Original Article

The Comparison of Hemodynamic Effect of Propofol and Thiopental During Electroconvulsive Therapy: A Prospective Randomized Controlled Trial

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Objective: To compare the hemodynamic effects of propofol with thiopental during electroconvulsive therapy (ECT) in psychiatric patients at the Faculty of Medicine Ramathibodi Hospital.

Materials and Methods: Fifteen patients with ASA physical status I-II undergoing 139 ECT sessions participated in this study. Each patient randomly received either propofol or thiopental followed by succinylcholine for muscle relaxation. The systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), heart rate (HR), oxygen saturation (SpO_2), and bispectral index (BIS) were recorded before anesthetic induction, after induction, before seizure, immediately at the end of the seizure, and at post anesthetic care unit (PACU).

Results: At two to seven minutes after induction, SBP, and DBP was significantly higher in thiopental group than propofol group after receiving treatments (approximately 11 to 22 mmHg, 6 to 13 mmHg, respectively). The HR was significantly decreased in propofol group at two and three minutes (p=0.002), but not significantly different from PACU (p=0.076). The SpO_2 was not significantly different between the two groups. Propofol significantly decreased electroencephalographic (EEG) and motor seizure duration (p<0.001).

Conclusion: Propofol anesthesia provided better hemodynamic responses than thiopental during ECT. Hence, propofol might be a useful alternative to thiopental in patients at higher risk of cardiac complications secondary to marked hemodynamic changes during ECT. However, the duration of seizure in the propofol group was shorter than in the thiopental group.

Keywords: Electroconvulsive therapy, Thiopental, Propofol, Bispectral index, Motor seizure

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Electroconvulsive therapy (ECT) is a valuable non-pharmacological intervention that is a rapid and highly effective psychiatric therapy. It is most commonly used to treat severe mental disorders including schizophrenia, schizoaffective, bipolar affective disorder, and medication resistant depression. ECT provokes a generalized tonic-clonic epileptic seizure, first described in 1938 with unclear exact mechanism of action[1,2]. In Thailand, ECT has been used since 1945[3]. It is performed without anesthetics for almost 30 years. Anesthetic techniques, such as general anesthetics, have evolved to improve the comfort and safety, and to prevent major complications such as cardiovascular instabilities, fracture, transient neurologic ischemic deficits, and intracerebral hemorrhages. The cardiovascular response is associated with the release of catecholamines. Occasional cardiac arrhythmia occurs by activating the autonomic nervous system during ECT stimulation[4,5]. The ideal anesthetic drugs for ECT should have rapid unconsciousness, minimum anticonvulsant properties, minimum effects on the hemodynamic system, rapid recovery, and be

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inexpensive. Nowadays, propofol and a short acting barbiturate such as methohexital, and thiopental are used for induction followed by a muscle relaxant that prevents muscle or bone injuries due to convulsion.

Succinylcholine (Sch) is the drug of choice for muscle relaxation. However, repetitive use of thiopental can cause drug tolerance leading to inadequate depth of anesthesia during the ECT. Therefore, the present study was designed to use depth of anesthesia monitoring to ensure adequate depth of anesthesia. The bispectral index (BIS) monitoring is a continuous, processed electroencephalographic (EEG) that provides a consistent and reliable index of state of consciousness and depth of anesthesia, with scores of 95 or greater typically indicating full consciousness, 65 to 85 for sedation, and 40 to 65 for general anesthesia[6,7].

Therefore, the authors conducted a randomized controlled trial that aimed to compare the hemodynamic effect of propofol with thiopental during ECT in psychiatric patients with BIS monitoring.

Materials and Methods

Informed consents were obtained from patients or their families as appropriate. All protocols were approved by the Medical Ethics Committee of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University (No. MURA2012/567). The study was conducted between January 2013 and January 2014. The participants were eligible for the study if they were adults, aged 18 to 50 years old, with the American Society of Anesthesiologist (ASA) physical status I-II, and scheduled for ECT treatments. All patients underwent at least seven sessions of ECT (three times per week at one- or two-days intervals). Psychiatric rating scales, including brief psychiatric rating scale (BPRS) for schizophrenia, Montgomery-Asberg Depression Rating Scale (MADRS) for depression, and Young Mania rating scale (YMRS) for mania, were used to assess the severity of the symptoms at baseline (24 hours before ECT), after every three sessions of ECT treatment, and after last ECT session. Assessment was performed by the staff and psychiatric residents who were trained. Interrater reliability was done. Intraclass correlation coefficient was 0.99. The definition for remission was determined by BPRS of less than 31 for schizophrenia[8], MADRS of less than 10 for depression[9], and YMRS of less than 10 for mania[10]. ECT was discontinued when patients achieved remission or plateau (no change of psychiatric symptoms after two consecutive ECT treatment).

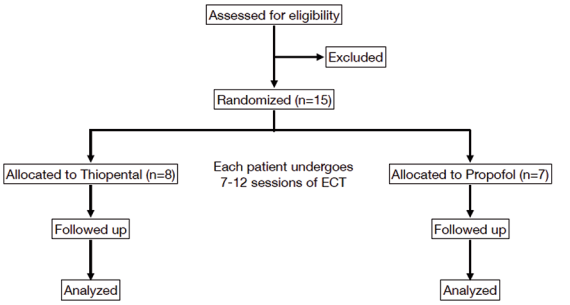

Figure 1. Flow diagram for patient enrollment.

The patients who had a history of cardiovascular or cerebrovascular disease, pregnancy, obesity (BMI greater than 30 kg/m²) and contraindication for using thiopental, propofol, and Sch were not eligible. Each patient was randomly allocated to receive either propofol or thiopental followed by Sch for muscle relaxation (Figure 1). Anesthesia was induced by propofol (1.0 mg/kg) or thiopental (2 mg/kg) intravenously, followed by Sch (0.5 mg/kg) intravenously. The ECT was started when BIS value was in the range of 55 to 60. A soft bite block was inserted before allowing the psychiatrist to administer the electrical stimulus. During the first and second ECT sessions, the authors confirmed that 1.0 mg/kg propofol, 2.0 mg/kg thiopental and 0.5 mg/kg Sch could provide adequate anesthetic conditions and muscle relaxation to all patients. The adequate depth of anesthesia was assured by the BIS value of 55 to 60. The adequacy of muscular relaxation was confirmed before applying the ECT stimulus by testing for a reduction in deep tendon reflexes and muscle tone[11]. In addition, the intensity of the ECT stimulus required to achieve minimal seizure duration of more than 25 seconds was determined during these sessions. The duration of motor and EEG seizure activity were recorded by a blinded investigator as the times from the electrical stimulus to cessation of tonic-clonic motor activity in the isolated foot, which an inflated tourniquet was applied at the beginning of the ECT session to prevent the distribution of Sch, and to postictal EEG suppression, respectively.

Assisted mask ventilation was initiated with 100% oxygen throughout the procedure until the patient has resumed spontaneous and regular respiration. Patients were thereafter transferred to the post anesthetic care unit (PACU). The present study outcomes of interest were hemodynamic parameters, BIS values, and the duration of convulsion. The hemodynamic parameters included systolic blood pressure (SBP), diastolic

blood pressure (DBP), heart rate (HR), and oxygen saturation (SpO_2). These parameters were recorded before and after administration of medications, before and immediately at the end of the seizure, and at PACU. BIS was recorded before and after anesthetic induction, at the beginning of ECT, motor convulsion, EEG convulsion, awakening time from the ECT stimulus to the patient's ability to open eyes and respond to simple verbal commands (squeezing the investigator's hand on command), and at PACU.

Statistical analysis

Simple randomization sequence was generated using Stata Statistical Software. Data were described using mean ± standard deviation (SD) and percentage for continuous and categorical outcomes, respectively. Demographics (age, gender, body mass index [BMI]) and clinical data at baseline (SBP, DBP, HR, and SpO_2) were then compared between the two groups using independent t-test and chi-square test for continuous and categorical data, respectively. A mixed-effect linear regression model was applied to assess treatment effects on SBP, DBP, SpO_2, BIS, and duration of seizure. Treatment, time, and interaction were fitted in the mixed-effect linear regression model. All analyses were performed using Stata, version 13.0 (StataCorp LP, College Station, TX, USA). A p-value of less than 0.05 was considered statistically significant.

Results

Fifteen patients met inclusion criteria and enrolled to the present study with 139 ECT treatment sessions (49 propofol and 90 thiopental). Each patient received at least seven ECT sessions. The ECT was discontinued when patients achieved remission or clinical effect plateau, which was no additional benefits observed for two or three successive ECT sessions[12]. Among the 15 patients, the mean age was 41.3 (SD 12.2) years, and the mean BMI was 24.9 (SD 6.1) kg/m². All patients had ASA class II. Six patients had bipolar affective disorder, four had schizoaffective disorder, three had paranoid schizophrenia, and two had severe depression episode. The baseline characteristics of the participants are displayed by treatment groups in Table 1, and most characteristics were non-statistically different, except gender (p=0.041).

Blood pressures at one to eight minutes after receiving treatments were compared between groups using a mixed linear regression model. This suggested that SBP was approximately 11 to 22 mmHg

Table1. Describe characteristics of the patients in the propofol and thiopental groups

Characteristics	Propofol (n=7) Mean±SD	Thiopental (n=8) Mean±SD	p-value
Age (years)	40.5±7.3	42.0±15.9	0.830
Sex; n (%)			0.041
Male	5 (71.4)	1 (12.5)	
Female	2 (28.6)	7 (87.5)	
BMI (kg/m²)	25.1±6.7	24.8±5.8	0.933
SBP (mmHg)	107.9±11.2	113±7.9	0.300
DBP (mmHg)	69.7±10.9	69.4±7.0	0.943
MAP	87.7±14.3	83.8±12.4	0.495
HR (beats/minute)	80.6±12.9	76.5±10.3	0.508
SpO_2 (%)	99.9±0.4	99.1±1.2	0.160
BIS index	92±8.0	95±2.0	0.290

BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; MAP=mean arterial pressure; HR=heart rate; SpO_2=oxygen saturation; BIS index=bispectal index

significantly higher in the thiopental group compared to the propofol group anytime except at one and eight minutes after receiving the treatments (Figure 2A). A similar trend was also observed for DBP, as the thiopental group had DBP approximately 6 to 13 mmHg significantly higher than the propofol group at two to seven minutes after induction (Figure 2B). Blood pressure observed every five minutes till 30 minutes at PACU, comparing SBP and DBP between groups, indicated that the SBP was not significantly different at each time except at time 5 (p=0.002) and 10 minutes (p=0.040), in which the thiopental group had higher SBP and DBP than the propofol group. A similar trend was observed for DBP, in which it was significant different only at five minutes at PACU (p=0.018), the rest was not significant different.

Treatment effects on HR were further assessed and found significant differences only at two and three minutes (p=0.002) after induction. The thiopental group had approximately 10 beats/minutes higher than the propofol group, whereas the rest of the observed time was not much different (Figure 3), and so did in the PACU.

The treatment effects on BIS were also assessed, which indicated that the BIS values were higher in the thiopental group than in the propofol group significantly, at started ECT, motor convulsion, and EEG convulsion (Figure 4). In addition, the duration of seizure for both motor and EEG were compared between the groups. The mean durations of motor convulsion were 29.9 and 16.0 seconds for

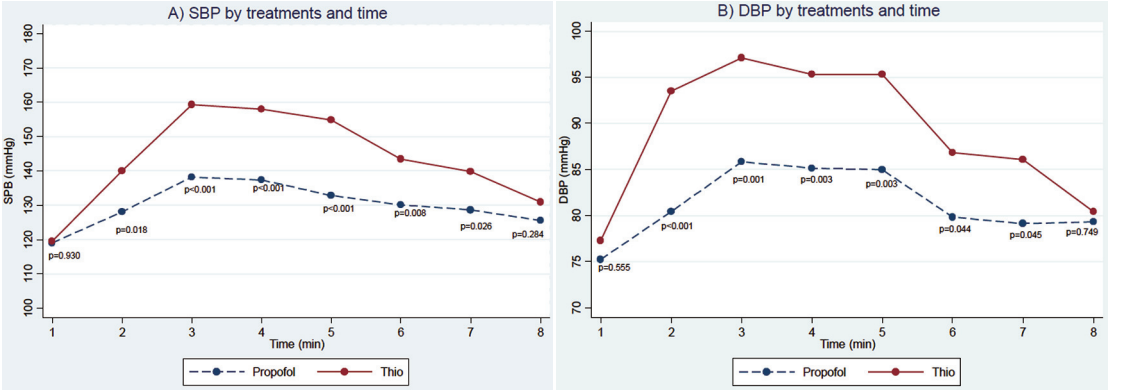

Figure 2. (A) Comparisons of systolic blood pressure between treatments at each time point. (B) Comparison of diastolic blood pressure between treatment at each time point.

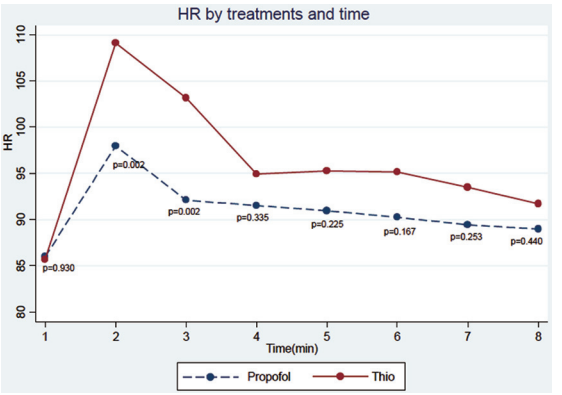

Figure 3. Comparisons of heart rate between treatments at each time.

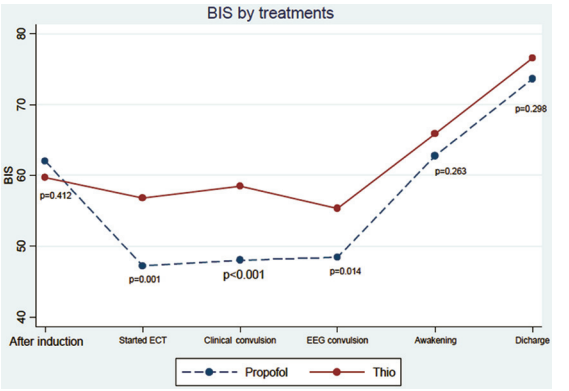

Figure 4. Comparisons of bispectral index (BIS) between treatments at different time points.

the thiopental and the propofol groups, respectively, which were statistically significant ($p<0.001$). Similar trend was found for the duration of EEG convulsion, at approximately 16 seconds significantly (43.3 versus 26.8, $p<0.001$) longer in the thiopental group than in the propofol group.

Patients in both groups required additional dose of propofol and thiopental for loss of responsiveness to verbal commands, and BIS value more than 60. The propofol requirement was 1.4±0.35 mg/kg and thiopental 2.3±0.52 mg/kg. The SpO_2 was similar between the two groups with no statistically significant difference (99.4 versus 99.8 for thiopental and propofol, $p=0.732$).

Discussion

During the electrical seizure of ECT, the typical cardiovascular response consists of an initial parasympathetic mediated bradycardia, followed immediately by a prominent sympathetic response lasting five to seven minutes[13]. The present study found that the thiopental group had increased mean arterial blood pressure more than the propofol group. Hence, propofol anesthesia provides more stabilized hemodynamic response than thiopental. The results of the present study indicate that propofol can reduce the increase of mean arterial blood pressure and DBP as compared to thiopental. A previous study demonstrated that recommended doses for both anesthetic agents in modified ECT ranged from 0.75 to 2.5 mg/kg for propofol and 2 to 5 mg/kg for thiopental[14]. However, sympathetic stimulation by electrical current and the following catecholamine increase overwhelm the hypotensive effects and elevates blood pressure by 20% to 50% as compared to a pre-stimulus value[15,16]. In the present study, the authors used the antihypertensive drug (labetalol) when SBP increased more than 40% from baseline in three sessions of ECT. Propofol has been associated with a reduction in seizure duration[14,17]. Nishihara et

al, 2002 and White et al, 2003 demonstrated that the index could be used to titrate the dose of propofol or methohexital in ECT[18,19]. Nishihara and Saito founded that adjustment of anesthetic depth by referring to the BIS value immediately before electrical stimulation to an elevation of 10% to 20% of BIS values, operators might be able to obtain an appropriate seizure duration for the second ECT treatment when the first treatment was inadequate[20]. The adequacy of muscular relaxation should be ascertained before applying the ECT stimulus. This process is done by testing for a reduction in deep tendon reflexes and muscle tone[11]. Thus, the present study used BIS to determine the depth of the anesthesia.

The current study found that propofol shortened motor and EEG seizure duration as compared to thiopental. The BIS values of propofol decreased more than that of thiopental during the clinical and EEG convulsion when started at the same BIS range (55 to 60) at induction. The lower BIS values in the propofol group might be the reason that causes shortened motor and EEG seizure duration. Further study to find the optimum dose of propofol to give adequate seizure response and stable hemodynamic response will be useful.

Limitation

There are three limitations of the present study. Firstly, the study was done between 2013 and 2014, which is 6 years ago. However, the authors are not aware of any other study related to ECT and anesthetic management in Thailand since then. Secondly, the psychiatric patients are a special group of patients who are vulnerable to anxiety, which may affect the study result. The informed consents in the present study were obtained by the psychiatrist in the research team either from the patients or from the caregivers as appropriate. A good rapport might only slightly affect the anxiety of patients, which was evidenced by no difference in baseline hemodynamic parameters (SBP, DBP, and HRs) in both study groups. Thirdly, the measurements were not blinded since the assessors were in the patient care team. However, all the measurements were objective.

Conclusion

Propofol anesthesia provided better in hemodynamic response than thiopental during ECT. Hence, propofol might be a useful alternative to thiopental in patients who were at higher risk of cardiac complications secondary to marked hemodynamic changes during ECT. However, the duration of seizure in the propofol group was shorter than in the thiopental group.

What is already known on this topic?

There are many studies that compare cardiovascular effects of thiopental and propofol. Some studies showed similar effects, and some revealed less changes in HR and blood pressure with propofol. In addition, it was found that anesthesia with propofol for ECT was associated with shorter seizure duration than with other anesthetics.

What this study adds?

The authors used BIS to ensure adequate depth of anesthesia before the conduct of ECT. This study showed that at the same depth of anesthesia with thiopental and propofol at the beginning, patients in the propofol group continued to have much lower depth of anesthesia significantly from the start of ECT and EEG convulsion. These findings may explain the lower change of hemodynamic parameters and shorter duration of seizure in the propofol group.

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Conflicts of interest

The authors declare no conflict of interest.

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