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Research Article

Intubation without Muscle Relaxant: The Role of Sevoflurane

Fatemeh Hajimohamadi, Abolghasem Yoosefi, Mehrdad Behzadi, Nader Ali Nazemian Yazdi, Hamed Abdollahi, Afshar Etemadi-Aleagha*, Samira Parvizi Omran

Department of Anesthesiology, Amir A'lam Hospital, Tehran University of Medical Sciences, Tehran, Iran.

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ABSTRACT

Background: Sevoflurane is preferred for induction of general anesthesia in pediatrics. We examined the minimum duration of sevoflurane administration resulting in most optimal intubation conditions.

Methods: We included 75 children, aged 2-12 years, undergoing tonsillectomy under general anesthesia at Amir-Alam Hospital. They were given midazolam 0.05 mg/kg and fentanyl 2 mic/kg IV, five minutes before induction with sevoflurane 8% in 60% N2O and 40% O2 with total gas flow of 10 lit/min via face mask for 90 seconds (group I), 120 sec (group II) or 150 sec (group III), randomly. After tracheal intubation, intubation condition was assessed using Steyn's modification of Helbo Hansen scoring system. The total scores were divided into clinically acceptable (≤10) or unacceptable (>10).

Results: There was no statistically significant difference among the three groups in demographic characteristics. Mean ± SD of intubation scores were 10.04±2.9, 8.12±3.2, and 5.64±1.15 in groups 1-3, respectively (P<0.001) with statistically significant differences between all three groups: between groups I and II (P=0.044), I and III (P<0.001), as well as II and III (P=0.004). Intubation conditions were acceptable in 11, 16, and 25 patients in each group, respectively (P<0.001).

Conclusion: Inhalation induction by sevoflurane 8% in 150s provides acceptable clinical situation for intubation in pediatrics.

In today's world, where many patients require anesthesia for different surgical procedures, the choice of anesthetic agent, which varies based on the type of surgery and patients' conditions, is the matter of discussion [1]. The choice of anesthetics can be more challenging in the pediatric population, as they may be more uncooperative, have lower tolerance, and higher resistance for induction [2-3]. Furthermore, the children's different anatomic and physiological structure necessitates changes in the choice of the anesthetic agents, as well as adjustment of dose, and duration of administration [4].

Inhaled anesthetics, including enflurane, halothane, isoflurane, desflurane, and sevoflurane, enhance the inhibitory postsynaptic channel activity and inhibit excitatory synaptic activity [5]. The inhaled anesthetics, particularly desflurane and sevoflurane are considered as safe and efficient anesthetics in children, although there are several considerations that should be taken into account, such as the transient emergence delirium after these two insoluble agents [6-7].

Sevoflurane has several advantages for general anesthesia in children; it has a pleasant smell and is nearly non-irritating for the airways, and has lower blood-gas partition coefficient and less cardiodepressant and hepatotoxicity effects, as compared with other volatile anesthetics [8-10]. Accordingly induction and recovery of anesthesia with sevoflurane is fast and adequate for many patients [11].

Sevoflurane is considered an appropriate anesthetic agent for intubation in children, as it can inhibit movement in response to laryngoscopy and intubation [12]; it is particularly preferred in short procedures, where prolonged muscle relaxation is not required or paralysis

The authors declare no conflicts of interest.
*Corresponding author.
E-mail address: afshetem@yahoo.com

is undesired, or when there is a contraindication for a neuromuscular blocking agent [13-14]. However, 100% excellent intubation conditions have not been yet reported with sevoflurane and different studies have suggested different dose adjustments, using additional drugs, and techniques to improve the intubation conditions [15-17]. Decreasing the duration of inhalation can minimize the adverse effects of sevoflurane in children.

In this study, we aimed to examine the efficacy of intubation with sevoflurane in children under 12 in three different durations to find the minimum duration of administration of sevoflurane, which can result in 100% acceptable intubation conditions.

Methods

Children aged 2-12 years, with ASA class I and II, who referred to Amir-Alam Hospital for tonsillectomy with or without adenoidectomy under general anesthesia were included in this study. Children with upper respiratory tract infection, cardiac, pulmonary, renal or musculoskeletal disorders, positive history of malignant hyperthermia, gastroesophageal reflux, or hiatal hernia, allergy to anesthetic drugs, and significant obesity were not included.

Participants were selected according to the inclusion criteria (sample size: 75); after 8 hours fasting for solid foods and 2 hours for clear liquids, the patients entered the operating theater without oral premedication and with an intravenous (IV) line inserted. After arrival to the operating theater, all patients were monitored for oxygen saturation (SpO2), EtCO2, vital signs, including respiratory rate (RR) and non-invasive blood pressure (NIBP) that measures the following parameters: systolic, diastolic, and mean arterial blood pressure, and heart rate). Also, all patients were continuously monitored by the electrocardiogram (ECG).

All patients were given midazolam 0.05 mg/kg and fentanyl 2 µg/kg IV and then induced with sevoflurane 8% in 60% nitrous oxide (N2O) and 40% oxygen (O2) with total gas flow of 10 lit/min via face mask for 90 sec (group I), 120 sec (group II) or 150 sec (group III). Patients' allocation into the three groups were based on simple randomization method (four-block randomization) and 25 children were placed in each group accordingly. Any patient with unsuccessful intubation was excluded from the study.

The face mask was connected to a semiclosed anesthetic circuit. Ventilation was controlled by positive pressure mask ventilation, in case of patient's apnea. An oral airway was inserted, in case of airway obstruction. Laryngoscopy and tracheal intubation were performed at preset times 90, 120, and 150 seconds by single anesthesiologist to avoid observer's variability and an appropriate cuffed endotracheal tube (ETT) size was obtained using the standard formula.

Intubation conditions were assessed during the laryngoscopy by the anesthesiologist using a standard grading system (Steyn's modification of Helbo Hansen scoring system) that includes five variables: ease of laryngoscopy, position of vocal cords, the degree of coughing, jaw relaxation, and limb movement.

A total score of ≤5 was considered excellent, 6-10 good, 11-15 poor, and 16-20 bad; patients, considered as impossible intubation, were given 0.5 mg/kg atracurium to facilitate intubation. The total scores were considered clinically acceptable when ≤10 and unacceptable when >10.

Statistical analysis

Results of the quantitative variables were presented by mean ± standard deviation (SD) and that of qualitative variables by frequency (percentage). One-sample Kolmogorov-Smirnov test showed that the data were normally distributed in the three groups (P>0.05). Equality of variances was also confirmed by the Levene's test (P=0.180). Continuous variables were thus compared using ANOVA test among the three groups and those with a significant difference were tested by Bonferroni test to see the difference was between which two groups. Also, variables were compared between the groups according to two age categories ≤6 and 7-12 years. All qualitative variables were compared using chi-square test. The association of variables were tested by Pearson's correlation coefficient. For the statistical analysis, the statistical software IBM SPSS Statistics for Windows version 21.0 (IBM Corp. 2012. Armonk, NY: IBM Corp.) was used. P values of 0.05 or less were considered statistically significant.

The study protocol was in conformity with the ethical guidelines of the 1975 declaration of Helsinki, as revised in 1983. Private information, name and surname were removed from datasheets to comply with ethical concern. According to Amir-Alam hospital Ethics Committee, the information about human subjects was fully confidential. Before patient selection, the researcher explained the research objectives to the parents of the participants and asked them to read and sign the written informed consent. The ethical considerations of Helsinki's declaration on human studies were met throughout the study steps. Also this study was done under the supervision of Tehran University of Medical Sciences (TUMS), Iran. The project was found to be in accordance to the ethical principles and the national norms and standards for conducting medical research in Iran and was approved under the registration number IR.TUMS.AMIRALAM.REC.1400.011.

Results

In this study, 23, 24, and 25 children were studied in three groups of 90, 120, and 150 seconds (Figure 1).

Most participants (73.3%, N=55) were boy and only 26.6% (N=20) were girls. There was no statistically significant difference among the three groups in terms of

mean age, mean weight, and sex distribution, and mean duration of anesthesia and surgery (Table 1).

Nonetheless, categorization of children into two groups of ≤6 and ≥7 showed that the groups had a significantly different frequency of these two age groups (P=0.026).

Mean ± SD of intubation scores were 10.04±2.9, 8.12±3.2, and 5.64±1.15 in groups 1-3, respectively (P<0.001). Pairwise comparison of the mean scores showed statistically significant differences between all three groups: between groups I and II (P=0.044), I and III (P<0.001), as well as II and III (P=0.004). Mean total score of children ≤6 years old was 7.91±3.28 and that of the children ≥7 years old was 7.79±2.97 (P≥ 0.05).

There was a significant difference in the frequency of categories based on clinical acceptance and four categories of excellent, good, poor and bad among the three groups (P<0.001) (Table 2).

Figure 1- Flow diagram for study enrollment.

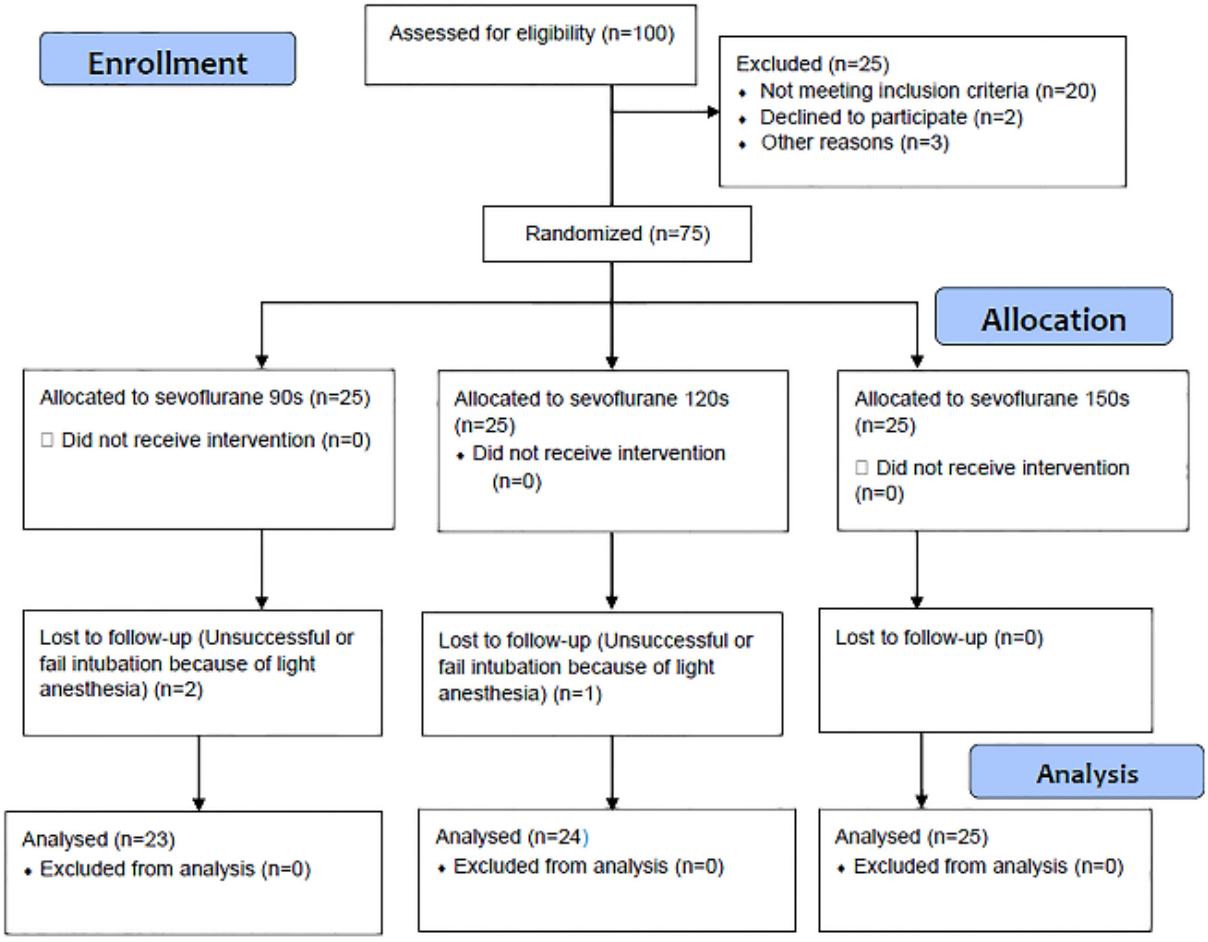

Table 1- Comparison of demographic characteristics of the studied patients among the three study groups.

Variables	Categories	Group I (90s)	Group II (120s)	Group III (150s)	P value
Age (years), mean±SD (range)		6.22±2.09 (3-10)	5.56±1.81 (3-9.5)	6.64±2.35 (2.5-11)	0.193
Age category	≤6 years, frequency (%)	17 (68.0%)	21 (84.0%)	12 (48.0%)	0.026
	≥7 years, frequency (%)	8 (32.0%)	4 (16.0%)	13 (52.0%)	
Weight (kg), mean±SD (range)		22.36±11.26 (11-60)	18.86±5.04 (13-30)	23.28±9.05 (12-42)	0.127
Sex (M/F)		19/6	15/10	21/4	0.148
Duration of anesthesia (min), mean±SD (range)		64.40±10.44 (45-90)	60.92±14.10 (35-90)	65.00±11.18 (40-90)	0.436
Duration of surgery (min), mean±SD (range)		53.72±8.49 (35-70)	49.44±14.87 (20-80)	54.92±12.30 (30-75)	0.253

Tracheal size, frequency (%)	3.5	0	4(16)	0	0.054
	4	7(28)	9(36)	7(28)	
	4.5	6(24)	6(24)	6(24)	
	5	9(36)	5(20)	7(28)	
	5.5	1(4)	1(4)	5(20)	
	6	2(8)	0	0	

Table 2- Comparison of score categories among the three study groups.

	Variables/Groups	Group I (90s)	Group II (120s)	Group III (150s)	P value
Qualitative categories	Excellent	0	8 (32.0%)	15 (60.0%)	<0.001
	Good	11 (44%)	8 (32.0%)	10 (40.0%)	
	Poor	11 (44%)	7 (28.0%)	0	
	Bad	1 (4.0%)	1 (4.0%)	0	
	Impossible Intubation	2 (8.0%)	1 (4.0%)	0	
Clinical categories	Acceptable	11 (47.8%)	16 (66.7%)	25 (100%)	<0.001
	Failure Of Intubation	12 (52.2%)	8 (33.3%)	0	

Discussion

In the present study, we compared the results of intubation condition of three groups receiving sevoflurane for three different durations (90s, 120s, and 150s) to find the shortest (minimum) time of inhalation of sevoflurane (with 0.05 mg/kg midazolam and 2 mic/kg fentanyl premedication, but without muscle relaxant) required for the best intubation condition with minimum adverse effects in children younger than 12 years old. For this purpose, the anesthesiologist scored the intubation condition based on Steyn's modification of Helbo Hansen scoring system and reported the scores based on qualitative categories and clinically acceptable.

According to the results, comparison of three groups with similar baseline characteristics showed the least mean score (5.64±1.15) in the group inhaling sevoflurane for the longest duration (150s) than the two other groups and higher mean score in the groups inhaling sevoflurane for 120s and 90s (8.12±3.2 vs. 10.04±2.9, respectively). Studying the scores based on categories showed that the group inhaling sevoflurane for the longest duration (150s) achieved 100% clinically acceptable intubation (score≥10); 60% achieved excellent intubation and 40% good intubation, while none had poor, bad, or impossible intubation. A closer look into cases with good intubation showed that the majority of them got a score of 6 (lost only one point) because of slight cough (4 cases), fair laryngoscopy (2 cases), or slight jaw relaxation (2 cases). Only one patient in this group got a score of 8 and another got a score of 10, which shows acceptable intubation results in this group. This was while none of the children in the group inhaling sevoflurane for the shortest duration (90s) achieved excellent intubation and less than half (47.8%) achieved clinically acceptable intubation; also, in the group inhaling sevoflurane for 120 seconds, 66.7% achieved clinically acceptable intubation and only 8 cases (32%) achieved excellent intubation. These results indicate the best intubation condition achieved by inhalation of sevoflurane for 150 seconds and recommends this dose and duration as the most appropriate.

Although the results of the present study confirmed that of previous studies suggesting no adverse effects and high tolerability of sevoflurane 8% by children [12-13,16], achieving 100% excellent intubation condition is still an important issue. Kumar and colleagues investigated 150 children ≤6 years with ASA I and II undergoing ophthalmic procedures under general anesthesia, induced by sevoflurane in 100% oxygen with 7 L/min flow (up to 8 vol% for 4.5 min), following 0.06 mg/kg glycopyrrolate and 1 µg/kg fentanyl and reported excellent intubation conditions in all patients without any complications [16]. These results are in line with ours in terms of confirming the safety and efficacy of anesthesia with sevoflurane for induction without the need for neuromuscular blocking agent in pediatric population, which plays a great role in reducing the risk of adverse events. Nevertheless, Kumar and colleagues reported excellent intubation in all patients [16], while the group with the best results in our study had only 58.3% excellent intubation conditions in children ≤6 years. These results could be due to the fact that they have considered 210 seconds for the induction time, while we used induction time of 90, 120, and 150 seconds. As suggested, induction time has a significant effect on the success rate of intubation and the required time to achieve 95% success rate was reported 189 seconds for children aged 1-4 years and 260 seconds for children aged 4-8 years [18], both of which are longer than that used in our study. One of the reasons that we have not achieved 100% success rate of intubation could be the fact that we did not use different durations of inhalation based on the child's age and randomized all children aged <12 years into three groups, while a longer duration of inhalation might have been required for achieving 100% excellent intubation

conditions in older children. Blair and colleagues reported 3 minutes of inhaling sevoflurane 8% in 60% N2O as a satisfactory alternative to propofol with succinylcholine in children aged 3-12 years [19]. The above-mentioned studies have reported a higher frequency of excellent intubation conditions, compared to that in the present study, which could be due to the fact that they have used longer durations than all of the groups in the present study. Hence, the longer duration of inhaling sevoflurane may increase the risk of adverse effects and is therefore undesirable [20].

Another factor supposed to affect the intubation success rate of sevoflurane is considered the dose and drug used after sevoflurane. As to the results of the study by Siddik-Sayyid and colleagues on 104 children aged 2-7 years, 2 mg/kg propofol resulted in a higher frequency of excellent intubation, compared to 1 mg/kg propofol (92% vs. 56%, respectively), after 8% sevoflurane with similar durations (249 vs. 231 seconds, respectively) [21]. However, for reduction of the adverse effects, we only induced the children by 8% sevoflurane in 60% N2O without any other medication for induction that has been suggested as the most appropriate choice for children in most recent studies [22-23]. Alternatively, we used fentanyl, which has been suggested to significantly reduce the risk of emergence agitation of sevoflurane [7] and the results of our study also showed no cases of emergence agitation among 75 children studied.

Sevoflurane has a low blood solubility that allows for rapid induction of anesthesia by fast equilibration between alveolar gas and arterial blood and is an appropriate choice for children due to their needle phobia and anxiety [24]. The results of the present study showed that induction was well tolerated by all children, as none refused to accept the clear plastic facemask. Furthermore, although we ventilated patients if required, the apnea time was very short. Another great advantage of using sevoflurane for induction, confirmed by the results of the present study, is that the apnea would be very short in this technique and the spontaneous ventilation could be reversed shortly and the patient can be awakened shortly, if required, for example in difficult intubation conditions. The apnea time is of great importance, as the shorter apnea time is directly associated with intubation success rate [17].

We compared three durations of inhaling 8% sevoflurane among three groups with similar baseline characteristics and determined the best approach, meanwhile this study also had several limitations. The first limitation was that this method was contraindicated to full stomach patients and we only included fasted children. Also, we did not use Bispectral index score for evaluating the depth of anesthesia. In addition, the children we included had a wide range of age and weight, which could affect the required duration and dose for an excellent intubation and we were unable to report the results separately, due to the small number of children in each category.

Conclusion

In conclusion, we found that inhaling 8% sevoflurane was tolerable for all children aged <12 years without any adverse effects. Additionally, comparison of three durations (90s, 120s, and 150s) showed that administration of 8% sevoflurane in 60% N2O for 150 seconds resulted in 100% clinically acceptable intubation condition, with the highest frequency of excellent intubation conditions, compared to the other groups. These results suggest a minimum of 150 seconds required for inhalation of 8% sevoflurane, although several factors affecting intubation success (such as child's age, weight, and sex) has to be taken into consideration. Future studies with a larger sample size and a longer follow up are required to determine the best duration for each category of children.

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