

**SEVOFLURANE VERSUS HALOTHANE FOR GENERAL ANESTHESIA IN PEDIATRIC PATIENTS – A COMPARATIVE STUDY OF INDUCTION TIME, INTUBATION TIME AND EMERGENCE TIME**Santosh K. Bhaskar<sup>1</sup>, Sameer Zutshi<sup>2</sup>, Roshan Chanchlani<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: AIM:** This study was conducted to compare the speed of induction, intubation, and speed of emergence with sevoflurane and halothane in pediatric patients. **METHODOLOGY:** All the patients had full preanesthetic check-up and the routine investigation (complete blood count, urine albumin) was done. Patients were kept fasting for 6 hrs. for solid food, 4 hours for semisolid and 2 hours for liquid. They were randomly divided into Gr S and Gr H each comprising of 30 patients each to receive sevoflurane and halothane with 60% nitrous and 40% oxygen respectively by inhalation. On arrival in the operation theatre, the standard monitors were applied including an electrocardiogram, pulse oximeter, non-invasive blood pressure and precordial stethoscope and the baseline readings of respective parameters were taken. Anesthetic induction was done with face mask application using incremental dosing of 0.5% for halothane and 1% for sevoflurane every three to five breath to deliver maximum inspired concentration of upto 5% halothane(maximum inspired concentration) or 8% sevoflurane (maximum inspired concentration). Spontaneous ventilation was maintained till loss of eye lash reflex. Following the loss of the eyelash reflex, the vaporizer concentration was decreased to 4% for sevoflurane and 0.86 % for halothane (approximately 2 MAC). Intravenous catheter was inserted. Inhalational agent at the same concentration was given until the loss of corneal reflex. After the intravenous line was secured, inj pentazocine 0.3 mg/kg was given. The patients were intubated with appropriate size endotracheal tube only after the loss of corneal reflex. After successful intubation, intravenous vecuronium 0.1 mg/kg was administered for muscle paralysis and the anesthetic concentrations was adjusted at 1.3 MAC with N<sub>2</sub>O (0.56% halothane and 2.6% sevoflurane). Time intervals measured: (induction time, intubation time, emergence time) were measured. Vitals recorded: Heart rate, systolic, diastolic blood pressures, and SpO<sub>2</sub>. The depth of anesthesia was assessed clinically by evaluation of changes in heart rate, and blood pressure during surgery and these were maintained within 20% of baseline values. **RESULTS:** Induction time was significantly shorter with Gr S [mean(SD) 136.0(19.343)secs] than with Gr H [mean (SD) 156.09(10.651)) secs] (P=0.0001). Intubation time was significantly shorter with Gr S [mean (SD) 242.400(9.940) secs] than with Gr H[mean(SD) 265.769(12.039) secs] (P<0.0001). Time to emergence was significantly shorter in Gr S [mean(SD) 217.667(22.831)secs] than with Gr H[mean(SD) 450.5(18.407) secs] (P<0.0001). **CONCLUSIONS:** We found that sevoflurane is an excellent agent for inhalational induction of anesthesia in pediatric patients. It facilitates a rapid induction of anesthesia, found to be 20 seconds faster than halothane in our study. Emergence time is relatively shorter with sevoflurane as compared to halothane.

**KEYWORDS:** sevoflurane, halothane, inhalational anesthesia.

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**INTRODUCTION:** Intravenous induction of anesthesia, although popular with adults, did not receive such widespread acceptance by children. Halothane was a considerable advance, as it heralded an improvement on ether as an alternative to the intravenous induction of anesthesia. Halothane has a relatively rapid onset, it smells nice (compared with ether), and it is not associated with vomiting during induction as well as Coughing and salivation are less. Halothane became the principal agent for inhalation induction of anesthesia for many anesthetists, and it has been a mainstay for anesthesia in children for almost forty years.

Sevoflurane, a volatile ether (methyl – isopropyl ether) anesthetic is a recent addition to the inhalational agents. It possesses several properties including low blood (0.6) and tissue solubility, non-pungency, non-inflammability and limited cardiorespiratory depression that may be desirable for use in infants and children.<sup>1, 2</sup> Sevoflurane is the most suitable agent for pediatric age groups because of its rapid onset of action, few intraoperative and postoperative complications, quick recovery and no risk of repeated sevoflurane exposure to patients.<sup>3</sup>

Inhalation induction by mask is the most commonly used technique in pediatric anesthesia because it can be achieved relatively easily and rapidly in most children and is less objectionable to most children than the insertion of an intravenous catheter. Isoflurane, enflurane, and desflurane which were introduced in clinical respectively have not improved either the comfort or safety of inhalation induction of anesthesia.

Coughing, breath-holding, and laryngospasm occur frequently with isoflurane, as confirmed by Cregg et al.<sup>4</sup> Sevoflurane considerably improves the ease of inhalation induction. It is less irritating to the airway than either isoflurane or halothane, and is associated with fewer cardiac arrhythmias<sup>5</sup>. This randomized controlled study directly compares sevoflurane with halothane in pediatric population in reference to induction time, intubation time, emergence time.

**METHODOLOGY:** This randomized double blind prospective study has been carried out after approval of local institutional ethics committee and explaining the procedure to the parents of the selected patient in local language and obtaining written informed consent from them. 60 patients were randomly allocated to be assigned to two groups, Group S which was to receive Sevoflurane and Group H to receive Halothane.

**Inclusion Criteria:** 1) Age 1-12 yrs. 2) Weight less than 20 kgs 3) Elective surgeries 4) ASA I, ASA II 5) Tracheal intubation.

**Exclusion Criteria:** 1) Parents refusal 2) ASA III, IV 3) Emergency surgeries. 4) Surgeries of less than 30 minutes duration and more than 2 hours duration. 5) Children with upper respiratory infections.

All the patients had full preanesthetic check-up and the routine investigation (complete blood count, urine albumin) was done. Patients were kept fasting for 6 hrs. for solid food, 4hours for semisolid and 2 hours for liquid. They were randomly divided into Gr S and Gr H each comprising of 30 patients each to receive sevoflurane and halothane with 60% nitrous and 40% oxygen respectively by inhalation. On arrival in the operation theatre, the standard monitors were applied including an electrocardiogram, pulse oximeter, non-invasive blood pressure and precordial stethoscope and the baseline readings of respective parameters were taken.

Anesthesia was administered via a primed Ayres's T piece and appropriate size face mask. All patients received N<sub>2</sub>O:O<sub>2</sub> 60:40 during induction and maintenance at standardized weight appropriated fresh gas flows. Halothane was started at 0.5% and sevoflurane at 1%. Anesthetic

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induction was done with face mask application using incremental dosing of 0.5% for halothane and 1% for sevoflurane every three to five breath to deliver maximum inspired concentration of upto 5% halothane(maximum inspired concentration) or 8% sevoflurane (maximum inspired concentration). Spontaneous ventilation was maintained till loss of eye lash reflex.

Following the loss of the eyelash reflex, the vaporizer concentration was decreased to 5% sevoflurane or 1.6 % halothane (approximately 2 Minimum Alveolar Concentration of both the agent). Intravenous catheter was then inserted for the infusion, continuing the inhalational agent at the same concentration until the loss of corneal reflex. The corneal reflex was assessed by assistant anesthetist. The patients then were intubated with appropriate size endotracheal tube only after the loss of corneal reflex. After successful intubation, intravenous vecuronium 0.1 mg/kg was administered for muscle paralysis and the anesthetic concentrations was adjusted at 1.3 MAC with N<sub>2</sub>O (0.56% halothane<sup>29</sup> and 2.6% sevoflurane<sup>30</sup>).

Elapsed time intervals from the face mask application to loss of the eyelash reflex (induction time), and intubation (intubation time) were measured. Heart rate, systolic, diastolic blood pressures, and SpO<sub>2</sub> were measured at induction, just before intubation and immediately after intubation, and then every 5 min until the end of the surgery.

The depth of anesthesia was assessed clinically by evaluation of changes in heart rate, and blood pressure during surgery and these were maintained within 20% of baseline values by adjustment of the inspired concentration of halothane or sevoflurane. At the end of the surgery, all the anesthetic agents were discontinued simultaneously. On regaining spontaneous respiratory efforts, intravenous neostigmine 50mcg/kg with glycopyrrolate 10mcg/kg was administered to antagonize the residual neuromuscular blockade.

The trachea was extubated when the gag reflex returns and the patients is breathing spontaneously and making purposeful movement. The time interval from the discontinuation of the anesthetic to patient response by hip flexion or bucking (emergence time) was noted. Data is presented as a mean, unless otherwise stated. Figures in the brackets indicated the Standard Deviation. To compare the study group, parametric data (age, sex, weight) was analyzed by students "t" test and non-parametric data was compared by chi square test with Yates continuity correction. "p" values less than 0.05 was considered the probability level to select significant difference. Statistical software "Epi Info 6" (version 7).

**RESULTS:** In each group there were 30 patients. Group- S received Sevoflurane and Group- H received Halothane. There was no statistically significant difference between both the groups with respect to the age and weight, sex, ASA functional status. (Table no.1)

Parameters	Group -S	Group-H	P value
Age	5.13 (2.713)	4.93 (2.716)	0.754
Weight	14.5 (5.355)	14.2 (5.448)	0.715
Sex (M:F)	19:11	20:10	0.393
ASA(I:II)	21:9	24:6	0.275

Table 1: Demographic profile of the patients

Figures in the parenthesis indicate Standard Deviation.

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There was statistically significant difference between both the groups in induction time and intubation time. The P value was less than 0.05. There was statistically significant difference between both the groups in emergence time. The P value was less than 0.05. The mean emergence time in group S was 217.667 seconds while it was 450.5 seconds in group H. (Table no.2)

Parameters	Group S	Group H	P value
Induction time (seconds)	136.0(19.343)	156.09(10.651)	0.0001
Intubation time (seconds)	242.400(9.940)	265.769(12.039)	0.00000
Emergence time (seconds)	217.667(22.831)	450.5(18.407)	0.0001

**Table 2: Difference in induction time, intubation time, and emergence time in study patients**

Figures in the parenthesis indicate Standard Deviation.

There is statistically no significant difference between the Groups in Baseline, Induction and Preintubation Mean Heart Rate as is clear from the P value which is more than 0.05. But the difference in the Post intubation Heart Rate is significant ( $p < 0.05$ ) among the Groups. There is statistically no significant difference between the Groups in preoperative, Induction Mean systolic blood pressure as is clear from the P value which is more than 0.05. But the difference in the Preintubation and Post intubation Mean systolic blood pressure is statistically significant ( $p < 0.05$ ) among the Groups. There is statistically no significant difference between the Groups in Baseline, Induction Mean Diastolic blood pressure as is clear from the P value which is more than 0.05. But the difference in the Preintubation and Post intubation Diastolic blood pressure is significant ( $p < 0.05$ ) among the Groups. (Table no.3)

Parameters	Group S	Group H	P value
Preoperative HR	111.067(9.333)	112.633(8.189)	0.56
Induction HR	114.000(9.366)	114.967(7.985)	0.80
Preintubation HR	116.267(9.032)	117.500(8.165)	0.66
Post intubation HR	119.800(8.0580)	139.933(4.586)	0.00
Preoperative SBP	100.400(8.041)	104.067(9.059)	0.107200
Induction SBP	98.733(7.511)	102.067(9.059)	0.108779
Pre intubation SBP	96.567(7.500)	104.067(8.905)	0.002618
Post intubation SBP	94.367(7.271)	107.467(8.597)	0.000001
Preoperative DBP	60.467(7.001)	59.333(5.738)	0.498881
Induction DBP	58.533(6.474)	57.333(5.738)	0.572120
Pre intubation DBP	56.867(6.574)	59.067(5.375)	0.1719915
Post intubation DBP	54.767(6.218)	61.667(5.175)	0.000055

**Table 3: Hemodynamic changes during peri-intubation period in study patients**

Figures in the parenthesis indicate Standard Deviation.

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**DISCUSSION:** In our study lot of emphasis was given for pre-operative visit to patient night before surgery the visit was to make them friendly and familiar to anesthesiologist. To avoid painful prick on arrival to operation theatre no premedication, intravenous or intramuscular route, was used and the mother was separated from child at O.T. door just before induction, thus avoiding agitation because of separation from parents.

**Induction time:** Induction time was calculated as time taken till loss of eyelash reflex from putting of face mask on child's face. The more rapid induction achieved with sevoflurane was probably because of its physical property of lower blood gas solubility resulting in rapid uptake compared with halothane, as well as the relatively faster increase in the inspired partial pressure of sevoflurane. It may be that the extreme lack of airway reactivity found with sevoflurane allowed for a more rapid increase in the inspired concentration compared with halothane.<sup>6</sup>

Our study found that the mean induction time of general anesthesia was 20 seconds faster with sevoflurane than with halothane. It was somewhat faster than reported by Naito et al<sup>1</sup> in a group of 30 healthy pediatric outpatients (about 3 min). Our faster induction times may be attributable to the fact that these investigators administered a maximum of 4.25% sevoflurane and 2% halothane during induction, while we gave upto 8% sevoflurane and 5% halothane in incremental doses.

Furuya et al<sup>7</sup> induced 50 pediatric patients with 3% to 5% sevoflurane in 60% N<sub>2</sub>O and 50 pediatric patients with halothane 1.5% to 2.5%; loss of consciousness took 2.10 minutes in the sevoflurane group and 2.4 minutes in the halothane group (p<0.05). This time saving was similar to that found in our study. In an adult volunteer study, Yurina and Kimura<sup>8</sup> induced anesthesia (time until failure to respond to commands) with sevoflurane (initially at 0.5% and increasing every 3 to 4 breaths by 0.5%, to maximum concentration of 4.5%) in 66 % N<sub>2</sub>O in 108 seconds, which was also similar to our results.

Sevoflurane is known to induce anesthesia faster due to rapid uptake of the agent. Some workers<sup>9-11</sup> experimented with high concentration of the agent from the very beginning of the anesthesia induction and they observed considerable amount of excitement during induction phase. To avoid this excitement phase of induction, gradual increase in concentration was carried out in the present study.

Piat et al<sup>12</sup> increased concentration every 5 breaths but they had varied increment in two groups –in sevoflurane group increment was in succession of 2%, 4%, 6% and 8%, while in halothane group it was 1%, 2%, 3% and 3.5%. This was done to obtain comparative value in terms of MAC(2-2.5) for both the agents. Black et al<sup>13</sup> used increments of 0.5% to 1% to maximum of 5% in halothane group and 1.5 to 2% to maximum of 7% in sevoflurane group. This way MAC value of both the agents is comparable as shown by Lerman.<sup>14</sup>

There were a number of factors in our study that may have attenuated the difference we measured in induction time between the two drugs. First, the maximum sevoflurane concentration delivered from our vaporizers is 8% (approximately 3.2 MAC<sup>15</sup> for the patients studied), while the halothane vaporizer delivers up to 5% (approximately 5.6 MAC<sup>16</sup>). During induction, the maximum settings were reached in all patients. This physical limitation of the sevoflurane vaporizer design was appreciated during the design of our protocol, but higher output sevoflurane vaporizers were not available.<sup>17</sup> We could have limited the inspired halothane concentration to the MAC equivalent of the maximum sevoflurane vaporizer output, but we felt it was inadvisable to subject the patients who

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would be receiving halothane to an induction sequence that had a greater risk of a prolonged excitement stage<sup>17</sup>. Thus, the expected increase in the speed of induction with sevoflurane due to its decreased solubility was somewhat offset by the overpressure used with halothane.

A second factor that may have lowered the observed difference in induction time was that the initial potent agent concentration delivered and the step increments were slightly lower in the sevoflurane group (1% or 0.4 MAC) than in the halothane group (0.5% or 0.5 MAC). This was a consequence of convenience, in that the vaporizer dials were calibrated in 0.5% increments. Finally, the rate at which we increased the sevoflurane concentration may have been the most important factor that limited the difference in induction times. This rate (about 0.5 MAC every 2-3 breaths) is what we ordinarily use when we induce anesthesia with halothane.

We arbitrarily chose to increase sevoflurane at the same rate as we increased the halothane. A more rapid increase in sevoflurane concentrations has been successfully accomplished by several investigators. Haga et al<sup>18</sup> induced anesthesia in 180 children using a constant inspired concentration of either 4% or 6.4% sevoflurane. These investigators measured induction times (time to spontaneous eye closure or cessation of vocalization) of 56 seconds and 47 seconds, respectively. In an adult volunteer study using a vital capacity rapid inhalation induction technique, induction of anesthesia (failure to respond to command) with sevoflurane was significantly faster than with halothane (81 seconds Vs. 153 seconds).<sup>19</sup>

In that study, no sevoflurane subjects had respiratory complications during induction, while 20 % of the halothane subjects developed coughing during induction. Each of these factors cited above served to limit the observed difference in induction time between the two drugs. One therefore might reasonably accept that the speed of induction with sevoflurane would be even faster if a higher starting and incremental concentration were chosen, the vaporizer setting increased more rapidly, or a higher output vaporizer were to be used.<sup>17</sup>

**Intubation Time:** Intubation time was measured from putting of face mask to loss of corneal reflex associated with regular respiration and loss of limb movements

Sarner<sup>20</sup> and colleagues recently compared times to intubation during sevoflurane and halothane anesthesia and showed that the two were almost identical. Intubation was performed successfully at first attempt in both the groups without using any muscle relaxant. Piat et al<sup>12</sup> and O'Brien et al<sup>21</sup> did not use muscle relaxant and intubated using inhalation agent only unlike Black et al<sup>13</sup> who used Atracurium for the purpose.

Vital signs during induction of anesthesia with sevoflurane were, on average, quiet stable. The most notable difference between the groups is that the halothane patients developed a marked tachycardia and moderate increase in blood pressure in response to tracheal intubation. Avoidance of use of muscle relaxant helped us to assess the direct hemodynamic response of two agents. We did not use pancuronium which would be expected to result in tachycardia and possibly an increase in blood pressure from their vagolytic actions.

For the similar reason vagolytic agents like atropine and glycopyrrolate were also avoided before intubation. Thus, if clinically one uses these drugs; one might not appreciate this difference between the two volatile agents. The tachycardia and hypertension were transient, and quickly resolved following intubation. We attribute this difference in the response to intubation between the two potent drugs to the fact that the sevoflurane patients were at a greater depth of anesthesia than the halothane patients.<sup>17</sup>

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**Emergence:** Emergence time was defined as time taken from discontinuation of anesthetic agent to hip flexion or bucking. Emergence from anesthesia was 3.8 minutes faster with sevoflurane. Mean emergence time was 3.62 minutes in group S while 7.5 minutes in group H ( $p < .05$ ).

Our findings were similar to that of Naito et al<sup>1</sup> in their outpatient study. In that investigation, patients who had received sevoflurane awoke 4.3 minutes after discontinuation of the agent versus 9.5 minutes after halothane was stopped. The patients in the Naito et al study did not receive any intraoperative analgesics. Furuya et al<sup>7</sup> observed wake up times of 10.1 and 13.0 minutes for sevoflurane and halothane, respectively.

Wellborn et al<sup>22</sup> noted that halothane and sevoflurane were not significantly different in respect to emergence time. The possible explanation for this difference seems to be the difference in definition of emergence time. Our study considered the time from discontinuation of anesthetic to hip flexion or bucking as emergence time whereas wellborn et al took time from discontinuation of anesthetic to extubation as emergence time.

**CONCLUSION:** We found that sevoflurane is an excellent agent for inhalational induction of anesthesia in pediatric patients. It facilitates a rapid induction of anesthesia, found to be 20 seconds faster than halothane in our study. Not only that, it also facilitates very smooth induction of anesthesia, when administered by face mask without any airway irritability. Emergence time is relatively shorter with sevoflurane as compared to halothane.

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