



Comparison of methohexital and etomidate as anesthetic agents for electroconvulsive therapy in affective and psychotic disorders

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ABSTRACT

Background: ECT is a well-established treatment for severe depression. The available data on psychosis are limited, but reliable. Its therapeutic potential relies on the induction of a generalized seizure. Besides other narcotics, methohexital and etomidate are used for general anesthesia in ECT. Since prolonged seizures have been reported following the use of etomidate, it can be deduced that the substances might differ in their anticonvulsant properties, resulting in a lower increase in stimulus intensity during the course of treatment under etomidate. Besides this hypothesis, we aimed to investigate the differential effects of etomidate and methohexital on clinical features, ECT parameters and side effects of the treatment.

Methods: We performed a retrospective analysis of treatment data of patients with affective and psychotic diagnosis who received general anesthesia for ECT either with etomidate or with methohexital. **Results:** ECT with etomidate and methohexital was equally effective. During the course of therapies the administered electric charge increased significantly and equally in both treatment groups. In the methohexital group, but not in the etomidate group, electroencephalographic seizure duration had a declining trend during the course of therapies. We observed more side effects during and immediately after ECT in the methohexital group than in the etomidate group.

Limitations: The limitations of this study are that the patients received various psychotropic co-medications, which influence ictal parameters differently, and, secondly, the study is based on a retrospective analysis.

Conclusion: The results of our analysis suggest that etomidate and methohexital affect ictal parameters to different extents. Longer seizure duration and fewer side effects are in favor of etomidate.

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1. Introduction

Electroconvulsive therapy (ECT) is a well-established, highly effective treatment for severe depression. The available data on psychosis are limited, but reliable (The UK ECT Review Group, 2003; Zervas et al., 2012). Although the exact therapeutic mechanisms remain to be clarified, repeated induction of a generalized seizure is viewed as decisive for a therapeutic response (Sackeim et al., 1991). General anesthesia and muscular relaxation are performed in order to prevent injuries during the seizure.

Cognitive-mnemonic impairments are the most frequent severe side effects (The UK ECT Review Group, 2003). Although these impairments have been shown to be fully reversible (The UK ECT Review Group, 2003), they are usually perceived by patients as being very defacing, and sometimes to such an extent as to render a further administration of ECT impossible. Besides electrode placement, the electric charge needed for seizure induction has been shown to be a pivotal parameter influencing cognitive side effects (Weiner et al., 1986). Thus, all measures that lead to a reduction of the electric charge might also help reduce cognitive side effects. There is widespread consensus that a generalized seizure of sufficient duration is necessary for the therapeutic effect of the treatment (American Psychiatric Association, 2001), but this alone is likely not sufficient (Robin and De Tissera, 1982; Sackeim et al., 2000). While recent studies have sought to identify EEG measures that are able to predict ECT outcome (Perera et al., 2007),

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the notion that ictal parameters influence therapeutic properties of ECT continues to persist. Higher amplitudes of the ictal EEG, especially in the δ -band, greater ictal coherence, stronger postictal suppression and a higher peak seizure heart rate are associated with greater success of the treatment (Perera et al., 2004; Folkerts, 1996). There is no relationship between seizure duration and ECT-effectiveness (Swartz, 2001).

Since seizures are longer under the influence of etomidate than under the influence of methohexital (Eranti et al., 2009), it can be assumed that the anticonvulsant effect seen by the gain of electric charge necessary to elicit a sufficient seizure is smaller after etomidate than after methohexital. One of the aims of this study was to test this hypothesis. Besides this, we wanted to test if the choice of the narcotic had an effect on other ictal and treatment parameters. Since the choice of the narcotic might influence both the main effect and the side effects induced by ECT, a better characterization of the narcotics used in ECT is needed for further optimization of this treatment.

Here we present a retrospective study with subjects who underwent ECT for clinical reasons in order to treat their affective disorder or their schizophrenia. One part of the patients received general anesthesia with methohexital, a short acting barbiturate, while the other part of the patients received etomidate, a non barbiturate. We sought to evaluate if these two patient groups differed in electric stimulation dose, main effect and the treatment's side effects. Moreover, we examined whether the group that improved better during ECT differed from the one that improved less in any other aspect.

2. Methods

2.1. Study design

This is a retrospective analysis of ECT treatments performed in our clinical institution from 2005 to 2007. All patients received general anesthesia. Originally, we performed ECT with methohexital as a narcotic. Then, with methohexital not being available in the market for some time, we resorted to using etomidate. None of the patients who received methohexital was included in the etomidate group. One reason for the choice of etomidate was that we thought the seizure parameters could be improved by this narcotic agent. In this analysis, 21 patients received methohexital and 47 patients received etomidate. Muscle relaxation was performed with the depolarizing muscle relaxant succinylcholine. Besides the use of two narcotic agents, all other treatment parameters stayed the same. The patients were suffering from major depression ($n = 51$; ICD-10: F32.x, F33.x), schizoaffective disorder ($n = 6$; F25.x) or treatment-resistant schizophrenia ($n = 11$; F20.x).

2.2. ECT treatment

Preoxygenation and post-seizure ventilation were performed by face mask until the patient's own ventilation was sufficient again. Before and immediately after the ECT noninvasive arterial blood pressure was measured. Oxygen saturation, heart rate and electrocardiogram (ECG) were monitored.

ECT treatment was performed using the Thymatron IV (SOMATICS, INC, Lake Bluff, IL) device. The treatment was started with right unilateral (RUL) stimulation as described by D'Elia et al. (1983). If a generalized EEG seizure of sufficient length could not be elicited even after raising the electric charge, or if no clinical response was seen, treatment was switched to left anterior right temporal (LART) stimulations (Swartz and Nelson, 2005). The seizures were monitored by two-channel EEG recording, with the EEG electrodes positioned bifrontally and over the mastoids. The energy administered during the first treatment was determined by the age

method, which is frequently used in Germany (Loh et al., 2012). If the seizure quality was poor, the administered electric charge was raised by 10–30% for the following stimulation; in most cases the electric charge was raised by 20%. At very low stimulus doses, i.e. below 252 mC, the electric charge was raised only by 10%. At very high stimulus doses, i.e. above 756 mC, the charge was raised by 30% where applicable. A seizure of sufficient length was classified as of poor quality if the amplitudes of the ictal EEG were low due to visual classification of an experienced clinician, or if the postictal suppression was poor, as the latter finding suggests that the stimulus was not high enough supra-threshold (Nobler et al., 1993; Suppes et al., 1996; Krystal et al., 1995, 1998; Perera et al., 2004; Riddle et al., 1993). If the electroencephalographic seizure was below 20 s, or if no seizure could be elicited, a restimulation was performed. If the seizure as detected by the electroencephalogram was between 20 and 24 s, a restimulation was only performed if the ictal EEG had low amplitudes (Folkerts, 1996). No restimulation was performed above 25 s. In order to avoid restimulation during the refractory period of the brain, we performed restimulation 2 min after termination of the insufficient seizure. The energy administered is referred to in mC. Pulse duration was 0.5 ms for electric charges of 504 mC and below, while it was 1 ms for higher electric charges. ECT was performed twice a week.

2.3. Data acquisition

We performed a retrospective analysis of treatment data of 68 patients who had been receiving ECT for clinical reasons. They were suffering from unipolar depression, bipolar depression, schizoaffective disorder or schizophrenia according to ICD-10. 21 patients received methohexital and 47 patients received etomidate as narcotic agent for ECT. For induction, 0.2–0.3 mg etomidate per kg body weight (20 ± 4 mg) or 1–1.5 mg methohexital per kg body weight (117 ± 28 mg) were administered. During and after each treatment session side effects were monitored. Pharmacological intervention was performed when necessary. The presence of cognitive side effects was assessed by the physician responsible for the patients' treatment on the ward and by the supervisor. Cognitive deficits caused by ECT were labeled as mild, if they were observable, but not disabling in every-day life. They were labeled as intermediate, if they were disabling in every-day life, but a sufficient level of daily functioning was not impossible due to ECT-induced cognitive deficits. ECT-induced cognitive deficits were labeled as severe, if they were so disabling that they extensively impaired daily functioning. In these cases ECT was stopped.

Information about the duration of the current episode, the duration of illness calculated from the first episode on, and history of hypertension or cardiac damage were gained from the patient's medical records.

GAF is a global parameter for daily functioning, which is applicable to severely ill patients not only with unipolar depression, but also schizoaffective disorder and schizophrenia. In order to compare the ECT-induced improvements of daily functioning of the etomidate and the methohexital group, GAF values were independently estimated before and after the course of ECT treatments by two psychiatrists responsible for the patients' treatment on the ward. The mean of these GAF values was used for the analysis. The patients were treated with antidepressants, high-potency antipsychotics, low-potency antipsychotics, mood stabilizers and benzodiazepines.

2.4. Statistical analysis

The following parameters of both treatment groups were compared by two-sided *t*-test: age, duration of illness, time from the first ECT treatment to discharge from hospital, GAF and alteration of

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