Evaluation of intubating conditions in children after sevoflurane induction using propofol or rocuronium bromide – a randomised, prospective, double blind study

S. GERA, J. S. DALI, K. R. SHARMA, R. GARG and M. ARYA

Abstract: Background: The use of sevoflurane without muscle relaxant for tracheal intubation has been widely investigated in children. Non-depolarizing neuromuscular blockers have long duration of action and do not provide rapid return of spontaneous ventilation. Use of succinylcholine has been found to be associated with various side-effects especially in children. Therefore, we aim to evaluate the effect of propofol 1.5 mg/kg without muscle relaxant, on intubating conditions in children 2-8 yrs of age and we compare them with those achieved with rocuronium 0.6 mg/kg, at moderate sevoflurane concentration.

Methods: Fifty children between 2-8 yrs, ASA I or II scheduled for elective surgery were randomly allocated to either Group P (propofol) or group R (rocuronium). After premedication with oral midazolam 0.5 mg/kg 30 min before surgery, anaesthesia was induced with 8% sevoflurane in oxygen. Intravenous fentanyl 1 µg/kg was administered after securing intravenous access and dial concentration of sevoflurane was reduced to 4%. At one minute with regards to time T1, the patients received the drug which was either intravenous rocuronium 0.6 mg/kg or an equal volume of 0.9% saline (D1) and at three minutes (two minutes after D1), second drug (D2) was given, which was either propofol 1.5 mg/kg or an equal volume of 0.9% saline according to the group allocated. At four minutes, laryngoscopy was done and intubation performed with appropriate sized uncuffed endotracheal tube. Incidence of acceptable and excellent intubating conditions, time to intubation and hemodynamic parameters were recorded.

Results: Incidence of acceptable or excellent intubating conditions was similar in both groups (p = 1.00). The difference in time to intubation was statistically not significant (25.03 ± 6.05s in Group P and 24.38 ± 5.58s in Group R, p = 0.694), at similar end-tidal concentration of sevoflurane (3.2 ± 0.20% in Group P and 3.1 ± 0.20% in Group R, p = 0.12).

Conclusion: Propofol (1.5 mg/kg) and rocuronium (0.6 mg/kg) produced similar intubating conditions in children induced with sevoflurane.

Key words: Sevoflurane; endotracheal intubation; propofol; neuromuscular blocking agent; rocuronium.

Background

Endotracheal intubation in children can be performed under deep inhalational anaesthesia or following neuromuscular blocking agents administration (1). More recently developed non-depolarizing neuromuscular blockers have intermediate duration of action and do not provide rapid return of spontaneous ventilation. Sevoflurane has been found to be suitable not only for induction by inhalation but also to provide optimal conditions for tracheal intubation (2, 3). However, it may not provide optimal relaxation of mandibular and laryngeal muscles. Occurrence of cough and limb movements during laryngoscopy and intubation can also be observed (4). Whereas, the use of high concentration of sevoflurane for intubation has the potential to produce hypotension and adverse effects such as epileptiform electroencephalographic activity, adjuvant drugs like propofol or opioids have been recommended to achieve rapid tracheal intubation with minimal adverse effects at moderate concentrations of sevoflurane (4, 5).

The use of optimal dose of propofol to achieve excellent intubating conditions in children without neuromuscular blockade at moderate and high alveolar concentration of sevoflurane has been reported previously by different authors (4, 5, 6). They observed that propofol 1.5-2 mg/kg and 2 mg/kg...
provide excellent intubating conditions at 3-4% end-tidal sevoflurane (5) and during 8% sevoflurane (4) induction respectively in children without using any neuromuscular blocking agent. We hypothesised that propofol when used as an adjuvant to moderate concentration of sevoflurane, could provide a suitable alternative to a neuromuscular blocking agent like rocuronium, to provide optimal intubating conditions at similar sevoflurane concentration. So, we planned to evaluate and compare the intubating conditions in children aged from 2 to 8 years old at moderate concentration of sevoflurane (4% dial setting) and using either propofol (1.5 mg/kg) or rocuronium (0.6 mg/kg).

METHODS

After approval of our institutional review board this randomised, prospective, double blind study was conducted in children 2-8 years old scheduled to undergo elective surgery, and requiring general anaesthesia with orotracheal intubation. Children with history of reactive airway disease, raised intracranial tension, any cardiovascular disease, with known allergy to any of the study drugs or anticipated difficult airway were excluded. After fasting for at least 6 hrs and premedication with oral midazolam 0.5 mg/kg 30 min prior to induction, the patients were shifted to the operating room. The 5 lead electrocardiogram (ECG), pulse oximeter (SpO2) and non-invasive blood pressure (NIBP) monitors (Excello, BPL Healthcare, India) were installed and baseline values of pulse rate, SpO2 and NIBP were recorded. A side- stream connector for the measurement of end-tidal sevoflurane concentration and end-tidal carbon dioxide was attached between the face mask and the breathing system. Anaesthesia was induced with sevoflurane 8% in 100% oxygen at a flow rate of 8 L/min using the Jackson Rees modification of Ayre’s T-piece circuit in patients weighing ≤ 20 kg and Mapleson D system in patients weighing > 20 kg. After loss of consciousness, ventilation was controlled or assisted when required and inspired sevoflurane concentration was decreased to 4% in pure oxygen. Intravenous line was secured and intravenous fentanyl 1 µg/kg was administered. This was recorded as time T0. Patients were randomly allocated using computer generated randomization to either one of the following two groups comprising 25 patients in each group. The randomized number was sealed in opaque envelope by an independent anaesthesiologist not involved in the study and opened just prior to intervention. Subsequent drugs were administered according to group allocated.

Group R (n = 25): Rocuronium 0.6 mg/kg (D1) + 0.9% saline (D2)

Group P (n = 25): 0.9% saline (D1) + Propofol 1.5 mg/Kg (D2)

At one minute with regards to time T0, the patients received the drug which was either intravenous rocuronium 0.6 mg/kg or an equal volume of 0.9% saline (D1) and at three minutes (two minutes after D1), second drug (D2) was given, which was either propofol 1.5 mg/kg or an equal volume of 0.9% saline according to the group allocated. The drugs were administered by an independent anaesthesiologist not involved in the present study. The limb receiving the drug was screened from the observer. At four minutes, laryngoscopy was done and intubation performed with appropriate sized uncuffed endotracheal tube. The mask ventilation and endotracheal intubation was done by experienced anaesthesiologist with over 500 intubations experience in children. The placement of endotracheal tube was confirmed by auscultation of chest and presence of square wave capnography.

The ‘time to intubation’ was noted as the time between insertion of laryngoscope blade and appearance of square wave capnography after intubation and connection of breathing circuit. The end-tidal sevoflurane was noted at the time of intubation. If intubation was not achieved within 1 minute and/or the SpO2 fell to < 92%, laryngoscope blade was removed and mask ventilation with pure O2 and 4% sevoflurane given for 30 seconds before another attempt was allowed. A maximum of three attempts were allowed. The intubation time in such a situation was the sum of time taken in these attempts. In the event that, the patients could not be intubated after three attempts the case was recorded as failure and the airway was managed according to difficult airway protocol. After intubation and confirmation of correct placement of endotracheal tube, ventilation was controlled using 66% nitrous oxide with 2-2.5% dial concentration of sevoflurane in oxygen after endotracheal intubation.

The ease of laryngoscopy, vocal cords position, coughing, jaw relaxation and limb movements were allocated a score of 1-4 using modified Helbo-Hansen score (6) (Table 1). Intubating conditions were excellent when all the scores were 1. Intubating conditions were judged acceptable when all scores were 2 or less. If any of the scores were 3 or 4, intubating conditions were judged unacceptable.

Haemodynamic parameters (NIBP, heart rate, and SpO2) were recorded before induction (base-
Intubating conditions in children after Sevoflurane induction

RESULTS

Fifty four patients were assessed for inclusion in the study and 50 were finally recruited as four patients did not meet our inclusion criteria. After recruitment no patient was excluded from the study and all 50 patients were included for study data analysis.

Both groups (group P and group R) were statistically similar with respect to age, weight and sex distribution of the patients (Table 2).

Incidence of acceptable intubating conditions i.e scores ≤ 2 as per modified Helbo-Hansen score (6) was 96% (24/25) in either group P or group R (Table 3). One patient in each group had one parameter with score 3, so intubating conditions were judged unacceptable in them (p = 1.00). Incidence of excellent intubating conditions (all scores as per modified Helbo-Hansen score (6) as 1) was 76% in both groups P and R (p = 1.00).

Trachea was intubated during first attempt in all patients. In Group P, mean time to intubation was 25.03 ± 6.1 sec while 25.8 ± 9.9 sec in group R (p = 0.755). At the time of intubation, the mean end-tidal sevoflurane concentration observed in group P was 3.2 ± 0.2% and 3.1 ± 0.2% in group R (p = 0.12).

As compared to baseline, increased heart rate was observed after induction (i.e. at time T0) in

Statistical analysis

The frequency of acceptable intubation with rocuronium 0.6 mg/kg was estimated to be 90% based on prior studies (7). We determined that a sample size of 50 children for the two groups based on detecting a 20% lower frequency of acceptable intubation conditions in the propofol group, with a power of 0.8 and alpha error of 0.05.

Statistical analysis was carried using SPSS software version-20. The quantitative data (time to intubation, hemodynamic parameters) were expressed as mean ± SD, and results (intubating conditions) were expressed as percentage. For quantitative data, mean of two groups was compared by student-t test or Mann-Whitney U test. Chi-square/ Fischer exact test was used to compare the difference between proportions. A p-value less than 0.05, was considered statistically significant.

Table 1

Intubating conditions parameters (modified Helbo-Hansen score (4))

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Score</th>
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<tbody>
<tr>
<td>Ease of Laryngoscopy</td>
<td>Easy Fair</td>
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<tr>
<td>Jaw relaxation</td>
<td>Complete Slight</td>
</tr>
<tr>
<td>Vocal cords position</td>
<td>Open Moving</td>
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<tr>
<td>Coughing</td>
<td>None Slight</td>
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<td>Limb movements</td>
<td>None Slight</td>
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Table 2

Demographic variables in the two groups

<table>
<thead>
<tr>
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<th>Group P (n = 25)</th>
<th>Group R (n = 25)</th>
<th>p-value</th>
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<tr>
<td>Age (yrs)</td>
<td>4.72 ± 2.15</td>
<td>4.62 ± 1.88</td>
<td>0.87</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>14.52 ± 4.25</td>
<td>15.58 ± 3.87</td>
<td>0.36</td>
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<tr>
<td>Male/Female N (%)</td>
<td>18/7 (72/28)</td>
<td>13/12 (52/48)</td>
<td>0.14</td>
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(Data represented as mean ± S.D or otherwise as specified).
both groups (Fig. 1) (p = 0.01). At T1 it decreased with respect to the heart rate at T0 in both the groups but didn’t reach the baseline value at any point time. MAP did not differ (p = 0.07) between the study groups at any point in time other than T6 when MAP in Group P was significantly lower than in Group R (62.04 ± 8.50 vs 67.20 ± 9.24) (p = 0.04).

No intraoperative or postoperative complications were observed in any patient in either group.

**Discussion**

In the present clinical study, we observed that intubating conditions achieved with either propofol (1.5 mg/kg) or rocuronium (0.6 mg/kg) at moderate concentration of sevoflurane are comparable without any added adverse effect. Time elapsed to reach successful tracheal intubation was also comparable in the two groups.

In our study, anaesthesia was induced with 8% sevoflurane in oxygen for faster induction than incremental increase in sevoflurane concentration (8, 9). Fentanyl was administered to blunt the hemodynamic response to laryngoscopy and intubation. Addition of narcotic to sevoflurane anaesthesia decreases also the target cerebral concentration of sevoflurane to perform tracheal intubation and consequently the risk of spike wave occurrences associated with high inhaled sevoflurane concentration (> 6%) (10, 11). Kato et al. (11) have reported that addition of fentanyl after sevoflurane induction reduces the MAC T1 of sevoflurane (sevoflurane requirements for achieving 50% probability of no movement in response to laryngoscopy and intubation). Dose of 1 µg/kg was used in our study so that it did not interfere with the discrimination of the effect of neuromuscular blocking agent as suggested by Good clinical research practice for pharmacodynamic study of neuromuscular blocking agents (GCRP) guidelines (12). The study drugs were administered according to group allocated such that intubation was performed 3 min after administration of rocuronium and 1 min after propofol administration in the respective groups with an overall timing of 4 minutes.

Propofol 1.5 mg/kg was used in our study. Kim et al. have found that the optimum dose of propofol
incidence of acceptable intubating conditions with rocuronium after induction with sevoflurane was found to be 96% in our study. This is in accordance with study by Lowry et al. (7) who have found an incidence of 90% with 0.6 mg/kg rocuronium after induction with 8% sevoflurane. However in comparison with one minute in the study by Lowry et al., we carried out intubation at three min after administration of rocuronium and also following nearly the same induction sequence. In their study the incidence of excellent intubating conditions has been found to be 20%, while in our study we were able to achieve excellent intubating conditions in 76% of subjects with the same dose (out of 96% patients with acceptable intubating conditions). The maximal neuromuscular block is reached after 1.5 min with rocuronium (14). Earlier it has been confirmed that a deeper neuromuscular block of laryngeal adductor muscles is associated with better intubating conditions. Since we performed intubation at three min, more profound neuromuscular block can explain our better results concerning intubating conditions. Nevertheless, excellent intubating conditions were achieved only in 76% patients in rocuronium group. Therefore, we conclude that satisfactory conditions for endotracheal intubation cannot be ensured even after two times the ED95 dose of a neuromuscular blocker if the depth of anaesthesia is not adequate (15).

A statistically significant but not clinically significant increase in the heart rate was observed after induction (time T0) in both groups which is in accordance with previous studies (5, 16, 17) but
opposite to the finding by Katoh et al. (11) who did not observe heart rate modification after induction of anaesthesia with sevoflurane. A much lower concentration of sevoflurane in their study can probably explain this difference. Subsequently after induction, heart rate decreased to the heart rate at T0 after administration of fentanyl 1 µg/kg in both groups. Nevertheless it didn’t reach the baseline value at any point. Statistically significant decrease in systolic blood pressure noticed in propofol group could be explained by the effect of propofol on cardiovascular system to decrease the systemic blood pressure (18). A decrease in systolic blood pressure was also observed by Siddik-Sayyid et al. in their study (4).

Our study may be limited by the fact that study included children of 2-8 years age group and results may not be applicable in other ages.

CONCLUSION

We found that intubating conditions in children achieved with propofol (1.5 mg/kg) or rocuronium (0.6 mg/kg) after induction with sevoflurane were similar. We conclude that propofol may be used as an alternative to neuromuscular blocking agents to provide acceptable intubating conditions under moderate concentration of sevoflurane in children.

References