Effect of methohexitone and propofol with or without alfentanil on seizure duration and recovery in electroconvulsive therapy


Summary
We have studied the effects of methohexitone and propofol with and without alfentanil on seizure duration and recovery in this observer-blinded, prospective, randomized, crossover study involving 24 patients undergoing electroconvulsive therapy (ECT). Each patient had four treatment sessions, and received the following four i.v. regimens in random order: methohexitone 0.75 mg kg$^{-1}$, methohexitone 0.50 mg kg$^{-1}$ and alfentanil 10 μg kg$^{-1}$, propofol 0.75 mg kg$^{-1}$, propofol 0.50 mg kg$^{-1}$ and alfentanil 10 μg kg$^{-1}$. Additional methohexitone or propofol was given as needed in 10–20-mg increments until loss of consciousness. Suxamethonium 1.0 mg kg$^{-1}$ i.v. was given for muscular paralysis. Mean motor and EEG seizure durations were longer with methohexitone–alfentanil (44.7 (SD 15.0) and 70.5 (29.7) s) than with methohexitone (37.6 (12.6) and 52.6 (15.3) s) and similarly, seizures were longer with propofol–alfentanil (36.8 (15.2) and 54.5 (20.9) s) than with propofol alone (27.2 (11.9) and 39.2 (3.9) s). Seizures were longest with methohexitone–alfentanil and shortest with propofol. Recovery time was statistically shorter in patients receiving propofol compared with methohexitone–alfentanil and methohexitone alone. Alfentanil with a reduced dose of methohexitone or propofol provided unconsciousness and increased seizure duration in patients undergoing ECT. We conclude that the combination of methohexitone with alfentanil is a good regimen for ECT, especially for patients with short seizure duration. (Br. J. Anaesth. 1997; 79: 801–803).

Key words

Electroconvulsive therapy (ECT) is a standard method for treating severe depression.$^1$ Methohexitone and propofol have been used to provide the brief period of unconsciousness needed for ECT$^2$; however, both produce a dose-dependent decrease in seizure duration.$^3$ Although no studies have proved a correlation between seizure duration and clinical outcome, prolonged seizures may be more efficacious$^4$ and a motor seizure duration of greater than 25 s has been recommended to ensure clinical adequacy of treatment.$^5$ A further reduction in methohexitone or propofol dose could increase seizure duration but might not provide adequate hypnosis. Alfentanil is a rapid acting opioid with an ultrashort duration of action and no known anti-convulsant effect. Combining alfentanil with propofol or methohexitone produces loss of consciousness with a smaller induction dose and thus could potentially increase seizure duration. We compared propofol and methohexitone with or without alfentanil with regard to seizure duration and haemodynamic stability after ECT.

Methods and results
After obtaining IRB approval and informed patient consent, we studied 24 patients, ASA I–III, during a series of four ECT. All patients presenting for a series of greater than or equal to four ECT were enrolled in this crossover, observer- and patient-blinded, prospective, randomized study. Non-invasive arterial pressure, heart rate, electrocardiogram (ECG) and oxygen saturation were recorded at 2-min intervals. Labetalol 20–40 mg was administered before ECT to patients with a history of hypertension. Each patient received the following four i.v. regimens of induction agents in a computer-generated random order: methohexitone 0.75 mg kg$^{-1}$, methohexitone 0.50 mg kg$^{-1}$ with alfentanil 10 μg kg$^{-1}$, propofol 0.75 mg kg$^{-1}$, propofol 0.50 mg kg$^{-1}$ and alfentanil 10 μg kg$^{-1}$. Patients were assessed clinically at approximately 60 s after administration of induction agent and additional methohexitone or propofol was given in 10–20-mg increments if needed until loss of eyelash reflex and response to verbal command. Neuromuscular block

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was produced with suxamethonium 1.0 mg kg\(^{-1}\) i.v. Patients’ lungs were ventilated with an air and oxygen mixture during the apnoeic phase. An arterial tourniquet was applied to the right arm of each patient to isolate the right hand for assessment of motor seizure duration. The stimulus was administered immediately after resolution of muscle fasciculations. Five patients received unilateral and 19 patients received bilateral ECT. Two frontal electrodes were placed to record continuous EEG seizure activity using a Thymatron device (Somatics Inc., Lake Bluff, IL, USA). Patients received ECT with 30–50% of the maximum output stimulus depending on the attending psychiatrist’s choice. The electrical stimulus used for each patient was kept constant during the study and none required an increase in the stimulus to achieve a longer seizure duration.

EEG seizure durations were determined from the EEG recording at the conclusion of the study by a blinded psychiatrist. Duration of motor seizure was recorded as the time from the beginning to the end of tonic–clonic motor activity in the isolated hand by a nurse who was also blinded to the induction agent used. Anaesthetic dose requirements, duration of stay in the post-anaesthesia care unit (PACU), and heart rate and arterial pressure were also recorded by a blinded nurse. Patients were discharged from the PACU when they met the following criteria: stable haemodynamic and respiratory status, response to verbal commands and ability to move from bed to wheelchair. Mental status was assessed before and after ECT by the same blinded nurse every 5 min until the patient returned to pre-ECT status.

Data were analysed using repeated measures ANOVA for comparison of anaesthetic dose requirements, EEG and motor seizure duration, and duration of stay in the PACU. Data were also analysed by post-hoc Student–Newman–Keuls test, where appropriate.\(P<0.05\) was considered significant.

Eight men and 16 women, mean age 52 (range 25–80) yr and weight 81 (SD 25) kg (range 55–160) kg were enrolled in the study for a total of 96 ECT. The doses of methohexitone and propofol with and without alfentanil are listed in table 1. Addition of alfentanil probably resulted from its additive effect leading to decreased requirements for groups who required 51% and 52% increases in their initial dose, respectively, to obtain the same response. The ratio between doses of methohexitone and propofol with and without pretreatment with alfentanil were 1:1.27 and 1:1.23, respectively.

Durations of motor and EEG seizures were longest in the methohexitone–alfentanil group and shortest in the propofol group (fig. 1). Durations of EEG and motor seizures were greater when patients were anaesthetized with methohexitone or propofol in combination with alfentanil than when methohexitone or propofol alone was used (fig. 1). All EEG seizures lasted longer than 25 s except for two of the treatments, performed using propofol alone. PACU duration was significantly shorter in patients receiving propofol or propofol with alfentanil (table 1). Patient mental status (anxiety level, clumsiness, fatigue and drowsiness) at the time of discharge was not affected by the induction agent administered. Alfentanil in combination with methohexitone or propofol had no significant effect on haemodynamic stability.

**Comment**

Our patients undergoing ECT with reduced doses of methohexitone with alfentanil had a longer duration of EEG and motor seizures than patients anaesthetized with methohexitone or propofol alone or propofol and alfentanil combined. Propofol with alfentanil was associated with longer EEG and motor seizures than propofol alone. This increase in duration of motor and EEG seizures with the addition of alfentanil probably resulted from its additive effect leading to decreased requirements for

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### Table 1

| Table 1 | Recovery room stay (PACU time) and drug doses for the four regimens (mean (SD)). \(P<0.05\) compared with *methohexitone, †methohexitone–alfentanil and ‡propofol |
|----------------|-----------------|-----------------|-----------------|-----------------|
|                | Pacu time (min) | initial dose (mg kg\(^{-1}\)) | Total dose (mg kg\(^{-1}\)) | |
| Methohexitone  | 34.0 (88)       | 0.75            | 0.92 (0.25)      | |
| Methohexitone–alfentanil | 35.0 (6.78) | 0.50            | 0.60 (0.18)*    | |
| Propofol       | 30.5 (5.46)†‡  | 0.75            | 1.13 (0.52)      | |
| Propofol–alfentanil | 31.8 (5.70)* | 0.50            | 0.76 (0.37)‡    | |

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**Figure 1** Mean (SD) duration of motor and EEG seizures in the four treatment groups. \(P<0.05\) compared with: *methohexitone; †methohexitone–alfentanil; ‡propofol–alfentanil.
methohexitone or propofol and the lack of effect of alfentanil on seizures.

A previous study by Weigner and colleagues demonstrated that pretreatment with fentanyl reduced seizure duration compared with a control group in patients undergoing ECT.6 In contrast, our study demonstrated prolongation of seizure duration when alfentanil was used to decrease the induction dose of methohexitone or propofol.

The doses of methohexitone and propofol in our study were higher than the doses used by Fredman and colleagues.2 This may be because there were younger subjects in our study requiring higher doses of anesthetics and different end-points for loss of consciousness between the studies (loss of eyelash reflex in our study in addition to loss of response to verbal commands in Fredman’s study). We could not establish a relationship between the dose of anaesthetic agent and seizure duration as there was minimal intra-patient dose variability.

The cardiovascular response to ECT is caused by activation of the autonomic nervous system. Initial parasympathetic activation results in bradycardia that is followed rapidly by sympathetically induced tachycardia and hypertension.7 Rampton and colleagues8 compared the cardiovascular response to ECT after administration of either methohexitone or propofol and reported improved haemodynamic stability after administration of propofol. However, in our study, there was no difference in haemodynamic stability between the four groups. The doses of methohexitone and propofol used in our study were tailored individually to achieve adequate anaesthesia for ECT and patients with a history of hypertension were pre-treated with labetalol. This could explain the absence of statistical difference in MAP and heart rate between the four groups. None of the patients in all four groups developed arrhythmias or showed ECG signs of myocardial ischaemia.

The small dose of alfentanil (10 µg kg⁻¹) allowed prolongation of seizure duration without adverse opioid side effects such as chest wall rigidity, respiratory depression or nausea and vomiting. Dinwidie and Isenberg used high-dose alfentanil (25 µg kg⁻¹) which resulted in nausea and vomiting in two of eight patients.9

There was a prolongation in duration of stay in the PACU in patients receiving methohexitone or methohexitone–alfentanil. This was probably a result of the increased seizure durations in these patients. Alternatively, the smooth recovery of propofol may have led to earlier PACU discharge as has been demonstrated in patients undergoing outpatient surgery.10

Although seizure duration may be affected by many factors such as sex, electrode placement (unilateral or bilateral), applied energy, individual seizure thresholds, previous ECT or concomitant drug therapy, the crossover design of this study should have eliminated potential bias from inter-patient variability.

In summary, using alfentanil to reduce the dose of methohexitone or propofol resulted in a longer seizure duration but no significant effect on recovery in patients undergoing ECT. Psychiatrists’ opinions vary regarding the importance of seizure duration. If it is assumed that short seizures may result in reduced therapeutic benefit, then combined methohexitone and alfentanil may be a better regimen for ECT than methohexitone alone, and propofol with alfentanil is a reasonable alternative.

References