RAPID INDUCTION OF HALOTHANE ANAESTHESIA IN MAN

J. M. RUFFLE, M. T. SNIDER, J. L. ROSENBERGER AND W. B. LATTA

The inhalation induction of general anaesthesia is usually avoided by both patients and anaesthetists, since a prolonged induction may terrify both adults and children. In addition, the anaesthetist may have difficulty maintaining the airway and restraining the muscular patient if excitement occurs. Intravenous induction is popular because these complications are usually avoided. However, venous access may be impossible in some patients and the slow termination of action of i.v. agents may delay the awakening of patients following outpatient surgery. In the past, cyclopropane offered an alternative (Bourne, 1954): loss of consciousness was rapid, arterial pressure was well maintained and emergence was rapid. The risk of explosion has, however, forced most anaesthetists to discard this method of rapid induction.

To provide a better method of gaseous induction of anaesthesia in co-operative adults, we devised a new halothane in oxygen technique. The patient takes a vital capacity breath of 4% halothane in oxygen and attempts to hold his breath until he is unconscious. The method has been used in approximately 200 patients in the past 5 years and appears to be effective, safe and acceptable. To understand this technique better, we attempted to anaesthetize healthy volunteers using vital capacity breath-holds of various concentrations of halothane in oxygen as delivered by clinical equipment, while monitoring cardiopulmonary responses.

SUBJECTS, MATERIALS AND METHODS

Selection of volunteers

Following approval by our Human Studies Committee, nine healthy men and women, aged 20–45 yr, were recruited. No volunteer had a history of liver disease and each had normal haematological values, serum bilirubin concentration, alkaline phosphatase concentration, transaminase concent-
rations, and negative titres for HBsAg and HBeAg. Informed consent included specific reference to the possibility of liver disease following exposure to halothane.

**Measurements**

Heart rate and rhythm were monitored on a standard operating room electrocardiograph. Arterial pressure was measured using an automatic non-invasive monitor (Dinamap No. 845XT with a model No. 950 recorder (Critikon)) (Looney, 1978). Arterial oxygen saturation was estimated using an ear oximeter (Biox model No. 11 A) (Fahey et al., 1983). Oxygen, nitrogen, carbon dioxide and halothane were detected continuously in the inspired and expired gas using a Perkin Elmer mass spectrometer (model MGA 1100A) which was calibrated using gravimetric standards of nitrogen, oxygen, carbon dioxide and halothane contained in compressed gas cylinders (Calibrated Standards, Airco Inc.) The signals were recorded on magnetic discs and processed subsequently on a DEC MINC 11/23 laboratory computer. The inspired concentrations of halothane, and the end-tidal concentrations of halothane (ET\textsubscript{hal}), oxygen (ET\textsubscript{O2}), and carbon dioxide (ET\textsubscript{CO2}) were tabulated on a breath-by-breath basis. Arterial oxygen saturation (SaO\textsubscript{2}), heart rate (HR) and arterial pressure were noted before induction, after 2 min of breathing halothane, and after awakening.

**Anaesthetic apparatus**

Mixtures of halothane in oxygen were delivered from a Drager Narkomed 2 anaesthetic machine fitted with either a Drager Halothane 19 or a Vapor vaporizer and a circle system. In place of the Y-connector in the circle, a Collins spirometer valve was used to allow the inspired gas to be switched rapidly between room air and the anaesthetic gas in the circle. The connector between the spirometer valve and the mask was the site for sampling inspired and expired gas for analysis. For each trial the circle was primed for about 2 min at a 10-litre min\textsuperscript{-1} oxygen flow with the vaporizer set at the desired halothane concentration.

**Experimental programme**

Each volunteer breathed a sequence of four concentrations of halothane in oxygen. Each exposure to halothane lasted no more than 4 min and a recovery period of at least 15 min was allowed between exposures.

After an 8-h fast, the volunteer lay supine on a stretcher and monitoring was commenced. At each anaesthetic concentration the volunteer inhaled a vital capacity breath of air through the mask and then exhaled to residual volume. The Collins valve was opened to the anaesthetic mixture and then, over a 10-s period, the volunteer inhaled (through his mouth) a vital capacity breath of halothane in oxygen from the primed anaesthesia circuit. The breath was taken slowly to avoid collapsing the reservoir bag. After the initial breath, the fresh gas flow was reduced to 5 litre min\textsuperscript{-1} to minimize positive pressure in the circle. After a breath-hold of 30–90 s the volunteer exhaled and then breathed spontaneously. He indicated the onset of tinnitus by a hand signal. After the breath-hold the same halothane in oxygen mixture was inspired for a maximum of 2 min. The Collins valve was then opened to room air and the volunteer emerged from anaesthesia.

Each volunteer inspired five mixtures of halothane and oxygen. Between trials the subject recovered until his expired halothane concentration was less than 0.01% and he felt fully awake. Four percent halothane in oxygen was administered first to determine a comfortable breath-hold time for subsequent trials, to accustom the volunteer to the experience of general anaesthesia, and to ascertain if the maximum inhaled concentration could be tolerated. The four subsequent trials of 1, 2, 3 and 4% halothane in oxygen were given in a random order to avoid biasing responses by a cumulative effect of halothane. In addition, the subjects were blind to the concentration of halothane. Onset of unconsciousness was defined as the time at which the subject would no longer open his eyes to verbal command. This command was repeated every 15 s until the subject no longer responded. Onset of awakening was defined as the time at which the subject first opened his eyes to verbal commands repeated at 15-s intervals.

**Data analysis**

The end-tidal halothane concentrations (ET\textsubscript{hal}) were evaluated by analysis of variance (ANOVA) to ascertain the effect of individual differences in volunteers $S$; nominal inspired halothane concentration, $C$; order of treatments administered, $O$; carry over effect from the halothane concentration of preceding trials, $R$; and finally breath number, $X$ (Winer, 1971). The model for the average response over all breaths $(ET_{hal})_{ijklm}$ was similar to that for a
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change-over design balanced for residual effects (John, 1971) with:

\[(\text{ET}_{\text{hal}})_{ijklm} = S_i + C_j + \Omega_k + \gamma_l + e_{ijkl} + \beta_1 X_{ijkl} + \beta_2 X_{ijkl} + f_{ijklm}\]

The \(e_{ijkl}\) error term represented the error variation among the trials and formed the error term for testing the above factors. The order factor was used to test for a cumulative effect over the five trials. The carry-over effect tested whether the concentration during the previous trial left a residual effect on the current trial. \(\beta\) represents the overall linear slope and \(\beta_1\) the separate slopes for the different halothane concentrations. The term \(f_{ijklm}\) represents the repeated measures error across all trials. The terms in the model indexed by \(m\) represent the repeated measures made after breaths 1–5 and at 2 min.

Three conditions were defined for analysis of cardiopulmonary responses. These included before induction, during anaesthesia and after awakening. ANOVA was used to evaluate the effects of subject; inspired halothane concentrations, condition and all first order interactions.

Because three observations were lost as a result of instrumentation malfunctions, calculations were adjusted for unbalanced and missing data using the general linear model routine in the SAS statistical package (Helwig and Council, 1979). All trials for subjects were considered stochastically independent. Diagnostic plots verified the assumption of homoscedastic errors. For all tests a value of \(P < 0.01\) was considered statistically significant.

RESULTS

During the induction of anaesthesia the inspired halothane concentrations, measured at the connector to the mask, were always greater than the vaporizer settings (table I). The relative percentage errors varied inversely with concentration and ranged from ±19.0 to ±6.1%.

End-tidal halothane concentrations increased rapidly and linearly with successive breaths at all inspired concentrations of halothane greater than 1% (fig. 1). However, at 1% halothane, the end-tidal concentrations appeared to plateau after the second breath. The slope of the 1% data was zero while the slopes of the 2%, 3%, and 4% data were greater than zero and did not differ significantly from each other (\(P < 0.01, F\) test). With subjects breathing 4% halothane, the mean end-tidal concentration was 1.5% at the end of the fifth breath. We observed a significant difference in the time course of end-tidal halothane between subjects (table II). There was no carry-over between successive trials of halothane exposure.

There were differences among subjects before induction in arterial pressure, heart rate, \(\text{ET}_{\text{CO}}\), \(\text{ET}_{\text{CO}_2}\), and arterial oxygen saturation, but these differences failed to influence the cardiopulmonary responses to halothane. Maximum changes in all variables were seen with 4% halothane (table III). Although decreases in arterial pressure were statis-

![Fig. 1. The end-tidal concentration of halothane (EThal) (mean values ± SEM) increased linearly with each successive breath at inspired concentrations of 2% (□), 3% (●) 4% (◆). At 1% (○) inspired concentration a plateau was reached by the third breath.](https://academic.oup.com/bja/article-abstract/57/6/607/272077)
Gas concentrations were measured at the end of the breath hold. Pressures were measured at the end of the 2-min period. Saturation and capacity breath of 4% inspired halothane followed by 2 min of spontaneously breathing 4% halothane (mean±SEM). Arterial TABLE III.

<table>
<thead>
<tr>
<th>Source of variance</th>
<th>df</th>
<th>Mean square</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject</td>
<td>8</td>
<td>0.236</td>
<td>2.57</td>
<td>0.040</td>
</tr>
<tr>
<td>Concentration</td>
<td>3</td>
<td>0.380</td>
<td>4.14</td>
<td>0.019</td>
</tr>
<tr>
<td>Order</td>
<td>4</td>
<td>0.169</td>
<td>1.84</td>
<td>0.159</td>
</tr>
<tr>
<td>Carry over effect</td>
<td>3</td>
<td>0.064</td>
<td>0.70</td>
<td>0.564</td>
</tr>
<tr>
<td>Error</td>
<td>21</td>
<td>0.0918</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Breath number</td>
<td>1</td>
<td>7.561</td>
<td>161.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Concentration × breath number</td>
<td>3</td>
<td>0.456</td>
<td>9.69</td>
<td>0.0001</td>
</tr>
<tr>
<td>Repeated measures error</td>
<td>159</td>
<td>0.0467</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

...cally significant, their magnitude was small. The greatest change was in systolic pressure and was less than 12 mm Hg. Heart rate did not change and no arrhythmias were observed. Inspired and expired oxygen tensions increased during induction and returned toward normal with awakening. Oxygen saturation remained stable during induction but decreased slightly while volunteers breathed room air during emergence. The vital capacity manoeuvre with room air decreased end-tidal carbon dioxide concentration to 4.5 kPa before induction. The end-tidal carbon dioxide concentration at the end of breath holding was 6.2 kPa.

The number of patients failing to respond to verbal command increased with breath number and percent inspired halothane (table IV). The onset of unconsciousness was rapid and was achieved in 15 of 16 trials after breath-hold plus 2 min of breathing 4% halothane. This represented 3.5 min of anaesthesia time. Although in only two of 16 trials were the volunteers unconscious at the end of the breath-hold of 4% halothane, they were unconscious in 10 of 16 trials by the fifth breath of 4% halothane. While breathing 2% halothane, seven of nine subjects were unconscious by 2 min.

**DISCUSSION**

Gaseous induction by a single vital capacity breath of 4% halothane in oxygen followed by 2 min of breathing the same mixture produced unconsciousness rapidly in healthy young volunteers without clinically important hypotension, arrhythmia, hypercarbia or hypoxia. Our volunteers found the experience relatively pleasant and stated they would accept this method for clinical anaesthesia. Indeed, those previously anaesthetized with either an i.v. induction or a conventional gaseous induction with gradually increasing concentrations of anaesthetic, expressed a clear preference for the single-breath technique.

This approach to anaesthesia is reminiscent of the gaseous induction of anaesthesia with cyclopropane: because of its low solubility and relatively high potency, both induction and awakening were rapid (Bourne, 1954). Our data demonstrate that this method of induction using halothane is similarly rapid and suggests that, in addition, in an unpremedicated patient awakening is rapid after a short anaesthetic. Variations in time to unconsciousness and rate of increase in end-tidal halothane concentrations among volunteers have several explanations. The minimum alveolar concentration (MAC) decreases with age (Stoelting, Longnecker and Eger, 1970). Since our volunteers ranged in age from 20 to 45 yr, we might expect the youngest volunteers to be least readily anaesthetized. This was not the case. Variable anaesthetic uptake may result if residual volume or vital capacity are not reached during induction. Specifically, if the initial breath is

**TABLE IV. Number of breaths or time required to produce unconsciousness at different inspired concentrations of halothane**

<table>
<thead>
<tr>
<th>Inspired halothane (%)</th>
<th>First breath</th>
<th>Fifth breath</th>
<th>1 min</th>
<th>2 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0/8</td>
<td>1/8</td>
<td>0/8</td>
<td>1/8</td>
</tr>
<tr>
<td>2</td>
<td>0/9</td>
<td>0/9</td>
<td>1/9</td>
<td>2/9</td>
</tr>
<tr>
<td>3</td>
<td>2/9</td>
<td>3/9</td>
<td>5/9</td>
<td>8/9</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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less than vital capacity, a submaximal amount of
halothane is available for uptake. If the first exhalation fails to reach residual volume, the subsequent
breath of halothane and oxygen to the vital capacity
point must be diluted with more air. Hence the sub-
ject's alveolar halothane concentration, at peak
inspiration, is lower and there is less anaesthetic
effect. Finally, variations in inspired halothane con-
centration supplied by vaporizers may occur. We
were surprised at the discrepancy between the nom-
inal vaporizer settings and actual concentration of
halothane delivered as measured by the mass spec-
trometer (table I). Some of the variation seen be-
tween subjects may be related to differences be-
tween nominal and actual inspired anaesthetic
concentrations.

Although it was difficult to measure precisely, the
onset of amnesia occurred substantially earlier than
the onset of unconsciousness. Volunteers usually
remembered only the first breath, even when obey-
ing commands after the fifth breath of halothane.
We believe that this early onset of amnesia may be an
important factor in acceptance and also contributes
to the flexibility of this technique. A concentration
of halothane as low as 2% is often adequate. This is
a potential advantage because 2% halothane is less
irritating to breathe than 4%. However, several of
the volunteers preferred the induction using 4%
halothane because it was more rapid. Only one vol-
unteer found the halothane sufficiently irritating to
cause coughing, but the coughing did not delay
induction.

Our data are consistent with previous descriptions
of halothane uptake and minimum alveolar concen-
trations (Gregory, Eger and Munson, 1969; Nicodemus et al., 1969; Stoelting, Longnecker and
Eger, 1970). There appears to be enough uptake
after five breaths or 2 min following a 30–90 s
breath-hold to achieve adequate anaesthetic con-
centrations in the brain. The increase in expired car-on dioxide at the end of a vital capacity breath-hold
of 4% halothane was 1.7 ± 0.3 kPa. Eger and Severinghaus (1961) measured an increase of
1.8 ± 0.3 kPa after the first 1 min of apnoea in
anaesthetized patients.

These investigations were carried out on healthy
volunteers, and our clinical experience with this
technique has been with patients of ASA status I and
II. This method of induction offers real benefits to
patients having brief procedures, in achieving both
rapid onset of unconsciousness and fairly prompt
awakening. Patients in whom venous access is dif-
ficult can be anaesthetized painlessly and safely
before the i.v. access is established. At present, we
regard patients with poor lung function having large
ventilation/perfusion mixmatches, greatly reduced
vital capacity or excessively large functional residual
capacity as poor candidates for this particular
 technique. In addition, the young, the retarded, the
senile and others who cannot or will not perform the
necessary steps are unsuitable, because co-operation
is required. Premedication with, for example, ben-
zodiazepines, or barbiturates and narcotics is com-
patible, but may modify the breath-hold time and
delay the resumption of regular breathing because of
the respiratory depressant effects of these drugs
(Patrick and Faulconer, 1952; Smith et al., 1967;
Gross, Smith and Smith, 1982).

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