

Alfentanil Mediated Activation of Epileptiform Activity in the Electrocorticogram During Resection of Epileptogenic Foci

Daniel L. Keene, David Roberts, William M. Splinter, Michael Higgins and Enrique Ventureyra

ABSTRACT: *Purpose:* Alfentanil is a potent, short-acting opioid agent which has been used during balanced anaesthesia in children undergoing the surgical excision of epileptic foci. After the observation that this agent had the potential to induce epileptic seizures, we questioned the frequency of this occurrence in this group of patients. *Method:* Twelve patients (6 males, 6 females) undergoing surgical excision of an epileptic foci were prospectively followed. For each patient an electrocorticogram was recorded for 30 minutes before and after receiving alfentanil 20 µg/kg intravenously. The frequency of epileptiform abnormalities before and after drug administration was evaluated. When the electrocorticogram no longer showed the effects of alfentanil administration, methohexital 0.5 µg/kg was given intravenously. *Results:* Alfentanil induced significant activation of epileptiform discharges among 83% of these patients. Twenty-five per cent had an electrographic seizure. In comparison, methohexital induced significant activation of epileptiform discharges in 50% of these patients. None experienced electrographic seizures. *Conclusions:* As alfentanil can induce electrographic seizures in patients known to have epilepsy, caution is advised in its use in this group of patients.

RÉSUMÉ: *Activation de l'activité épileptique médiée par l'alfentanil à l'électrocorticogramme pendant la résection d'un foyer épileptogène. But:* L'alfentanil est un agent opioïde puissant de courte durée qui a été utilisé pendant l'anesthésie équilibrée chez des enfants qui subissent une excision chirurgicale d'un foyer épileptique. Suite à l'observation que cet agent pouvait induire des crises épileptiques, nous en avons évalué la fréquence chez ce groupe de patients. *Méthodes:* Douze patients (6 garçons et 6 filles), qui ont subi une excision chirurgicale d'un foyer épileptique, ont été suivis de façon prospective. Un électrocorticogramme a été enregistré chez tous les patients pendant 30 minutes avant et après l'administration intraveineuse de 20 µg/kg d'alfentanil. Nous avons évalué la fréquence d'anomalies épileptiformes avant et après l'administration de l'alfentanil. Quand l'électrocorticogramme ne montrait plus d'effet de l'alfentanil, du méthohexital à la dose de 0.5 µg/kg a été administré par voie intraveineuse. *Résultats:* L'alfentanil induit une activation significative des décharges épileptiformes chez 83% de ces patients. 25% ont eu une crise électrographique. Par contre, le méthohexital a induit une activation significative des décharges épileptiformes chez 50% de ces patients et aucun n'a présenté de crise électrographique. *Conclusions:* Comme l'alfentanil peut induire des crises électrographiques chez les patients connus comme épileptiques, on doit l'employer avec prudence chez ces patients.

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Unlike in the adult, the resection of epileptogenic foci in a child with epilepsy often requires general anaesthesia. At our institution we have used balanced anaesthesia (halothane or isoflurane, nitrous oxide, narcotic agent and a non-depolarizing muscle relaxant). Initially alfentanil appeared to be a narcotic agent that was well-suited for this procedure, as it has a rapid onset of action and a short duration of action.¹ With rapid onset and elimination of this drug, we had hoped that there would be minimal effect on the electrocorticogram.

Recently we observed seizure-like activity after a patient who was undergoing surgery of the excision of epileptogenic foci received alfentanil during the induction phase of the anaes-

thesia. Based on this observation and a case report of alfentanil inducing a seizure in the literature,² we decided to further evaluate the role of this drug in children and adolescents undergoing surgery for excision of epileptogenic foci.

From the Division of Neurology, Department of Pediatrics (D.L.K.); Department of Anaesthesia (D.R., W.M.S.) Division of Neurosurgery (M.H., E.V.), Department of Surgery Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa.

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Reprint requests to: Dr. Daniel L. Keene, Division of Neurology, Department of Pediatrics, Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa, Ontario, Canada K1H 8L1

METHOD

Twelve consecutive patients undergoing surgical resection of epileptic foci were prospectively followed. All had partial epilepsy which had proven refractory to standard anticonvulsant medication. Surgical excision of the epileptic focus was considered the best treatment option. All had extensive pre-operative electrographic and imaging studies in attempt to localize the area of epileptogenic abnormality. All patients had their regular anticonvulsant medications discontinued at least one week prior to their surgery. A general anaesthetic consisting of 0.2-0.4% halothane or isoflurane, 70% nitrous oxide, and a non-depolarizing muscle relaxant was administered in all cases. The volatile anaesthetic agent was discontinued 20 minutes before doing electrocorticographic recordings.

Following the surgical exposure of the brain, twenty electrocorticographic electrodes were placed on the exposed brain over the area of surgical interest. The electrocorticogram was recorded using a Nihon Kohden 21 channel electroencephalographic recording machine. A baseline electrocorticogram was recorded for 20 minutes. Alfentanil 20 $\mu\text{g.kg}^{-1}$ intravenously was then given. Once the electrocorticographic recording had returned to baseline, methohexital 0.5 $\mu\text{g.kg}^{-1}$ intravenously was administered. Electrocorticographic recording was continued for a further 20 minutes after the methohexital administration.

The tracings were reviewed by the same electroencephalographer in the operating room at the time of the surgical procedure and again at the time the data were being reviewed for possible publication (several months later).

Activation of epileptiform activity was considered significant if there was greater than or equal to 50% enhancement of this activity after administration of the drug when compared to the baseline recording. Electrographic seizures were stated to have occurred if there was constant epileptiform activity for greater than 60 seconds.

RESULTS

Twelve patients (six males and six females) between the ages of 15 months and 17 years were included in this review. Alfentanil activated epileptiform abnormalities in ten patients (83%) of which three (25%) had evidence of electrographic seizures. The epileptiform abnormalities appeared within five minutes of the administration of the drug. The morphology and initial localization of discharge was unchanged when compared to the baseline tracing. Muscle relaxation prevented any movement during these electrographic seizures. In contrast, six patients (50%) had activation of their epileptiform abnormality after receiving methohexital. No patients had electrographic seizures recorded after receiving this drug. No differences in location of the epileptiform abnormalities were seen in those cases in which activation occurred with both drugs.

DISCUSSION

Seizure-like activity during or after induction of anesthesia with fentanyl, sufentanil and alfentanil has been reported.²⁻⁷ Electroencephalographic confirmation of the epileptic origin has been missing in these reports. Smith et al.⁸ reported on forty-six cases in which seizure-like activity was associated with narcotic anaesthetic agents. The seizure-like activity was recorded elec-

trographically using two leads (FP1-O1 and FP2-O2). After or during the administration of the narcotic anaesthetic agent, they noted the following: sudden onset of flexion of the upper extremities, extension of the lower limbs, flexion of the chin onto the chest, severe rigidity of the abdominal and chest wall musculature, frequent athetoid or myoclonic movements of the limbs, and vertical nystagmus. Electrographic recordings at the time of the clinical event was reported to have shown sharp wave activity superimposed onto underlying slow waves. After the administration of neuromuscular blocking agent, the sharp waves disappeared. Based upon these data, they concluded that the majority of the reported cases of seizure-like activity previously reported was due to opioid-induced rigidity rather than epileptic seizures.⁸⁻¹⁰ Seizure associated with high dose opioid anaesthesia were felt to be a rare event. The authors further stated that an association between these drugs and seizures could only be established if simultaneous electrographic seizure activity was recorded. Three patients in our series who had electrographic seizures after receiving alfentanil meet these criteria. The elevated heart rate and blood pressure that occurred simultaneously with the continuous epileptiform abnormalities was strongly suggestive that clinical seizures were also occurring. As muscle relaxants were used as part of our balanced anaesthesia protocol, the other physical features were blocked.

One of our patients had a "seizure" occur after the administration of alfentanil during induction phase of anaesthesia and before the onset of muscle relaxation. The physical description of the "seizure" was similar to the previously described by Smith et al.⁸ This patient was also administered alfentanil after the administration of a muscle relaxant while under electrocorticographic control. We observed an elevated blood pressure and heart rate associated with a period of continuous epileptiform discharge on electrocorticogram.

The reason for the discrepancy between our observations and those of Smith et al.⁸ may be either technical or due to patient selection or a combination of both. The use of electrocorticographic tracings with multiple electrode placement used in series and recorded using both bipolar and referential montages allows for a optimal clinical assessment of the temporal distribution of the electric activity of the brain. Montages using only two electrodes are not sufficient to adequately represent the electrical activity of the brain, particularly when the abnormality may be subcortical or temporal in location. This is even more problematic when the electrodes are placed at long distances from each other.

All subjects included in our review had a known underlying epileptic condition. Many epileptic foci were mesial temporal in location. Narcotic agents have been felt to have the ability to induce seizures in this group.¹⁶ These selection criteria could be another reason for the differences between the studies.

Methohexital has been shown to induce epileptiform discharges on electrocorticographic recordings in approximately 50% of cases.¹¹⁻¹⁵ The degree of activation of epileptiform abnormalities on electrocorticographic recordings by this drug in our cases compares favourably to that reported. When we compared the degree of enhancement of epileptiform abnormalities in the electrocorticogram of alfentanil to methohexital, alfentanil would appear to be superior.

The findings of this paper suggest that alfentanil can activate epileptiform abnormalities in the electrocorticogram in

patients undergoing surgery for the removal of epileptogenic tissue in patients with chronic epilepsy. This drug has the ability to induce clinical seizures in patients with underlying epilepsy. Caution in using alfentanil in patients with epilepsy *or* neurological handicaps is advised.

REFERENCES

1. Stanski D, Hug C. Alfentanil – a kinetically predictable narcotic analgesia. *Anesthesiology* 1982; 57: 435-438.
2. Strong W, Matson M. Probable seizure after alfentanil. *Anesth Analg* 1989; 68: 692-693.
3. Roa T, Mummaneni N, El-Etr A. Convulsions: an unusual response to intravenous fentanyl administration. *Anesth Analg* 1982; 61: 1020-1021.
4. Safwat A, Daniel D. Grand mal seizure after fentanyl administration. *Anesthesiology* 1983; 59: 78.
5. Baraka A, Haroun S. Grand mal seizures following fentanyl-lidocaine. *Anesthesiology* 1985; 62: 206.
6. Brain J, Seifen A. Tonic-clonic activity after sufentanil. *Anesth Analg* 1987; 66: 481-483.
7. Goroszeniuk T, Albin M, Jones R. Generalized grand mal seizure after recovery from uncomplicated fentanyl-etomidate anesthesia. *Anesth Analg* 1986; 65: 979-981.
8. Smith N, Benthuyens J, Bickford R, et al. Seizures during opioid anesthetic induction – are they opioid-induced rigidity? *Anesthesiology* 1989; 71: 853-862.
9. Tommasino C, Maekawa T, Shapiro H. Fentanyl-induced seizures activate subcortical brain metabolism. *Anesthesiology* 1984; 60: 283-290.
10. Benthuyens J, Smith T, Sanford T, et al. Physiology of alfentanil-induced rigidity. *Anesthesiology* 1986; 64: 440-446.
11. Harel D, Sharf B, Bental E. Methohexital as an activator in epileptic patients with normal electroencephalograms. *Israel J Med Sc* 1975; 10: 986-990.
12. Ford E, Morrell F, Whisler W. Methohexital anesthesia in the surgical treatment of uncontrollable epilepsy. *Anesth Analg* 1982; 61: 997-1001.
13. Wilder B, Musella L, Van Horn G., Schmidt BP. Activation of spike and wave discharge in patients with generalized seizures. *Neurology* 1971; 21: 517-527.
14. Gumpert J, Paul R. Activation of electroencephalogram with intravenous Brietal (methohexitone): the findings in 100 cases. *J Neurol Neurosurg Psychiatry* 1971; 34: 646-648.
15. Musella L, Wilder BJ, Schmidt RP. Electroencephalographic activation with intravenous methohexital in psychomotor epilepsy. *Neurology* 1971; 21: 594-602.
16. Frenk H. Pro- and anticonvulsant actions of morphine and the endogenous opioids: involvement and interactions of multiple opiate and non-opiate systems. *Brain Res Rev* 1983; 6: 197-210.