

# The Effect of Fentanyl on the Emergence Characteristics After Desflurane or Sevoflurane Anesthesia in Children

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Desflurane and sevoflurane anesthesia are associated with emergence agitation in children. In this study, we examined the effect of a single intraoperative dose of fentanyl on emergence characteristics in children undergoing adenoidectomy. One hundred children, 2–7 yr old, were randomly assigned to receive desflurane or sevoflurane for maintenance of general anesthesia after an inhaled induction with sevoflurane and a 2.5  $\mu\text{g}/\text{kg}$  dose of fentanyl. An observer blinded to the anesthetic technique assessed the times to achieve emergence, extubation and recovery criteria, as well as emergence behaviors. The results showed a

similar incidence of severe emergence agitation after general anesthesia with desflurane (24%) and sevoflurane (18%). Times to achieve extubation and postanesthesia care unit discharge criteria were shorter with desflurane than with sevoflurane. With this technique, desflurane allows for a more rapid emergence and recovery than sevoflurane. In children receiving desflurane or sevoflurane, the concurrent use of fentanyl in a dose of 2.5  $\mu\text{g}/\text{kg}$  results in a small incidence of emergence agitation.

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**B**oth desflurane and sevoflurane, which have low blood gas solubility coefficients, allow for rapid emergence and recovery from general anesthesia (1,2). However, desflurane and sevoflurane, as sole anesthetics, are often associated with emergence agitation in children (3–6). The need to treat emergence agitation with analgesics and sedatives postoperatively delays recovery and discharge from the postanesthesia care unit (PACU) (7,8). In a previous study, we demonstrated that the concurrent use of fentanyl, 2.5  $\mu\text{g}/\text{kg}$ , with a desflurane anesthetic, decreased the incidence of emergence agitation while preserving quick recovery (9). The purpose of this study was to compare the effect of this previously determined dose of fentanyl on emergence characteristics of children undergoing adenoidectomy with either desflurane or sevoflurane.

## Methods

Informed consent and IRB approval were obtained. One hundred ASA physical status I and II children, 2–7 yr of age, undergoing adenoidectomy, with or without bilateral myringotomy and insertion of tubes, were studied. None of the patients had a history of sleep apnea, developmental delay, or psychological disorders. The same inclusion and exclusion criteria were used to determine the subjects studied in finding the mean effective dose of fentanyl to reduce emergence agitation (9).

Patients were not premedicated. Anesthesia was induced with an inhaled technique consisting of nitrous oxide/oxygen (70%:30%) and sevoflurane. An IV catheter was placed, mivacurium 0.25 mg/kg was given to facilitate endotracheal intubation, and the previously calculated mean effective dose of fentanyl (2.5  $\mu\text{g}/\text{kg}$ ) was given. Ondansetron 0.1 mg/kg was given to reduce the incidence of postoperative nausea and vomiting. For anesthesia maintenance, patients were randomly assigned to receive either desflurane 4%–6% or sevoflurane 1.5%–2.0% with  $\text{N}_2\text{O}$  2 L/min and  $\text{O}_2$  1 L/min via the endotracheal tube. Ventilation was controlled to maintain an end-tidal  $\text{CO}_2$  of  $35 \pm 4$  mm Hg. Vital signs were monitored and recorded throughout the study. Standard monitoring included electrocardiogram, blood

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pressure cuff, pulse oximeter, temperature, and end-tidal gas measurements.

At the completion of surgery, defined as the time when the mouth gag was removed, desflurane or sevoflurane and nitrous oxide were discontinued simultaneously. Controlled ventilation was continued at the same settings and a total gas flow of 3 L/min of oxygen, without any attempt to stimulate the patient. With the return of the cough reflex, patients were allowed to breathe spontaneously. When patients demonstrated recovery of neuromuscular function and complete emergence from anesthesia by displaying a regular respiratory pattern, facial grimacing, and purposeful movement, they were tracheally extubated and transferred to the PACU. An observer who was blinded to the anesthetic used, recorded time to first cough, facial grimacing, purposeful movement, eye opening, and extubation. Agitation was scored on a 3-point scale (1 = calm, 2 = agitated but consolable, 3 = severely agitated, inconsolable). Pain was assessed by using the objective pain scale (10) and recovery was determined by using the Steward recovery score (11) by the same observer. Times until the child was ready for discharge from the PACU (Steward recovery score = 6) to the short stay (Phase 2) recovery unit (SSRU), and from the SSRU to home were recorded. Each patient was contacted 24 h after surgery to follow up on the incidence of agitation, pain, and vomiting at home.

A power analysis determined the total number of observations needed to be 88 by comparing both the range of emergence times and the mean incidence of emergence agitation controlling for the probability of Type I and Type II errors. Emergence agitation was the primary endpoint using an incidence of previously published results. The sample size was increased by 5% to allow for the use of nonparametric tests and another 5% for attrition protection.

Statistical analysis of the results was preformed by using the SAS software (12) (SAS, Cary, NC), and the significance tests used were the Student's *t*-test and Kruskal-Wallis test when comparing the demographic data and the measured time intervals. Nonparametric data including sex, agitation scores, pain scores, and the incidence of vomiting were compared by using  $\chi^2$  analysis and Fisher's exact test. All tests were considered significant if  $P < 0.05$ .

## Results

There were no significant ( $P > 0.05$ ) differences between the two study groups in age, weight, sex, or surgical time (Table 1). Times to emergence, extubation, and ready for discharge from PACU (Steward recovery score of 6) were significantly shorter in the Desflurane group ( $P < 0.05$ ). Patients who received

sevoflurane required an average of 3 additional min to emergence compared with those who received desflurane. There were no significant differences between the two treatment groups in the times to discharge from the SSRU. These results are summarized in Table 2. The incidence of severe agitation (a score of 3), severe pain (an objective pain scale score  $\geq 6$ ), and vomiting were similar between the two groups (Table 3).

## Discussion

Rapid emergence with dependable return of airway reflexes and cognitive abilities is important in the ambulatory patient. In a previous study, we found that concurrent use of fentanyl at a dose of 2.5  $\mu\text{g}/\text{kg}$ , immediately after induction, significantly reduced the incidence of emergence agitation while preserving speedy recovery after desflurane anesthesia in children undergoing adenoidectomy (9). The proposed causes of emergence agitation seen with desflurane and sevoflurane included rapid emergence, variable neurological recovery, and increased pain sensation (2-6,13-16). In this study, we did not try to delineate the cause of emergence agitation. No control group was used because of the unacceptably frequent incidence of severe emergence agitation in children receiving only these anesthetics. Prevention is ethically indicated and opioids have long been considered the only consistent and reliable therapy for emergence agitation (13).

In our previous study, the dose of fentanyl effective in reducing emergence agitation in desflurane-anesthetized children was determined by implementing the classic up-down method (9). Using the same age group, surgical procedure, extubation criteria, and emergence behavior scales, we observed similar emergence times and incidence of emergence agitation in this study. When comparing the incidence of severe agitation between the 2 treatment groups, no significance difference ( $P = 0.624$ ) was found. Approximately 20% of all patients were assessed to have severe emergence agitation.

There was a statistically significant delay in meeting emergence criteria, extubation, and PACU discharge in the Sevoflurane group as compared with the Desflurane group. We found that emergence was faster with desflurane than sevoflurane by approximately three to five minutes. Similar results and times have been reported in adults (17). This amount of time in a busy, rapid turnover surgical setting can be particularly important in high acuity/high cost areas as the operating room and PACU. In an operation that is typically  $<30$  minutes, a 10% prolongation of emergence can be important.

The lack of any difference between the treatment groups in the time to be discharged to home is not

**Table 1.** Demographics

	No.	Age (mo)	Weight (kg)	Sex (male/female)	Surgical time (min)
Desflurane	50	50.4 ± 16.1	17.9 ± 3.9	29/21	27.1 ± 10.6
Sevoflurane	50	46.4 ± 16.8	16.8 ± 4.1	32/18	25.9 ± 12.7
Kruskal-Wallis		<i>P</i> = 0.23	<i>P</i> = 0.10	<i>P</i> = 0.68*	<i>P</i> = 0.35

Values are mean ± SEM.  
\* Fischer's exact test.

**Table 2.** Emergence and Recovery Times in Minutes

	Cough	Grimace	Purposeful movement	Extubation	Eye opening <sup>a</sup>	Discharge to home
Desflurane	4.3 ± 3.2	4.7 ± 3.2	7.2 ± 4.9	6.5 ± 2.8	10.7 ± 6.2	127 ± 38
Sevoflurane	6.9 ± 3.7	7.5 ± 3.3	10.0 ± 4.5	9.3 ± 3.3	13.9 ± 8.3	129 ± 37
Kruskal-Wallis	<i>P</i> = 0.0002	<i>P</i> = 0.0001	<i>P</i> = 0.0001	<i>P</i> = 0.0001	<i>P</i> = 0.0054	<i>P</i> = 0.99

Values are mean ± SEM.  
<sup>a</sup> Ready for postanesthesia care unit discharge/Steward score = 6.

**Table 3.** Incidence of Untoward Effects

	Severe agitation (score = 3)	Severe pain (score ≥ 6)	Vomiting
Desflurane	24	42	16
Sevoflurane	18	48	12
Fischer's exact test	<i>P</i> = 0.624	<i>P</i> = 0.688	<i>P</i> = 0.715

Values are percentages.

surprising. With average time to discharge being approximately two hours and multiple factors (such as nursing care, patient willingness to drink, walk, and get dressed, and parental readiness to depart) impinging on discharge, a difference of three to five minutes can become obscured.

The frequent incidence of severe postoperative pain is unexpected in these children pretreated with a relatively large dose of fentanyl. The pain score results are reported as the highest score achieved during recovery. Pain experienced after adenoidectomy is typically described as moderate and not requiring repeated doses of potent analgesics. In past studies with desflurane and sevoflurane, the increased need for analgesics has been reported. Although this can be attributed to the severe emergence agitation causing a high score on an observational pain scale, in this study, the percent of patients exhibiting severe agitation is decidedly less than those experiencing severe pain. Also, the high pain scores were often recorded later in the recovery course and self reported by patients.

It should be noted that no premedication was used in this study; midazolam and other sedatives significantly prolong emergence when used to facilitate induction or reduce the incidence of emergence agitation (18,19). Prophylactic treatment with the antiemetic ondansetron was

included in the study design secondary to the frequent incidence of vomiting in our previous study (9). The incidence of vomiting was small in both treatment groups.

We conclude that when using the highly insoluble anesthetic gases, a balance needs to be achieved between maintaining rapid emergence and minimizing the incidence of agitation. In children undergoing adenoidectomy with desflurane or sevoflurane, 2.5 µg/kg fentanyl reduces the incidence of emergence agitation compared with previously reported results (3-6) whereas delaying emergence and recovery in those patients who received sevoflurane compared with those who received desflurane. Although in this study there were no incidences of upper airway obstruction or apnea, well supervised postanesthesia care and avoidance of additional sedatives when using this dose of fentanyl are recommended. In addition, the need for antiemetics with this technique should be anticipated.

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