Activation of Epileptogenic Activity by Etomidate

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Etomidate (Amidate®), a new ultra-short-acting hypnotic chemically unrelated to barbiturates has not been noted to cause activation of electroencephalographic fast activity or epileptogenic abnormalities. We describe two cases of marked EEG activation, including enhancement of both fast activity and epileptogenic discharges.

REPORT OF TWO CASES

Patient 1: This 10-year-old boy with medically refractory complex partial seizures underwent electrocorticography and excision of a left cingulate gyrus seizure focus. Without premedication, anesthesia was induced with etomidate, 0.3 mg/kg, and fentanyl, 0.005 mg/kg iv; after administration of metocurine, 0.018 mg/kg iv. Intubation of the trachea was facilitated by succinylcholine, 1.0 mg/kg iv. Anesthesia was maintained with 70% nitrous oxide, fentanyl as needed, and metocurine titrated according to nerve stimulation. A field block with a local anesthetic was performed by the neurosurgeon to enhance analgesia and to allow lighter levels of anesthesia. The local anesthetic used was a mixture of bupivacaine, 0.17%, lidocaine, 0.23%, and epinephrine, 0.0002% in normal saline. This was used only subgaleally as a local block. End-tidal Pco2 was maintained at 28–32 mmHg. A left frontotemporal craniotomy was performed without further local anesthesia. After exposure of the left hemisphere, N2O was reduced to 50%, and a 16-lead electrocorticography crown was placed over the exposed cortex. In addition, depth electrodes were placed in the left cingulate gyrus. Frequent bursts of spike and wave and polyspike and wave discharges were recorded and were isolated to the cingulate gyrus and to the rostral lateral frontal region (fig. 1). Etomidate, 0.3 mg/kg, was administered iv, which produced a marked activation of large amplitude, sharp appearing, 20–50 Hz activity intermingled with polyspikes over the entire exposed cortex of the left frontal and temporal lobes (fig. 2). In addition, the activity from the cingulate gyrus was enhanced further, evolving into an electrographic seizure, lasting approximately 3 min. Over the next 10 min, the induced fast activity gradually lessened, with the background activity returning to baseline. A partial left frontal lobectomy was performed, which included the epileptogenic focus in the left cingulate gyrus. A second dose of etomidate, 0.2 mg/kg, was administered iv, which again produced an activation of fast activity lasting several minutes; however, no epileptogenic discharges were recorded (fig. 3).

Patient 2: This 11-year-old boy with medically refractory complex partial seizures underwent a right craniotomy for seizure control with no premedication. Anesthesia was induced with etomidate, 0.5 mg/kg, fentanyl, 0.005 mg/kg, and pancuronium, 0.008 mg/kg, after which the trachea was intubated with the aid of succinylcholine, 1 mg/kg iv. Anesthesia was maintained with 70% nitrous oxide, fentanyl, and pancuronium as needed. A field block was performed by the surgeon to enhance analgesia and to allow lighter levels of general anesthesia. The local anesthetic used was the same as used in patient 1. A 16-lead electrocorticography crown was placed over the lateral surface of the right temporal lobe as well as the right prerolandic and postrolandic suprasylvian region. Depth electrodes also were placed in the middle temporal gyrus at approximately the level of the amygdala and hippocampus. Baseline recording revealed very active spikes, polyspikes, and spike and wave discharges from the depth electrodes and from the anterior pole of the lateral temporal lobe. In addition, rare spikes were recorded from the suprasylvian region in the postrolandic gyrus. Etomidate, 0.2 mg/kg, was administered iv, which produced a marked activation of fast activity from the central regions. In addition, spike discharges were activated, occasionally occurring as bursts lasting up to 2 s in duration. The discharges became more diffuse and were recorded from all the electrodes of the right frontal and temporal areas. A right temporal lobectomy then was performed, which included the amygdala and the anterior 2 cm of the hippocampus. A second dose of etomidate, 0.2 mg/kg, was administered iv, again producing a marked activation of fast activity over the central regions but without activation of epileptogenic activity.

DISCUSSION

These patients demonstrate two prominent electrophysiologic effects after the administration of etomidate, including enhancement of fast activity lasting several minutes and enhancement of epileptogenic activity. In patient 2, the etomidate-induced epileptogenic activity culminated in an electroencephalographic seizure. Although activation of fast activity is an effect common to many anesthetics, especially barbiturates, it is controversial whether etomidate produces this effect. Several studies do note activation of electroencephalographic fast activity after administration of etomidate.1–3 In these studies, administration of etomidate was followed by a brief period (5–10 s) of fast activity which then was followed by slow wave activity. However, these studies may not be directly comparable to our report in that higher doses of etomidate were administered. Also in
the human study, at least one subject was premedicated with diazepam, which is known to induce fast activity. Using atropine as sole premedication, Ghoneim and Yamada\(^4\) did not note fast activity, an effect expected with most drugs used to induce anesthesia.

No investigator previously noted an epileptogenic effect in patients recorded with EEG after administration of etomidate.\(^1\)\(^-\)\(^3\) In fact, etomidate antagonizes pentylenetetrazol (Metrazol\(^\circledR\))-induced seizures in rats. The myoclonus produced after administration of etomidate may be quite dramatic and at times may simulate tonic seizures;\(^4\) however, these movements have not been correlated with any epileptogenic activity. In decerebrate cats, spike-shaped waves were noted after administration of etomidate.\(^5\) In both of our patients, activation of epileptogenic activity was seen. This effect, however, was only noted before resection of epileptogenic foci and did not recur after the cortical resections. Perhaps the use of lidocaine and bupivacaine for local anesthesia altered the threshold for production of epileptogenic activity. However, the amounts used were small, and none was used intracranially. While high doses of lidocaine may cause convulsions, low doses have anticonvulsant properties.\(^6\) Activation of epileptogenic activity concomitant with induction of anesthesia, is an effect that seems paradoxical, but is not unique to etomidate. Methohexital (Brevital\(^\circledR\)), another ultra-short-acting drug enhances the epileptogenic activity in patients with focal seizures and is utilized to help localize epileptogenic foci during seizure surgery.

In summary, two patients are described with medically refractory complex partial seizure disorders. During electrocorticography, before excision of the epileptic tissue, etomidate enhanced the epileptogenic activity, and, in addition, produced activation of fast activity lasting several minutes. Therefore, etomidate should be used with caution in patients with focal epilepsy. However, etomidate's apparent lack of cardiovascular effects

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**Fig. 1.** Interictal activity recorded from the cortex (electrodes 1–16) and from depth electrodes (A and B) placed in the cingulate gyrus.

**Fig. 2.** A. Twenty seconds after etomidate (0.3 mg/kg iv) administered demonstrating the increase in fast activity and in epileptogenic activity that culminated in an electrographic seizure. Calibration is the same as in Figure 1. B. Three minutes later, the electrographic seizure stops and is followed by postictal suppression.
makes it a potentially useful drug to deliberately enhance epileptogenic activity in patients undergoing electrocorticography as part of cortical resection of epileptogenic tissue for the treatment of refractory epilepsy and would be an acceptable alternative to methohexitone, especially in those patients allergic to barbiturates.

REFERENCES


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Precurization Inhibits Maximal Ventilatory Effort

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Pretreatment with 3–5 mg d-tubocurarine (dTC) prevents succinylcholine- (SCh) induced muscle fascicula-

tion.1–3 This has been shown to attenuate the increased intragastric4 and intraocular5 pressures that usually accompany fasciculation and to reduce the incidence of post-SCh myalgia.6 Most patients today are given SCh before tracheal intubation, and many of these are pre- treated with a nondepolarizing drug such as dTC. In the interval between injection of dTC and the induction agent, an occasional patient becomes dysneic and, very rarely, one develops apnea and must be ventilated.7 In these circumstances, dyspnea may be due to respiratory muscle weakness, airway obstruction, or apprehension. Previous studies of low-dose dTC effect on muscle power of awake subjects employed doses of 0.1 mg/kg or greater.8,9 The usual dose of dTC used clinically to pretreat adults is 3 mg,10 which is 0.043 mg/kg for a 70-kg patient. We chose a comparable dose, 0.05 mg/kg, to study dTC effect on negative inspiratory pressure (NIP) and respiratory flow-volume loops of premedicated