J Anesth (1996) 10:72–75

Journal of
Anesthesia

Clonic convulsive movements during and on emergence from sevoflurane anesthesia

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Key words: Sevoflurane, Clonic convulsion, Bronchospasm

Introduction

Sevoflurane is a new potent volatile anesthetic which is useful in pediatric anesthesia because of its rapid induction of and emergence from anesthesia with nonpungency and limited cardiorespiratory depression. However, clonic and tonic seizure-like movements of the extremities during induction of anesthesia with sevoflurane-nitrous oxide have been reported [1]. We previously described electrical seizures during induction of anesthesia with sevoflurane-oxygen in two pediatric patients with epilepsy [2]. In the present report, two cases are described of seizure-like activity associated with bronchospasm during induction but no bronchospasm on emergence from anesthesia with nitrous oxide-sevoflurane.

Case reports

Case 1

A 4-year-old, ASA class I, 98-cm-tall, 15.1-kg girl was scheduled for cystoscopy and biopsy for a possible recurrence of rhabdomyosarcoma of the bladder. Fifteen months earlier, she had received chemotherapy with a combination of vincristine sulfate, cyclophosphamide, and actinomycin D. The results of a preoperative examination of her general condition were completely within normal limits. Both her own and her family's medical histories revealed neither convulsive disorders nor asthmatic experiences. Three hours before anesthesia, the patient had 150 ml of a sports drink (Pocari Sweat, Otsuka Pharmaceuticals, Tokyo) containing sugar and was given triclofos sodium (150 mg, p.o.) as premedication 45 min prior to the induction of anesthesia. She was well sedated on arrival at the operating room. Oxyhemoglobin saturation measured by pulse oximetry (Spo_2) was 99% under room air, and auscultation of her chest was clear, with neither rales nor wheezes. Anesthesia was induced with a mixture of 21 oxygen (O_2)·min^{-1} and 4 l nitrous oxide (N_2O)·min^{-1}. Sevoflurane was added to the mixture, with stepwise increases in concentration by 0.5% every 20 s. The induction was tolerated well with no coughing or breath holding. When the inspired sevoflurane concentration increased to 7.0% (and Spo_2 was still 99%), 2- to 3-Hz, regular, bilateral clonic convulsions of the upper eyelids and the upper and lower extremities were noticed, and the patient's heart rate and blood pressure increased from 86 bpm, 101/46 mmHg to 159 bpm, 107/59 mmHg, followed by a sudden decrease to 115 bpm and 94/49 mmHg. The sevoflurane concentration was reduced to 4.0%, and the ventilation rate decreased. During the rhythmic convulsive movements, ventilation became difficult and expiratory time was prolonged. Auscultation of the lung revealed a dry rale and wheezing. Despite an increase in FIo_2 to 1.0, the Spo_2 and heart rate decreased to 86% and 85 bpm. Consecutive intravenous administration of atropine 0.2 mg and aminophylline 50 mg produced relief of the bronchospasm and bradycardia. The Spo_2 and heart rate increased to 100% and 163 bpm. Noticeable durations of convulsions and bronchospasms were within 1 min and a few min, respectively. Anesthesia was maintained with O_2 2 l·min^{-1}, N_2O 4 l·min^{-1}, and sevoflurane 2.5%. An arterial blood sample showed no abnormal findings (pH 7.373, Pco_2 38.3 mmHg, Po_2 119.3 mmHg, base excess (BE) 1.9 mmol·l^{-1}, blood sugar level 136 mg/dl) and the electroencephalogram (EEG) recorded during mainte-

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Received for publication on March 6, 1995; accepted on July 28, 1995

nance of anesthesia with nitrous oxide and sevoflurane 2.5% revealed high-amplitude slow waves with no spike activities. She awoke uneventfully following 130 min of anesthesia, and the results of a complete neurological examination at her ward were within normal limits. On the 2nd postoperative day, the EEG recording, including both awake and asleep tracings, showed no abnormal findings.

Case 2

A 21-month-old, ASA class I, 13.3-kg girl was scheduled for radical surgery for a bilateral inguinal hernia. Both her own and her family's medical histories were normal with no convulsive disorders. She was taken to the operating room with adequate sedation 30 min after premedication with scopolamine (0.15 mg, s.c.). Anesthesia was induced with O_2 2 l·min^{-1}, N_2O 4 l·min^{-1}, and sevoflurane 1.0%, with increases in concentration by 0.5% every 1 min. When the inspired concentration of sevoflurane was 5.0%, the trachea was intubated uneventfully. During the operation, anesthesia was maintained with 2%–3% sevoflurane and 67% nitrous oxide, and was replaced by 100% oxygen at the end of the operation. Eight minutes later, spontaneous respiration began to be restored, followed by abrupt, 2- to 3-Hz, regular, rhythmic convulsive movements of the bilateral eyelids, and upper and lower extremities. The patient's heart rate increased from 88 bpm to 108 bpm. The convulsions stopped within 1 min after intravenous administration of thiamylal 50 mg. No respiratory problems were observed. Ten minutes later the trachea was extubated and she returned to the ward uneventfully after an additional 30-min observation period. During anesthesia the heart rate, blood pressure, Spo_2 (100%), and rectal temperature were kept entirely within the normal range. The following day, the child's neurologic examination results were within normal limits.

Discussion

In the present report, we described two cases of clinically obvious clonic convulsive movements associated with possible bronchospasm during induction and without bronchospasms on emergence from sevoflurane anesthesia. Although seizure-like movements [1] during induction of anesthesia with sevoflurane and nitrous oxide were reported, to our knowledge, clinically obvious, generalized, clonic convulsions (that is, generalized, bilaterally synchronous, rhythmic, regular movements) have not been demonstrated. In particular, clonic convulsions associated with bronchospasms during anesthesia have never been reported.

The occurrence of convulsions was associated with increases in heart rate, blood pressure, and bronchospasms, suggesting an autonomic disorder. In general, the autonomic symptoms during seizure include tachycardia, increased blood pressure, flushing, salivation, and increased bronchial secretion [3].

What are the pathological mechanisms that play an important role in causing clonic convulsive movements?

Although in adult male volunteers sevoflurane (up to 10%) did not produce any evidence of seizure activities including EEG [4], sevoflurane has reportedly caused seizure activity in some humans and animals. We previously demonstrated two cases wherein electrically generalized but clinically silent seizure activity occurred during induction of anesthesia with sevoflurane and oxygen in epileptic children [2]. Exposure of unpremedicated volunteers to an initial inspired sevoflurane concentration of 4.0% initially induced a sudden appearance of high-amplitude rhythmic, slow waves of 2–3 Hz on the EEG at 1–3 min when the arterial blood level of sevoflurane increased to the maximum [5]. This EEG pattern was similar to that of cyclopropane, ether, and ketamine, which activate the reticular neurons in humans and strongly suggest CNS stimulation during anesthesia [5]. Our previous study in mice demonstrated that the order of incidence of opisthotonus during induction of volatile anesthetics in air was sevoflurane > isoflurane > enflurane > methoxyflurane > halothane [6]. In cats, 2-Hz repetitive peripheral stimulation during 5% sevoflurane-induced anesthesia elicited high-frequency spike activities of the grand-mal-type generalized electrographic seizures in 2 of 13 animals. These EEG seizures were associated with small twitches of a few muscles, and myoclonic jerking was noted by visual inspection of these partially paralyzed preparations [7]. The initiation of generalized seizure activity was confirmed by the appearance of repetitive high-frequency spike activities independently of the peripheral stimuli. Sevoflurane can therefore potentially cause the convulsions observed in our cases.

Nitrous oxide was also supplementally used with sevoflurane in our cases. In volunteers, diffuse paroxysmal bursts of high-voltage theta activity without convulsions were observed immediately after cessation of nitrous oxide [8]. There appears to be only one case report, without EEG documentation, in which nitrous oxide alone precipitated convulsions [9]. In a child who convulsed with exposure to halothane-nitrous oxide, halothane alone did not produce a convulsion, whereas nitrous oxide alone did [10]. However, EEG studies performed in patients receiving nitrous oxide alone have not revealed seizure activity [9]. Furthermore, in animals, a potent anticonvulsant action of nitrous oxide

was demonstrated in the study of the effect of nitrous oxide on the epileptogenic property of enflurane [11]. Nitrous oxide was also found to elevate the local anesthetic seizure threshold [12]. Thus, in our cases, the possibility of a convulsive effect resulting from nitrous oxide should not be eliminated completely. However, nitrous oxide remains the oldest and most widely used anesthetic in clinical practice. In view of this long-standing record of safety and the available evidence regarding its cerebral stimulatory effect, its epileptogenic potential appears to be extremely low [9].

As premediction, our case 1 and 2 patients were given trichlophos sodium and scopolamine, respectively. The former is least likely to cause convulsions because it is effective against convulsions produced by strychnine, pentylenetetrazol, and electroshock and has been used in the treatment of eclampsia and tetanus [13]. In therapeutic doses, scopolamine normally causes drowsiness, euphoria, amnesia, fatigue, and dreamless sleep with a reduction in rapid eye movement (REM) sleep. These effects are sometimes sought when scopolamine is used as an adjunct to anesthetic agents or for preanesthetic medication. Although the same doses of scopolamine can cause excitement, restlessness, hallucinations, or delirium, especially in the presence of severe pain, these excitatory effects occur regularly after large doses of scopolamine. However, no seizure activities were described [14,15]. On the contrary, in animals, scopolamine significantly reduces the maximal seizure stage of electrical kindling of the amygdala [16], soman-induced seizures [17], limbic seizures produced by pilocalpine [18], chemical kindling by muscarinic amygdaloid stimulation [19], and generalized epileptiform activities produced by topical succinylcholine [20]. Thus scopolamine is unlikely to have caused convulsions on emergence from anesthesia in case 2.

Sevoflurane itself may eliminate the possibility of causing bronchospasms because 1 MAC sevoflurane significantly attenuates the increase in pulmonary resistance, which is the sum of airway resistance and lung tissue resistance, produced by the A. suum antigen challenge in dogs [21]. Other evidence of sevoflurane eliminating the possibility of bronchospasms is the case of a child who experienced bronchospasms during isoflurane-nitrous oxide anesthesia, in whom subsequent anesthesia with sevoflurane alone after 4 days did not produce bronchospasms [22].

Thus, the bronchospasm in case 1 was possibly due to the autonomic disorder associated with the convulsion. No anaphylactoid symptoms such as eruption and hypotension were observed, which may support the above-mentioned conclusion.

In conclusion, we herein report two cases of clonic convulsive movements with sevoflurane anesthesia. In the first case, convulsion occurred with 7% sevoflurane and was associated with possible bronchospasm, which is extremely rare. In the second case convulsion occurred on emergence from sevoflurane anesthesia.

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