The Effect of Hypocapnia on the Level of Halothane Anesthesia in Man

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The minimum alveolar concentration (MAC) of halothane required to eliminate movement in 50 per cent of patients in response to a surgical skin incision was determined for two groups. The first group breathed spontaneously and had a mean arterial PaCO₂ of 37.5 ± 2.2 mm. of mercury. Ventilation in the second group was controlled so as to maintain PaCO₂ at 20.8 ± 2.7 mm. of mercury. No difference in MAC was found between the groups; in either case, the halothane concentration required to eliminate movement in 50 per cent of patients was between 0.74 and 0.76 per cent.

By measuring the lowest alveolar concentration of halothane required to suppress movement in response to a painful stimulus in dogs, Merkel and Eger derived values which they described as "minimum alveolar concentrations" (MAC) of anesthetic. Using this technique, Eger et al. found in dogs that reducing arterial carbon dioxide pressure (PaCO₂) from 42 to 14 mm. of mercury did not affect the MAC. These results are in contrast to the current belief that hypocapnia reduces anesthetic requirements. It appeared to us that the MAC concept might be used to test this belief in man.

Methods

Twenty-eight healthy patients scheduled for elective surgery were studied. Premedication consisted of atropine, 0.4 mg. intramuscularly, given approximately one hour prior to induction. Anesthesia was induced with halothane and oxygen and endotracheal intubation was accomplished after the intravenous administra-

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made, and the patient observed for presence or absence of movement.

The second group of 12 patients were studied as above except that in order to lower Pa\textsubscript{CO\textsubscript{2}}, ventilation was controlled following endotracheal intubation.

**Results**

The results are summarized in table 1 and in figures 1 and 2. Pa\textsubscript{CO\textsubscript{2}} and pH values were significantly different (P < 0.001) between the two groups. No significant difference could be shown for any other parameter. For both groups, the end-tidal halothane concentration required to suppress movement in 50 per cent of patients in response to incision lay between 0.74 and 0.76 per cent. No patient moved above a concentration of 0.78 per cent and all moved below a concentration of 0.74 per cent.

**Discussion**

This study suggests that anesthetic requirements are not affected by an acute reduction in Pa\textsubscript{CO\textsubscript{2}}. One may question whether the end-tidal samples in the case of hypocapnia are representative of cerebral halothane partial pressures since cerebral blood flow is reduced by a lower Pa\textsubscript{CO\textsubscript{2}}. This may be examined theoretically as follows: Assume a mean normal cerebral blood flow of 0.5 ml. ml./minute of brain tissue which is reduced to 0.25 ml. ml./minute at a Pa\textsubscript{CO\textsubscript{2}} of 20; and, assume a brain-blood partition coefficient of 2.5 for halothane.\textsuperscript{\textdagger} The time constant (i.e., time to 63 per cent change)\textsuperscript{\textdagger\textdagger} for such a system is 2.5 \(0.25\) = 10 minutes. If one assumes a stepwise increase in arterial halothane concentration, then in 25 minutes (21/2 time constants and the mean time in our study) the partial pressure of halothane in brain would be 92 per cent of that in arterial blood (or end-tidal gas). This would mean a maximum error in our halothane concentrations of about 0.06 per cent halothane. For two reasons we believe this is an overestimate of the error. First, although the time of constant alveolar

![Table 1](image)

<table>
<thead>
<tr>
<th></th>
<th>Normocapnia (Spontaneous)</th>
<th>Hypocapnia (Hyper-ventilation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Subject's age</td>
<td>41.7±9.2</td>
<td>35.2±9.2</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>36.4±0.4</td>
<td>36.2±0.3</td>
</tr>
<tr>
<td>Minutes of anesthesia to incision</td>
<td>43.6±10.1</td>
<td>46.3±6.7</td>
</tr>
<tr>
<td>Minutes of constant alveolar halothane prior to incision</td>
<td>20.9±6.5</td>
<td>24.7±9.2</td>
</tr>
<tr>
<td>Pa\textsubscript{CO\textsubscript{2}} (mm. Hg)</td>
<td>37.5±2.2</td>
<td>29.8±2.7</td>
</tr>
<tr>
<td>pH</td>
<td>7.384±0.022</td>
<td>7.583±0.114</td>
</tr>
<tr>
<td>BE (mEq./liter)</td>
<td>-2.2±1.5</td>
<td>-1.0±5.2</td>
</tr>
</tbody>
</table>

Values are followed by the standard deviation.

**Fig. 1.** The results obtained for both normocapnia and hypocapnia are shown. The alveolar concentration at the time of surgical incision is plotted on the horizontal axis. An upward deflection denotes movement, in response to the incision. Downward deflection indicates that the patient did not move.

**Fig. 2.** From figure 1, the patients were divided into groups of four, starting with the lowest alveolar concentration. The average alveolar concentration of each of these groups is plotted on the horizontal axis. The percentage of patients moving is then shown on the vertical axis.
halothane averaged 25 minutes, the actual time of exposure of the brain to halothane was considerably longer—46 minutes. This would further reduce the difference between alveolar and brain partial pressures. Second, the cerebral blood flow to the brain as a whole is less than that to grey matter, the latter receiving 0.8 to 1.2 ml./ml./minute.\(^7\) Even were this halved by hypoxemia to 0.4 ml./ml./minute it would mean a time constant of 2.5/0.4 or 6.25 minutes. If grey matter is the site of action of anesthetics, then in 25 minutes the partial pressure of halothane in brain would be 98 per cent of that in arterial blood—i.e., the two would be essentially identical.

Our findings are in contrast to much of the literature on the subject of hyperventilation in anesthesia which states that hyperventilation increases the depth of anesthesia produced by any one inspired concentration of inhalation anesthetic. However, the apparent disagreement between these concepts may not be real. Hyperventilation increases the alveolar concentration and hence the cerebral concentration of anesthetic, even though the inspired concentration is unchanged. This increase in alveolar concentration with no change in inspired concentration can account for “deepening” of the anesthetic level. An additional possibility is that although anesthetic requirements as defined by MAC may not be altered by hyperventilation, anesthesia as defined by muscular relaxation may be profoundly affected. Katz and Wolf have shown that the integrated electrical activity of abdominal muscles is reduced by hyperventilation.\(^8\)

Nevertheless, the impression persists that the anesthetic level may be deepened by hyperventilation and lowered by Pa\(_{CO_2}\) per se. This impression is supported by numerous observations. For example, Dundee\(^9\) reported that plasma thiopental levels increase with hyperventilation. He suggested that this was the result of changes in the pH of blood that affect binding and distribution of that agent. In addition, Clutton-Brock\(^10\) reported it to be a common observation among anesthetists that overventilation appeared to increase the depth of anesthesia produced by any given dose of an anesthetic. He also reported a significantly increased pain threshold in conscious subjects (including himself) whose lungs were being hyperventilated. The threshold was decreased to normal with inhalation of amyl nitrite, presumably causing cerebral vasodilation. He concluded that the effect on pain was the result of cerebral hypoxia secondary to vasoconstriction. This conclusion is based, in part, on the work of Kety and Schmidt\(^4\) who showed that cerebral blood flow is decreased when Pa\(_{CO_2}\) is reduced. In further support of this conclusion, Sugioita found in anesthetized dogs that reduction of Pa\(_{CO_2}\) by hyperventilation resulted in a decreased partial pressure of oxygen in cerebral tissue.\(^11\) However, Wollman has presented evidence that during anesthesia, the cerebral blood flow approaches a lower limit as Pa\(_{CO_2}\) is reduced below 25 mm. of mercury.\(^12\) Reduction of Pa\(_{CO_2}\) below this level resulted in little further decrease in cerebral blood flow, suggesting that the brain limits the extent of the oxygen reduction to tolerable levels, and that cerebral hypoxia is not likely to be responsible for “deepening” anesthesia. That there is at least no permanent significant impairment of cerebral function with hyperventilation is supported by the clinical observation that patients subjected to the nitrous oxide/oxygen-relaxant technique with vigorous hyperventilation usually awaken rapidly on termination of anesthesia.

Clutton-Brock and Sugioita suggest that cerebral function may be impaired during hyperventilation—at least in the awake state. In contrast, McAlcevay et al.\(^13\) found that a decrease in Pa\(_{CO_2}\) increases the concentration of nitrous oxide necessary to obtund coordination and consciousness.

In at least two aspects, the study we have undertaken differs from those listed above. We have not used “reactive” anesthetics (for example, thiopental) since the distribution of these anesthetics is altered by changes in pH. We studied only anesthetized patients since one may question the extrapolation of findings in the awake to the anesthetized subject. The two conditions have not been proved directly comparable nor even extensions of one another. Extrapolation is further questionable since, as noted above, the data now available permit the opposite conclusion as to the impact of Pa\(_{CO_2}\) in the conscious state.
EFFECT OF HYPOCAPNIA ON HALOTHANE LEVEL

Summary

The minimum alveolar concentration (MAC) of halothane necessary to prevent movement of 50 per cent of patients in response to a surgical skin incision was determined in two groups of patients. In one group, breathing spontaneously, arterial $P_{CO_2}$ values were 37.5 ± 2.2 mm. of mercury. In the other group, arterial $P_{CO_2}$ values were held at 20.8 ± 2.7 mm. of mercury by controlling respiration. No difference in MAC could be demonstrated between the two groups, the concentration required to eliminate movement in 50 per cent of the patients being 0.74 to 0.76 per cent, in either case. These data indicate that hyperventilation per se has no effect on anesthetic depth.

References


MUSCLE RELAXANTS Decamethonium in doses of 39–52 µg/kg, virtually eliminated ability of human volunteers to raise their heads. At this dosage, both inspiratory and expiratory pressures and flows were well maintained. This response to decamethonium resembles response to $d$-tubocurare observed in earlier experiments. Following decamethonium, head lift was better preserved than hand grip; whereas, following $d$-tubocurare, the opposite response occurred. Fasciculations occurred following decamethonium administration in all subjects, and two of the subjects experienced muscle soreness on the following day. (Jorgensen, M., Molbech, S., and Johansen, S.: Effect of Decamethonium on Head Lift, Hand Grip and Respiratory Muscle Power in Man, J. Appl. Physiol. 21: 509 (Mar.) 1966.)