A within-subject comparison of seizure duration with etomidate and methohexital in electroconvulsive therapy

Kevin J Black

Objective: To determine whether etomidate is associated with longer seizures than methohexital in ECT anesthesia. **Methods:** Retrospective chart review in 39 patients who were switched from one anesthetic to the other. We compared motor and EEG seizure duration in the last ECT session on one anesthetic and the first session on the other anesthetic. **Results:** Motor seizures were about 10 seconds longer with etomidate ($p < 0.05$). However, few of the increases in seizure duration had obvious clinical import. **Conclusions:** Etomidate can lengthen ECT seizure time compared with methohexital, but the clinical significance of this observation requires further study.

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A within-subject comparison of seizure duration with etomidate and methohexital in electroconvulsive therapy

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Note

The manuscript below was written in 1997. Changes in 2013 are marked.

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Introduction

Seizure duration is thought to be important for the antidepressant efficacy in electroconvulsive therapy (ECT) [1,2], though beyond a certain minimum of about 25 seconds this is controversial [3]. Among several strategies for increasing seizure length is the use of the non-barbiturate anesthetic agent etomidate [4,5].

Seizure times are longer with etomidate than with thiopental [2,6], but methohexital also shares this advantage [1]. Initial comparisons of seizure length between methohexital and etomidate showed no significant benefit for the latter [7-9]. However, a later methodologically superior study did show longer seizure times with etomidate [10]. A recent small case series supports this finding [11].

Considering these contradictory earlier reports, we felt it might be helpful to report our experience with the effects on seizure duration of changing between methohexital and etomidate anesthesia.

Methods

Setting: Our ECT center is in a large, university-affiliated general hospital. Inpatients are usually treated three times a week, while outpatient ECT frequency varies from three times a week to about once a month. Major depression is the most common referring diagnosis. Medications between ECT sessions are prescribed by the patients' private physicians.

We searched ECT anesthesia records for all etomidate orders for the period 1990-1992, when etomidate was commonly used at our center. We only included patients who were changed between etomidate and methohexital on consecutive treatments. The study was approved by the Washington University Human Studies Committee (#93-0171).

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We compared seizure times for the last ECT session before the change of anesthetic and the first session following the change. We used data only from these two sessions to minimize any effects of other variables on seizure length (including progressive shortening of seizures during a course of ECT and medication changes by the patient's private physician). We recorded all medications given in the ECT suite, and all medications received by inpatients over the 24 hours preceding each session.

The primary outcome measures were motor and EEG seizure duration as recorded in the ECT chart. Motor seizure time was measured by the cuff method. EEG seizure time was determined by the attending ECT physician by visual inspection of a bifrontal EEG recording.

In comparing seizure times between anesthetics, we analyzed results first in all patients, and second in those patients without potential confounds ("pure"); *i.e.* inpatients who were known to be taking no medications that affect seizure duration, and had no changes in electrode placement, stimulus parameters, or doses of caffeine or adrenergic antagonists. In the larger group we used a two-tailed *t* test without assuming equal variance, and in the smaller "pure" group we used a two-tailed paired *t* test.

Results

Etomidate was ordered for 56 patients, of whom 39 switched between the two anesthetics on consecutive treatments. Three patients changed anesthetics twice, and one changed three times, resulting in 44 before-after comparisons. Six of these changes were from etomidate to methohexital, while 38 were in the opposite direction. Most ECT sessions used unilateral electrode placement and intravenous atropine and succinylcholine; several patients also received intravenous caffeine, labetalol or esmolol. Only 6 patients met the more stringent criteria for the

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"pure" group.

The mean EEG seizure time was similar with either drug ($p > 0.75$). However, the mean seizure duration by the cuff method was about 10 seconds longer, whether we considered all patients or only the pure group ($p < 0.05$ in each case; see Table 1). Succinylcholine dose was nearly identical in the two drug conditions ($p > 0.75$).

Group comparisons aside, how often did the change of anesthetic produce a potentially meaningful change in seizure duration? In the whole group, 25 patients had increased motor seizure times on etomidate while 11 had decreases and 3 had no change. Three patients had no motor seizure on methohexital; of these, two still had no motor seizure after the change to etomidate while the third had a seizure by EEG after the change but motor seizure duration was not recorded. In the 6 "pure" patients, 5 had longer seizures on etomidate and one did not change. Four of these 6 started out with methohexital motor seizure times less than 25 seconds, of which two increased to over 25 seconds with etomidate.

Discussion

The main finding of this study is that seizure duration measured by the cuff method was on average about 10 seconds longer with etomidate than with methohexital. This result is not due to differences in concomitantly administered drugs including succinylcholine. Furthermore, since etomidate usually followed methohexital, our finding is not due to the anticonvulsant effect of prior ECT sessions.

The primary limitations of our study include its retrospective design and the modest number of subjects.

These results support the findings of Avramov et al. [10]. Assuming an average of 70kg

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for our patients, our anesthetic doses fall between their “medium” and “high” doses, at which they found mean seizure times with etomidate to be 7 to 13 seconds longer by the cuff method and 6 to 30 seconds longer by EEG. The fact that we did not find statistically longer EEG seizure times may relate to any of several factors. (1) Our sample is not large and a Type II error is likely. (2) Mean seizure length by EEG is affected by outliers, since our *median* EEG duration in both groups was actually 9-15 seconds longer with etomidate than methohexital. (3) Clinician estimates of EEG seizure duration may be more variable than motor seizure times. (4) We used methohexital doses somewhat lower than those at which Avramov et al. found the largest difference in EEG seizure length. (5) Etomidate and methohexital may differ in their relative anticonvulsive effects on prefrontal *vs* motor cortex.

Earlier studies did not find significant differences in seizure duration between methohexital and etomidate [7-9]. However, of these, only Greenberg et al. report seizure times using the cuff method, and average motor seizure duration was actually a few seconds longer for etomidate (see Table 2 in [8]).

A more interesting question relates to the clinical significance of the difference in seizure duration between the two drugs. Ilivicky et al. [11] report potentially clinically meaningful changes with etomidate in four patients who had short seizures on methohexital. However, we did not see motor seizures on etomidate after missed seizures on methohexital. A few patients crossed the 25-second threshold after the change in anesthetics, but this threshold, though widely accepted, is of unproven significance to the antidepressant efficacy of ECT [3].

In summary, our data support the view that etomidate can lengthen ECT seizure times in some patients, compared to methohexital. However, the clinical significance of this finding remains an important question for further study.

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Table 1. Etomidate caused an increase in seizure duration (by the cuff method) compared to methohexital. Seizure duration by visual inspection of EEG, and succinylcholine dose, were similar between the two anesthetic agents.

	motor seizure duration (mean, sec)	EEG seizure duration (mean, sec)	anesthetic dose (mean, mg)	succinylcholine dose (mean, mg)
all patients (39 patients, 44 anesthetic changes)				
methohexital	29.1	54.0	97.4	104.2
etomidate	38.7	55.3	22.1	107.0
p (2 tails, paired)	**0.047**	0.871	--	0.781
“pure” group (6 patients, 6 anesthetic changes)				
methohexital	22.8	52.8	88.3	95.0
etomidate	33.5	46.8	18.7	93.3
p (2 tails, paired)	**0.033**	0.786	--	0.809

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