Sevoflurane EC$_{50}$ and EC$_{95}$ values for laryngeal mask insertion and tracheal intubation in children

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The laryngeal mask airway (LMA$^\text{ â}$) is a simple, easy to use and safe method for airway control in children. Its insertion needs less anaesthetic, and haemodynamic responses and post-operative sequelae are less than with laryngoscopy and tracheal intubation. This study was designed to determine the end-tidal concentrations of sevoflurane where 50% (EC$_{50}$) and 95% (EC$_{95}$) of the attempts to secure the airway would be successful. We randomly assigned 40 children aged 4–12 yr undergoing general surgery to either LMA insertion (n=20) or to laryngoscopy and tracheal intubation (n=20) under sevoflurane anaesthesia. The initial end-tidal concentration of sevoflurane for each child was determined according to the response of the previous child in the same group. Up to three attempts to secure the airway with increasing sevoflurane end-tidal concentrations in 0.3% steps were allowed for each child. The logistic regression model was used to calculate the EC$_{50}$ and EC$_{95}$ values. Sevoflurane provided good conditions for both LMA insertion, and laryngoscopy and tracheal intubation without serious adverse effects. The EC$_{50}$ and the EC$_{95}$ of sevoflurane were 1.57 (SD 0.33)% and 2.22% for LMA insertion and 2.20 (SD 0.31)% and 2.62% for laryngoscopy and tracheal intubation. Thus, less sevoflurane is required for LMA insertion in children than for laryngoscopy and tracheal intubation.

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The laryngeal mask airway (LMA$^\text{ â}$) is widely used for anaesthesia in children. Compared with laryngoscopy and tracheal intubation, it is easy to use, causes less haemodynamic response to insertion and removal, and fewer complications such as coughing and sore throat.$^1$ Less sevoflurane seems to be required for LMA insertion than for laryngoscopy and tracheal intubation.$^2$ In patients with upper respiratory tract infection it seems to cause less bronchoconstriction than the tracheal tube.$^3$–$^5$

Previous studies have only assessed the concentration where 50% of the attempts to secure the airway have succeeded (effective concentration EC$_{50}$).$^2$–$^7$ We designed a study to determine both the EC$_{50}$ for LMA and laryngoscopy and tracheal intubation, and also the concentration where 95% of the attempts would succeed (EC$_{95}$).

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$^1$LMA$^\text{ â}$ is the property of Intavent Limited.

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Materials and methods

We obtained ethics committee approval, written informed consent from the parents, and assent from children aged 7 yr or older, from 40 healthy children undergoing elective surgery under general anaesthesia (see Table 1 for patient characteristics). We excluded patients with a history of significant cardiorespiratory, renal or hepatic dysfunction or concurrent treatment with medication known to affect anaesthetic requirements, if the weight of the patient exceeded 150% of the ideal weight, or if the patient had symptoms of upper respiratory tract infection. The child was excluded from the study if premedication was needed after randomization and obtaining informed consent.

The children were randomly allocated either to LMA insertion or to laryngoscopy and tracheal intubation using a randomization table. The patients arrived in the surgical unit fasted and unpremedicated. They were connected to an electrocardiogram and a peripheral pulse oximeter. End-
tial sevoflurane concentration and carbon dioxide partial pressure during induction and maintenance of anaesthesia were monitored using a Datex Capnomac airway gas monitor (Datex-Ohmeda, Helsinki, Finland). After loss of the eyelash reflex a catheter was positioned via one of the nostrils in the oropharynx for sampling of the inspired and exhaled gases.8

Anaesthesia was induced with sevoflurane in a mixture of air and oxygen (FIO2 30%) at a concentration of 8% until loss of eyelash reflex, which occurred usually in less than 10 breaths. The patients breathed spontaneously from a Mapleson D circuit with a fresh gas flow of 6–9 litre min−1 throughout the study. If the end-tidal carbon dioxide partial pressure increased over 6.0 kPa ventilation was gently manually assisted, targeting an end-tidal carbon dioxide partial pressure of 4.5–6.0 kPa. After loss of the eyelash reflex, anaesthesia was maintained with the predetermined end-tidal concentration of sevoflurane. We used previous data2 6 7 to give 1.8% end-tidal sevoflurane to the first patient allocated for laryngeal mask insertion and 2.2% the first patient allocated for laryngoscopy and tracheal intubation. The anaesthetist in charge of the patient was not aware of the end-tidal sevoflurane concentration throughout the study. The predetermined end-tidal concentration of sevoflurane was maintained for 10 min to allow adequate time for alveolar and brain sevoflurane partial pressures to equilibrate.9 An attempt to secure the airway was then performed using either a standard multiple-use LMA or an uncuffed single-use tracheal tube. If the attempt failed (a failure was defined as any visible relevant spontaneous movement such as withdrawal or flexor movement of the arms or legs, frowning of the forehead muscles, coughing or bucking within 1 min of LMA insertion or laryngoscopy and tracheal intubation),2 6 7 the end-tidal sevoflurane concentration was increased by 0.3% end-tidal and another 10 min was allowed to elapse before the next attempt. If this second attempt failed the end-tidal sevoflurane concentration was increased again by 0.3% end-tidal and another 10 min was allowed to elapse before the third attempt. The difference between the inspired and end-tidal sevoflurane concentration was less than 10% at the time of each attempt to secure the airway.10 If the third attempt to secure the airway failed no further attempts were made as it was considered unethical to expose the patient to further attempts and the patient was then managed as considered appropriate by the anaesthesiologist in charge of the patient. The study ended at the first successful attempt or after the third unsuccessful attempt to secure the airway. If the attempt to secure the airway succeeded, the assigned end-tidal sevoflurane concentration for the next patient in that group was decreased by 30% of that of the successful attempt. If the third attempt to secure the airway failed, the assigned sevoflurane end-tidal concentration for the next patient in that group was that used at the third failed attempt. The sevoflurane concentration and the result of each attempt of securing the airway were recorded. The conditions of each successful LMA insertion or laryngoscopy and tracheal intubation were recorded as poor, good or excellent. Adverse effects, particularly excitation, during sevoflurane induction and maintenance were also recorded and graded none, mild, moderate or severe.

Statistics
All statistical analyses were performed using the SAS (SAS Institute Inc., Cary, NC, USA) statistical software. Fisher’s exact test was used to compare the groups regarding excitation and conditions of the successful attempts to secure the airway. Success of the LMA insertion or laryngoscopy and tracheal intubation was analysed using the logistic regression model to determine those sevoflurane end-tidal concentrations where 50% (EC50) and 95% (EC95) of the attempts were successful.11 Differences between the groups in EC50 and EC95 values were evaluated by t-tests. Data are presented as mean (SD) except were indicated and a P value of less than 0.05 was considered statistically significant.

Results
The patient characteristics of the groups were similar (Table 1). Eleven patients allocated to LMA insertion and four patients allocated to laryngoscopy and tracheal intubation (data of three patients missing) experienced mild to severe excitation during induction (Table 2). No

### Table 1 Patient characteristics as mean (SD) and range

<table>
<thead>
<tr>
<th></th>
<th>LMA</th>
<th>Tracheal intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>7.70 (2.70)</td>
<td>7.15 (2.30)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>130.3 (17.5)</td>
<td>125.1 (15.3)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>29.48 (11.71)</td>
<td>28.43 (13.83)</td>
</tr>
<tr>
<td>ASA class (n)</td>
<td>13/7</td>
<td>13/7</td>
</tr>
</tbody>
</table>

### Table 2 Excitation during induction of anaesthesia and the conditions of the successful attempts to secure the airway

<table>
<thead>
<tr>
<th></th>
<th>LMA</th>
<th>Tracheal intubation</th>
<th>P-value (Fisher’s exact)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excitation during</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>induction</td>
<td></td>
<td></td>
<td>0.251</td>
</tr>
<tr>
<td>None</td>
<td>9</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>7</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Conditions of</td>
<td></td>
<td></td>
<td>0.193</td>
</tr>
<tr>
<td>successful attempts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>16</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>
other adverse effects were observed during the study. The conditions during the successful attempts were generally good in both groups (Table 2). The EC₅₀ and the EC₉₅ of sevoflurane were 1.57 (0.33)% and 2.22% end-tidal for LMA insertion and 2.20 (0.31)% and 2.62% end-tidal for laryngoscopy and tracheal intubation, respectively (P<0.001 for both variables; Fig. 1).

Discussion
The minimum alveolar concentration (MAC), for example the concentration for achieving a 50% probability of no response to skin incision is the most widely used measure of anaesthetic potency for volatile anaesthetics.

However, it represents only one measure of potency, and other points on the concentration response curve are also of interest. Indeed, the concentration of the volatile anaesthetic that prevents a response to a stimulus in 95% of patients (EC₉₅) is clinically more useful than the EC₅₀. Previous studies on securing the airway under sevoflurane anaesthesia in children have focused on the EC₅₀. Therefore, our study was designed to determine both the EC₅₀ and the clinically more relevant EC₉₅ for LMA insertion and for laryngoscopy and tracheal intubation in children.

We found that (1) sevoflurane in general provided good conditions in unpremedicated children for both LMA insertion and for laryngoscopy and tracheal intubation and (2) both the EC₅₀ and the EC₉₅ of sevoflurane were significantly less for LMA insertion than for laryngoscopy and tracheal intubation. Our values for the EC₅₀ of sevoflurane are slightly less than those presented previously. The EC₅₀ of sevoflurane has been reported to be approximately 2.0% end-tidal for LMA insertion and in the range of 2.66–2.83% end-tidal for laryngoscopy and tracheal intubation.⁶⁷ There is one report of an EC₉₅ of 3.54% end-tidal of sevoflurane for laryngoscopy and tracheal intubation.⁷ These differences may be caused by several methodological differences between these studies and our study. In all previous studies, only one attempt to secure the airway was allowed for each child. In two of these studies, the up-and-down method was used which only allows EC₅₀ values to be measured.²⁶ Our study design, with three attempts at increasing sevoflurane concentrations for each child, increases the number of observations, particularly for unsuccessful attempts. This allowed us to assess both ends of the concentration response curve more closely than if only one attempt was allowed for each child. However, the possible carry-over effect of sevoflurane from the previous step of sevoflurane and attempt cannot be excluded. The 10 min equilibration period that we used for alveolar and brain sevoflurane partial pressures to equilibrate between each attempt should have been sufficient for sevoflurane, which has a blood-gas partition ratio coefficient of approximately 0.65.⁷⁹¹⁰ We also used a smaller step of sevoflurane changes (0.3% vs 0.5% end-tidal) than the other studies.²⁶⁷ This may have increased the accuracy in our study when the response to securing the airway was determined. Finally, we utilized the logistic regression model to calculate the EC₅₀ and the EC₉₅ values, instead of using a more simple method applied in the up-and-down technique. The use of the logistic regression model in the assessment of dose-response curves has recently been evaluated. The accuracy of the parameter estimates has been questioned, particularly when small samples such as the present one are being evaluated.¹³

In spite of this criticism the logistic regression model remains the only robust method to estimate both the EC₅₀ and the EC₉₅ values and it allows comparison of these values with those of previous similar studies.¹¹¹³ These
differences in methods probably cause small differences in the EC50 and EC95 values in our study and those reported previously. However, the results of our study are essentially in the same range as those reported previously.2 6 7

We conclude that, the LMA provides a safe and feasible alternative to secure the airway in children with significantly less sevoflurane requirements than needed for laryngoscopy and tracheal intubation. The LMA might be particularly practical for securing the airway in children during procedures that do not require deep levels of anaesthesia or during procedures that are performed under sedation and regional anaesthesia.

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