Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2014, Vol. 42(1) 111–119

DOI: 10.1177/0300060513509036
imr.sagepub.com
SAGE

Sevoflurane/remifentanil versus propofol/remifentanil for electroconvulsive therapy: Comparison of seizure duration and haemodynamic responses

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Abstract

Objective: To compare the anaesthetic and convulsive effects of sevoflurane/remifentanil versus propofol/remifentanil combination in electroconvulsive therapy (ECT).

Methods: In this prospective, randomized double-blind study, patients diagnosed with treatment-resistant depression were included for ECT. Prior to treatment, 1 μg/kg remifentanil was intravenously administered to all patients, followed by anaesthetic induction with either 0.5 mg/kg propofol or 8% sevoflurane. Following muscular paralysis with succinylcholine and hypnosis, bitemporal ECT was applied. Vital signs, depth of sedation, recovery parameters, motor and electroencephalography (EEG) convulsion activity and postictal suppression index scores were recorded.

Results: A total of 120 sessions of ECT were administered to 12 patients. Heart rate was higher in the sevoflurane group than the propofol group. Compared with the sevoflurane group, bispectral index level was lower in the propofol group during the induction period and higher during the recovery period. Anaesthetic induction and recovery times were lower, and average motor and EEG convulsion activity was longer, in the propofol group than in the sevoflurane group.

Conclusion: Propofol/remifentanil is more successful compared with sevoflurane/remifentanil in anaesthesia management during ECT since it provides quick induction and recovery, longer seizure activity and stable haemodynamics.

These data were presented as a poster at the 46th Turkish Anesthesia Association Congress (TARK), 7–10 November 2012, Girne, Turkish Republic of Northern Cyprus.

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Keywords
Anaesthesia, electroconvulsive therapy, sevoflurane, propofol, seizure

Date received: 30 May 2013; accepted: 22 September 2013

Introduction

Electroconvulsive therapy (ECT) is an efficient and fast therapy for treatment-resistant depression. Modern ECT, termed 'modified' ECT, is performed under general anaesthesia and muscle relaxation.[1] An ideal anaesthetic agent for ECT must have a rapid onset, no effect on seizure efficacy and should ensure cardiovascular stability during administration.[2]

Different anaesthetic agents have different effects on seizure duration. Seizures of 20–25 s duration are generally required for therapeutic efficacy, with shorter seizures viewed as a negative outcome for ECT.[3,4] An anaesthetic agent with a stabilizing effect on the cardiovascular system is considered to be beneficial.[5] Propofol is a nonbarbiturate hypnotic agent that is widely used in ECT anaesthesia because of its associated rapid recovery and haemodynamic stability advantages.[6–8] Propofol may increase the efficacy of ECT[9,10] and can decrease post-ECT confusion,[11] however, its use is associated with a dose-dependent decrease in seizure duration.[12] Decreasing the dose of propofol is associated with longer seizures, and one means of decreasing the propofol dose (for example to 0.5 mg/kg) is to use it in combination with 1 μg/kg remifentanil.[13–15]

In circumstances where venous access is difficult due to dehydration or agitation of the patient, inhaled anaesthetics can be administered. Sevoflurane is an inhaled anaesthetic used in ECT,[16,17] however, it's use may be disadvantageous because it causes acute haemodynamic changes following ECT.[16,18] Compared with anaesthesia using propofol, sevoflurane-induced anaesthesia has been associated with a faster recovery time and longer convulsion duration, however, it has also been associated with a longer induction and greater haemodynamic response.[16,19–21]

Opioid analgesics decrease the negative anaesthetic effects on haemodynamics and seizure duration in ECT anaesthesia. Remifentanil is a potent ultrashort-acting opioid used as an analgesic in ECT,[22] with no systematic anticonvulsant effect,[23] and is associated with haemodynamic stability and fast recovery times.[13–15,24] The addition of remifentanil to propofol anaesthesia in ECT has been shown to enable a decrease in propofol dose by 50–75%, and be associated with increases in seizure duration.[13–15] Remifentanil is associated with a dose-dependent decrease in the bispectral index (BIS).[25] The BIS is an automated, single measure of scalp electroencephalography (EEG). It is an index of depth of anaesthesia, with scores of $\geq$95 being associated with full consciousness, scores of 65–85 being associated with sedation and scores of 40–65 indicating general anaesthesia.[26]

The present study aimed to compare the effects of propofol/remifentanil or sevoflurane/remifentanil combinations on induction rate, convulsion time, haemodynamics and recovery profile during anaesthetic induction for ECT, in patients whose anaesthetic depth was measured using the BIS.

Patients and methods

Study population

The present study was conducted at the Department of Psychiatry, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey between January 2010 and June 2012 on patients with depression aged 18–65 years (American Society of Anesthesiologist [ASA] I–II), who were

considered appropriate for ECT and whose depression was resistant to medical treatment. Patients with poorly controlled cardiovascular disorders, arrhythmia, chronic obstructive pulmonary disease, renal or hepatic failure and organic brain diseases were excluded.

The study was conducted using a prospective, randomized, double-blind plan and conducted using a randomization method. The study was approved by the faculty ethical committee of Karadeniz Technical University Faculty of Medicine, reference No. 2007/13. Written informed consent was obtained from the patients or their legal proxies.

ECT randomization and treatment

Prior to each ECT treatment, patients were randomized using a computer-generated randomization program to an ECT anaesthesia protocol: Group P, 0.5 mg/kg propofol intravenously (i.v.) + 1 μg/kg remifentanil i.v.; or Group S, 8% sevoflurane + 100% oxygen by inhalation + 1 μg/kg remifentanil i.v.

Patients received no premedication. Prior to anaesthetic induction, all patients were preoxygenated with 6 l/min oxygen for 5 min via a face mask. 0.3 mg atropine i.v. was administered 5 min prior to ECT. Pulse oximetry, noninvasive blood pressure, three-lead electrocardiogram, BIS score (0–100 where: ≥95, full consciousness; 65–85, sedation; and 40–65, anaesthesia) and Thymatron® EEG (Somatics, LLG, Lake Bluff, IL, USA) monitoring was performed for each patient at each treatment. A tourniquet was placed on the contralateral forearm to use the isolated forearm technique. Systolic blood pressure, heart rate, peripheral oxygen saturation (SpO_2), and BIS score were recorded preanaesthesia (baseline), 1 min following anaesthesia induction and after loss of eyelash reflex, during ECT, at reversal of spontaneous respiration, at eye opening and at resumption of spontaneous breathing. Arrhythmia episodes, bradycardia (<50 pulse/min), desaturation (<96%), hypotension (>20% decrease from baseline) and hypertension (>20% increase from baseline) were recorded during the anaesthesia and recovery periods.

Within 90 s of administering 1 μg/kg remifentanil i.v., patients allocated to group P received 0.5 mg/kg propofol i.v. over 15 s and patients allocated to group S treatment received sevoflurane 8% in 100% oxygen 6 l/min fresh gas flow. For all patients in group S, when BIS values fell below 50, sevoflurane gas flow was stopped and ventilation was assisted with 100% oxygen. Loss of eyelash reflex and eye-opening response to verbal instruction were recorded during this period. All patients received 0.75 mg/kg succinylcholine i.v. for muscular paralysis. Once no muscular fasciculation was observed, ECT was applied with the AKMED ECT-F-180 machine (Akmed, Istanbul, Turkey) using bitemporal electrodes. Mask ventilation with 100% oxygen continued until spontaneous ventilation began.

The EEG seizure duration, postictal suppression index (degree of suppression at end of the seizure) and motor convulsion time (using isolated upper limb technique) were recorded. ECT therapies were scheduled by the same psychiatrist (C.H.) who was unaware of the randomized assignment. The first ECT dose received by each patient was performed at 30% of maximum stimulus amplitude, depending on the decision of the psychiatrist. Stimulus amplitude after the first treatment was planned by the same psychiatrist based on the EEG seizure duration, postictal suppression index and motor convulsion time for the patient. Successful ECT session criteria were postictal suppression index ≥70%, and EEG and motor convulsion time >15 s.

Patients were transferred to recovery when spontaneous ventilation resumed

(SpO_2 >96% without supplemental oxygen) and they could respond to verbal instruction. Patients were transferred from recovery to a ward when the modified Aldrete score was >9.[27] Times of onset of spontaneous inhalation and response to verbal instruction, and side-effects such as headache, nausea and vomiting during this period were recorded.

Statistical analyses

Study data were analysed using SPSS® software, version 13.0.1 (SPSS Inc., Chicago, IL, USA) for Windows®. Kolmogorov–Smirnov dispersion test was used to evaluate normal dispersion. Differences between the qualitative data were analysed using Pearson's χ^2-test; quantitative data were analysed using Mann–Whitney *U*-test. Wilcoxon signed–rank test was used for within-group comparisons. All findings were evaluated bidirectionally at a significance level of $P \leq 0.05$ and an advanced significance level of $P \leq 0.01$. The study was powered to detect a 0.5 effect size with (1-β) 0.47499, with 10.5 degrees of freedom.

Results

The present study included a total of 120 ECT sessions administered to 12 patients with depression (aged 18–65 years; weight range, 49–113 kg). This study design resulted in exactly the same number of patients being exposed to each treatment (sevoflurane- or propofol-based anaesthesia) (Table 1). Each patient received between two and twelve ECT sessions.

Mean heart rate during ECT and the follow-up period was found to be statistically significantly higher in the sevoflurane group than in the propofol group ($P < 0.001$; Table 2). The higher heart rate values were not related to any differences in clinical results. Mean systolic blood pressure changes were similar between the two types of treatment (Table 2).

The BIS values in the propofol group were lower than in the sevoflurane group during the induction and loss of eyelash

Table 1. Demographic data presented on a per-treatment basis in patients with treatment-resistant depression ($n = 12$) assigned to receive electroconvulsive therapy under two types of anaesthesia: Group P, 0.5 mg/kg propofol i.v. + 1 μg/kg remifentanil i.v.; Group S, 8% sevoflurane + 100% oxygen by inhalation + 1 μg/kg remifentanil i.v.

	Treatment group	
Characteristic	Group P $n = 63$	Group S $n = 57$
Age, years	43.53 ± 17.26	43.53 ± 17.26
Weight, kg	67.00 ± 18.00	67.00 ± 18.00
Patients, female/male	5/7	5/7
Number of treatments, female/male	31/32 (63)	25/32 (57)
Medications		
Antidepressants	27 (42.9)	24 (42.1)
Antipsychotics	21 (33.3)	19 (33.3)
Benzodiazepines[a]	15 (23.8)	14 (24.6)

Data presented as mean ± SD or *n* (%) incidence.
[a]Lorazepam.

reflex periods, and higher than in the sevoflurane group during periods when spontaneous inhalation began, and eye opening and motor responses returned ($P < 0.05$; Table 3).

Anaesthetic induction time, recovery time following ECT, motor and EEG convulsion activity time, and postictal suppression index scores are shown in Table 4. Anaesthetic induction time and recovery time were shorter in the propofol group compared with the sevoflurane group ($P < 0.05$). Mean motor and EEG convulsion activity were longer in the propofol group than the sevoflurane group ($P < 0.05$). There were no between-group differences with regard to postictal suppression index score (72.42 ± 22.06 and 77.15 ± 18.22, respectively). In addition, there were no significant between-group differences regarding charge delivered during ECT.

Nausea and vomiting following ECT or side-effects relating to the anaesthesia were similar in both groups ($df = 1$); data not shown.

Discussion

The present study showed that propofol/remifentanil combination used in anaesthesia for ECT was more effective than sevoflurane/remifentanil combination in terms of rapidity of induction and recovery time, and length of seizure duration.

Efficacy of ECT may be related to seizure duration and seizure quality.[19] While there

Table 2. Haemodynamic data presented on a per-treatment basis in patients with treatment-resistant depression ($n = 12$) assigned to receive electroconvulsive therapy (ECT) under two types of anaesthesia: Group P, 0.5 mg/kg propofol i.v. + 1 μg/kg remifentanil i.v.; Group S, 8% sevoflurane + 100% oxygen by inhalation + 1 μg/kg remifentanil i.v.

	Treatment group		
Haemodynamic parameter	Group P $n = 63$	Group S $n = 57$	Statistical significance
Heart rate, pulse/min			
Baseline	76.43 ± 14.08	83.86 ± 20.28	NS
Induction	$73.95 \pm 13.68^{\dagger}$	$79{,}95 \pm 20.86^{*}$	NS
Loss of eyelash reflex	$71.98 \pm 14.06^{*}$	$76.77 \pm 18.65^{*}$	NS
ECT	$85.44 \pm 15.43^{\dagger}$	$100.23 \pm 19.56^{*\ddagger}$	$P = 0.0001$
Reversal of spontaneous respiration	81.21 ± 15.43	$91.67 \pm 11.71^{*\ddagger}$	$P = 0.0001$
Eye opening	80.30 ± 15.55	$92.74 \pm 18.47^{*\ddagger}$	$P = 0.0001$
Reversal of motor response	$80.73 \pm 14.15^{\dagger}$	$92.39 \pm 17.28^{*\ddagger}$	$P = 0.0001$
Systolic blood pressure, mmHg			
Baseline	126.52 ± 19.74	127.29 ± 18.05	NS
Induction	125.26 ± 20.15	128.21 ± 25.67	NS
Loss of eyelash reflex	$120.339 \pm 20.83^{*}$	124.87 ± 25.79	NS
ECT	$139.73 \pm 30.30^{\dagger}$	$157.17 \pm 33.63^{*}$	NS
Reversal of spontaneous respiration	$143.79 \pm 31.09^{*}$	$146.98 \pm 29.05^{*}$	NS
Eye opening	133.93 ± 27.66	$138.85 \pm 26.70^{*}$	NS
Reversal of motor response	132.06 ± 25.03	$136.31 \pm 26.26^{\dagger}$	NS

Data presented as mean ± SD.

†Statistically significant difference compared with baseline ($P < 0.05$, Wilcoxon signed–rank test); *Statistically significant difference compared with baseline ($P < 0.01$, Wilcoxon signed–rank test); ‡Statistically significant between-group difference ($P < 0.05$, Mann–Whitney *U*-test).

NS, no statistically significant between-group difference ($P > 0.05$).

Table 3. Bispectral index (BIS) values presented on a per-treatment basis in patients with treatment-resistant depression ($n = 12$) assigned to receive electroconvulsive therapy (ECT) under two types of anaesthesia: Group P, 0.5 mg/kg propofol i.v. + 1 μg/kg remifentanil i.v.; Group S, 8% sevoflurane + 100% oxygen by inhalation + 1 μg/kg remifentanil i.v.

	Treatment group		
Treatment timepoints	Group P $n = 63$	Group S $n = 57$	Statistical significance
Baseline	94.95 ± 3.89	95.42 ± 3.57	NS
Induction	78.19 ± 10.41*	87.80 ± 10.26*‡	$P = 0.0001$
Loss of eyelash reflex	61.88 ± 13.65*	74.08 ± 17.84*‡	$P = 0.0001$
ECT	39.04 ± 9.56*	40.43 ± 14.98*	NS
Reversal of spontaneous respiration	62.09 ± 11.25*	55.59 ± 11.73*‡	$P = 0.007$
Eye opening	74.96 ± 6.75*	66.00 ± 11.71*‡	$P = 0.0001$
Reversal of motor response	84.38 ± 5.20*	76.12 ± 9.51*‡	$P = 0.0001$

Data presented as mean ± SD BIS score (0–100) where: ≥95, full consciousness; 65–85, sedation; 40–65, anaesthesia.
*Statistically significant difference compared with baseline ($P < 0.01$, Wilcoxon signed–rank test); ‡Statistically significant between-group difference ($P < 0.05$, Mann–Whitney *U*-test).
NS, no statistically significant between-group difference ($P > 0.05$).

Table 4. Times for induction of anaesthesia, recovery and motor and electroencephalograph (EEG) seizure activity, and postictal suppression index scores, presented on a per-treatment basis in patients with treatment-resistant depression ($n = 12$). Patients were assigned to receive electroconvulsive therapy under two types of anaesthesia: Group P, 0.5 mg/kg propofol i.v. + 1 μg/kg remifentanil i.v.; Group S, 8% sevoflurane + 100% oxygen by inhalation + 1 μg/kg remifentanil i.v.

	Treatment group		
Parameter	Group P $n = 63$	Group S $n = 57$	Statistical significance
Induction time			
Time to loss of eyelash reflex, s	50.07 ± 20.62	75.89 ± 31.38*	$P = 0.0001$
Time to loss of verbal response, s	110.69 ± 39.61	138.40 ± 60.02*	$P = 0.0001$
Recovery time			
Time to reversal of spontaneous respiration, s	259.60 ± 89.89	319.63 ± 128.36*	$P = 0.002$
Time to eye opening, s	351.90 ± 97.31	477.28 ± 137.28*	$P = 0.0001$
Time to reversal of motor response, s	450.142 ± 109.82	556.63 ± 114.86*	$P = 0.0001$
Time to Aldrete score≥9, s	552.63 ± 136.83	654.68 ± 98.05*	$P = 0.0001$
Mean motor convulsion duration, s	25.44 ± 17.41	17.26 ± 9.21*	$P = 0.002$
Mean EEG convulsion duration, s	33.00 ± 25.35	16.89 ± 15.07*	$P = 0.003$
Postictal suppression index, %	72.42 ± 22.06	77.15 ± 18.22	NS

Data presented as mean ± SD.
*Statistically significant between-group difference ($P < 0.01$, Mann–Whitney *U*-test).
NS, no statistically significant between-group difference ($P > 0.05$).

are data showing that propofol decreases convulsion time of ECT, there are no data available showing that sevoflurane increases the convulsion duration.[28]

A study investigating the effects of sevoflurane (8%) anaesthesia induction versus propofol (1 mg/kg), found the mean motor convulsion time was higher in the sevoflurane group.[19] Postictal suppression index score was determined to be higher in the propofol group compared with the sevoflurane group, however, no significant difference was found in EEG convulsion time. Sevoflurane was emphasized as an alternative to propofol anaesthesia in patients in whom ECT was applied.[19] A similar study evaluating induction time, recovery profile and convulsion time associated with 2 mg/kg propofol i.v. versus 8% sevoflurane by inhalation for anaesthesia induction during ECT, found that recovery was faster and seizure duration was longer in the sevoflurane group.[21] In contrast, the present study showed that administration of propofol resulted in longer convulsion time compared with sevoflurane. Consistent with the results of the present study, an investigation into the effects of propofol alone, sevoflurane alone and propofol-sevoflurane combination on haemodynamic responses, convulsion time and recovery characteristics determined that propofol had a longer motor and EEG convulsion time compared with sevoflurane.[16]

The effects on convulsion time of using an opioid in combination with propofol or other anaesthetic agents in anaesthesia, have been investigated in previous studies. Compared with 1 mg/kg propofol alone, 0.5 mg/kg propofol plus 1 μg/kg remifentanil has been shown to enable reduction of the propofol dose, and resulted in a significant increase in seizure duration, without interfering with the cardiovascular parameters and recovery time.[15] Another study of the effects of propofol alone compared with propofol plus remifentanil found that the addition of remifentanil significantly increased postictal suppression index score and EEG seizure duration.[29] In both studies, the addition of remifentanil decreased the propofol dose necessary for loss of consciousness and resulted in increased convulsion time. In contrast to previous studies comparing sevoflurane with propofol, which report different results,[19,21] the present study used remifentanil infusion in both groups. The results of the present study which used remifentanil in combination with propofol, facilitating a reduction in the propofol dose, suggest that the adverse effects of propofol on seizure duration in previous studies may have been dose dependent.[19,21]

Remifentanil has been reported to decrease the haemodynamic variability accompanying ECT treatment.[30] In a study investigating the acute cardiovascular depressant effect of remifentanil in patients receiving ECT, addition of 1 μg/kg remifentanil i.v. to 1 mg/kg thiopental i.v. decreased the acute haemodynamic response.[30] The present study showed that the mean heart rate at the time of ECT and during the follow-up period was higher in the remifentanil/sevoflurane group compared with the remifentanil/propofol group.

The present study showed that the rapid induction and rapid recovery objectives in ECT anaesthesia can be achieved with propofol/remifentanil combination anaesthesia. The propofol/remifentanil combination was more effective compared with sevoflurane/remifentanil in terms of length of EEG and motor convulsion, which are important for therapeutic efficacy in ECT.

There are various approaches to dosing strategy in ECT. The titration method involves stimulating a patient with a gradually increasing electrical dose, starting at a low dose to determine the threshold for an induced seizure.[31] Alternatively, starting the ECT dose based on half or three-quarters according, to the patient's age, is recommended for bilateral ECT.[32] The starting ECT dose for patients in the present study was determined to be 30% of the maximum recommended output for the age of the patient.

The authors believe that further large-scale case series studies in ECT are required, to reveal effective drug combinations for anaesthesia that offer good safety profiles and provide ideal conditions for effective seizures.

The results of the present study are limited, however, by the lack of measurement of end-tidal sevoflurane concentrations, since it was not possible to reveal the relationship between depth of anesthesia and sevoflurane concentration during ECT.

In conclusion, propofol/remifentanil combination in ECT anaesthesia management is more effective in providing rapid induction and recovery time, longer seizure activity and stable haemodynamics compared with sevoflurane/remifentanil combination.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not for-profit sectors.

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