

Use Of Sevoflurane With Or Without Nitrous Oxide For Inhalational Induction In Paediatric Patients

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Citation

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Abstract

Background

Sevoflurane is a commonly used agent for inhalational induction in paediatric anaesthesia. There is no consensus on the use of nitrous oxide in combination with sevoflurane induction in children. This study was designed to compare anaesthesia induction time (time when sevoflurane vaporizer was dialed to 8% after facemask application till the time of end tidal sevoflurane concentration of 5% was achieved), response to IV and LMA insertion and any adverse events during induction and until LMA insertion.

Methods

We studied 182, ASA 1, 2 and stable 3 paediatric patients between two and 15 years of age undergoing elective surgery who were randomly assigned to a control group (sevoflurane and oxygen induction) or an intervention group (sevoflurane, nitrous oxide (50%) with oxygen). The observers were blinded to the patient groups. The anaesthesia circuit was primed with 100% oxygen.

Results

Median induction time was 120 seconds in both groups with IQR 65 in sevoflurane oxygen and 70 in sevoflurane, nitrous oxide and oxygen group. Combined adverse events were 20% in former and 28% in the later group.

Conclusion

Addition of nitrous oxide to sevoflurane oxygen did not provide a significant advantage in terms of induction time, haemodynamic and adverse effects

INTRODUCTION

Sevoflurane has the advantage of a pleasant non-irritating odour and a low blood gas solubility coefficient; resulting in rapid and smooth induction of general anaesthesia.[1] Its use in inhalational induction in paediatric patients is an accepted technique. When used in combination with nitrous oxide (N₂O), it provides satisfactory anaesthetic induction and intubating conditions. The safety of routine use of N₂O has been questioned in recent literature because of its effects on the developing human brain.[2,3] Elimination of nitrous oxide at the time of induction did not result in a decrease in complications, neither did it affect the speed of induction in adults.[4] Studies in children on the subject are limited. The rate and quality of induction with and without N₂O with a single vital capacity breath induction using 8% sevoflurane was found to be similar in both groups.[5] Sarner et al on the other hand showed a higher incidence of excitement and

prolonged induction time without the use of nitrous oxide in the induction sequence in children.[6] In view of conflicting evidence, we compared the anaesthesia induction in a cohort of paediatric patients receiving sevoflurane inhalational induction with or without nitrous oxide.

MATERIALS AND METHODS

This study was conducted in the department of Anaesthesia, Aga Khan University between April 2008 to August 2008. Ethical approval for this study (Ethical Committee No. 742-ANE/ERC/07) was provided by the Ethical Committee of the Aga Khan University, Karachi, Pakistan (Chairman, Prof Q Nizami) on 15th June 2007. Assent was obtained from older children. The study design was double blind randomised clinical trial. One hundred and eighty two patients of either gender aged between 2 to 15 years, ASA grade 1, 2 and stable 3 undergoing surgery requiring general anaesthesia with laryngeal mask (LMA) were included.

Obesity, anticipated difficult intubation, raised intracranial pressure, history of pneumothorax and patients on drugs that could affect heart rate were excluded. The sample size was calculated using induction time as the primary outcome and was based on testing for equivalence. The reference was from two previous studies using the assumption that the difference between the two groups was either more than 7 seconds in absolute terms[4] or 4% or more[5], between sevoflurane alone group and sevoflurane with nitrous oxide group. A 0.05 significance level and a power of 80% was taken.

Patients were randomized into two groups based on anaesthesia induction with sevoflurane, nitrous oxide and oxygen (sevoflurane and N₂O) or with sevoflurane, oxygen and air (sevoflurane alone). A sealed opaque envelope technique was used for randomization. An envelope was randomly selected for a recruited patient by a research officer and handed over to an unblinded anaesthetist responsible for dialing gas flow and vaporizer concentration. This anaesthetist was not responsible for patient airway management at the time of induction.

Induction time was predefined as the time when sevoflurane vaporizer was dialed at 8% after mask application (time zero) till the time that the end-tidal sevoflurane concentration of 5% was achieved (time end). A SevoTec 7 vaporizer was used for delivering the inhalational agent.

Each patient was premedicated based on weight with either oral tablet midazolam 3.75 mg (half tablet) in older children or syrup midazolam calculated at 0.5 mg per kilogram, administered one hour before arrival to operation room. Baseline heart rate, mean arterial pressure and oxygen saturation were recorded in the holding area of the unit. The parents did not accompany the child to the operating room. Two anaesthetists were assigned in the operating room A and B. Anaesthetist A being responsible for inhalational induction and was blinded to the study group. The anaesthesia machine used was Aestiva/5 Datex Ohmeda (USA) and was placed at an angle so that the rotameters and vaporizer dials were not visible to anaesthetist A. Anaesthetist B was responsible for dialling gas flow and concentrations of vaporizers, and was not blinded. Anaesthesia was administered with Mapleson F or Bains circuit in children weighing more than 15 kg. After flushing the circuit with 100% oxygen an initial gas flow rate was set at 10 liters per minute oxygen. A well fitting anaesthesia mask was then applied. The head movements of the child were controlled by the anaesthetist A by placing one hand

behind the occiput and other holding the mask firmly. After three breaths, the gas flow was reduced to four litres per minute of oxygen with four litres per minute nitrous oxide or air introduced according to the group allocation. At the same time, 8 % sevoflurane was dialled on the vaporizer (time zero). When an end tidal concentration value of 5% was achieved on the monitor, time was noted (time end) by the research assistant and anaesthetist B informed anaesthetist A. Haemodynamic measurements were taken. An intravenous canula was then inserted. An appropriately sized LMA was inserted after IV placement. Sevoflurane end tidal concentration was measured by Datex Ohmeda S/5 (Helsinki, Finland) monitor. The patients were observed for any fall in oxygen desaturation below 90%, breath holding, coughing or laryngospasm during induction time, and until the LMA was in place. An end tidal concentration of five percent with sevoflurane was maintained till the LMA was inserted. Limb or head movement during IV insertion or inability to insert LMA due to presence of muscle tone was also noted. Rest of anaesthesia was continued as clinically appropriate. All the observations during the study period were recorded by an assigned research assistant who was blinded to the study groups.

Data was collected on a structured format and was compiled in SPSS version 16 (copyright © SPSS Inc, 1989-2007, Chicago, USA). Distributions of continuous variables was checked for normality and frequencies were calculated. Mean and median of induction times (SD) in two groups, changes in heart rate and mean blood pressure between baseline and post induction values were compared between the two groups using Mann Whitney U test as the data was not normally distributed. Qualitative data like occurrence of adverse events was compared using Chi square test. P value of less than 0.05 was considered as significant.

RESULTS

A total of 182 patients were studied. The demographic characteristics and baseline data of the two groups is given in Table 1.

Table 1

Comparison of baseline characteristics between study groups

Variables	Groups		p-value
	Sevoflurane alone n = 91	Sevoflurane and nitrous oxide n = 91	
	Median (IQR)	Median (IQR)	
Age (months)	60 (60)	60 (57)	0.78
Weight (kg)	18 (12)	17 (12)	0.71
Baseline heart rate	102 (29)	100 (31)	0.46
Baseline MAP (mm Hg)	72 (17)	76 (20)	0.08
Gender (n)			
Male	81	79	
Female	10	12	0.65

IQR means interquartile range
MAP means mean arterial pressure

In table 2 there was no missing data and no drop outs. No significant difference was observed in baseline characteristics of age, gender, weight, baseline heart rate and mean arterial pressure between the groups (p value > 0.05).

Table 2

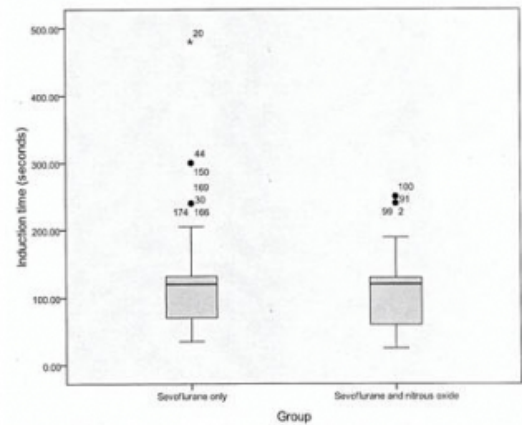
Age distribution in the study group

Age	Group	
	Sevoflurane alone n = 91	Sevoflurane and nitrous oxide n = 91
Less than 36 months	21	17
3 years – 7 years	36	46
7 years – 12 years	27	25
More than 12 years	7	3

Median induction time in both groups was 120 seconds with Interquartile range (IQR) 65 in sevoflurane alone and IQR 70 in sevoflurane nitrous oxide group (Figure 1: Boxplot showing induction time in two groups). The mean induction time was 120 seconds (SD 69) in sevoflurane and 109 seconds (SD 81) in sevoflurane N2O group.

Figure 1

Boxplot showing induction time in two groups



- Indicates outliers of induction time in two groups
- * Indicates extreme outlier

A posthoc subgroup analysis based on gender showed a significant difference in induction time in female patients where median induction time was 120 (IQR 73) in sevoflurane alone compared to 100 (IQR 60) in sevoflurane nitrous oxide group (Table 3). This difference was not seen in male patients. Female patients were 12 percent of the total sample size.

Table 3

Comparison of induction time in seconds based on gender

Gender	n	Group		P value
		Sevoflurane alone Median (IQR)	Sevoflurane and nitrous oxide Median (IQR)	
Female	22	120 (73)	100 (60)	0.042*
Male	160	116 (64)	120 (74)	0.96

*P value less than 0.05 considered significant

No significant difference in percentage change in the mean heart rate and mean arterial pressure (taken once immediately after time end) compared to baseline were noted between the two groups (p value >0.05). Movements during intravenous cannulation were noted in 3% (n=3) of patients in both groups. Movements during LMA insertion were noted in 13% of patients in sevoflurane alone group and in 8% of patients in sevoflurane and nitrous oxide group. There was difficulty in LMA insertion due to presence of muscle tone in one patient in sevoflurane alone and in two

patients in sevoflurane and N2O group. The incidence of total adverse events was 20% (n = 19) in sevoflurane alone group and 28% (n = 26) in sevoflurane and nitrous oxide group (p value > 0.05) (Table 4). A subgroup analysis based on age categories showed a statistically significant difference in occurrence of adverse events above and below 36 months of age. The incidence of adverse events in children more than 36 months was comparable in both groups whereas adverse events in children less than 36 months were more in sevoflurane alone (12 events) compared to sevoflurane and nitrous oxide group (one event) (p value 0.045). This is shown in Table 4 with value in brackets referring to children less than 36 months. A subgroup analysis based on gender did not show any significant difference in occurrence of adverse events.

Table 4

Adverse events	Groups	
	Sevoflurane alone n=91	Sevoflurane and nitrous oxide n=91
Oxygen saturation below 90%	2 (0)	1 (0)
Coughing	3 (2)	2 (0)
Difficulty in LMA insertion	1 (0)	2 (0)
Limb movements during IV cannulation	3 (2)	3(0)
Breath holding (apnea)	8 (6)	5 (0)
Laryngospasm	1 (0)	1 (0)
Head and neck movements	8 (2)	5 (1)

Values in brackets () represents values for children below 36 months age

DISCUSSION

CONCLUSION

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