SOMATIC MOVEMENT AND OESOPHAGEAL MOTILITY DURING ISOFLURANE ANAESTHESIA

C. MATHER, S. RAFTERY AND C. PRYS-ROBERTS

SUMMARY

The quantal responses for somatic movement, and spontaneous and provoked lower oesophageal contractions (motility) were noted at the time of incision in 72 patients aged 40-65 yr, receiving varying concentrations of isoflurane. Probit analysis of the alveolar concentration of isoflurane required to prevent somatic movement revealed an MAC or EC95 (95% confidence limits) of 1.00 (0.83-1.17)% and EC99 of 2.16 (1.69-3.89)%. The EC95 of isoflurane to suppress spontaneous lower oesophageal contractions was 1.27 (1.12-1.43)%, and the EC99 2.13 (1.78-3.22)%. The EC95 for provoked lower oesophageal contractions was 1.31 (0.93-3.48)% and the EC99 was 6.18% (unable to compute confidence limits).

KEY WORDS:
Lower oesophageal contractions Anaesthesia, gaseous.

The concept of minimum alveolar concentration (MAC) as an index of potency and means by which various inhaled anaesthetic agents may be compared, was introduced by Merkel and Eger in 1963 [1]. MAC is defined as the alveolar concentration that prevents gross somatic movement in 50% of subjects after a surgical incision; it is equivalent to the median value read from the concentration-response curve (the EC50 or median effective concentration), although in the past MAC has been determined by the Dixon "up and down" method [1,2]. However, the MAC is just one "point" and gives no indication of the shape or slope of the complete concentration-response curve. More significantly, the EC96 and the "slope" of the curve have been extrapolated from the EC95 studies [3].

We studied the quantal concentration-effect relationships for somatic motor and for spontaneous (SLOC) and provoked (PLOC) lower oesophageal contractions (visceral motility) during isoflurane anaesthesia, to validate the published values for MAC (equivalent to EC95) and to allow accurate definition of both the EC95 and the slope of the concentration-effect curve. Evans and others [4-6] have suggested that lower oesophageal contractions (LOC) may provide an index of anaesthetic adequacy, but there has been little to link oesophageal contraction indices to MAC for inhalation anaesthetics. Our objectives in the present study were to determine if it is feasible to use a quantal measure of a visceral reflex (in the same way that one uses somatic "move/no move" responses to reflect anaesthetic adequacy), which would not only be unaltered during somatic muscle paralysis, but also predict the likelihood of somatic movement in patients anaesthetized with inhalation agents. Other investigators have tried to quantify various aspects of LOC to identify a threshold above which "awareness" or anaesthetic inadequacy may be said to be present: in particular, the rate of SLOC, the amplitude of PLOC and the oesophageal contractility index [7]. The quantal relationship between LOC and the i.v. anaesthetic, propofol [8], has already been established, but we have been unable to trace any previous attempts to quantify the quantal relationship between LOC and inhalation anaesthetic concentrations.

PATIENTS AND METHODS

The study was approved by the district Ethics Committee and informed consent was obtained from each patient. Seventy-two healthy patients, aged 40-65 yr, presenting for lower abdominal and extraperitoneal surgery under general anaesthesia were allocated randomly to one of seven groups, each to receive differing end-tidal concentrations of isoflurane (table I). Patients were premedicated with temazepam 20 mg orally 2 h before anaesthesia, which was

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induced by spontaneous breathing of increasing concentrations of isoflurane in oxygen, via a face mask and Lack breathing system. When regular breathing and centrally fixed pupils were noted, suxamethonium 1 mg kg⁻¹ was given to facilitate tracheal intubation and passage of an oesophageal probe to 35 cm below the teeth (marked on the probe). Correct position of the probe was confirmed by hearing breath and heart sounds through the integral stethoscope. The probe was connected to a Lectron 302 oesophageal contractility monitor (Antec Systems Ltd) set to monitor spontaneous lower oesophageal contractions (SLOC) and provoked oesophageal contractions (PLOC) [5]. A threshold of 15 cm H₂O was set to eliminate the interpretation of any ventilatory artefacts that may be transmitted to the oesophageal probe, such as coughing or straining, from being interpreted as oesophageal contractions.

After intubation of the trachea, spontaneous ventilation was allowed to return and neuromuscular function was confirmed by peripheral nerve stimulation, if any doubt remained. Maintenance was by spontaneous breathing of the preselected end-tidal isoflurane concentration in oxygen, achieved by adjustment of the inspired isoflurane concentration. In every patient, greater than 20 min elapsed between induction and incision. End-tidal isoflurane concentrations were measured by a precalibrated gas analyser (Datex Capnomac).

At incision, the patient’s motor response was noted as either movement or no movement; a positive result was defined as movement of one or more extremities occurring within 60 s of skin incision. The presence or absence of SLOC and PLOC within 60 s of skin incision were also noted. If the patient moved at any time, surgery was halted and increments of propofol 20 mg were given and recorded. After incision, anaesthesia was continued by spontaneous breathing of 1.5-2% isoflurane with 70% nitrous oxide in oxygen.

Analysis of data was performed using SAS software (SAS for PC, version 6.03, SAS Institute, Cary, NC, U.S.A.) [9] Data relating to patient characteristics were analysed for statistical significance using one-way analysis of variance. Probit analysis of the ratio of movers to non-movers and the ratio of those patients with SLOC or PLOC to those without was used to determine the alveolar isoflurane concentration—response curves for somatic movement and for oesophageal contractions (Slope [9]).

Calculated values and 95% confidence limits for EC₅₀ and EC₉₅ of isoflurane for somatic movement and for oesophageal contractions are displayed in Table III.

Figure 1 shows the log concentration–response curves for somatic motor responses, and spontaneous and provoked oesophageal contractions as functions of the end-tidal concentration of isoflurane.

**DISCUSSION**

The results of our study confirm the value for MAC, in this age group, derived in the original study by Stevens and colleagues [10], but are at variance with the values for EC₅₀ then derived, by extrapolation, by de Jong and Eger (table IV) in patients from the same study [3]. Because the Dixon up-and-down method [2] generates a central tendency around the eventual mean value, it provides an inadequate method of determining the EC₅₀ and the true slope of the central part of the log concentration–response

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### Results

Patients in each group were similar in terms of age, weight and sex distribution (table I). The time of incision after induction of anaesthesia, numbers of patients who moved in response to the initial surgical incision and those who had spontaneous (SLOC) or provoked (PLOC) oesophageal contractions are shown in table II.

### Table II. Mean (SD) time of surgical incision after induction of anaesthesia (no significant difference between groups) and the incidence of somatic movement, spontaneous and provoked oesophageal responses

<table>
<thead>
<tr>
<th>Group (end-tidal isoflurane (%))</th>
<th>n</th>
<th>Time (min)</th>
<th>Movement SLOC (No.)</th>
<th>PLOC (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>10</td>
<td>26.0 (5.4)</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>0.8</td>
<td>11</td>
<td>27.7 (7.6)</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>1.0</td>
<td>10</td>
<td>27.5 (6.7)</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>1.2</td>
<td>10</td>
<td>23.3 (4.3)</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>1.4</td>
<td>10</td>
<td>23.6 (7.3)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1.6</td>
<td>11</td>
<td>25.7 (7.0)</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>1.8</td>
<td>10</td>
<td>28.7 (6.8)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table III. Computed end-tidal (alveolar) isoflurane concentrations required to abolish responses to surgical incision (value (95% confidence limits)). Probit analysis of the ratio of movers to non-movers and the ratio of those patients with SLOC or PLOC to those without was used to determine the alveolar isoflurane concentration–response curves for somatic movement and for oesophageal contractions (Slope [9]). n.c. = Not calculable

<table>
<thead>
<tr>
<th>Response</th>
<th>EC₅₀ (%)</th>
<th>EC₉₅ (%)</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Movement</td>
<td>1.00 (0.82-1.17)</td>
<td>2.16 (1.69-3.89)</td>
<td>4.94 (1.13)</td>
</tr>
<tr>
<td>SLOC</td>
<td>1.27 (1.12-1.43)</td>
<td>2.13 (1.78-3.22)</td>
<td>7.30 (1.59)</td>
</tr>
<tr>
<td>PLOC</td>
<td>1.31 (0.93-3.48)</td>
<td>6.18 (n.c.)</td>
<td>2.44 (1.05)</td>
</tr>
</tbody>
</table>

**FIG. 1.** Concentration–response curves for somatic movement (—), spontaneous (—) and provoked (—) lower oesophageal contractions as functions of the end-tidal concentration of isoflurane.
of the three (table IV). Their data might also suggest that the concentration–response curves of the common volatile anaesthetics for somatic movements have differing slopes (table IV), but this must be regarded as speculative until full concentration–
response curves have been determined for enflurane and halothane.

Our quantal concentration–response curve relating SLOC and isoflurane concentration is steeper and lies to the right of that for somatic movement (table III, fig. 1), consistent with the findings during total i.v. anaesthesia (fig. 2) [8]. Thus a greater concentration of isoflurane is necessary to suppress visceral motility than for somatic movement. At the EC50 for SLOC, one would predict that 70 % of patients would not move. The quantal concentration–
response curve for PLOC was distinctly flatter than either of the two other curves (fig. 1), indicating that PLOC was more difficult to suppress than either somatic movement or SLOC. Changes in PLOC activity would, therefore, seem to have less value in distinguishing between the adequately and the inadequately anaesthetized patient. This is consistent with previous studies which concluded that PLOC were unhelpful in assessing adequacy of anaesthesia [8, 12]. Measurements of PLOC have not been found to correlate with brainstem death, as do SLOC [13].

We can find no evidence that concentration–response curves for loss of consciousness have ever been estimated for volatile anaesthetics, but recent studies [14] of an i.v. anaesthetic, propofol, suggest that the dose–(concentration)–response curve for consciousness lies well to the left of that for somatic movement in response to incision. It is generally assumed that, if unparalysed patients do not move in response to a noxious stimulus, it can be accepted that they are unconscious and unlikely to have any explicit recall of events during anaesthesia. Can one then monitor in paralysed patients an index of visceral motility, such as SLOC, the concentration–response curve of which lies further to the right of that for somatic movement, to predict the adequacy of anaesthesia? In Evans' study of an i.v. anaesthetic, propofol, the authors suggested that lower oesophageal contractions (LOC) might be a useful index of adequacy. Many other investigators have related LOC activity qualitatively with clinical signs of anaesthesia, haemodynamic changes, autonomic responses, movement of an isolated limb, EEG and EMG changes [4, 15–18]. Thornton and her colleagues [19] showed a good correlation between the amplitudes and latencies of auditory evoked potentials and venous concentration of propofol, whereas neither SLOC nor PLOC correlated. Their results in only six patients are, however, at variance with those of Raftery, Enever and Prys-Roberts [8], who showed a clear dose– and concentration–response with both SLOC and PLOC, during propofol and alfentanil anaesthesia. Figure 1 shows the concentration–response curves for somatic movement and oesophageal visceral motor activity as functions of the end-tidal isoflurane concentration; theoretically, the end-tidal concentration reflects the arterial concentration, but in practice this cannot always be said to be valid for

<table>
<thead>
<tr>
<th>Anaesthetic</th>
<th>EC50 (%)</th>
<th>EC95 (%)</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>1.05 (0.05)</td>
<td>4.94 (1.1)</td>
<td>8.60 (3.8)</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>1.50 (0.01)</td>
<td>2.16 (1.7–3.9)</td>
<td>15.2 (6.7)</td>
</tr>
<tr>
<td>Enflurane</td>
<td>1.00 (0.8–1.2)</td>
<td>1.63</td>
<td>27.3 (14.0)</td>
</tr>
<tr>
<td>Halothane</td>
<td>1.68</td>
<td>27.3 (14.0)</td>
<td>2.16 (1.7–3.9)</td>
</tr>
</tbody>
</table>

**TABLE IV.** Comparison of results from our study with those from Stevens and colleagues [10] and de Jong and Eger [3]. EC50, EC95 and slopes of the log-concentration probit response (somatic movement) "curves" of isoflurane (SE or 95 % confidence interval). The slopes only of the "curves" for halothane and enflurane are given here for comparison. Ages of patients studied were mean 55 yr (range 40–65 yr) in the present study, mean 64 yr (range > 55 yr) in [10] and mean 55 yr (range 40–65 yr) in [3].

![Figure 2](image-url)
OESOPHAGEAL MOTILITY

individuals. Concentration–response curves have also been determined previously for total i.v. anaesthesia with propofol and alfentanil [8]; figure 2 shows these oesophageal visceral responses as functions of the venous concentration of propofol (values are taken from [8]). Although the slopes in figures 1 and 2 are not directly comparable, it is of interest that the relationships appear to hold true for both propofol and propofol, in that, first, the concentration–response curve for SLOC lies close to, and to the right of, that for somatic movement and, second, that for PLOC is the flattest of the three curves.

Some aspects of our methods in this study merit discussion. Theoretically, indices such as MAC (ECB6) and ECB6 should be based on measurements made under steady state conditions, when equilibrium of isoflurane, between alveoli, blood and brain should be achieved. However for equilibrium to be complete would take many hours, and previous studies have compromised therefore and accepted at least 10 min at a stable end-tidal concentration. Unlike most studies, we not only performed a gaseous induction (“loading dose”), but also allowed at least 20 min before surgical incision, and our inspiratory to end-expiratory concentration ratios of isoflurane were close to unity. The bias towards the number of females in our study should cause no error, as no significant differences have been shown for MAC between the sexes [10]. There were occasions when interpretations of LOC were difficult, in that PLOC could be confused with coincidental SLOC, or vice versa. This problem occurred mainly at smaller concentrations of isoflurane, when increased numbers of SLOC would result. If it was not possible to state whether or not a PLOC had occurred, these patients were noted and omitted from the final analysis. LOC could be confused also with extraneous disturbances of intra-thoracic pressure, transmitted to the oesophageal probe. We therefore excluded contractions which did not exceed our monitoring threshold, set at 15 cm H2O. Premedication with temazepam 20 mg may have contributed to a slight reduction in our MAC, although such effects are probably minimal in the absence of an opioid premedication [20].

Several unanswered questions have been raised during the course of this study. First, the consequences on LOC of using spontaneous ventilation and not controlling arterial carbon dioxide partial pressures (PAco2) are unknown. Spontaneous ventilation was chosen because this was the method of the original studies on MAC; it was also tolerated better by “lightly” anaesthetized patients, than controlled ventilation. The values of PAco2 encountered during spontaneous ventilation do not influence MAC [20], but the effect of PAco2 on LOC activity remains to be established.

Second, we compared LOC with somatic movement after the incision, in order to establish the relationship of the concentration–response curves at the same moment in time, and at the same “level” or adequacy of anaesthesia. Others claim to be able to predict the motor responses to incision on the basis of more than two SLOC in 6 min before incision [21], or the absence of SLOC in patients receiving halothane or isoflurane, but not with nitrous oxide–opioid anaesthesia [4, 5, 15, 17, 21].

In conclusion, the present study has shown that the quantal relationship between SLOC and end-tidal isoflurane concentration lies to the right of that for somatic movement in response to surgical incision. The relationship is similar to that shown previously for an i.v. anaesthetic combination. Based on this premise, we conclude that the absence of SLOC may be used to predict the adequacy of anaesthesia in paralysed patients anaesthetized with isoflurane, and that the presence of SLOC may lead the anaesthetist to question the adequacy of anaesthesia. Use of the quantal SLOC response to incision as an index of anaesthetic adequacy, when its concentration–response curve does lie to the right of that for somatic movement, may result in individual patients receiving excessive anaesthetic; ideally, we need to identify the visceral (or other) response for which the concentration–response curve coincides either with that for somatic movement or, perhaps better, with that for unconsciousness/lack of awareness. Finally, we suggest that the term motility [22, 23] is preferable to contractility to describe the phenomena of SLOC and PLOC, in that contractility suggests, by analogy with studies of cardiac and other smooth muscle, an inherent property related to the force of contraction.

REFERENCES