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# Convulsions on anaesthetic induction with sevoflurane in young children

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Increased worldwide use for paediatric anaesthesia of the volatile anaesthetic agent sevoflurane has mainly resulted from its low blood-gas partition coefficient and low airway irritability, providing smooth conditions for rapid induction of anaesthesia. Nevertheless, there are several clinical and experimental reports suggesting a correlation between exposure to sevoflurane and generalized clonic or tonic seizure activity. We report two clinical episodes of convulsions associated with the induction of sevoflurane anaesthesia in young children.

Case 1: during induction of anaesthesia with sevoflurane by facemask in a 3-year-old healthy boy, there were symmetrical clonic seizure-like movements of the upper extremities for 60 s. Case 2: on re-induction of anaesthesia with sevoflurane because of profuse bleeding following nasal adenoidectomy in a 4-year-old healthy girl with a family history of epilepsy, there were symmetrical tonic and clonic seizure-like movements for

30–40 s in the upper and lower extremities. Both episodes ceased spontaneously.

Although no EEG was recorded, it cannot be excluded that both episodes resulted from seizure activity within the CNS. Based on our observations and reports by others we suggest that, until further notice, sevoflurane should be avoided or at least used cautiously in patients where clinical epileptic activity has been verified or is strongly suspected.

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SINCE commercial release of sevoflurane on the global market in 1990, there have been several clinical reports of tonic and clonic seizure-like movements in patients undergoing sevoflurane anaesthesia (1–4). Some authors (3–13) have even suggested a correlation between the exposure to sevoflurane and electrocortical seizure activity.

We report two episodes of convulsive movements observed in young children anaesthetized with sevoflurane. Although no EEG was recorded in either child, it cannot be excluded that the episodes were associated with electrocortical seizure activity.

## Case report

### Case 1

During the induction of anaesthesia with sevoflurane by facemask in a 3-year-old healthy boy, symmetrical clonic seizure-like movements of the upper extremities were observed. These movements lasted for 60 s and ceased spontaneously.

A 3-year-old healthy boy weighing 17 kg with no previous experience of anaesthesia was scheduled for abrasion of the nasal adenoid. He had never had seizures, nor did he have a family history of epilepsy.

Twenty minutes before anaesthesia was induced, the child was given midazolam 5.1 mg, paracetamol 250 mg and atropine 0.34 mg rectally for premedication. He was well sedated on arrival in the operating room. The boy was subjected to preoxygenation via facemask for 2–3 min and was then exposed to gradually increased concentrations (range 0.5–6%) of sevoflurane in oxygen  $2.5 \text{ l min}^{-1}$  and nitrous oxide ( $\text{N}_2\text{O}$ )  $2.5 \text{ l min}^{-1}$  provided via a rebreathing anaesthesia circuit equipped with a Penlon vaporiser (Penlon Ltd, UK) and a soda lime  $\text{CO}_2$  absorber.

After 3–4 min, when the patient was clinically anaesthetized (parallel and centralized eye axes, medium-sized pupils) at an expiratory sevoflurane concentration of 3%, as well as adequately oxygenated ( $\text{SpO}_2$  99%) and ventilated (endtidal  $\text{CO}_2$  4.7 kPa), there were sudden symmetrical regular slow clonic movements of both upper extremities. The  $\text{N}_2\text{O}$  was

immediately exchanged for oxygen, and a teflon cannula was rapidly inserted in a dorsal hand vein, but by that time the movements had stopped spontaneously. The episode of convulsions lasted approximately 60 s, and during this period the heart rate decreased to  $100 \text{ min}^{-1}$  from  $130 \text{ min}^{-1}$  immediately after the end of induction.

After this point, anaesthesia was uneventful. The patient had 30 µg of fentanyl and 30 mg of suxamethonium administered intravenously (i.v.), and an oral endotracheal tube was inserted. After intubation the sevoflurane was exchanged for isoflurane to maintain further anaesthesia.

Surgery was carried out as planned, and there were no problems during emergence from anaesthesia or later in the postoperative period.

### Case 2

A 4-year-old healthy girl with a family history of epilepsy had undergone uneventful nasal adenoidectomy under general anaesthesia with sevoflurane. On emergence from anaesthesia there was sudden profuse bleeding from the nose. During re-induction of anaesthesia with sevoflurane via the endotracheal tube there were tonic and slow clonic seizure-like movements for 30–40 s in the upper and lower extremities.

A girl aged 4 years and weighing 14 kg was scheduled for abrasion of the nasal adenoids and bilateral tympanic paracentesis. She had no previous history of epilepsy, but her mother and elder sister were both reported to be epileptics.

Approximately 20 min before induction of anaesthesia, the girl was given midazolam 4.2 mg, paracetamol 250 mg and atropine 0.28 mg rectally for premedication. She was adequately sedated when brought to the operating room.

The girl was preoxygenated by facemask for approximately 2 min. She was then given increasing inspiratory concentrations (0.5–6%) of sevoflurane in oxygen  $31 \text{ min}^{-1}$  and  $\text{N}_2\text{O}$   $31 \text{ min}^{-1}$ . Approximately 4 min later, the patient had centralized, parallel eye-axes and medium-sized pupils at an endtidal sevoflurane concentration of 3.0–3.2%, and was adequately oxygenated ( $\text{SpO}_2$  99%) and ventilated (endtidal  $\text{CO}_2$  4.5–4.7 kPa). The  $\text{N}_2\text{O}$  was then exchanged for oxygen. A dorsal hand vein was cannulated and 0.15 mg of atropine together with 20 mg of suxamethonium and 30 µg of fentanyl were given i.v. Oral endotracheal intubation was carried out, and anaesthesia was then maintained with sevoflurane in an even  $11 \text{ min}^{-1}$  mixture of oxygen and  $\text{N}_2\text{O}$ .

On emergence from anaesthesia, after the supplies of  $\text{N}_2\text{O}$  and sevoflurane had been turned off for

several minutes and the patient had regained control of her gag reflex, there was sudden profound nasal bleeding calling for rapid surgical re-intervention.

Anaesthesia was rapidly re-induced by controlled ventilation via the endotracheal tube with up to 8% (vaporiser setting) sevoflurane in an even  $61 \text{ min}^{-1}$  mixture of oxygen and  $\text{N}_2\text{O}$ . After approximately 90 s, when a sinus tachycardia of  $160 \text{ min}^{-1}$  had just appeared, tonic generalized convulsions were observed for 5–10 s and immediately followed by symmetrical, regular, slow, clonic movements of the upper and lower extremities. The sevoflurane and the  $\text{N}_2\text{O}$  were both turned off and pure oxygen supplied, and roughly 30 s later the convulsions disappeared. By then the heart rate was  $130 \text{ min}^{-1}$ . Throughout this episode the  $\text{SpO}_2$  was 97–99% endtidal  $\text{CO}_2$  at an 4.6–4.8 kPa. Thiopentone 75 mg i.v. was administered and isoflurane in pure oxygen was used to maintain further anaesthesia while the bleeding was stopped successfully. Emergence from anaesthesia was uneventful, and so was the further postoperative course.

## Discussion

Since global introduction of sevoflurane more than a decade ago, there have been several reports of clinical (1–4) and electrocortical (3–13) seizure activity in patients anaesthetized with sevoflurane. Nevertheless, almost no serious neurological adverse effects have been reported over these years despite the extensive use of sevoflurane.

It is tempting to believe that the convulsions observed in our two patients were primarily caused by sevoflurane itself, although the response to sevoflurane could certainly have been influenced by the extent of ventilation, by the speed of change in alveolar drug concentration over time or by the concomitant use of other anaesthetics.

Both seizure episodes were certainly associated with tachycardia – still a common, almost regular, finding on clinical induction of sevoflurane anaesthesia, although recently reported to be associated with epileptiform EEG activity in children (12). No patient was hypocapnic before or during these episodes. In the late nineties, hypocapnia was suggested to promote epileptiform EEG activity in patients exposed to sevoflurane, particularly during the induction period (7), but recently clinical epileptiform EEG patterns have also been found to persist (12) or even decrease (9) in patients subjected to hyperventilation during sevoflurane anaesthesia.

A rapid increase in the alveolar concentration of sevoflurane during re-induction of anaesthesia could have contributed to the episode of clinical convulsions in the second patient, although sevoflurane is considered to be associated with more paroxysmal electrocortical excitability than isoflurane, as shown in three recent studies in epileptic patients (4, 8, 9).

Epileptiform EEG activity in nonepileptic patients has been found to be associated with the use of sevoflurane for induction of anaesthesia in children (12) and adults (10, 11, 13) as well as for maintenance of anaesthesia in adults (3, 6). In contrast, no EEG seizure activity was found in patients also given midazolam (14), thiopental (15) or fentanyl (16), and nitrous oxide has accordingly been reported to attenuate (9) or to have no effect on (4) the EEG response to sevoflurane. Apart from the sevoflurane, the only drugs possibly associated with the seizure-like activity in our patients were midazolam, fentanyl and N<sub>2</sub>O. Based on findings by others (4, 9, 14, 16) we propose that the administration of these drugs together with sevoflurane would rather have attenuated than facilitated clinical convulsions similar to those found in our patients.

In summary, the first child with no history of convulsions had regional clonic seizure-like movements at an adequate depth of anaesthesia while being exposed to 2.5–3% of sevoflurane, whereas the second child with a family history of epilepsy had general tonic and clonic seizure-like movements at a more superficial level of anaesthesia while inhaling high concentrations of sevoflurane. Although no EEG was recorded in either case, we cannot exclude that the convulsive movements observed were actually associated with electrocortical seizure activity, particularly in the second child. Based on our observations and previous reports (3, 4, 6, 8–12) we conclude that sevoflurane should be avoided, or at least used cautiously, in those patients where epilepsy has been verified or is strongly suspected.

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