PAROXYSMAL ELECTROENCEPHALOGRAPHIC DISCHARGES DURING ENFLURANE ANAESTHESIA IN PATIENTS WITH A HISTORY OF CEREBRAL CONVULSIONS

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If general anaesthesia is required for dental outpatients, agents with the fewest side effects and the most rapid recovery should be selected. Enflurane is one of the best drugs for this purpose when one considers its physicochemical properties and its pharmacological characteristics (Virtue et al., 1966; Dobkin et al., 1968; Chase et al., 1971; Ogli and Saki, 1975).

While seizure activity has been reported in association with enflurane, it is considered that a history of cerebral convulsions is not a contraindication to its use (Dukes, 1980).

The present study was undertaken in patients receiving long-term anticonvulsant therapy in whom the incidence of epileptogenic activity was noted during the administration of enflurane.

PATIENTS AND METHODS

We present three patients who underwent dental treatment as outpatients under general anaesthesia. Each had a previous history of cerebral convulsive disorders and had been receiving appropriate anticonvulsant medication regularly; none had shown clinical evidence of convulsions for at least 5 years. In regard to their general health, no other noteworthy tendencies were observed, except for mild mental deficiency. The patients were allowed to continue their regular anticonvulsant treatment until the morning of the operation. Atropine 0.01 mg kg\(^{-1}\) was administered i.m. 30 min before the induction of anaesthesia. The EEG was monitored through all phases of anaesthesia. The electrodes were attached to Fp\(_{1}\), Fp\(_{2}\) according to the International Ten-Twenty System. The time constant and the high cut were set at 0.3 s and 30 Hz, respectively. Both were connected to a bioelectric amplifier (AB 621 G, Nihon Kohden). During anaesthesia the EEG and ECG were displayed on an oscilloscope and were stored simultaneously on tape (Elcaset DR. FE-30 Series, Instrumentation Tape Recorder, Sony Magnescale Inc. Tokyo); a permanent record could be obtained, when required. The inspired concentration of enflurane (Engström Emma), and the end-expiratory carbon dioxide concentration (FE\(_{\text{CO}_2}\)) and the arterial carbon dioxide partial pressure (Pa\(_{\text{CO}_2}\)) (Normocap, Datex), were monitored.

Anaesthesia was induced with enflurane and sodium thiopentone. Nasotracheal intubation was facilitated by the administration of suxamethonium 1 mg kg\(^{-1}\), and anaesthesia maintained with 1–3% enflurane and nitrous oxide in oxygen.

CASE REPORTS

Patient I

A 16 year-old boy, weighing 54 kg was being treated with phenobarbitone, acetazolamide and carbamazepine. No abnormalities were noted in...
EEG DURING ENFLURANE ANAESTHESIA

Fig. 1. Patient I. A: Polyspike bursts appeared at intervals of 5–10 s during 2% enflurane and hyperventilation. B: Enflurane 3% and hyperventilation shows an increase in the slow-wave components of the background activity and a lessening of the fast wave components. C: Polyspike bursts appeared when the patient's lungs were hyperventilated and during 1.5% enflurane administration. D: Even during normoventilation under assisted respiration with 1% enflurane, epileptiform activity as shown in the previous figure was observed for a period of approximately 5 min. E: Neither spikes nor high voltage slow waves were observed. Inhalation of 100% oxygen at rest.

the EEG during the induction of anaesthesia with enflurane.

After tracheal intubation, with the inspired enflurane concentration at 2% and at an $F_{CO_2}$ of 3.5% ($P_{CO_2}$ 3.5–3.7 kPa), clusters of spikes (fig. 1A) appeared, and continued at 5–10 s intervals. This spike activity disappeared when artificial ventilation was instituted and the $F_{CO_2}$ maintained at approximately 5% ($P_{CO_2}$ 5.1–5.6 kPa). Twenty minutes later, in order to maintain the necessary depth of anaesthesia, controlled ventilation was carried out for approximately 5 min. Although the $F_{CO_2}$ was 3.5%, no abnormal findings were recorded, with the exception of those for the EEG which were characteristic of 3% enflurane (Neigh, Garman and Harp, 1971) (fig. 1B). For approximately 20 min subsequent to normoventilation with 1.5% enflurane, no abnormalities were observed. However, bursts of spike activity appeared when the patient was, once again, hyperventilated (fig. 1C). When this occurred normocapnia was maintained (1% enflurane); however, the paroxysmal activity (fig. 1D) persisted for about 5 min. The EEG observed during inhalation of 100% oxygen, after all other procedures were finished, contained neither high voltage slow waves nor spikes (fig 1E).

**Patient II**

The patient was a 14 year-old boy who weighed 34 kg. He had a history of Lennox syndrome as an infant. Since that time, he had been taking anticonvulsant drugs regularly. When he presented, he was taking clonazepan by mouth.

Anaesthesia was commenced using 0.5% enflurane for 3–5 breaths. The enflurane concentration was then gradually increased to 4% by 5 min.

Since the patient had received 4% enflurane for approximately 1 min only, there was no decrease in arterial pressure. Anaesthesia was then maintained with 1% enflurane.

No abnormalities were noted in the EEG before induction (fig. 2A). During induction (1–3% enflurane), when respiration was assisted intermittently to maintain normocapnia, neither spikes nor high voltage slow waves were observed. Figure 2B shows the EEG during induction with 2% enflurane. However, when 4% enflurane was inhaled during induction, bursts of high voltage spike activity and sharp waves appeared superimposed on a background of low amplitude activity (fig 2C). Diazepam 5 mg was injected i.v., suxamethonium 1 mg kg$^{-1}$ administered and the trachea intubated. During intubation, 3 min after the administration of diazepam the EEG revealed high voltage spike and wave complexes (fig. 2D). These complexes began to decrease 5 min after the injection of diazepam. Paroxysmal activity was completely absent during the maintenance of anaesthesia(normocapnia with assisted ventilation) and the administration of 1% enflurane (fig. 2E). Thereafter, no abnormalities were noted on the EEG until the end of anaesthesia. The EEG during inhalation of 100% oxygen after extubation is shown in figure 2F.

**Patient III**

A 7 year-old girl, weighing 19.5 kg, was receiving sodium dipropylacetate and clonazepam.
Fig. 2. Patient II.  A: During induction with administration of 100% oxygen. No abnormalities were observed at rest while awake.  B: An increased frequency of the basic activity but no epileptiform activity was observed in patient II during induction with 2% enflurane and assisted respiration.  C: Bursts of high voltage polyspikes and sharp waves superimposed on a low amplitude background activity were observed during induction with 4% enflurane and assisted respiration.  D: During tracheal intubation,
when the blood concentration of diazepam was probably at a peak (3 min after i.v. administration) the epileptiform discharge had not disappeared. E: The epileptiform discharge disappeared completely 10 min after diazepam administration with 1% inspired enflurane and normocapnia. F: After extubation and under 100% oxygen. No EEG abnormalities were noted.
EEG DURING ENFLURANE ANAESTHESIA

The induction of anaesthesia was performed with sodium thiopental in combination with enflurane. During the inhalation of 3% enflurane at the time of induction, a characteristic EEG pattern for 2 MAC enflurane (Neigh, Garman, and Harp, 1971) was observed (fig. 3A). When 2% enflurane was inhaled after tracheal intubation and a state of hyperventilation developed, multiple spike and wave complexes appeared (fig. 3B). These disappeared during the maintenance of normocapnia (assisted ventilation) and the administration of 1% enflurane. Thereafter, bursts of high voltage slow wave activity appeared during the inhalation of 3% enflurane as a result of the decrease in PaCO₂ (fig. 3C). The spikes and high voltage slow waves persisted for a few minutes, even after the inhalation of enflurane was discontinued. Figure 3D shows the EEG during inhalation of 100% oxygen following extubation of the trachea.

DISCUSSION

Enflurane has minimal effects on hepatic function, renal function and the metabolic system, its rate of biotransformation is less than that of other inhalation anaesthetics, and recovery is rapid. These factors render it suitable for general anaesthesia in outpatients. However, the possibility of seizure activity remains a problem. Muscle movement is observed frequently during enflurane anaesthesia. Julien and Kavan (1972) reported epileptoid bursts on the EEG with deeper anaesthesia, and a decrease in PaCO₂ may accelerate enflurane-induced seizure activity (Bart, Homi, and Linde, 1971). Furthermore, Darimont and Jenkins (1977) stated that barbiturates, typical anticonvulsants, intensified such enflurane-induced seizure activity.

These data suggest that the use of enflurane in high concentrations, when the PaCO₂ is decreased, or when it is used in combination with a barbiturate, increases the probability of the induction of seizures.

On the other hand, Mori (1980) and Urabe (1981) reported that enflurane has an anticonvulsive effect in the cat experimental seizure model, at low and high concentrations. Gallagher, Galindo, and Richey (1978) observed the disappearance of seizure activity noted during anaesthesia by the inhalation of enflurane at a high concentration (4%). Opitz and Oberwetter (1979) reported that they were able to give enflurane safely, even to epileptic patients. Thus, at the present time, enflurane is not generally considered to be contraindicated in patients with a history of cerebral convulsive disorders (Dukes, 1980).

In the three cases presented in this paper, the fact that no convulsions had occurred for at least 5 years, suggested that control was adequate. Following the precedent of Opitz and Oberwetter (1979), we permitted the oral administration of anticonvulsants until the morning of the day when anaesthesia was given. A previous report (Bart, Homi, and Linde, 1971) which noted that the seizure activity associated with enflurane was enhanced by hypocapnia, was confirmed by our observations. The spikes, polyspikes, spike and wave complexes and high voltage slow waves which appeared in the EEG in the present cases, and which differed from background activity, resembled those attributable to epilepsy. It has been suggested that, when the enflurane concentration is less than 1.5 MAC (about 2.5%) and hypocapnia is avoided, the occurrence of seizures can be minimized (Michenfelder and Cucchiara, 1974). However, even when the inhalation concentration of enflurane was 1.5% or 2%, we recognized paroxysmal discharges in the EEG.

In the first patient, once clusters of spikes had appeared, they did not disappear for a few minutes even though normocapnia was maintained by assisted respiration and the enflurane concentration was only 1%. Therefore, enflurane may induce paroxysmal discharges during normocapnia and at a concentration commonly considered not to induce seizures.

In the second patient, polyspike and sharp waves superimposed on low amplitude background activity appeared suddenly during induction when 4% enflurane was being administered. In patients with mental deficiency or severe anxiety, the establishment and maintenance of the i.v. route

Fig. 3. Patient III. A: During induction with 3% enflurane and assisted ventilation the characteristic EEG of approximately 2 MAC enflurane was obtained with slightly high amplitude 7-12-Hz waves. B: Polyspike and wave complexes appeared during 2% enflurane administration and hyperventilation. C: With a decrease in PaCO₂, spikes and high voltage slow waves appeared during 3% enflurane administration and hyperventilation. D: After extubation and under 100% oxygen administration, high voltage slow waves predominate, but no polyspikes or polyspike and wave complexes can be recognized.
before anaesthesia induction is often difficult. Therefore, while it is believed that 4% enflurane may involve a greater possibility of seizure induction, as high a concentration as permissible should be used to complete induction quickly in such patients.

Gallagher, Galindo and Richey (1978) and Mori (1980) stated that a concentration of 4% was not necessarily dangerous. However, when enflurane is administered to patients with a history of cerebral convulsive disorders, burst of paroxysmal activity may occur, even when anticonvulsants are administered and inhalation is carried out using a low concentration. In the second patient, the polyspike activity which appeared during the induction of anaesthesia had not disappeared 3 min after diazepam 5 mg i.v. during intubation, when the blood concentration of diazepam was considered to have reached its peak. During the administration of 1% enflurane and the maintenance of normocapnia with assisted ventilation, the clusters of spikes disappeared about 8 min after the commencement of the injection of diazepam. Abnormal findings, for example spike or sharp-wave bursts in the EEG observed in patients with epilepsy ordinarily disappear immediately after an i.v. injection of diazepam 2.5–8 mg and the basic activity becomes rhythmical or fast (Murata, 1969). Since this patient had been receiving an anticonvulsant of the same benzo-diazepine class over a long period of time, it is possible that he had a greater tolerance to diazepam, with the result that the dose was insufficient.

Although it has been reported that the combined use of barbiturates and enflurane intensifies enflurane-induced seizures (Darimont and Jenkins, 1977), our experience revealed that, in some patients, the EEG was more stable than it was before the induction of anaesthesia. In the third patient, on the other hand, when 3% enflurane was administered during induction, EEG findings consisted mainly of slow waves mingled with spikes. These are considered to be the EEG characteristics of approximately 2 MAC enflurane (Neigh, Garman and Harp, 1971). The injection of sodium thiamylal 100 mg i.v. did not produce any marked changes in the EEG. The combined use of the barbiturate and enflurane did not appear to intensify enflurane-induced paroxysmal activity in any of these patients.

Actual convulsions or twitching of the limbs were not observed in these three patients. However, clusters of spikes, spike and wave complexes and high voltage slow wave bursts which appeared in the EEG during the course of anaesthesia resembled those observed during epileptic attacks (Shimazono, Kitamura and Ōtomo, 1976). Therefore, the possibility exists that when such paroxysmal discharges are noted, convulsions may develop with a resultant increase in cerebral oxygen consumption.

Enflurane was administered to patients with a history of cerebral convulsive disorders who had been examined regularly by specialists, treated with anticonvulsants for long periods, and in whom no abnormalities were found in the EEG before anaesthesia. However, abnormal EEG findings differing clearly from background activity were recognized during anaesthesia.

Based on our experience, we suggest that anaesthetics without epileptogenic properties be used in patients with a history of cerebral convulsions, in order to avoid the possibility of producing overt seizures during anaesthesia.


