

## Original Article

# Comparison of two different sevoflurane expelling methods on emergence agitation in infants following sevoflurane anesthesia

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**Abstract:** Purpose: To investigate the effects of two different inhalation anesthetic expelling methods on emergence agitation in infants following sevoflurane anesthesia. Methods: 100 infants (1~3 years old) with cleft lip and palate and ASA classification I~II were randomized into two groups, a sevoflurane concentration decreasing expelling group (group N = 50 cases) and a low fresh gas flow expelling group (group D = 50 cases). The operation for cleft lip and palate repair was under general anesthesia, in which 30 minutes after initiation of narcosis ending extubation was indicated and after the tubes were removed the patients were sent to the post-anesthesia care unit (PACU) to record anesthesia times, emergence agitation scores, Ramsay scores and adverse reactions including drowsiness, respiratory depression, nausea and vomiting, chills, hiccup or laryngospasms. Results: There were no differences in anesthesia times, awaking time and time until extubation between the two groups. 10 min after start of expelling sevoflurane, blood pressure and heart rates were higher in group N than in group D ( $P < 0.05$ ). The postoperative agitation incidence and the degree of agitation were lower in group D than in group N ( $P < 0.05$ ). Conclusion: Postoperative agitation is prone to occur in patients with sevoflurane concentration decreasing expelling. Avoiding sevoflurane application maintenance in the stage of sevoflurane expelling reduces the occurrence of postoperative agitation and diminishes physiological and psychological harm.

**Keywords:** Infants, emergence agitation, sevoflurane, methods of expelling inhalational anesthetics

## Introduction

Surgical procedures involving pediatric patients have frequently to be done under general anesthesia and the children are too young for cooperation during or immediately following the operation. Sevoflurane is an inhalational anesthetic agent used in general anesthesia and characterized by a sweet smell, low blood gas partition coefficient, short induction time and rapid recovery while causing little airway irritation [1]. At present, sevoflurane is already widely in use for general anesthesia induction and maintenance for various kinds of pediatric surgeries [2]. However, the incidence of emergence agitation following sevoflurane anesthesia is higher in children than in adults [3] and has been reported to be 10%~67% [4] and in children receiving ear-nose-throat and eye surgery, postoperative agitation occurs even more

frequently than after other surgical procedures [5]. In addition, pre-school children aged 2-5 years old are documented to have higher incidences of agitation after general anesthesia than school-age children aged 6-10 years old [6, 7]. Postoperative agitation is mostly self-limited, but it can have negative consequences, for example, increasing bleeding, affecting sutures and drainage tubes due to body movement and struggling and may even affect relevant medical equipment [8-10]. Currently, the method used most often to intervene with emergence agitation in children involves the application of drugs, such as fentanyl, benzodiazepines as well as selective  $\alpha_2$  adrenoceptor agonist [11-13]. There has been less research, however, examining whether the ways of breathing out inhalational anesthetics can affect emergence agitation in children following sevoflurane anesthesia. According to a 2011 inhala-

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**Table 1.** Comparison of the age, weight, operation time, awaking time, extubation time, HR and MAP 10 min after expelling sevoflurane between the two groups ( $n = 50$ , mean  $\pm$  SD)

Groups	Age (years)	Weight (kg)	Operation time (min)	Awaking time (min)	Extubation time (min)	HR (beats/min)	MAP (mmHg)
Group N	2.70 $\pm$ 0.70	12.56 $\pm$ 2.50	100.10 $\pm$ 25.10	6.70 $\pm$ 2.30	7.80 $\pm$ 2.10	98.00 $\pm$ 18.00***	64.00 $\pm$ 10.00***
Group D	2.30 $\pm$ 0.90	11.56 $\pm$ 3.65	102.45 $\pm$ 36.28	6.90 $\pm$ 1.80	8.10 $\pm$ 1.80	83.00 $\pm$ 15.00	50.00 $\pm$ 12.00
P	0.148	0.1073	0.7072	0.6293	0.4449	0.0000	0.0000

\* $P < 0.05$ , \*\*\* $P < 0.001$  when compared with group D.

tion anesthesia expert consensus, expelling ways of inhaled anesthetics include a sevoflurane concentration decreasing method and a low fresh gas flow method [14]. The study described here is focused on the analysis of the effect of the two different sevoflurane leaching methods on postoperative agitation in children, who received cleft lip and palate repair surgery under sevoflurane anesthesia.

### Materials and methods

#### Patients

The study included 100 children aged 1~3 years old in a physical status of I~II according to the American Society of Anesthesiologists (ASA) guidelines, who visited the First Peoples' Hospital of Shijiazhuang for cleft lip and palate repair surgery. The hospital ethics committee approved the study and the parents of all children provided informed written consent. All children had no prior history of surgery, congenital heart disease, serious organ dysfunction, drug abuse, epilepsy or obvious respiratory tract infection before surgery. Routine chest X-ray and laboratory examinations were done before surgery for all the patients. The patients were randomly assigned into two groups each including 50 patients, which were treated with different methods for expelling sevoflurane. Group N received a concentration decreasing leaching and group D received a low flow leaching treatment. Exclusion criteria included: (1) sensitivity to inhaled anesthetics, (2) mental retardation, (3) emergency operation, (4) taking part in other clinical studies, (5) the need of intravenous drugs to induce and maintain the anesthesia or combined inhalation and intravenous drug anesthesia and (6) known or suspected susceptibility to malignant hyperthermia.

#### Anesthesia methods

All patients were deprived of water for 4 h and were fasted for at least 6 h in the morning of

the operation day and atropine was intramuscularly injected 30 min before surgery. Patients were kept warm with an electric blanket and connected to a monitor who recorded blood pressure, pulse,  $\text{SPO}_2$  and respiration once every 5 min. For anesthesia induction we adopted a tidal volume method and the equipments were an Ohmeda 7100 anesthesia machine and an Ohmeda Tec 7 sevoflurane exclusive volatilizer. The anesthesia machine was in manual mode and the APL valve was set in the open position, with the evaporator open and the initial scale adjusted to 8% pre-charge sevoflurane in the breathing circuit, while the children were given sevoflurane mixture inhalations using suitable size masks. When the patient's eyelash reflexes disappeared and the submaxilla relaxed, the oral tube intubation was performed. Volume controlled ventilation (VCV) was performed with tidal volume of 10 ml/kg and respiration rates of 20~30 bpm, while end-tidal carbon dioxide partial pressure ( $\text{PETCO}_2$ ) was maintained at 35-45 mmHg. At the start of the operation, the inhalation concentration was adjusted to 2.5% (1MAC) and according to the children's vital signs, further inhalation concentrations were adjusted and the inhaled sevoflurane was stabilized to 0.8-1.2 MAC with an oxygen flow rate of 2 L/min.

#### Sevoflurane expelling methods

**Group N:** 30 min prior to the operation end, the inhaled anesthetic concentration was reduced and maintained at about 0.5 MAC. After surgery was completed, the inhaled anesthetic supply was ceased with fresh gas flow increased to 8 L/min in order to accelerate the sevoflurane clearance. **Group D:** 30 min minutes ahead of the surgery end, the sevoflurane influx was turned off with reduced fresh gas flow of 0.5 L/min until subcuticular skin suturing was completed and then the fresh gas flow was increased to 4 L/min in order to accelerate the expelling of sevoflurane.

**Table 2.** Comparison of Sevoflurane concentrations ( $C_{ET}Sev$ ) between the two groups just before start of expelling and just before extubation ( $n = 50$ )

Group	$C_{ET}Sev$ prior to leaching	$C_{ET}Sev$ prior to extubation
Group D	$2.5 \pm 0.4$	$0.11 \pm 0.05^{***}$
Group N	$2.6 \pm 0.3$	$0.21 \pm 0.06$
<i>P</i>	0.1605	0.0000

\* $P < 0.05$ , \*\*\* $P < 0.001$  when compared with group D.

**Table 3.** The incidence and degree of postoperative agitation between the two groups [ $n = 50$ ,  $n$  (%)]

Groups	Mild (%)	Moderate (%)	Severe (%)	Total incidence (%)
Group N	10 (20)*	14 (28)*	6 (12)***	30 (60.0)***
Group D (%)	6 (12)	2 (4)	0 (0.0)	8 (16)
<i>P</i>	0.0413	0.0011	0.0007	0.0000

\* $P < 0.05$ , \*\*\* $P < 0.001$  when compared with group D.

For our study, we selected children aged from 1 to 3 years as patients, whose average age was 2 years. Because these patients are not able to follow verbal instructions such as to open their eyes as the criteria for extubation, after the surgery they were extubated when the spontaneous breathing tidal volume was  $> 8$  ml/kg and blood oxygen saturation ( $SpO_2$ ) was  $> 98\%$  with suction phlegm after swallowing reflex recovery. Patients were then sent to the post-anesthesia care unit (PACU). When the Modified Aldrete Score was greater than 9 (see **Table 1**), oxygen supply had been stopped for over 5 min and  $SPO_2$  was higher than 95%, the patients were sent out of the PACU.

#### Observation indices

Patients' mean arterial pressure (MAP) and heart rate 10 min after expelling sevoflurane were recorded. In addition, anesthesia time, awaking time (time from post-operation to opening eyes), and extubation time (time from post-operation to pulling out the tube) were monitored. Agitation score and Ramsay score [15] were observed once every 5 min after extubation until 20 min after awaking and recorded. Postoperative agitation score, incidence and degree were evaluated using a five-point scale method: 0-drowsy, unable to wake up; 1-awake, quiet, cooperative; 2-crying but consolable; 3-agitated, crying inconsolably, no need to control agitation; 4-agitated, disorientated, need to control agitation. A score  $\geq 2$  was considered positive for agitation and scoring was 2-mildly

agitated, 3-moderately agitated whereas 4-severely agitated. Ramsay scores were as follows: 1-awake, anxious and agitated; 2-cooperative, orientated, quiet; 3-drowsy, responsive to order; 4-drowsy, sensitive to tapping eyebrow or loud auditory stimulating; 5-drowsy, slow to respond to tapping eyebrow or loud auditory stimulating; 6-drowsy, no response. A Ramsay score of 1 was therefore the only score considered positive for agitation. A score of 2-4 indicated satisfactory sedation, whereas a score of 5-6 indicated excessive sedation. After 3 days of surgery, patients were finally monitored for any ad-

verse reactions such as drowsiness, respiratory depression, nausea and vomiting, chills, hic-cough or laryngospasm.

#### Statistical analyses

Measurement data were expressed as mean  $\pm$  SD. Analysis of variance (ANOVA) and *t*-tests were used for comparisons. Count data were presented as  $n$  (%) and *Chi*-squared test was used for comparison. Data were analyzed using SPSS software (version 13) and  $P < 0.05$  was considered statistically significant.

#### Results

There were no differences in age, weight or time under anesthesia between the two groups ( $P > 0.05$ ) (**Table 1**), which showed that the basic characteristics of the two groups were equal. The overall concentration of sevoflurane was maintained to the same level of 1 MAC in both groups before sevoflurane expelling and there was no significant difference in the operation time between the two groups. 10 min after start of expelling sevoflurane, the heart rate (HR) and mean arterial pressure (MAP) in group N were higher than in group D ( $P < 0.05$ ) and no significant difference was noted in the awaking time or the extubation time ( $P > 0.05$ ) (**Table 1**). We conclude therefore, that the method of expelling sevoflurane in group N affected the depth of anesthesia in the later stage of the operation causing a relatively shallow anesthesia. Vital signs thus fluctuated in the stage of

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**Table 4.** Comparison of the Ramsay score after extubation between the two groups (n = 50, mean  $\pm$  SD)

Groups	5 min after extubation	10 min after extubation	15 min after extubation
Group N	4.6 $\pm$ 0.2	3.4 $\pm$ 0.7	3.3 $\pm$ 0.3
Group D	4.3 $\pm$ 0.5	3.6 $\pm$ 0.4	3.4 $\pm$ 0.4
P	0.1642	0.0825	0.1605

**Table 5.** Comparison of sevoflurane concentrations just before start of expelling and just before extubation between male and female patients in the two groups

Group	Gender (male/female)	Gender	C <sub>ET</sub> Sev of just before start of expelling	C <sub>ET</sub> Sev of just before extubation
Group N	23/27	Male (n = 23)	2.6 $\pm$ 0.4	0.11 $\pm$ 0.04
		Female (n = 27)	2.5 $\pm$ 0.3	0.12 $\pm$ 0.05
P			0.3182	0.4443
Group D	24/26	Male (n = 24)	2.5 $\pm$ 0.3	0.21 $\pm$ 0.04
		Female (n = 26)	2.6 $\pm$ 0.5	0.22 $\pm$ 0.06
P	0.8412		0.3255	0.4952

**Table 6.** Comparison of postoperative agitation between male and female patients in the two groups

Group	Gender (male/female)	Gender	Mild	Medium	Severe	Total incidence
Group N	23/27	Male (n = 23)	4	6	2	12
		Female (n = 27)	6	8	4	18
P			0.6704	0.7810	0.5069	0.2971
Group D	24/26	Male (n = 24)	3	1	0	4
		Female (n = 26)	3	1	0	4
P	0.8412		0.9167	0.9539	0.0000	0.9017

**Table 7.** Comparison of Ramsay scores after operation between male and female patients in the two groups

Group	Gender (male/female)	Gender	5 min after extubation	10 min after extubation	15 min after extubation
Group N	23/27	Male (n = 23)	4.5 $\pm$ 0.4	3.3 $\pm$ 0.5	3.2 $\pm$ 0.2
		Female (n = 27)	4.6 $\pm$ 0.3	3.5 $\pm$ 0.7	3.3 $\pm$ 0.3
P			0.3182	0.2585	0.1800
Group D	24/26	Male (n = 24)	4.2 $\pm$ 0.6	3.5 $\pm$ 0.4	3.4 $\pm$ 0.4
		Female (n = 26)	4.3 $\pm$ 0.5	3.6 $\pm$ 0.4	3.3 $\pm$ 0.3
P	0.8412		0.5239	0.3815	0.3199

expelling sevoflurane as compared with group D. Both groups started to expel sevoflurane 30 min before operation end and we compared the concentration of sevoflurane (C<sub>ET</sub> Sev) just before start of sevoflurane expelling, which was the same in both groups (group D = 2.5  $\pm$  0.4; group N = 2.6  $\pm$  0.3). In contrast, at the time of extubation, the C<sub>ET</sub> Sev for the group D was 0.11  $\pm$  0.05, whereas for group N it was 0.21  $\pm$  0.06,

(P < 0.05) (Table 2). Mild agitation was more common in group D. Higher incidence of mild, moderate and severe agitation occurred in group N. There was a significant difference in the incidence and in the degree of postoperative agitation between the two groups (P < 0.05) (Table 3). Postoperative Ramsay scores between the two groups were not significantly different (P > 0.05), indicating that the two ways of expelling sevoflurane had no effect on the sedation degree in the stage of awaking or the time until awaking (Table 4).

Further analyses on gender differences revealed, that there was no statistically significant difference between male and female patients regarding C<sub>ET</sub> Sev just before start of expelling and just before extubation (Table 5) or postoperative agitations (Table 6) and Ramsay scores after operation (Table 7).

## Discussion

An inhalation anesthesia expert consensus published in 2011 suggested that both the concentration decreasing leaching method and the low flow leaching method could be used for the recovery of inhalation anesthesia. However, there is no report regarding the effect of the two methods for expelling inhalational anes-

thetics on emergence agitation in children following sevoflurane anesthesia. In our study, all inhaled anesthetic eliminations were achieved by means of gas exchange among blood, tissue and cells. Gas molecules diffuse from the high partial pressure side to the low pressure side. The oxygen exchange thus conforms to the following rule: outside atmosphere → respiratory tract → pulmonary blood capillary → blood circulation → tissue blood capillary → tissue cells and carbon dioxide exchange occurs in the opposite direction. *In vitro* uptake, distribution and discharge process of inhaled anesthetics occur in an identical manner and sevoflurane is not an exception. Although the solubility of sevoflurane is relatively low, even with operation time extension, the time for the reduction of 60% or even 80% alveolar gas concentration is not affected by the anesthesia duration. However, getting rid of more than 90% anesthetics is needed for pharyngeal reflex to return to normal and when the anesthetic concentration exceeds 0.5%-0.8% MAC obvious pharyngeal dysfunctions appear [16]. Adverse reactions caused by incomplete sevoflurane elution are the main causes of emergence agitation in children. The results of our study showed, that with the same anesthesia time, there was a higher incidence of postoperative emergence agitation using the concentration decreasing leaching method compared to the low flow leaching method. We suggest that the difference is probably due to the fact, that during the process of sevoflurane elution, the depth of anesthesia became relatively shallow by inhaling 0.5 MAC sevoflurane and because of that, 10 min after sevoflurane expelling, HR and MAP in group N was higher than in group D ( $P < 0.05$ ). In addition, the sevoflurane concentration was fast adjusted from 1 MAC to the stable 0.5 MAC concentration during end of surgery, while undesirable stimulation during this time might have also stimulated the occurrence of postoperative agitation. We suggest that because of the rapid recovery from sevoflurane anesthesia, the time of central recovery differs between the groups. While the cerebral cortex is in an inhibitory state, the subcortical regions have been liberated thus causing sensitization of local centers. Loss of this functional completeness affects children's sensory response and processing ability. Children in the stage of awaking after general anesthesia are sensitive to undesirable stimulation under the role of stimulants. The central nervous system mani-

festes overexcitement, so that agitation induction occurs [7]. However, the depth of anesthesia is moderate during the leaching stage using the low flow leaching method and the leaching process is in a stable state. The main reason for the occurrence of agitation using the low flow leaching method may be due to the still relatively incomplete elution of sevoflurane. Taken together, a small amount of remaining residual drugs in the awaking stage is the main reason for postoperative agitation and it was significantly higher in the N group. It has been reported that sevoflurane concentrations of 0.1-0.2 MAC in the awaking stage are the cause for tracheal tube irritation, wound pains [17], hypoxia, respiratory tract obstruction [16], while noisy environment triggers the occurrence of postoperative agitation [18]. In our study, comparisons of  $C_{ET}Sev$  just before start of expelling and just before extubation, postoperative agitations and Ramsay scores after operation between female and male patients did not reveal any statistically significant difference. This is in agreement with previous reports of gender influence on sevoflurane anaesthesia [19, 20]. On the other hand, it has been noted that the early recovery time after sevoflurane anesthesia was shorter in male than in female patients, which the authors explained with a lower minute ventilation of women, which may contribute to a slower initial washout of the inhalational agents [21].

In conclusion, postoperative agitation is prone to occur in preschool children, who receive a concentration decreasing leaching method after cleft lip and palate repair surgery under sevoflurane anesthesia. Proper drug use and combined anesthesia should be used for such little operations, especially avoiding pure inhalation anesthesia maintenance in the stage of sevoflurane leaching in order to stably and fully elute sevoflurane, thereby reducing the occurrence of postoperative agitation.

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### Disclosure of conflict of interest

None.



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## References

- [1] Gueli SL and Lerman J. Controversies in pediatric anesthesia: sevoflurane and fluid management. *Curr Opin Anaesthesiol* 2013; 26: 310-317.
- [2] Goldman LJ. Anesthetic uptake of sevoflurane and nitrous oxide during an inhaled induction in children. *Anesth Analg* 2003; 96: 400-406, table of contents.
- [3] Malviya S, Voepel-Lewis T, Ramamurthi RJ, Burke C and Tait AR. Clonidine for the prevention of emergence agitation in young children: efficacy and recovery profile. *Paediatr Anaesth* 2006; 16: 554-559.
- [4] Silva LM, Braz LG and Modolo NS. Emergence agitation in pediatric anesthesia: current features. *J Pediatr (Rio J)* 2008; 84: 107-113.
- [5] Kuratani N. [Emergence agitation in pediatric anesthesia]. *Masui* 2007; 56: 554-559.
- [6] Sikich N and Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. *Anesthesiology* 2004; 100: 1138-1145.
- [7] Herlenius E and Lagercrantz H. Neurotransmitters and neuromodulators during early human development. *Early Hum Dev* 2001; 65: 21-37.
- [8] Dahmani S, Delivet H and Hilly J. Emergence delirium in children: an update. *Curr Opin Anaesthesiol* 2014; 27: 309-315.
- [9] Galinkin JL, Fazi LM, Cuy RM, Chiavacci RM, Kurth CD, Shah UK, Jacobs IN and Watcha MF. Use of intranasal fentanyl in children undergoing myringotomy and tube placement during halothane and sevoflurane anesthesia. *Anesthesiology* 2000; 93: 1378-1383.
- [10] Bakhamees HS, Mercan A and El-Halafawy YM. Combination effect of low dose fentanyl and propofol on emergence agitation in children following sevoflurane anesthesia. *Saudi Med J* 2009; 30: 500-503.
- [11] Jung HJ, Kim JB, Im KS, Oh SH and Lee JM. Effect of ketamine versus thiopental sodium anesthetic induction and a small dose of fentanyl on emergence agitation after sevoflurane anesthesia in children undergoing brief ophthalmic surgery. *Korean J Anesthesiol* 2010; 58: 148-152.
- [12] Ozcengiz D, Gunes Y and Ozmete O. Oral melatonin, dexmedetomidine, and midazolam for prevention of postoperative agitation in children. *J Anesth* 2011; 25: 184-188.
- [13] Ghosh SM, Agarwala RB, Pandey M and Vajifdar H. Efficacy of low-dose caudal clonidine in reduction of sevoflurane-induced agitation in children undergoing urogenital and lower limb surgery: a prospective randomised double-blind study. *Eur J Anaesthesiol* 2011; 28: 329-333.
- [14] Xue QS, Luo Y, Zhang FJ, Yu BW, Wang GL, Tian YK, Tian M, Liu J, Wu XM, Su F, Lian QQ, Yue Y, Zheng H, Yu WF, Guo QL, Guo XY, Huang YG, Huang QW, Xiong LZ and Xue ZG. Inhalation anesthesia clinical practices expert consensus (in chinese with English abstract). *Continuing Medical Education* 2011; 3: 108-112.
- [15] Reschreiter H, Maiden M and Kapila A. Sedation practice in the intensive care unit: a UK national survey. *Crit Care* 2008; 12: R152.
- [16] McKay RE, Large MJ, Balea MC and McKay WR. Airway reflexes return more rapidly after desflurane anesthesia than after sevoflurane anesthesia. *Anesth Analg* 2005; 100: 697-700, table of contents.
- [17] Mayer J, Boldt J, Rohm KD, Scheuermann K and Suttner SW. Desflurane anesthesia after sevoflurane inhaled induction reduces severity of emergence agitation in children undergoing minor ear-nose-throat surgery compared with sevoflurane induction and maintenance. *Anesth Analg* 2006; 102: 400-404.
- [18] Kain ZN, Caldwell-Andrews AA, Maranets I, McClain B, Gaal D, Mayes LC, Feng R and Zhang H. Preoperative anxiety and emergence delirium and postoperative maladaptive behaviors. *Anesth Analg* 2004; 99: 1648-1654, table of contents.
- [19] Kodaka M, Johansen JW and Sebel PS. The influence of gender on loss of consciousness with sevoflurane or propofol. *Anesth Analg* 2005; 101: 377-381, table of contents.
- [20] Shen X, Hu C and Li W. Tracheal extubation of deeply anesthetized pediatric patients: a comparison of sevoflurane and sevoflurane in combination with low-dose remifentanyl. *Paediatr Anaesth* 2012; 22: 1179-1184.
- [21] Tercan E, Kotanoglu MS, Yildiz K, Dogru K and Boyaci A. Comparison of recovery properties of desflurane and sevoflurane according to gender differences. *Acta Anaesthesiol Scand* 2005; 49: 243-247.