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Greater Incidence of Delirium during Recovery from Sevoflurane Anesthesia in Preschool Boys

Jun Aono, M.D.,* Wasa Ueda, M.D.,† Kikyo Mamiya, M.D.,‡ Eri Takimoto, M.D.,* Masanobu Manabe, M.D. §

Background: **In the authors' clinical experience, preschool children are more likely to show delirium after sevoflurane than are older children.**

Methods: **Sixty-three preschool boys aged 3–5 yr (classified as American Society of Anesthesiologists [ASA] physical status I), and 53 school-age boys aged 6–10 yr (ASA physical status I) who underwent minor urologic surgery were randomly assigned to receive either halothane or sevoflurane, thus creating four groups: preschool-halothane (n = 32), preschool-sevoflurane (n = 31), school-halothane (n = 27), and school-sevoflurane (n = 26). Anesthesia was induced by inhalation of halothane or sevoflurane in oxygen and was maintained at 1 minimum alveolar concentration of each agent throughout surgery. For intra- and postoperative analgesia, caudal block with 0.5–1.0 ml/kg 0.25% plain bupivacaine and topical infiltration with 3–5 ml 1% lidocaine were provided for all patients. Recovery characteristics and incidence of delirium on emergence were compared among the four groups.**

Results: **Two patients in the preschool-halothane group, one in the preschool-sevoflurane group, and one in the school-halothane group were excluded from the comparison because of insufficient analgesia or agitation before induction. In both age groups, the time to emergence from sevoflurane was significantly faster (about 3 min) than from halothane. The incidence of delirium during recovery in the preschool-sevoflurane group (40%) was significantly greater than that in the other groups (preschool-halothane, 10%; school-halothane, 15.4%; school-sevoflurane, 11.5%).**

Conclusion: **Sevoflurane provided quicker emergence and early recovery compared with halothane, but the incidence of delirium was greater in preschool boys after sevoflurane. (Key words: Age, pediatrics. Anesthetics, volatile: sevoflurane; halothane. Complications: delirium.)**

SEVOFLURANE has advantages over halothane in terms of quicker recovery in children given anesthesia.[1-3] The quick recovery from sevoflurane, however, is likely to be accompanied by postoperative delirium, which is considered due to the early appearance of pain.[4,5] In our clinical experience, however, we have noticed that postoperative delirium often occurs after sevoflurane in children even when sufficient analgesia is provided. In addition, the delirium seemed more common in preschool children (younger than 6 yr) than in older children. In previous studies, however, such age-related differences in the incidence of the delirium after sevoflurane has not been reported.[4,5]

Therefore, to examine the effect of age on the recovery characteristics of sevoflurane anesthesia, we compared the incidence of postoperative delirium between preschool and school-aged children anesthetized with either sevoflurane or halothane under pain-free conditions.

Patients and Methods

After obtaining approval of the ethics committee at our institution and informed parental consent, we studied 116 healthy boys aged 3-10 yr. They consisted of 63 preschool-aged (3-5 yr) boys who underwent circumcision, and 53 school-aged (6-10 yr) boys who underwent inguinal hernia repair. The boys were randomly assigned, using a dice throw to receive either halothane or sevoflurane, into one of four groups: the preschool-halothane group, preschool-sevoflurane group, school-halothane group, and school-sevoflurane group.

None of the patients was given any solid food overnight before surgery, but each was encouraged to take clear fluids until 2 h before anesthesia was induced. All patients received 0.2 mg/kg diazepam orally 1 h before induction. Monitoring during anesthesia included heart rate, electrocardiography, blood pressure, and percutaneous oxygen saturation together with end-tidal sevoflurane, halothane, and carbon dioxide concentrations measured by a Datex Ultima (Datex, Finland).

Anesthesia was induced with either halothane (5%)

* Senior Staff.

† Associate Professor of Anesthesiology.

‡ Junior Staff.

§ Professor and Chair.

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Address reprint requests to Dr. Aono: Department of Anesthesiology, Kochi Medical School, Kochi, 783 Japan. Address electronic mail to: aonoj/KMS

or sevoflurane (6–7%) in 100% oxygen by mask through an open circuit without a soda lime absorber. After 1 ml 4% lidocaine was sprayed onto the trachea under an adequate depth of anesthesia, the trachea was intubated without a muscle relaxant. With controlled ventilation, we maintained the end-tidal carbon dioxide concentration at 35–40 mmHg and at 1 minimum alveolar anesthetic concentration.

Then all patients received a caudal block with 0.5 to 1 ml/kg body weight of plain 0.25% bupivacaine. After 10–15 min, surgery started after 3–5 ml 1% lidocaine was infiltrated into the incision.

At the end of surgery, we immediately discontinued anesthetic agents and placed the patient in the lateral decubitus position. The trachea was extubated when the patient showed purposeful movement of all extremities, grimaced, coughed, or gagged.

The time to extubation, time to emergence (defined as the time until eye opening on command or the time of first response to command), and behavior during the emergence period were recorded by the same anesthesiologist, who did not know which agent was used in each patient. Behavior was rated on the following four-point scale: 1 = calm; 2 = not calm but could be easily calmed; 3 = not easily calmed, moderately agitated or restless; and 4 = combative, excited, or disoriented. For statistical purposes, grades 1 and 2 were considered nonproblematic behavior, and grades 3 or 4 were considered delirium. The observed delirium was not treated with any drug.

None of the parents were allowed to be present during emergence and recovery. The criteria for transfer from the operating room to the ward included being pain free, awake, and moving all limbs voluntarily. Adverse events during the recovery period in the operating room were also recorded.

We excluded the following patients from the study: those who showed agitation or crying before or during anesthesia induction; those who showed more than a 10% increase in the preoperative stable value of heart rate or systolic arterial pressure after skin incision; and patients who reported pain during the recovery period.

Statistical analysis of differences in measured variables among groups was conducted using two-way analysis of variance. If significance was detected, Scheffé's F test was applied for comparison between groups. Fisher's exact test was applied to determine whether any association was present between the group and the incidence of delirium. All tests were two-tailed, and a probability value less than 0.05 was considered significant.

Results

We excluded three boys (two in the preschool-halothane group and one in the preschool-sevoflurane group) from the study because of signs of incomplete pain relief. One boy in the school-halothane group was also excluded because of agitation or crying before induction. Thus the remaining 60 preschool and 52 school-aged boys were studied. All of these boys were calm or easily accepted the mask before and during induction of anesthesia. No major complications, such as oxygen desaturation (percutaneous oxygen saturation $< 95\%$), were observed in any patient at any time during the study period.

Table 1 shows patient demographic data, duration of surgery, time to extubation, time to emergence, and incidence of delirium. There was no significant difference in age, weight, or duration of surgery between the two anesthetic groups for each age group. Time to emergence from sevoflurane was significantly less than that in halothane in both age groups, but the difference (about 3 min) was not so large.

The incidence of delirium during recovery in the preschool-sevoflurane group (40%) was significantly greater than that in the other groups.

Discussion

The present study showed that the incidence of delirium was greater in preschool-aged boys after sevoflurane than in school-aged boys after sevoflurane, and in both preschool- and school-aged boys after halothane.

Possible causes of postoperative delirium include hypoxemia, metabolic disturbance, pain, and the effect of drugs.[6] In this study, all of the patients were healthy and received adequate fluid therapy during the study period, and none showed oxygen desaturation. Furthermore, all patients were free of pain because of adequate regional analgesia. Thus the high incidence of the delirium observed after sevoflurane anesthesia was not considered to be due to pain, hypoxia, or metabolic disturbance.

In the past, drug-related postoperative delirium was more common after cyclopropane anesthesia and recently after desflurane.[7,8] Previous investigators postulated that the rapid return to consciousness in a strange area with strangers may exacerbate a child's underlying sense of apprehension and fear, thereby causing a high incidence of delirium during recovery. But after remifentanil anesthesia in chil-

Table 1. Demographic Data of the Subjects, Duration of Surgery, and Recovery Characteristics

Variable	Preschool		School	
	Halothane	Sevoflurane	Halothane	Sevoflurane
n	30	30	26	26
Age (yr)	3 ± 1	3 ± 1	8 ± 1	9 ± 1
Weight (kg)	18.9 ± 3.4	18.6 ± 3.3	29.5 ± 3.7	28.3 ± 2.8
Duration of surgery (min)	29 ± 4	28 ± 6	41 ± 6	43 ± 6
Time to extubation (min)	13 ± 3	8 ± 2*	12 ± 2	8 ± 3*
Time to emergence (min)	15 ± 3	12 ± 3†	15 ± 4	12 ± 4‡
Incidence of delirium on emergence	3/30 (10%)	12/30 (40%)§	4/26 (15.4%)	3/26 (11.5%)

Values are mean ± SD. Time to extubation and time to emergence after sevoflurane anesthesia were significantly less than those after halothane anesthesia in each age groups (* $P < 0.0001$, † $P < 0.01$; ‡ $P < 0.05$ by Scheffe's F test). Among the four groups, the incidence of delirium on emergence was most frequent in the preschool-sevoflurane group (§ Fisher's exact test: preschool-sevoflurane *vs.* preschool-halothane, $P < 0.0087$; preschool-sevoflurane *vs.* school-sevoflurane, $P < 0.032$, school-halothane *vs.* school sevoflurane, $P > 0.9999$).

dren, on the contrary, even though the emergence is rapid, such high incidence of delirium is not observed.[9] Thus the rapid emergence alone may not be the cause of delirium.

In contrast to our findings, Welborn *et al.*[10] reported that the incidence of excitement after desflurane was 55%, and after sevoflurane it was 5%. On the other hand, Lerman *et al.*[11] observed a greater incidence of agitation after sevoflurane (18%) compared with that after halothane (7%). The reason for the differences in the incidence of delirium on emergence between our results and their studies is not clear, but different age groups studied may have yielded different results.

Preschool children may be psychologically less mature than school-aged children and less able to cope with sudden awakening in a strange environment. We speculate that psychological immaturity, coupled with the rapid recovery potential of sevoflurane, might have caused the greater incidence of delirium in the preschool-sevoflurane group in this study.

Agitation and excitement on emergence has been treated with 1–2 μg/kg fentanyl.[10,12] Although we did not treat delirium with any drugs, this treatment might be recommended especially for preschool-aged children after sevoflurane. A rational method of controlling this problem should be studied in the future.

In conclusion, sevoflurane provided quicker emergence and early recovery than halothane, but a high incidence of delirium was observed in preschool-aged boys after sevoflurane.

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