Sevoflurane-maintained anesthesia induced with propofol or sevoflurane in small children: induction and recovery characteristics

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Purpose: To compare the induction and recovery characteristics of sevoflurane anesthesia induced with either propofol or sevoflurane in pediatric outpatients.

Methods: Fifty-two children, aged 1-3 yr, presenting for ambulatory adenoidectomy were randomly allocated to receive 3 mg·kg⁻¹ propofol iv or sevoflurane 8% inspired concentration for induction of anesthesia. Tracheal intubation was facilitated with 0.2 mg·kg⁻¹ mivacurium. Anesthesia was maintained with nitrous oxide/oxygen (FIO₂ 0.3) and sevoflurane approximately 3-5% inspired concentration with controlled ventilation. Intubation was assessed by an anesthetist blinded to the induction method. Recovery characteristics were compared using the modified Aldrete scoring system, the Pain/Discomfort scale and measuring specific recovery times. A postoperative questionnaire was used to evaluate the children's well-being at home.

Results: Intubating conditions were similar in both groups. Emergence from anesthesia occurred earlier with sevoflurane for induction than with propofol (11 ± 4 vs 17 ± 7 min (mean $\pm$ SD), $P = 0.0002$). More children in the sevoflurane group achieved full points on the modified Aldrete scoring system during the first 20 min after anesthesia ($P < 0.05$). However, children in the sevoflurane group scored higher in the Pain/Discomfort scale at 10 min after anesthesia ($P = 0.04$) and were given postoperative analgesics earlier than children in the propofol group (13 ± 5 min vs 18 ± 11 min, $P = 0.03$). The time to meet discharge criteria and recovery at home were similar.

Conclusions: Induction of sevoflurane anesthesia with propofol for day-case adenoidectomy results in longer, but more calm, early recovery but does not delay discharge or affect recovery at home.

Objectif : Comparer les caractéristiques de l'induction, réalisée avec du propofol ou du sévoflurane, et de la récupération d'une anesthésie avec du sévoflurane chez des patients ambulatoires de pédiatrie.

Méthode : Cinquante-deux enfants, âgés de 1 à 3 ans, qui se sont présentés pour une adénoïdectomie ambulatoire, ont été répartis de façon aléatoire et ont reçu 3 mg·kg⁻¹ de propofol iv ou de sévoflurane 8 % par inhalation pour l'induction de l'anesthésie. L'intubation endotrachéale a été facilitée par 0,2 mg·kg⁻¹ de mivacurium. L'anesthésie a été maintenue avec un mélange de protoxyde d'azote et d'oxygène (FiO₂ 0,3) et du sévoflurane d'une concentration approximative de 3 à 5 % administré par inhalation et accompagné d'une ventilation contrôlée. L'intubation a été évaluée par un anesthésiste impartial qui ne connaissait pas la méthode d'induction. Les caractéristiques de la récupération ont été comparées en utilisant le système de cotation modifié d'Aldrete, l'échelle Douleur/Inconfort et les mesures spécifiques des temps de récupération. Un questionnaire postopératoire a été utilisé pour évaluer le bien-être des enfants de retour à la maison.

Résultats : Les conditions de l'intubation ont été similaires dans les deux groupes. La récupération de l'anesthésie s'est produite plus tôt avec l'induction au sévoflurane qu'avec l'induction au propofol (11 ± 4 vs 17 ± 7 min (moyenne $\pm$ écart-type), $P = 0,0002$). Un plus grand nombre d'enfants du groupe sévoflurane a obtenu tous les points au système de cotation modifiée d'Aldrete pendant les 20 premières min après l'anesthésie ($P < 0,05$). Toutefois, les enfants de ce groupe ont eu des scores de Douleur/Inconfort plus élevés à 10 min après l'anesthésie ($P = 0,04$) et on leur a administré des analgésiques postopératoires plus tôt qu'aux enfants du groupe propofol (13 ± 5 min vs 18 ± 11 min, $P = 0,03$). Le temps nécessaire pour satisfaire aux critères de sortie de l'hôpital et de récupération à la maison a été semblable dans les deux groupes.

Conclusion : L'utilisation du propofol à l'induction de l'anesthésie au sévoflurane a donné lieu à une récupération précoce plus longue, mais plus calme, d'une adénoïdectomie ambulatoire et n'a pas eu d'effet sur le moment de la sortie et sur la récupération à la maison.

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S EVOFLURANE is an inhalational anesthetic with low blood-gas solubility and nonpungent smell. In children, it provides smooth, uncomplicated induction and rapid emergence from anesthesia^{1,2} which makes it especially suitable for ambulatory anesthesia. Propofol is a short-acting intravenous anesthetic, which has also become popular in the pediatric outpatient setting because of its rapid recovery characteristics^{3,4} and antiemetic properties.^{5,6}

In ambulatory procedures of short duration, the induction agent may affect emergence and recovery from anesthesia. In adults, inhalational induction with sevoflurane provided more rapid emergence from sevoflurane anesthesia than did an *iv* induction with propofol.^{7,8} However, when the duration of anesthesia increased, recovery characteristics and discharge times were similar.^{9,10}

No study has investigated the possible effect of propofol as an induction agent on recovery from sevoflurane-based anesthesia in children. We decided to compare intravenous induction with propofol with inhalational induction with sevoflurane in children undergoing ambulatory adenoidectomy. Our aim was to evaluate the induction characteristics of the two anesthetics with special regard to their effect on recovery from anesthesia.

Methods

We studied 52 children, ASA physical status I or II, aged 1-3 yr, presenting for ambulatory adenoidectomy

my with or without myringotomy. The study was carried out in two centres, the Helsinki University Central Hospital and the Central Hospital of Seinäjoki. The study was approved by the Ethics Committees of both hospitals. Informed written consent was obtained from the parents of each child investigated. All children had EMLA® cream (Astra, Sweden) applied over the dorsum of the hand one hour before induction of anesthesia. No sedative premedication was used. Each child was randomly assigned, by computer-based random numbers listing, to receive intravenous induction with 3 mg·kg⁻¹ propofol (propofol group) or inhalational induction with sevoflurane 8% (inspired concentration) via a face mask (sevoflurane group). In both groups anesthesia was continued with sevoflurane in nitrous oxide 70% in oxygen.

After arrival in the operating room, pre-induction heart rate, blood pressure (Dinamap, Critikon, Tampa, Florida, USA) and oxygen saturation (Capnomac Ultima, Datex, Helsinki, Finland) were recorded. All children received 0.01 mg·kg⁻¹ atropine *iv* immediately after venous cannulation and 10 µg·kg⁻¹ alfentanil *iv* 60 sec

TABLE I Intubating condition score according to Helbo-Hansen *et al.*¹¹

Score	1	2	3	4
Laryngoscopy	easy	fair	difficult	impossible
Vocal cords	open	moving	closing	closed
Coughing	none	slight	moderate	severe

TABLE II The modified Aldrete score^{12,13,14} and the Pain/Discomfort Scale¹⁵

Modified Aldrete Score		Pain/Discomfort Scale	
Parameter	Score	Parameter	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	2
O₂ saturation			
< 90%	0		
90-94%	1		
≥ 95%	2		

TABLE III Demographic data

	<i>Propofol</i>	<i>Sevoflurane</i>
<i>n</i>	26	26
Age (months)	27 ± 11	24 ± 9
Weight (kg)	13 ± 2	13 ± 3
Duration of surgery (min)	14 ± 6	16 ± 10
Duration of anesthesia (min)	22 ± 7	25 ± 11

Mean ± SD

TABLE IV Recovery times in the two study groups

<i>Recovery variable (min)</i>	<i>Propofol</i>	<i>Sevoflurane</i>	<i>P</i> ‡
Emergence	17 ± 7	11 ± 4	0.0002
CI	14-19	9-12	
Making sounds	15 ± 7	10 ± 4	0.002
CI	12-18	8-11	
Interaction	23 ± 7	17 ± 6	0.01
CI	19-26	14-20	
Elective drinking	64 ± 32*	41 ± 18†	0.05
CI	45-83	29-52	
Walking	58 ± 32	51 ± 24	0.5
CI	45-72	40-62	
Discharge criteria met	75 ± 27	70 ± 24	0.2
CI	65-87	60-79	

Mean ± SD and 95% confidence intervals (CI)

* *n* = 13; † *n* = 12.‡ Mann-Whitney *U* test.

before induction of anesthesia. In the propofol group, 10 mg lidocaine *iv* was used to minimize pain on injection with propofol. An initial dose of 3 mg·kg⁻¹ propofol *iv* was injected slowly. Additional increments of 0.5 mg·kg⁻¹ propofol *iv* were administered until the child tolerated the application of the face mask and gentle manual ventilation with oxygen 100%. In the sevoflurane group, inhalational induction was started with sevoflurane 1-2% (inspired concentration) in nitrous oxide 70% in oxygen via a face mask with gradual increase every few breaths up to sevoflurane 8%. When the child had 'fallen asleep' (pupils small and midline), ventilation was assisted and the sevoflurane inspired concentration decreased to 3-5%. In both groups, the trachea was intubated two minutes after administration of 0.2 mg·kg⁻¹ mivacurium *iv*. Intubation was performed and assessed by an anesthetist blinded to the method of induction. This anesthetist entered the operating room only after the attending anesthetist considered the child to be ready for intubation. At this time all signs of the induction agent were concealed (sevoflurane turned off, syringes hidden). Assessment of the intubating conditions was made according to a 4- point scoring system for laryngoscopy,

TABLE V Adverse events and need for additional pain relief after anaesthesia in the recovery room

	<i>Propofol</i>	<i>Sevoflurane</i>
Vomiting	2 (8)	4 (15)
Laryngospasm	2 (8)	0
Bleeding from surgical site	0	1
Emergence delirium	5 (19)	10 (38)
Additional analgesia required	23 (88)	24 (92)

Number (%).

No differences between groups.

TABLE VI Recovery details at home during the first 24 hr after discharge

	<i>Propofol</i> <i>n</i> = 24	<i>Sevoflurane</i> <i>n</i> = 26
Pain		
on same day	14 (58)	20 (77)
next morning	8 (33)	5 (19)
Medication for pain given		
on same day	16 (67)	16 (61)
next morning	3 (13)	7 (27)
Vomiting	1 (4)	2 (7)
Bad tempered	5 (21)	3 (12)
Drinking less	3 (13)	4 (15)
Tiredness *	7 (29)	9 (35)
Disturbed sleep †	7 (29)	8 (31)

Number (%). No differences between groups.

* Playing less than normal or lying down. † Waking up often or nightmares.

position of vocal cords and coughing after placement of the tracheal tube¹¹ (Table I). Immediately after intubation a suppository of 20 mg·kg⁻¹ acetaminophen was given for postoperative analgesia.

Anesthesia was maintained with sevoflurane in nitrous oxide 70% in oxygen. The sevoflurane concentration during surgery was adjusted to maintain blood pressure within ± 20% of pre-induction values, usually between 3-5% inspired concentration. Oxygen saturation and end-tidal carbon dioxide values were monitored continuously (Capnomac Ultima, Datex, Helsinki, Finland). Ventilation was controlled to maintain end-tidal carbon dioxide values between 33-42 mmHg. Vital signs (heart rate, blood pressure) were recorded immediately before intubation (end of induction), after intubation, every five minutes during surgery, and before and after extubation.

At the end of surgery sevoflurane was discontinued and oxygen 100% delivered. The oropharynx was suctioned and the trachea extubated when spontaneous breathing was regarded as adequate. Extubation time was defined as the time from discontinuation of sevoflurane and nitrous oxide to recovery of spontaneous breathing and removal of the tracheal tube.

FIGURE 1 Heart rate (HR) during anesthesia in the two study groups.

Mean $\pm$ SD. * Significant difference between groups according to post-hoc comparison.

Pre = pre-induction, ind = end of induction, int = after tracheal intubation, end = end of surgery, ext = after extubation.

FIGURE 2 Mean arterial pressure (MAP) during anesthesia in the two study groups.

Mean $\pm$ SD. * Significant difference between groups according to post-hoc comparison.

Time points as in Figure 1.

In the recovery room, heart rate, blood pressure and oxygen saturation were monitored until the child was fully awake. If required, $0.05 \text{ mg} \cdot \text{kg}^{-1}$ oxycodone *iv* was given for postoperative pain relief. The time from extubation to the first dose of analgesic and the total amount of analgesic needed were recorded. Recovery was assessed by a specially trained nurse who was unaware of the induction method. A modified Aldrete scoring system¹²⁻¹⁴ was used to assess recovery from

FIGURE 3 Number of patients achieving full points (8) on the modified Aldrete score at different times in the recovery room. * $P = 0.05$, † $P = 0.04$ between groups.

FIGURE 4 Total group score for pain/discomfort at different times in the recovery room.

* $P = 0.04$ between groups.

anesthesia and the Pain/Discomfort scale according to Hanallah *et al.*¹⁵ was used to evaluate the quality of emergence from anesthesia (Table II). If the total score on the Pain/Discomfort scale at any evaluation point exceeded the sum of three, emergence was regarded as delirious. The modified Aldrete and Pain/Discomfort scores were evaluated every 10 min after arrival in the recovery room for the first half hour then every 15 or 30 min until discharge. In addition, the following recovery times (from discontinuation of sevoflurane)

were recorded: (1) time to emergence (spontaneous eye opening), (2) time to making sounds, (3) time to interaction (responding to the nurse or parent), (4) time to elective drinking, (5) time to be able to walk and (6) time to achieve discharge criteria. Discharge criteria included being fully awake, stable vital signs for 30 min, no bleeding, no pain, no nausea or vomiting and able to ambulate according to age.

A postoperative questionnaire was given to the parents who were asked to record the well-being (pain, nausea, tiredness, drinking ability, sleep) of the child at home until 24 hr after surgery.

Statistical analysis

Analyses were performed with a Statistical Package for the Social Sciences (SPSS) version 6.0 for Windows and STATISTICA for Windows. Results are presented as mean $\pm$ SD, 95% confidence intervals (CI) or number (%) where appropriate. A *P* value of < 0.05 was considered significant. Differences in demographic data were assessed by Student's *t* test. Differences in extubation times, recovery times, time to first analgesic and pain scores between the groups were analyzed with the Mann-Whitney *U* test. The Chi-square and Fisher's Exact test were used to compare the distribution of intubation scores and the incidences of patients with full Aldrete scores and postoperative sequelae. Changes in heart rate and mean arterial pressure (MAP) were analyzed with two-way ANOVA for repeated measurements (baseline values as a covariant) with the Spjotvall-Stoline test for post-hoc comparisons. It was predicted that, in order to detect a five minute difference between groups regarding emergence from anesthesia, with an estimated emergence time of 14 min and a SD of six minutes in the sevoflurane group, a minimum of 23 patients would be required in each group. This would give the study an 80% power at a significance level of 5%.

Results

The two groups were comparable in terms of patient characteristics and duration of surgery and anesthesia (Table III).

The required mean dose of propofol for induction of anesthesia was 3.2 ± 0.3 mg·kg⁻¹. Successful intubation was achieved in all patients. Intubating conditions were similar in the two groups. All patients scored 1 or 2 for laryngoscopy. Three patients from each group scored 3 for the position of vocal cords, and one patient from each group had moderate coughing (score = 3) after intubation. No scores of four were seen.

Movement related to tracheal intubation occurred in seven (31%) children in the propofol group com-

pared with two (9%) children in the sevoflurane group ($P = 0.06$). Two children from the propofol group and one child from the sevoflurane group started to breathe spontaneously immediately after intubation. One child in the propofol group developed a rash on the arm after the administration of mivacurium, which resolved spontaneously.

The hemodynamic responses to induction and intubation are shown in Figures 1 and 2. Heart rate (HR) decreased after induction and increased after tracheal intubation in both groups (Figure 1). When analyzing HR, the groups differed significantly ($P = 0.008$). The period effect (time) ($P < 0.0001$) and the interaction between the groups and periods ($P = 0.003$) were significant. The post-hoc comparison showed that the interaction was due to the time points after induction and intubation, where the HR in the sevoflurane group was higher than in the propofol group (Figure 1). No bradycardia (heart rate < 70 beats·min⁻¹) was seen in either group. Mean arterial pressure (MAP) decreased after induction in both groups. After intubation MAP increased in the propofol group but remained depressed in the sevoflurane group (Figure 2). When analyzing MAP, the period effect ($P < 0.0001$) and the interaction between the groups and periods ($P = 0.048$) were significant. Post-hoc analysis revealed that the interaction was due to the time point after intubation (Figure 2).

All children started breathing spontaneously after discontinuation of sevoflurane without reversal of neuromuscular block. Extubation time was 3.3 ± 1.7 min in the propofol group and 3.0 ± 1.1 min in the sevoflurane group ($P = 0.7$). After extubation, one child in the propofol group coughed and one child from each group developed laryngospasm.

The time to emergence, making sounds, interaction and drinking occurred earlier in the sevoflurane group than in the propofol group but discharge time was similar in both groups (Table IV). More children in the sevoflurane group scored full points on the modified Aldrete scoring system at 10 and 20 min after anesthesia (Figure 3) but obtained higher scores on the Pain/Discomfort scale at 10 min after anesthesia compared with the propofol group (Figure 4). The Pain/Discomfort scores remained higher in the sevoflurane group at 20 min after anesthesia but this did not reach statistical significance ($P = 0.06$).

Adverse events in the recovery room were few and did not differ between the study groups (Table V). The first dose of oxycodone in the recovery room was administered earlier to the children in the sevoflurane group than to those in the propofol group (13 ± 5 min vs 19 ± 12 min, $P = 0.03$) but the total amount administered was the same in both groups.

All the questionnaires except for two from the propofol group were returned. No severe adverse reactions were reported. Recovery from anesthesia at home was similar in both study groups (Table VI). The total incidence of vomiting during the first 24 hr after surgery was 13% and 22% in the propofol and sevoflurane groups, respectively (NS).

Discussion

In our study intravenous induction with propofol provided similar intubating conditions to inhalational induction with sevoflurane but heart rate during induction of anesthesia was better preserved with sevoflurane. Early recovery was faster with sevoflurane than with propofol for induction but late recovery was not affected by the induction agent. On the other hand, children in the sevoflurane group were in more discomfort at 10 min after anesthesia and postoperative analgesics were administered earlier than to the children in the propofol group.

Intubating conditions were similar between the groups but movement related to tracheal intubation occurred more often after propofol for induction, though this did not reach statistical significance. Furthermore, two children in the propofol group and one child in the sevoflurane group started to breathe spontaneously immediately after intubation. Incomplete neuromuscular block has been reported after 0.2 mg·kg⁻¹ mivacurium in children,^{16,17} which may in part explain the movement and the return of spontaneous breathing after tracheal intubation. The higher incidence of movement in the propofol group may also have been due to an insufficient induction dose of propofol in some of the children. It has been recommended to use 4 mg·kg⁻¹ propofol *iv* for induction of anesthesia in children 1-3 yr because of the larger volume of the central compartment in this age group.¹⁸ We chose to use an initial dose of 3 mg·kg⁻¹ with additional doses of 0.5 mg·kg⁻¹ in order to achieve acceptance of the face mask and assisted ventilation, a common clinical end-point. All movements during intubation were slight movements of the hands or feet and did not compromise tracheal intubation or hemodynamics.

Both HR and MAP decreased during induction of anesthesia in both groups. The lower HR after induction with propofol than with sevoflurane may reflect the impairment of the baroreflex caused by propofol in this age group.¹⁹ However, no bradycardia was seen in either group which was probably due to the effect of atropine given before induction. The blood pressure response to tracheal intubation was better attenuated with sevoflurane than with propofol which

possibly reflects a deeper depth of anesthesia with sevoflurane at the time of laryngoscopy.

Adverse reactions related to anesthesia were few in both groups. All children started breathing spontaneously at the end of surgery and neuromuscular reversal agents were not needed. The 95% recovery after a single dose of 0.2 mg·kg⁻¹ mivacurium is 16-18 min^{17,20} which is within the range of the duration of anesthesia in our study. The reversal of neuromuscular block was not used routinely in our study because in earlier studies, spontaneous recovery after a single intubating dose of mivacurium occurred in every child after sevoflurane anesthesia¹⁶ and the risk of residual block is low even after an infusion of mivacurium.²¹

Children in the sevoflurane group opened their eyes, made sounds, interacted with the environment and scored full points on the modified Aldrete scale earlier than in the propofol group. The difference in early recovery characteristics in our study was most likely due to the short duration of anesthesia (< 30 min) which would allow propofol to have some residual effect in the immediate recovery period. Our findings are consistent with adult studies where induction of sevoflurane anesthesia with propofol resulted in longer emergence times than when sevoflurane alone was used for anesthesia of short duration.^{7,8}

The attending anesthetist administering sevoflurane was not blinded to the induction agent. However, the concentration of sevoflurane was adjusted strictly according to the study protocol (maintaining mean arterial pressure within $\pm$ 20% of initial readings). We believe this would not allow for differences between groups in regard to the concentration of the maintenance agent.

More children in the sevoflurane group were crying, restless or agitated upon awakening than in the propofol group, which was seen in the higher scores for Pain/Discomfort in the recovery room at 10 min after anesthesia. The increased incidence of emergence delirium would account for the earlier administration of analgesics to the children in the sevoflurane group. In previous studies in children, awakening from sevoflurane anesthesia has been associated with discomfort, excitement or agitation,^{13,22-24} the mechanism of which is still unclear. In our study, pain may have been a contributing factor, as the rectal absorption of acetaminophen - used for postoperative analgesia - can be delayed and incomplete.²⁵ Because of the faster emergence, pain could have occurred earlier in the sevoflurane group. However, the Pain/Discomfort scale does not differentiate between pain and anxiety. Westrin *et al.* found that the occurrence of postanesthetic agitation was related to the age

of the child and not to the perception of pain.²² This effect of age on increased incidence of emergence delirium has been confirmed in other studies^{23,26} and could, in part, have accounted for the unruly awakenings in our study. It has also been suggested that the shorter time to emergence may contribute to the occurrence of delirium postoperatively.²⁶ The use of propofol as an induction agent in our study reduced the incidence of emergence delirium (19%) to nearly half the incidence (38%) with sevoflurane alone for anesthesia though this did not reach statistical significance ($P = 0.1$). This may have resulted from the slightly prolonged early recovery with propofol. Though the small sample size in our study precludes drawing statistical conclusions, our findings suggest that propofol - as an induction agent for sevoflurane anesthesia - may be beneficial in reducing the incidence of emergence delirium in this age group.

The incidence of vomiting (13-22%) in both groups during the first 24 hr after surgery is in accordance with the incidence reported in a previous study using sevoflurane anesthesia in children.² An induction dose of propofol did not affect the incidence of vomiting significantly after operation.

In conclusion, induction of sevoflurane anesthesia with propofol resulted in similar intubating conditions as after induction with sevoflurane. Recovery occurred earlier but children were in more discomfort during the first 10 min after anesthesia with sevoflurane induction than with propofol. Discharge or recovery at home was not affected by the induction agent.

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