ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS: Anesthesia, pediatric, outpatient, sevoflurane, halothane

RECOVERY CHARACTERISTICS OF SEVOFLURANE VERSUS HALOTHANE IN CHILDREN AGED 1-3 YEARS -- A COMPARATIVE STUDY.

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ABSTRACT

Background: The main objective of this study was to compare the recovery characteristics of sevoflurane and halothane for day-care anaesthesia in children aged 1–3 yr.

Methods: 40 children undergoing day-care surgery were randomly divided into 2 groups of 20 each to receive inhalational induction with either sevoflurane or halothane and nitrous oxide in oxygen (70/30) via a face mask. Tracheal intubation was performed without a muscle relaxant. Anaesthesia was continued with the volatile anaesthetic, adjusted to maintain heart rate and blood pressure within ±20% of initial values. Recovery was evaluated using a modified Aldrete score, a Pain/ Discomfort scale and by measuring recovery end-points. A postoperative questionnaire was used to determine the well-being of the child at home until 24 h after discharge.

Results: Emergence and interaction occurred significantly earlier after sevoflurane than halothane but discharge times were similar. More children in the sevoflurane group achieved full Aldrete scores within the first 30 min after anaesthesia, although this group suffered more discomfort during the first 10 minutes. The amount of postoperative analgesic administered was higher and the first dose given earlier in the sevoflurane group. Postoperative vomiting was more common with halothane, but side-effects in the two groups were otherwise similar in the recovery room and at home.

Conclusions: In children 1–3 yr, sevoflurane provided more rapid early recovery but not discharge after anaesthesia of < 30-min duration. Apart from more vomiting with halothane and more discomfort during the first 10 min after awakening with sevoflurane, the quality of recovery was similar with the two anaesthestics.

INTRODUCTION

SEVOFLURANE (fluoromethyl 2,2,2-trifluoro-1-[trifluoromethyl] ethyl ether), an inhalational anesthetic agent, has a low blood-gas partition coefficient (0.6–0.7) and a pleasant, nonpungent odor and provides a rapid, smooth induction and a rapid emergence from anesthesia (1). Because of its pleasant smell and lack of respiratory irritant properties, mask induction is a feasible alternative to other inhalant agents. However, it is degraded by carbon dioxide absorbents into an haloalkane known commonly as 'compound A.' Compound A at high doses has been shown to be nephrotoxic in nonhuman primates, causing proximal tubular necrosis. It has replaced halothane in many hospitals, especially in the paediatric setting. Sevoflurane's induction and maintenance characteristics appear to be similar to or slightly better than those of halothane (2–5), and a majority of studies have demonstrated its superior recovery characteristics (3, 6–9). However, recent attention has focused on the practical advantages – if any – of sevoflurane over halothane (5, 10). Though early recovery is more rapid with the former, discharge times have not differed (2, 3, 8, 9, 11). Moreover, postoperative agitation and excitement appear to be more common after sevoflurane anaesthesia (2, 8, 11). Differences in the design of the studies could affect their outcome as recovery from anaesthesia can be influenced by the dose of anaesthetic, age of the patient, premedication and opioid treatment. We therefore attempted to determine the recovery characteristics of sevoflurane and halothane in a specifically defined age group (1–3 yr) of children undergoing a similar type of surgery and standardized anaesthetic administration. Our hypothesis was that after elimination of certain confounding factors, differences in recovery after sevoflurane and halothane would be minimal in this group of children.

Methods After obtaining approval from the Ethical Committee and informed parental consent, 40 children were randomly divided into 2 groups of 20 each to receive either sevoflurane or halothane for induction of anaesthesia. The children were aged 1–3 yr, ASA physical status 1 or 2, and were scheduled for short elective operative procedures under general anaesthesia. All children had a eutectic mixture of local anaesthetic cream applied on the dorsum of the hand one hour before venous cannulation. The parent(s) accompanied the child into the operating room. Pre-induction heart rate, non-invasive arterial pressure and oxygen saturation were recorded. Inhalational anaesthesia was induced via a facemask with either sevoflurane or halothane and nitrous oxide in oxygen (70/30) using a Bain circuit with a fresh gas flow. As soon as consciousness was lost an intravenous cannula was inserted and a solution of NaCl started at an age-appropriate hourly rate. When induction was complete (small pupils with central gaze), tracheal intubation was accomplished without a muscle relaxant. After tracheal intubation, anaesthesia was continued with 1 MAC of the inhaled anaesthetic (halothane (12), sevoflurane (13)). Nitrous oxide and oxygen were administered at the same 70/30 concentration. The end-tidal concentration of the inhalational anaesthetic was measured continuously from the elbow connector of the tracheal tube. Ventilation was controlled to maintain normocapnia and the fresh gas flow was kept high enough to prevent rebreathing. The inspired concentration of the inhalational anaesthetic was adjusted according to the response of the patient to surgery (e.g. movement, tearing, swallowing) while attempting to keep heart rate and arterial pressure within ± 20% of initial values. Standard monitoring (arterial pressure, heart rate and oxygen saturation) was used throughout anaesthesia. After completion of surgery, the inhalational anaesthetic was discontinued and 100% oxygen delivered. The oropharynx was suctioned and extubation performed when spontaneous breathing returned. End-tidal anaesthetic concentrations were recorded during anaesthesia and the age-adjusted MAC-value calculated. The MAC-hour was obtained by multiplying the mean age-adjusted MAC-values during maintenance of anaesthesia with the duration of anaesthetic gas administration. In the

recovery room, heart rate, arterial pressure and oxygen saturation were monitored until the child was fully awake. The parent(s) of the child was allowed into the recovery room once the child had regained consciousness. Recovery of all the children was evaluated by the same trained recovery nurse, who was blinded to the the anaesthetic method used. The rate of recovery was assessed using a modified Aldrete score (14) (Table 1) and the behaviour of the child using a modified Pain/Discomfort scale based on that by Hannallah et al. (15) (Table 1).

Table 1. *The modified Aldrete score (14) and the Pain/ Discomfort Scale (15)*

Modified Aldrete Score	Score	Pain/Discomfort Scale	Score
Activity		Crying	
Not moving	0	Not crying	0
Non-purposeful movement	1	Responding to comforting	1
Moving limbs purposefully	2	Not responding to comforting	2
Respiration		Moving	
Apnoeic/needs maintenance	0	None	0
Shallow or limited	1	Restless	1
Deep breathing or coughing	2	Thrashing	2
Consciousness		Agitation	
Unresponsive	0	Asleep or calm	0
Responding to stimuli	1	Mild agitation	1
Fully awake	2	Severe agitation/hysterical	2
O_2 saturation			
<90%	0		
90–94%	1		
≥95%	2		

If the sum on the Pain/Discomfort scale at any evaluation point exceeded 3, the child was regarded as suffering from post-anaesthetic excitement. Evaluation of the Aldrete and Pain/Discomfort scores was performed every 5– 10 min after cessation of anaesthesia for the first hour, then every half hour until discharge. In addition, predetermined recovery end-points were measured: time to emergence (spontaneous eye opening to non-painful stimuli), time to interaction (responding to the nurse or parent), time to achieving full points on the modified Aldrete score, time to drinking fluids, time to ambulating according to age, and time taken to achieve the criteria for discharge. The discharge criteria were: stable vital signs, full points on the modified Aldrete score, no vomiting, no excessive pain, and able to drink fluids and ambulate according to age. Adverse events in the recovery room were noted. Intravenous pethidine in increments of 5 mg was administered for postoperative analgesia at the discretion of the recovery nurse. The total amount given and the time to the first dose were recorded. The parents were asked to record, in a postoperative questionnaire, the well-being of the child at home until 24 h after discharge.

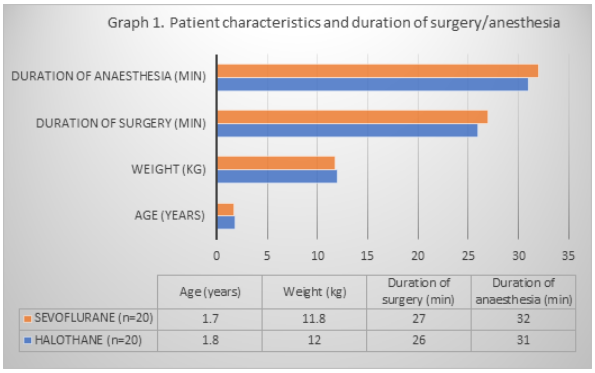
STATISTICAL ANALYSIS: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS and Microsoft Excel were used to carry out the statistical analysis of data. Descriptive statistics of data including percentages and means were reported. Values for continuous data were expressed as mean ± SD and categorical variables as proportions. Continuous variables with normal distribution were compared using Student t test while those not normally distributed were analysed using Mann Whitney U test. Categorical data were analysed using Chi-square test. Graphically the data was presented by bar diagrams. A P-value of less than 0.05 was considered statistically significant.

Results The two study groups were comparable in age, weight, duration of surgery and anaesthesia (Table 2 and Graph 1) and the difference was not statistically significant. The age-adjusted end-tidal MAC-values and doses of anaesthetic during anaesthesia did not differ between the groups (Table 2 and Graph 1).

Table 2. *Patient characteristics and age-adjusted MAC concentrations during anaesthesia. Results are expressed as mean ± SD. No significant differences between groups.*

PARAMETER	HALOTHANE (n=20)	SEVOFLURANE (n=20)
Age (years)	1.8 ±0.5	1.7 ±0.5
Weight (kg)	12 ±1.5	11.8 ±1.6
Duration of surgery (min)	26 ±7	27 ±7
Duration of anaesthesia (min)	31 ±8	32 ±9
Anaesthetic concentrations: a		
Maintenance	0.90 ±0.3	0.80 ±0.1
End of surgery	0.86± 0.3	0.80 ±0.1
MAC- hour	0.45 ±0.2	0.40 ±0.1

MAC: minimum alveolar concentration. aAnaesthetic concentrations are expressed as end-tidal age-adjusted MAC multiples, as described in Methods



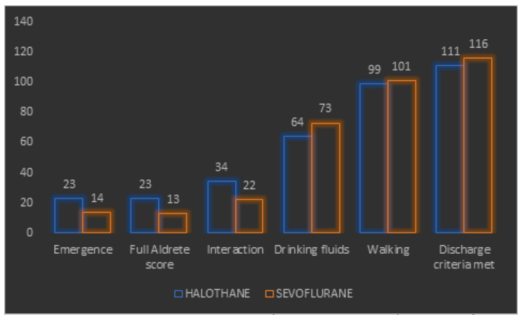
Recovery times are shown in Table 3 and Graph 2. Children in the sevoflurane group opened their eyes (emergence), interacted and scored full points on the modified Aldrete score earlier. The number with full Aldrete scores was higher in the sevoflurane group during the first 30 min after anaesthesia (P<0.05), although the discharge time did not differ from the halothane group (Table 3 and Graph 2).

Table 3. *Recovery times (min) from end of anaesthesia in the two study groups. Results are expressed as mean ± SD*

PARAMETER	Halothane	Sevoflurane	P*
Emergence	23 ±11	14 ±11	0.0001
Full Aldrete score	23 ±17	13±12	0.0001
Interaction	34 ±18	22 ±15	0.0001
Drinking fluids	64 ±25	73 ±35	0.3
Walking	99 ±32	101 ±31	0.3
Discharge criteria met	111 ±36	116 ±25	0.3

**Mann-Whitney U test.*

Graph 2. Recovery times (min) from end of anaesthesia in the two study groups

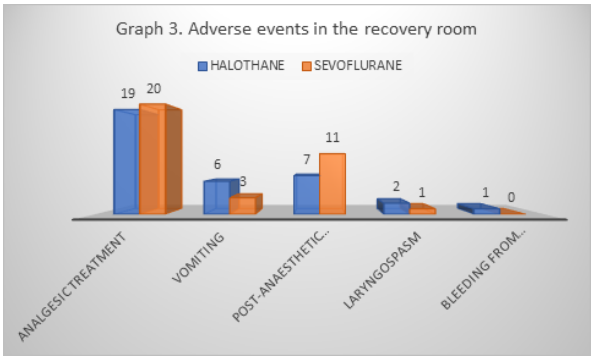


Vomiting in the recovery room was more common with halothane than sevoflurane (P<0.05). Bleeding from the surgical site occurred in two patients with halothane, delaying discharge. Otherwise adverse events were not statistically significant between the groups (Table 4 and Graph 3).

Table 4. Adverse events in the recovery room in the two study groups. Results are expressed as number (%)

PARAMETER	Halothane	Sevoflurane
Analgesic treatment	19 (95)	20 (100)
Vomiting	6 (30) *	3 (15)
Post-anaesthetic excitement	7 (35)	11 (55)
Laryngospasm	2 (10)	1 (5)
Bleeding from surgical site	1(5)	0 (0)

**P=0.05 between groups (Chi-square test)*



After sevoflurane anaesthesia, children were in more discomfort during the first 10 min after anaesthesia, while those in the halothane group scored higher on the Pain/Discomfort scale at 30 min after anaesthesia. Time to administering the first intravenous dose of pethidine was significantly shorter in the sevoflurane group (mean ± SD= 7± 4 min) compared to the halothane group (19 ± 12) min) (P< 0.0001). Also, the total analgesic dose was higher in the sevoflurane group (mean ±SD) 12= ±7 mg) than in the halothane group (10 ±7) mg. At home, recovery was similar in both groups. Of the children who vomited in the recovery room, one from each group also vomited at home. The total incidence of vomiting during the first 24 h after anaesthesia was 30% and 25% in the halothane and sevoflurane groups, respectively.

Discussion

Our hypothesis that differences in recovery would be small after sevoflurane and halothane anaesthesia in children 1–3 yr was not confirmed. Early recovery was significantly more rapid after sevoflurane although discharge times were similar with both agents. In addition, children in the sevoflurane group were in more discomfort upon awakening and required more analgesics at an earlier stage. These findings are in accordance with earlier studies in children of varying age where recovery with halothane was delayed during the first 20–30 min after anaesthesia, but did not subsequently differ (3, 6–9). In the present study, the children belonged to a limited age group undergoing a similar type of surgerWe expected recovery times to be similar because of the young age of the children. The more rapid recovery with sevoflurane is consistent with the lower solubility of sevoflurane (0.6 (1)) than halothane (2.4 (17)), resulting in faster elimination of the anaesthetic from blood after its discontinuation (18). However, the solubility of the anaesthetic determines the effect of age on recovery. The solubility of halothane in blood (17, 19) and tissues (20) decreases with younger age. In contrast, age has little effect on the solubility of sevoflurane in blood (19). It could thus be postulated that the younger the child, the less impact the solubility of the anaesthetic would have on recovery, thus reducing the differences between sevoflurane and halothane. However, the dose of the anaesthetic also correlates with recovery (21). We attempted to deliver an equipotent dose of the anaesthetics by restricting their concentration during maintenance to 1 MAC, when haemodynamically possible. Neither the MAC-hour nor the concentrations at the end of anaesthesia differed between the groups. However, nitrous oxide decreases the MAC of halothane more (60% (22)) than that of sevoflurane (24% (13)). In consequence, the children in the halothane group would have been at a deeper level of anaesthesia at the end of surgery, which could help to explain the slower awakening. Our emergence times are similar to the findings of Rieger et al. (2) and Lerman et al. (11) for both anaesthetics, but longer than in the studies by Kataria et al. (1), Greenspun et al. (9) and Welborn et al. (23). Differences in anaesthetic doses between studies may explain the disparity in emergence times after discontinuation of the anaesthetic. In addition, tapering of the anaesthetics towards the end of surgery was not done in our study and consequently higher concentrations than needed may have been delivered at the end of anaesthesia. In spite of more rapid emergence and earlier recovery, sevoflurane did not provide earlier discharge in our study population. Apart from the study by Naito et al. (24), where discharge was delayed by 50 min with halothane, discharge times after sevoflurane have differed by 10 min (4) or been equal to halothane (2, 3, 8, 9, 11). The time to discharge can be influenced by many factors, e.g. the administration of postoperative opioids, nausea and vomiting, and by discharge criteria. In our study, postoperative pethidine was used more often with sevoflurane. This possibly counteracted its benefit of more rapid recovery by increasing postoperative sedation and consequently delaying discharge in some of the children. Differences in adverse events were small in the recovery room and at home. Both agents caused minimal airway complications postoperatively. A lower incidence of vomiting (13%) in the recovery room occurred with sevoflurane than with halothane (30%), which is consistent with previous studies (3, 11). The Pain/Discomfort scores were higher during the first 5–10 min after anaesthesia in the sevoflurane group. Also, more children suffered from post-anaesthetic excitement after sevoflurane than after halothane, although this did not reach statistical significance. Similar findings have been reported in several previous studies (2, 8, 11). Pain may have been a contributing factor as rectal diclofenac may not have provided adequate analgesia at the time of awakening in some children. However, young age has also been shown to predispose to postoperative agitation or delirium, the effect being more pronounced after sevoflurane anaesthesia (25, 26). Recently, the benefits of sevoflurane over halothane have been questioned (5, 10). The induction and maintenance characteristics of sevoflurane and halothane during a short anaesthetic can be indistinguishable to a blinded anaesthetist (10). In addition, sevoflurane does not necessarily provide more rapid recovery (5, 10) or decrease length of stay in the operating room (27). On the other hand, provided that the quality of recovery of the two agents is similar, a delayed early recovery is not necessarily a disadvantage. After surgery requiring postoperative analgesia with no possibility of regional block or intraoperative opioids, a child may even benefit from a slightly delayed recovery (28). In view of our findings, halothane may be a worthy alternative to sevoflurane for short-lasting procedures in these situations. In conclusion, in children aged 1–3 yr, early recovery was more rapid with sevoflurane than with halothane, but discharge times were similar. In spite of similar MAC-hours, the greater additive effect of nitrous oxide to the MAC of halothane may have delayed the speed of recovery in this group. However, initial awakening was associated with more distress with sevoflurane and this created a need for more analgesics. Except for a slightly higher incidence of vomiting in the

recovery room, adverse events did not differ between the groups in the recovery room or at home.

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