Seizures Induced by Methohexital

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Methohexital sodium (Brevital®) is frequently used by anesthesiologists to induce sleep. This agent is particularly advantageous in pediatric anesthesia practice because it may be administered either rectally (20–30 mg/kg as a 10 per cent solution), or intramuscularly (6–10 mg/kg as a 5 per cent solution). When carefully used, it has been demonstrated to be both safe and effective.1,2 For some brief noninvasive procedures additional anesthetic agents are often unnecessary.

We recently observed two children who developed seizures after the administration of methohexital. Despite the widespread use of methohexital in children, this complication has not previously been reported. Furthermore, since barbiturates are the most commonly used drugs for seizure control during childhood, this response was totally unexpected. These two cases are presented, and the role of methohexital in induction of seizures is discussed.

REPORT OF TWO CASES

Patient 1. A 14-month-old child was scheduled for computerized transaxial tomography (CT scan) under general anesthesia, one week after experiencing episodes of staring, eye fluter, and loss of consciousness. These events lasted approximately 10–20 s and occurred every few hours. Neurologic examination was otherwise unremarkable. An awake electroencephalogram (EEG) was normal, but, during sleep revealed focal rightsided spikes consistent with temporal lobe dysfunction. There was a strong family history of seizures occurring in a 6-year-old sibling, a maternal uncle, and the maternal grandfather. Phenobarbital therapy was begun, and the seizures increased in frequency.

Anesthesia was induced with rectal administration of 200 mg (25 mg/kg) of methohexital dissolved in 2 ml of sterile water. Within 3 min the child became markedly sedated and developed a seizure similar to his previous episodes, which included generalized stiffening. The seizure ceased spontaneously in 30 s. An intravenous infusion was started and electrocardiographic leads applied. Within 5 min, the child developed another seizure similar to the first. Diazepam, 1 mg, was administered intravenously, and the seizure promptly abated. The study was performed over 40 min using contrast material without any additional anesthetic agents or further complications. No abnormality was demonstrated on the CT scan, and the child awakened as he was removed from the scanning device.

After discussion of these events with the neurologist, phenobarbital was discontinued, and phenytoin therapy begun. Within a week the child was free of seizures, and has remained asymptomatic since discharge 2 months ago.

Patient 2. A three and a half-year-old child was scheduled for a CT scan under general anesthesia. He had previously been evaluated at the age of 14 months for seizures and rightsided weakness. EEG then revealed spike and slow waves in the left temporal area. At that time, a Grade III astrocytoma was discovered in the left temporal lobe, extending to the cerebellomedullary angle and was partially excised. His condition gradually improved, and tumor size was evaluated at two and three years of age with CT scans on an outpatient basis. On both occasions two doses of rectal methohexital (20–25 mg/kg/dose) failed to induce sleep. For the first scan, general endotracheal anesthesia was induced with halothane; for the second, intramuscular methohexital was given with satisfactory results, and without any mention of unusual reaction. We presumed the successful induction of sleep with intramuscular methohexital after the rectal route failed was probably due to the less predictable absorption which occurs with rectal administration. The child was maintained on phenobarbital and phenytoin and had been free of seizures for the last two years.

During the present admission the only residual finding on neurologic examination was mild hemiparesis. Intramuscular methohexital was again used for anesthesia. One hundred fifty mg of the drug (10 mg/kg) dissolved in 3 ml of sterile water was administered in the buttock. Within 2 min, as the child started to fall asleep, he developed a predominantly rightsided clonic seizure which lasted approximately 30 s before resolving spontaneously. An intravenous infusion was started; the CT scan with contrast material was performed uneventfully. The results demonstrated a decrease in size of the cystic component in the

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left cerebellopontine angle. He was discharged from the recovery room one hour after completion of the study.

**Discussion**

Barbiturates have been used for many years in the treatment of seizure disorders, especially among children. Generalized or nonfocal seizures are often controlled by phenobarbital alone or in combination with other anticonvulsants. However, focal cortical seizures are more difficult to treat. Among the cortical epilepsies, psychomotor seizures originating in the temporal lobe are the most common. Occasionally, barbiturates exacerbate these conditions.

 Methohexital was introduced into clinical practice because of its great potency and ultrashort duration of action. Originally, it was abandoned in clinical trials because its use was noted to cause seizures in animals and EEG abnormalities in humans. Ultimately, fractionation of this drug into isomeric forms resulted in a high-melting point isomer, allegedly devoid of these undesirable effects, and is the compound presently available as methohexital sodium. This agent has gained widespread acceptance in anesthesia practice.

 However, only a few years after methohexital was clinically introduced, Galley reported a patient with a history of epilepsy who developed a brief seizure after intravenous induction with this agent. Later reports noted the usefulness of intravenous methohexital to activate EEG abnormalities in patients with seizures in whom awake recordings were unrevealing. It has also been used to provoke epileptic foci during temporal lobectomy while recording from the exposed hemisphere.

 Our cases indicate that even the intramuscular or rectal administration of methohexital may activate seizure foci in susceptible patients and can induce clinical seizures. Furthermore, the fact that the patient's epilepsy is controlled with medication (as in our second case), or that the EEG abnormalities are not clinically apparent (as in the case reported by Galley), does not appear to lessen the convulsant effects of methohexital.

 The epileptogenic effects of methohexital appear to be limited to individuals with psychomotor seizures. Musella et al. examined the EEG effects of intravenous methohexital in three groups of patients. Seventy-two per cent of the patients with well-documented histories of psychomotor epilepsy demonstrated marked electrical activation of their foci. The others in this group developed distinct but less impressive changes. A control group of normal, healthy individuals showed only nonspecific drug effect (bilateral slowing and superimposed fast rhythms), as did a group of patients with a history of generalized seizures or poorly documented seizure-like episodes. No patients in any group developed a clinically apparent seizure. Interestingly, muscle twitching and hiccup sometimes seen in normal patients following methohexital are not associated with EEG abnormalities. The cause of methohexital provocation of temporal lobe seizures is unknown.

 Thiopental does not appear to produce EEG activation in patients with psychomotor epilepsy. The first patient reported by Galley to experience a clinical seizure with methohexital did not develop seizures during two identical procedures performed with thiopental. If induction of sleep by the rectal route is desirable, as it often is with small children, it is important to note that thiopental can also be given rectally.

 Although EEG abnormalities or brief seizures provoked by methohexital may not be harmful, it would be prudent to avoid use of this agent in patients with psychomotor, temporal or complex seizure disorders. Thiopental may be a safer induction agent for such patients.

**References**

Diazepam and Intracranial Pressure

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In neurosurgical anesthesia, drugs which decrease cerebral blood flow (CBF) are assumed to decrease intracranial pressure (ICP) probably as a result of a decrease in cerebral blood volume (CBV).²³ Diazeplam is known to decrease CBF in both humans³ and animals,⁴⁵ and hence may decrease ICP. However, in dogs, Campan et al.⁶ observed no significant change in ICP with diazeplam. The effect of diazeplam on ICP in humans has not been described except for a case report by Phirman and Shapiro.⁷ Therefore, we measured ICP after intravenous injection of diazeplam in neurosurgical patients.

METHODS

The study was approved by the Human Experimentation Committee of the Hospital and was performed during the induction of general anesthesia on ten neurosurgical patients who were divided into two groups of five patients each: hypertensive (ICP > 15 torr) and normotensive (ICP < 15 torr). Their age ranged from eleven to seventy-six years old. Four cases of intracranial hematoma, three cases of brain tumor, two cases of hydrocephalus and one case of subarachnoid hemorrhage were included. Glasgow coma scale was 15 in five patients, 14 in two patients, and 13, 11, and 10, respectively, in the remaining three patients. An intraventricular catheter or a subdural balloon, which was connected to a transducer (Statham® P231D), was installed one or two days before surgery, under local anesthesia. On the day of surgery, a central venous catheter was inserted from the basilic vein, and a catheter inserted in the radial artery. Direct arterial pressure, ICP, ECG, and rectal temperature were monitored continuously. Arterial pressure, central venous pressure (CVP) and ICP were zero-referred to the level of external auditory canal. Cerebral perfusion pressure (CPP) was calculated as the difference between mean arterial pressure (MAP) and mean ICP. After monitoring was started, at least 10 min elapsed to permit the measured variables to become constant. The measurements were performed before, and for 15 min after diazeplam (0.25 mg/kg for one min) administration. CVP was measured by open manometry before, 5, 10, and 15 min after diazeplam. Arterial blood gases, heart rate, and hematocrit were measured before and 10 min after diazeplam was given. After the measurements, all the patients were hyperventilated and neuroleptanesthesia was started. The subsequent course of anesthesia in all cases was uneventful. Results were analyzed statistically using a Student's t test for paired data to compare the values before and after diazeplam in each group, and for unpaired data to compare the values before diazeplam between both groups. P < 0.05 was considered to be significant.

RESULTS

Figure 1 shows individual ICP before and after diazeplam. Table 1 shows mean values of ICP, MAP.

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