. Its effectiveness, however, has been somewhat controversial, and the optimal parameters of hyperventilation for this purpose have not been completely delineated. Considerable attention has been paid to the effect of CO₂ on cerebral blood flow but relatively little to the fact that airway pressure can influence cerebral venous drainage. Since these are the two main factors contributing to changes in intracranial pressure during passive hyperventilation, it would appear important to assess their effects, both as independent variables as well as in combination.

This study has been designed to examine the effects on intraventricular pressure of various levels of end-tidal pCO₂ and airway pressure, including a comparison of positive-negative and positive-atmospheric pressure ventilation.

Methods

Twelve healthy but otherwise unselected adult dogs weighing 10 to 14 kg were used. Anesthesia was induced intravenously with pentobarbital (33 mg/kg) and the trachea intubated. Supplemental doses of pentobarbital (10 mg/kg) were administered as needed. The femoral artery was cannulated for arterial pressure monitoring and the femoral vein for intravenous infusion (5% dextrose in ½ normal saline at a rate of 5 ml/kg/hr). Rectal temperature was maintained at 37 ± 0.5°C throughout the experiment by a servo-controlled heater placed under the animal. To monitor central venous pressure, in four animals a catheter was placed in a
cephalic vein with its tip within the superior vena cava. The animal was placed prone, the head fixed in a stereotaxic instrument, and the skull exposed by a midline incision. A No. 19-gauge thin-walled needle was inserted into the right lateral ventricle through a burr hole, with stereotaxic coordinates of anterior 15 mm and lateral 7 mm. The ventricle was encountered at depths varying between 10 and 17 mm from the cortex. The needle was fixed to the skull with dental cement covering the burr hole. Pressure in the lateral ventricle, femoral artery, trachea, and superior vena cava were continuously monitored throughout the experiment using Sanborn Model 267BC and 268B pressure transducers connected to a Hewlett-Packard Model 7700 Recorder. Tidal air was sampled from the endotracheal tube and its pCO₂ was continuously monitored with a Beckman Model LB-1 Gas Analyzer and the Sanborn Recorder.

During all recording phases of the experiment, the animals breathed 100% oxygen through a circle system. Controlled ventilation was achieved with a Bennett Anesthesia Ventilator after adding gallamine triethiodide to the intravenous infusion (concentration 0.1%). The parameters of ventilation, tidal volume and airway pressure, were controlled by regulating the escape valve setting of the pressure-cycled Bennett Ventilator. In the phase of the experiment in which airway pressure was kept constant and pCO₂ varied, a gradual increase in pCO₂ was produced by removing the soda lime from the canister and ventilating at a slower rate, and a decrease in pCO₂ by reversing the procedure. In experiments in which airway pressure was varied, end-tidal pCO₂ was kept constant by adjusting the inflow rate of oxygen with the soda lime removed.

At the completion of each experiment, the animals were sacrificed by administering 100% nitrous oxide. Immediately following death, the circle system was removed and the airway tightly sealed. Bilateral pneumothoraces were then created by opening the thoracic wall. The resulting rise in the airway pressure gave the static recoil pressure of the lung. The brain was removed, fixed with 10% buffered formaldehyde, and later sectioned to verify that the needle track had entered the lateral ventricle, and that no hemorrhage had occurred.

**Results**

**Conventional Hyperventilation (Positive-Atmospheric)**

With the animals breathing 100% oxygen spontaneously 12 to 20 times per min, the average end-tidal pCO₂ was $51.7 \pm 2.1$ (x ± S.E.) torr. After neuromuscular blockade, ventilation was gradually increased by raising the positive inspiratory airway pressure from 5 to 30 cm water in 5 cm water increments, keeping the respiratory rate constant at 20 per min. Under these conditions there was a gradual increase in tidal volume and a gradual decrease in end-tidal pCO₂ (Table 1). Intraventricular pressure initially decreased as the degree of ventilation was increased to an airway pressure of 20/0 cm water; above this the intraventricular pressure showed a gradual rise despite a further fall in end-tidal pCO₂ (Fig. 1). Graphic representation of the effect of positive-atmospheric pressure ventilation upon the mean intraventricular pressure is shown in Fig. 2. It demonstrates a statistically sig-

<table>
<thead>
<tr>
<th>airway pressure (cm water)</th>
<th>Spontaneous Respiration</th>
<th>Positive-Atmospheric Ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>near zero</td>
<td>5/0 10/0 15/0 20/0 25/0 30/0</td>
</tr>
<tr>
<td>tidal volume (ml)</td>
<td>&lt;60</td>
<td>80-100 180-200 280-330 380-450 500-600 680-800</td>
</tr>
<tr>
<td>end-tidal pCO₂ (x ± S.E. torr)</td>
<td>51.7±2.1</td>
<td>43.3 36.4 29.6 23.5 18.2 15.2</td>
</tr>
<tr>
<td></td>
<td>±1.0 1.5 1.2 0.9 0.7</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 1**

*Effect of conventional hyperventilation on tidal volume and end-tidal pCO₂ in 12 dogs*
Passive hyperventilation and intraventricular pressure

![Graphs showing venous pressure, ventricular pressure, airway pressure, and arterial pressure with corresponding data and statistical significance.](image)

**Fig. 1.** Conventional hyperventilation (positive-atmospheric) in a typical animal. Column 1, spontaneous respiration; Columns 2-4, increasing levels of ventilation. With an airway pressure greater than 20/0 cm water, the intraventricular pressure started to rise despite continuing fall in end-tidal pCO₂.

significant (p < 0.05) fall of the mean intraventricular pressure to a positive airway pressure of 20/0 cm water, above which a statistically significant (p < 0.05) rise in the mean intraventricular pressure occurred.

In contrast to spontaneous respiration during which both central venous pressure and intraventricular pressure exhibited phasic decrease with inspiration, there occurred a phasic rise in both parameters with controlled positive-pressure ventilation. The mean central venous pressure during spontaneous respiration was $-1.1 \pm 0.3$ (X ± S.E.) torr, and it rose gradually during the positive-pressure controlled ventilation. As shown in Fig. 3, the mean central venous pressure was $+2.8 \pm 0.7$ (X ± S.E.) torr when airway pressure rose to 30/0 cm water. This rise was statistically significant (p < 0.05) when Student’s t-test was applied.

**Airway Pressure Constant, pCO₂ Varied**

As shown in Fig. 4, when the end-tidal pCO₂ was gradually increased by removing the soda lime but with ventilation kept constant (airway pressure 10/0 cm water, respiratory rate 7 to 10 per min), there was a gradual rise in intraventricular pressure. Following accumulation of CO₂, pCO₂ was then gradually decreased by adding soda lime and ventilating at faster but constant rate (30 to 40 per min) while airway pressure was kept constant (10/0 cm water). Paralleling the fall in pCO₂, the intraventricular pressure gradually decreased (Fig. 5). The intraventricular arterial pulse amplitude was noted to
be larger at higher mean intraventricular pressures than at lower pressures. A study of this phenomenon is reported elsewhere.\textsuperscript{10} The arterial pressure was stable except for a slight elevation with hypercarbia.

**PCO\textsubscript{2} Constant, Airway Pressure Varied**

Under usual conditions, an increase in airway pressure during controlled ventilation produces an increase in tidal volume and a decrease in end-tidal pCO\textsubscript{2}. However, by removing soda lime from the system and adjusting the inflow rate of oxygen it is possible to maintain end-tidal pCO\textsubscript{2} constant and study the effect of changes in airway pressure. Pressure-volume relationships, of course, remain unchanged. Under these conditions, with end-tidal pCO\textsubscript{2} constant at 40 ± 2 torr, a rise in airway pressure resulted in a corresponding rise in intraventricular pressure (Fig. 6). Fig. 7 illustrates a typical recording of intraventricular pressure in one

![Fig. 2. Conventional positive-atmospheric pressure hyperventilation. Relationship between intraventricular pressure and varying levels of passive hyperventilation (12 animals). Note rise in intraventricular pressure at a positive airway pressure of 20/0 cm water.](image)

![Fig. 3. Changes in central venous pressure induced by positive-atmospheric pressure ventilation (4 animals).](image)

![Fig. 4. Relationship between intraventricular pressure and end-tidal pCO\textsubscript{2} at constant airway pressure of 10/0 cm water and respiratory rate of 7/min (12 animals).](image)
Passive hyperventilation and intraventricular pressure

An example of decline in intraventricular pressure with CO₂ washout at a constant airway pressure of 10/0 cm water. Initial end-tidal pCO₂ = 90 torr; final end-tidal pCO₂ = 40 torr.

The rise in intraventricular pressure was associated with a significant rise in mean central venous pressure (also see Fig. 3).

Positive-Negative Versus Positive-Atmospheric Pressure Ventilation

Following completion of the studies above, a comparison of the effect on intraventricular pressure of positive-negative and positive-atmospheric pressure ventilation was made in each animal. Animals were subjected to successive periods, each approximately 10 to 15 min, of positive-atmospheric pressure ventilation and two degrees of positive-negative pressure ventilation. Levels of positive-atmospheric pressure ventilation again ranged from 5/0 to 30/0 cm water in 5 cm water increments. Tidal volumes of each successive period of positive-negative pressure ventilation was made to correspond to that of the preceding period of positive-atmospheric pressure ventilation. The negative pressures exerted were: 1) static recoil pressure of the lung (minus 4 ± 0.5 cm water as measured by the method described above; and 2) the maximum negative pressure this particular ventilator could exert (minus 8 cm water).

As shown in Table 2 and Fig. 8, when compared to the corresponding level of positive-atmospheric pressure ventilation, there was a statistically significant (p < 0.05) decrease in the intraventricular pressure associated with a fall in the central venous pressure when the negative pressure exerted was equal to static recoil pressure of the lung. The end-tidal pCO₂ was also significantly decreased.

As compared to static recoil pressure ventilation, with the use of a negative pressure of minus 8 cm the intraventricular pressure and the end-tidal pCO₂ increased at low levels of ventilation but were decreased slightly at higher levels of ventilation.

Discussion

Since the work of Kety and Schmidt (1948) relating carbon dioxide tension to
L. M. Kitahata, J. H. Galicich and I. Sato cerebral blood flow, it has been recognized that there is a point beyond which further reduction of pCO$_2$ causes little or no further decrease in cerebral blood flow (Wasserman and Patterson, 1961) and, therefore, in intracranial pressure. The significance of this study lies mainly in the demonstration of other limits in the reduction of intracranial pressure by hyperventilation, namely excessive positive or negative airway pressure.

The limit in the reduction of intraventricular pressure by positive-atmospheric pressure hyperventilation demonstrated in this experiment was an airway pressure of 20/0 cm water. At this airway pressure, the end-tidal pCO$_2$ was 23.5 ± 1.2 (X ± S.E) torr (Table 1). From extrapolation of the curves shown in Fig. 4, from the work of Wasserman and Patterson and considering increase in arterial-alveolar pCO$_2$ gradient by passive hyperventilation, one would expect further reduction in intracranial pressure in response to a further decrease in pCO$_2$. However, intraventricular pressure rose with higher levels of passive hyperventilation in spite of the fact that there was a further reduction in end-tidal pCO$_2$ (Fig. 2). This effect of airway pressure on intraventricular pressure.

![Graph](image-url)  
**Fig. 6.** Relationship between intraventricular pressure and airway pressure with end-tidal pCO$_2$ constant at 40 ± 2 (X ± S.E.) torr (12 animals). Compare with Fig. 3.

![Graph](image-url)  
**Fig. 7.** Typical polygraph display of intraventricular pressure, airway pressure, and central venous pressure at constant end-tidal pCO$_2$. Increase in airway pressure from 5/0 cm water to 25/0 cm water resulted in increase in intraventricular pressure and central venous pressure.

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**TABLE 2**

*Difference in intraventricular pressure (p\textsubscript{VENT}) and end-tidal pCO\textsubscript{2} between positive-atmosphere ventilation and two degrees of positive-negative ventilation*

<table>
<thead>
<tr>
<th>Level of Positive-Atmospheric Ventilation (cm water)</th>
<th>Positive-Negative Ventilation</th>
<th>((-4\text{ cm water}))</th>
<th>((-8\text{ cm water}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>((\bar{x} \pm \text{S. E. torr}))</td>
<td>((\bar{x} \pm \text{S. E. torr}))</td>
<td>((\bar{x} \pm \text{S. E. torr}))</td>
</tr>
<tr>
<td>5/0</td>
<td>p\textsubscript{VENT}</td>
<td>-0.3 \pm 0.1*</td>
<td>+0.5 \pm 0.3</td>
</tr>
<tr>
<td>10/0</td>
<td>p\textsubscript{VENT}</td>
<td>-0.8 \pm 0.2*</td>
<td>+0.2 \pm 0.2</td>
</tr>
<tr>
<td>15/0</td>
<td>p\textsubscript{VENT}</td>
<td>-0.8 \pm 0.2*</td>
<td>-0.1 \pm 0.1</td>
</tr>
<tr>
<td>20/0</td>
<td>p\textsubscript{VENT}</td>
<td>-0.8 \pm 0.1*</td>
<td>-0.1 \pm 0.1</td>
</tr>
<tr>
<td>25/0</td>
<td>p\textsubscript{VENT}</td>
<td>-0.4 \pm 0.1*</td>
<td>-0.2 \pm 0.1</td>
</tr>
<tr>
<td>30/0</td>
<td>p\textsubscript{VENT}</td>
<td>-0.6 \pm 0.2*</td>
<td>-0.4 \pm 0.2</td>
</tr>
<tr>
<td></td>
<td>pCO\textsubscript{2}</td>
<td>-0.4 \pm 0.2</td>
<td>+2.0 \pm 1.0</td>
</tr>
<tr>
<td></td>
<td>pCO\textsubscript{2}</td>
<td>-1.4 \pm 0.7</td>
<td>+0.9 \pm 0.5</td>
</tr>
<tr>
<td></td>
<td>pCO\textsubscript{2}</td>
<td>-1.9 \pm 0.7*</td>
<td>-0.2 \pm 0.2</td>
</tr>
<tr>
<td></td>
<td>pCO\textsubscript{2}</td>
<td>-1.2 \pm 0.4*</td>
<td>-0.1 \pm 0.1</td>
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<tr>
<td></td>
<td>pCO\textsubscript{2}</td>
<td>-1.5 \pm 0.3*</td>
<td>-0.3 \pm 0.1</td>
</tr>
<tr>
<td></td>
<td>pCO\textsubscript{2}</td>
<td>-1.0 \pm 0.1*</td>
<td>-0.4 \pm 0.2</td>
</tr>
</tbody>
</table>

* \(p < 0.05. (\_ \_ = \text{decrease}; + = \text{increase.})*

pressure was also seen in the phase of the experiment in which end-tidal pCO\textsubscript{2} was kept constant and airway pressure was altered independent of pCO\textsubscript{2}. Under these conditions, each increment of airway pressure elevation produced a corresponding rise in intraventricular pressure. This increase in intraventricular pressure was associated with an increase in central venous pressure (Fig. 3). This relationship between the two in terms of pressure is essentially one to one.

During excessive negative-pressure ventilation (Table 2), the segment of the airway above the equal pressure point was constricted due to a pressure gradient (Fig. 9). This phenomenon results in air trapping\textsuperscript{2,7,12} and consequently impeded CO\textsubscript{2} washout (Table 2). Air trapping, however, does not occur with a negative pressure that equals the static recoil pressure of the lung.

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![Fig. 8. Comparison of effects on intraventricular and central venous pressures of positive-atmospheric and positive-negative pressure ventilations. Respiratory rate and tidal volume identical. Note reduction in both parameters with positive-negative pressure ventilation.](image-url)

*Fig. 8. Comparison of effects on intraventricular and central venous pressures of positive-atmospheric and positive-negative pressure ventilations. Respiratory rate and tidal volume identical. Note reduction in both parameters with positive-negative pressure ventilation.*

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that does not exceed the static recoil pressure results in further significant reduction in central venous pressure, end-tidal pCO₂, and intraventricular pressure. These results defining an optimal range of negative pressure explain the controversy related to negative-pressure hyperventilation⁴,⁶,¹⁵,¹⁸ and confirm those reports showing its advantage.⁸,⁹,¹¹,¹³,¹⁹,²⁰,²²,²⁸

The present study has been carried out in animals with normal intracranial pressure and presumably normal pulmonary function. To apply principles derived from this study to clinical situations, it must be realized that certain individual modifications may be necessary. It might be expected that excessive airway pressure in patients with raised intracranial pressure would have an exaggerated effect. Bulging of the brain described by Schettini, et al.,²⁴ with the use of extreme hyperventilation (minute volumes greater than 15 liters per min) in man is probably explained on this basis, namely, an impeded venous return due to elevated airway pressure. However, further experimental studies are necessary to fully evaluate the effect on subjects with increased intracranial pressure.

The optimal parameters of hyperventilation may also vary with the pulmonary status of the patients. For instance, decreased pulmonary compliance associated with chronic lung disease presents difficulties because airway pressures higher than normal are required to obtain adequate tidal volume. A decrease in the static recoil pressure of the lung associated with, for instance, pulmonary emphysema, presents the hazard of air trapping, especially with the application of negative pressure ventilation. Because of such individual variations, the optimal range of hyperventilation found in this study should not be taken as a strict limit.

Summary

With dogs as experimental animals, it was found that:

1. When end-tidal pCO₂ is kept constant, intraventricular pressure and central venous pressure rise as airway pressure is elevated.
2. When airway pressure is kept constant, mean intraventricular pressure falls as end-tidal pCO₂ is lowered.
3. The conventional positive-atmospheric pressure hyperventilation results in a gradual decrease in mean intraventricular pressure in proportion to the degree of hyperventilation to a certain point above which intraventricular pressure increases due to an elevated airway pressure in spite of a further decrease in end-tidal pCO₂.
4. When negative pressure equals the static recoil pressure of the lung, positive-negative pressure hyperventilation lowers end-tidal pCO₂, mean intraventricular pressure, and central venous pressure, more than positive-atmospheric pressure hyperventilation with identical tidal volume and respiratory rate. Extreme negative pressure, however, does not cause any further significant decrease in end-tidal pCO₂ or mean intraventricular pressure.

This study has demonstrated the limits in the reduction of intracranial pressure by passive hyperventilation, namely, excessive positive or negative airway pressure. It is concluded that optimal ventilation for reducing the intracranial pressure is that ventilation which lowers end-tidal pCO₂ without excessive positive or negative airway press-
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sure. The clinical difficulties associated with positive-atmospheric and positive-negative pressure hyperventilation have been discussed.

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References


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