Minimum Alveolar Concentration of Halothane: An Ethnic Comparison

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SUMMARY: The minimum alveolar concentration (estimate of spread) of halothane which was determined in 42 Chinese, Nepalese or European patients was found to be 0.70% (0.66-0.74%) in Chinese and 0.70% (0.65-0.76%) in Nepalese and 0.68% (0.65-0.72%) in Europeans, using the Spearman Kärber method of analysis. This preliminary trial suggests that there is no ethnic difference in the minimum alveolar concentration of halothane between Asians and Europeans.

Introduction
There has been anecdotal evidence of the Chinese being more susceptible to general anaesthetic agents and, more recently, there have been reports of ethnic differences in the rate of recovery following anaesthesia (1-3) which could be related to a difference in sensitivity to anaesthetic agents. However no comparative work studying the potency of volatile anaesthetic agents in different ethnic groups appears to have been done. This trial set out to examine the problem.

Methods
Healthy adults patients (ASA I) of Chinese, Nepalese, and European descent living in Hong Kong, who had been scheduled for elective lower abdominal surgery, were studied. All gave their consent to the trial which was approved by the Army Medical Research Executive. Without being premedicated, they received an inhalational induction with halothane (up to 5%) in oxygen through a mask with a Magill breathing attachment and Ambu E valve (Ambu International, Glostrup, Denmark). A flow rate of 8 l.min⁻¹ was used. After five minutes, the inspired halothane concentration was reduced to that concentration required to maintain a constant predetermined expired concentration chosen between 0.6 and 0.9%. After a further period of at least 15 minutes, the patient was prepared for surgery. Just before (three breaths) the skin incision, which was used as the maximal stimulus, the inspired halothane concentration was reduced below the expired concentration so as to sample alveolar gas, uncontaminated by an overpressure of halothane. Presence or absence of purposeful movement in response to the incision was noted and the halothane concentration at which the inspired and expired concentrations were equal was noted. Expired alveolar gas was sampled at the opening to the larynx via a modified Guedel airway; halothane and carbon dioxide concentrations were measured with a mass spectrometer (Medishield Edwards, England — MS2) which had been calibrated with a refractometer (Riken-Keiki, Japan — Type 18). After the determination, anaesthesia was deepened and altered as necessary, and the patient’s trachea was intubated if appropriate for the surgery.

Data were analysed by chi-square tests, analysis of variance and the Spearman Kärber method (4) as appropriate. Details of the method for the estimation of the spread of the data when using the Spearman Kärber method are available from the authors.
Results
Forty-two patients were studied, the breakdown by ethnic group and sex being shown in Table 1. The Europeans were significantly taller than the Asian groups, more of them drank alcohol and all had had a previous anaesthetic. Arterial blood pressures and incidence of nocturnal waking and dreaming were similar in the three groups.

The details of the concentration of halothane and the patient response to maximal stimulation are shown in Table 2. The minimum alveolar concentration (estimated spread) of halothane was 0.70 (0.66-0.74)% in the Chinese, 0.70 (0.66-0.74)% in the Nepalese and 0.68 (0.65-0.72)% in the Europeans.

Discussion
This study suggests that there is no difference in the minimum alveolar concentration (MAC) of halothane in Chinese, Nepalese or European patients. Until recently, virtually all studies on the MAC of anaesthetic agents had originated from Eger’s department and the subject has been well reviewed by Quasha, Eger, and Tinker (5). The determination assumes that cerebral anaesthetic agent concentration approximates to that in the cerebral blood which in turn approximates to the alveolar concentration. For halothane, it has been calculated, using a cerebral blood flow of 50ml.100g-1.min-1 and a blood/brain partition coefficient of 2.5, that three time constants is 15 minutes and there will be at least 95% equilibration between arterial and brain tensions if a constant alveolar concentration is maintained. MAC has been shown not to vary with length of anaesthesia.

Table 1
Mean ages, weights, and heights; sex distribution; incidence of smoking, consumption of alcoholic beverages, nocturnal waking, and previous general anaesthesia; mean systolic and diastolic arterial pressures, and end tidal carbon dioxide concentrations in Chinese, Nepalese, and European patients.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Chinese n = 18</th>
<th>Nepalese n = 12</th>
<th>Europeans n = 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>63.5±24.4</td>
<td>57.8±10.7</td>
<td>60.1±13.3</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.56±0.35</td>
<td>1.54±0.09</td>
<td>1.65±0.09</td>
</tr>
<tr>
<td>Sex</td>
<td>M9 F9</td>
<td>M1 F11</td>
<td>M3 F7</td>
</tr>
<tr>
<td>Smoking</td>
<td>19%</td>
<td>25%</td>
<td>40%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>43%</td>
<td>50%</td>
<td>90%</td>
</tr>
<tr>
<td>Dreaming incidence</td>
<td>76%</td>
<td>92%</td>
<td>80%</td>
</tr>
<tr>
<td>Nocturnal waking</td>
<td>1.53±0.92</td>
<td>1.83±1.21</td>
<td>1.75±1.86</td>
</tr>
<tr>
<td>Previous anaesthetic</td>
<td>44%</td>
<td>33%</td>
<td>100%</td>
</tr>
</tbody>
</table>

A number of factors affect the MAC value including age, body temperature, partial pressure of carbon dioxide, circadian rhythm and potentiation by other drugs. MAC is lower with increasing age but as the mean ages of our groups were similar, no corrections were made for age (6). Although changes in partial pressure of carbon dioxide affect MAC (7), minor degrees of hypocarbia or hypercarbia do not (8) and to reduce the influence of circadian rhythm, all our determinations were done in the morning or early afternoon. Sedatives or other anaesthetic agents, including lignocaine, are additive in their affect on MAC rather than one agent modifying the effect of another (9). For this reason our patients received no other drugs or agents prior to the determination. Our sexes were not well balanced which reflects the patient mix of our hospital, however, Tanifuji and associates (10) have shown that MAC is unaffected by menstrual cycle or gender.

<table>
<thead>
<tr>
<th>Halothane Concentration</th>
<th>Chinese</th>
<th>Nepalese</th>
<th>Europeans</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.57</td>
<td>0</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>0.65</td>
<td>0</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>0.66</td>
<td>2</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>0.68</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>0.70</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>0.71</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>0.75</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>0.76</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>0.77</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>0.80</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>0.87</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2
Response of Chinese, Nepalese, and European patients at different concentrations of halothane.

- 0.64 0 1 4 1 0.20
- 0.65 2 0 4 1 0.20
- 0.69 0 2 2 3 0.60
- 0.70 1 1 2 4 0.67
- 0.73 0 1 2 5 0.71
- 0.77 0 1 1 6 0.86
- 0.80 0 1 1 7 0.88
- 0.87 1 0 1 7 0.88

- 0.46 1 0 5 0 0.00
- 0.67 2 1 4 1 0.20
- 0.69 0 1 2 2 0.50
- 0.70 0 1 2 3 0.60
- 0.71 0 1 2 4 0.67
- 0.72 0 1 2 5 0.71
- 0.73 1 0 2 5 0.71
- 0.77 0 1 1 6 0.86
- 0.80 0 1 1 7 0.88
- 0.87 1 0 1 7 0.88

- 0.64 0 1 4 1 0.20
- 0.65 2 0 4 1 0.20
- 0.69 0 2 2 3 0.60
- 0.70 1 1 2 4 0.67
- 0.73 0 1 1 5 0.83
- 0.76 1 0 1 5 0.83
- 0.81 0 1 0 6 1.00
A number of factors may affect the accuracy of the determination. Whilst an endotracheal tube facilitates sampling of alveolar gas, drugs used to assist intubation such as lignocaine, suxamethonium or other neuromuscular blocking agents may affect MAC. We chose not to use an endotracheal tube but to sample through a specially modified airway at the entrance of the larynx. An airtight seal was maintained with a mask and the airway kept open with jaw thrust. The airway tissues will absorb halothane from the inspired gas and the alveolar gas may be contaminated by halothane diffusing out during expiration. The effect is greater with more soluble agents but the effect can be reduced by lowering the inspired halothane concentration below that of the alveolar gas just before measurement of MAC. The point at which inspired and expired concentrations were equal was taken as the true value of the alveolar concentration of halothane.

A failure to randomise or predetermine the concentration of volatile agent may prejudice the results. The results are based on small numbers which were analysed, therefore, with a modification of the Spearman-Kärber method (4), rather than the more usual Waud’s method of statistical analysis. These preliminary results suggest there are no ethnic differences in the MAC of halothane in Asians and Caucasians.

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