

# Efficacy of Thiopental and Propofol as Anaesthetic Agents in Electroconvulsive Therapy: A Randomised Double-blind Clinical Study

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## ABSTRACT

**Introduction:** Electroconvulsive Therapy (ECT) is a well-established treatment for severe psychiatric disorders, often requiring the use of anaesthetic agents to ensure patient safety and comfort during the procedure. Thiopental and propofol are two commonly used anaesthetics in this context, each with distinct pharmacological properties and effects on seizure activity.

**Aim:** The present study aimed to assess the differences in seizure characteristics, haemodynamic stability, recovery times, and complications between propofol and thiopental in a tertiary care hospital setting.

**Materials and Methods:** The present randomised, double-blind clinical study was conducted at Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India, from January 2024 to December 2024. Fifty patients were randomly assigned into two groups to receive either thiopental (2 mg/kg) or propofol (1 mg/kg). First-time seizure occurrence and duration of seizure activity were recorded. Haemodynamic stability was assessed through serial measurements of systolic blood pressure,

diastolic blood pressure, and heart rate. Additionally, recovery time and adverse events during 30-minute post procedure period were documented. Continuous variables were analysed and compared using an independent t-test. The association between categorical variables was tested using Chi-square tests and p-value <0.05 was considered statistically significant.

**Results:** In both groups, demographic data including age, sex, and American Society of Anaesthesiologists (ASA) physical status were comparable. First time seizure occurrence in thiopental group was seen in 21 (84%) patients while in the propofol group it was seen in 14 (56%) patients which was statistically highly significant (p=0.03). Seizure duration was statistically significant longer in the thiopental group than in the propofol group (38 sec vs 26 sec, p=0.001). Recovery time and haemodynamic stability were comparable in both groups.

**Conclusion:** Thiopental appears to be a better choice than propofol for induction in patients undergoing ECT due to its association with a significantly higher occurrence of first-time seizure activity and longer duration of seizure activity compared to propofol.

**Keywords:** Anaesthetics, Haemodynamics, Psychiatric disorders, Recovery time, Seizures

## INTRODUCTION

The ECT is a well-established treatment modality for various severe psychiatric disorders, including major depressive disorder, bipolar disorder, and certain forms of schizophrenia [1]. The choice of anaesthetic agents during ECT is crucial, as it can significantly influence both the efficacy of the treatment and the safety profile for patients [2]. Among the commonly used anaesthetics, thiopental and propofol have emerged as two prominent options [3].

Thiopental is an ultra-short-acting barbiturate that has been traditionally used for ECT anaesthesia due to its rapid onset, minimal anticonvulsant properties, and established seizure-facilitating effects [4]. Propofol is a newer intravenous (i.v.) anaesthetic agent with a favourable recovery profile though it possesses stronger anticonvulsant properties that may potentially interfere with seizure induction [5]. Both agents exhibit distinct pharmacological profiles that may differentially impact seizure parameters, haemodynamic stability, and recovery characteristics [6].

The modified ECT approach incorporates the use of general anaesthesia and muscle relaxants, allowing for a more controlled and humane treatment experience [7]. Recently, there has been an increasing interest in incorporating additives such as opioids alongside induction agents for ECT [8]. The addition of an opioid to hypnotics can enhance the overall effect on consciousness levels and help reduce the required dosage of hypnotic agents [9]. Previous studies have demonstrated that propofol was associated with

greater decrease in blood pressure [10,11]. Utilising lower doses of both anaesthetic agents, in conjunction with opioid premedication, could lead to improved haemodynamic stability [12].

Current literature shows inconsistent findings on recovery profiles between thiopental and propofol, with limited data on first-time seizure success rates [11,13,14]. As ECT protocols evolve to incorporate opioid adjuncts in anaesthetic regimens, there is a growing need for evidence-based guidance on optimal anaesthetic selection to maximise therapeutic outcomes while ensuring patient safety [15]. The present study aimed to assess the differences in seizure characteristics, haemodynamic stability, recovery times, and complications between thiopental and propofol in a tertiary care hospital setting. By elucidating these differences, the findings of this study may contribute to optimising anaesthetic practices in ECT and improving patient care in psychiatric treatment.

## MATERIALS AND METHODS

The present randomised, double-blind clinical study was conducted in the Department of Anaesthesiology, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India, from January 2024 to December 2024. The study complied with the ethical standards of Institutional Scientific and Ethical Committee and received formal approval (STU/IEC/2023/202-A).

**Sample size calculation:** Sample size was calculated based on seizure duration as suggested by previous study using the formula

$$n=2 \times (Z\alpha/2 + Z\beta)^2 \times \sigma^2 / \Delta^2 \quad [13].$$

Where:

$n$ =sample size required for each group;

$Z\alpha/2=1.96$  (critical value from standard normal distribution for  $\alpha=0.05$ , two-tailed);

$Z\beta=1.28$  (critical value from standard normal distribution for 90% power);

$\Delta$ =Mean difference ( $36.3-25.7=10.6$ );

$\sigma$ =Pooled Standard Deviation (SD) ( $\sigma=\sqrt{\{(13.2^2+8.3^2)/2\}} \approx 11.03$ );

In the study, mean seizure duration for the thiopental group was  $36.3 \pm 13.2$  seconds, while for the propofol group, it was  $25.7 \pm 8.3$  seconds.

$$n=2 \times (1.96+1.28)^2 \times 11.03^2 / 10.6^2$$

$$n=2 \times (3.24)^2 \times 121.66 / 112.36$$

$$n=2 \times 10.50 \times 1.08$$

$$n \approx 23 \text{ patients per group}$$

Based on this formula, they calculated that enrollment of a minimum of 46 patients (23 per group) was needed, with a 95% confidence interval, 90% power, and an alpha level of 0.05. To account for potential dropouts, we enrolled 50 patients (25 per group).

**Inclusion criteria:** Patient admitted to the hospital for ECT in the age group >18 years and having ASA I or II were included in the study.

**Exclusion criteria:** Patients who had ASA III or IV, history of adverse reactions to the studied anaesthetic drug, substance abuse disorder in the last 12 months and patients unwilling to be a part of the study were excluded in the study.

## Study Procedure

Fifty patients were randomised into two groups using computer-generated randomisation numbers to receive either thiopental or propofol [Table/Fig-1]. The random allocation sequence generation and patient enrollment were done by the index Anaesthesiologist (not a part of study). The preparation of the drugs was also performed by the index Anaesthesiologist according to group. The second Anaesthesiologist conducting the case as well as collecting the data was unaware of the drug being given. All patients underwent a preoperative evaluation, which included an airway assessment, and written consent was obtained. Patients were prepared for ECT according to institutional policy. Non-invasive Blood Pressure (NIBP), Electrocardiogram (ECG), and pulse oximetry were

monitored throughout the ECT procedure. A tourniquet was applied to the contralateral arm from which i.v. drugs were administered to exclude that arm from neuromuscular blocking action and to allow for the assessment of seizure duration (from the administration of ECT to the complete subsiding of tonic-clonic movements).

Before induction, patients were preoxygenated with 6-8 L/min of 100% oxygen. Anaesthesia was induced with fentanyl (1.0 mcg/kg bolus), followed by a bolus of either thiopental (2 mg/kg) or propofol (1 mg/kg) over a period of 20 seconds, according to the allocated group [16,17].

After the loss of the eyelash reflex, succinylcholine (0.5 mg/kg bolus) was administered to achieve muscular paralysis and prevent trauma from seizures. At the end of the muscular fasciculation phase, ECT was performed. Manual ventilation assistance through a face mask with 100% oxygen was provided during induction and after the electrical stimulus until the return of spontaneous respiratory activity. Patients were transferred to the recovery room after achieving adequate consciousness and psychomotor recovery.

The primary outcomes of the present study were to measure first-time seizure occurrence and the duration of seizure activity. First-time seizure occurrence was evaluated by measuring the success rate of first-attempt seizure following initial electrical stimulus administration, recorded as a binary outcome. Seizure duration in seconds was timed from the moment of electrical stimulus delivery until the complete cessation of tonic-clonic movements in the isolated limb.

Secondary outcomes included haemodynamic stability, recovery profile, and safety parameters. Haemodynamic stability was evaluated through serial measurements of systolic blood pressure, diastolic blood pressure, and heart rate at five time points: baseline (preinduction), immediately after induction, and at 1, 5, and 30 minutes post-ECT. Recovery profile was determined by measuring the time interval (in seconds) from anaesthetic induction to first eye opening in response to verbal commands, which were issued at one-minute intervals following seizure cessation. Safety assessment consisted of monitoring for adverse events during the 30-minute post-procedure period, including oxygen desaturation episodes ( $\text{SpO}_2 < 90\%$ ), respiratory complications (laryngospasm, bronchospasm), post-ECT nausea and vomiting, and any other anaesthesia-related adverse effects.

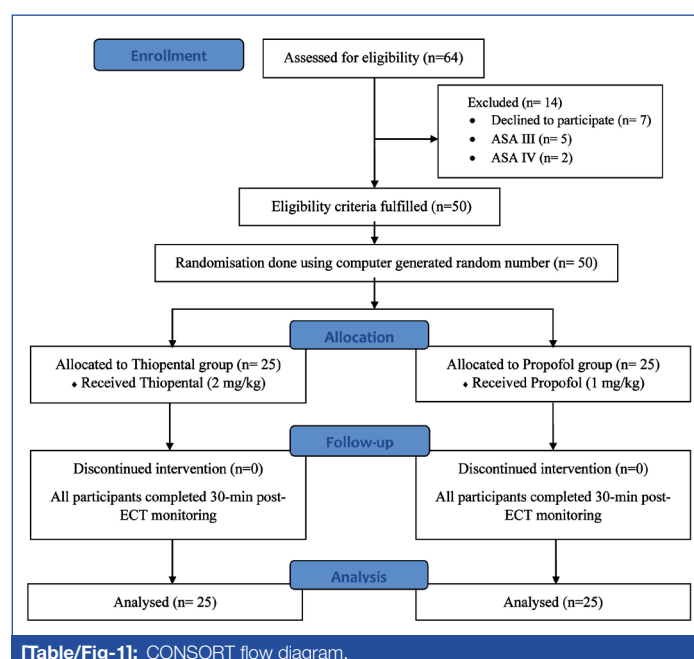
## STATISTICAL ANALYSIS

The statistical analysis for the study was conducted using IBM Statistical Package for Social Sciences (SPSS) version 25.0 (SPSS Inc., IBM Corporation, NY, USA), with the data compiled and organised in a Microsoft Excel spreadsheet. Descriptive statistics were computed to determine percentages, means, and Standard Deviation (SD) of the collected data. Statistical tests, such as the independent t-test for continuous variables and Chi-square test for ASA physical status were employed for data analysis. A p-value  $\leq 0.05$  was considered significant.

## RESULTS

A total of 50 patients were included in this study, 25 patients in each group. In thiopental group, the mean age was  $52 \pm 12.1$  years, while in the propofol group, it was  $48 \pm 10.8$  years with no statistically significant difference between them ( $p=0.11$ ) [Table/Fig-2]. Out of the total 50 participants, 15 were males in the Thiopental group, and 13 were males in the propofol group, while 10 females were in the thiopental group, and 12 females were in the propofol group which was also not statistically significant ( $p=0.56$ ) [Table/Fig-2].

First time seizure occurrence in the thiopental group was seen 21 patients (84%) while in the propofol group it was seen in 14 patients (56%) which was statistically significant ( $p=0.03$ ) [Table/Fig-3]. The mean seizure duration in the thiopental group was  $38 \pm 4.6$  seconds while in the propofol group it was  $26 \pm 5.9$  seconds, difference was statistically highly significant ( $p=0.001$ ) [Table/Fig-3].



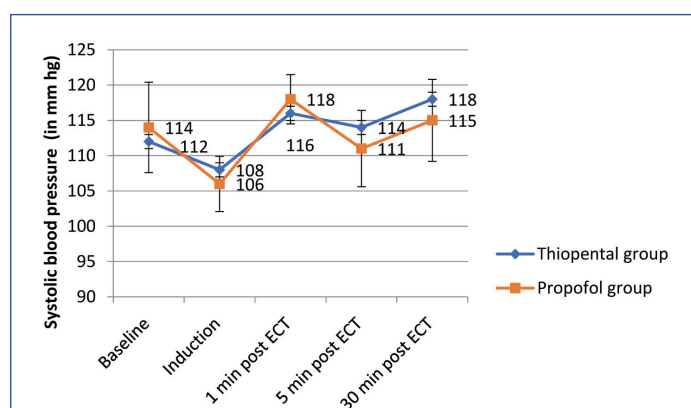
Baseline	Thiopental group (n=25)	Propofol group (n=25)	p-value
Age, years	52±12.1	48±10.8	0.11
Male, n (%)	15 (60 %)	13 (52 %)	0.56
Female, n (%)	10 (40 %)	12 (48 %)	0.56
ASA physical status I/II	19/6	21/4	0.48

[Table/Fig-2]: Baseline characteristics of included patients.

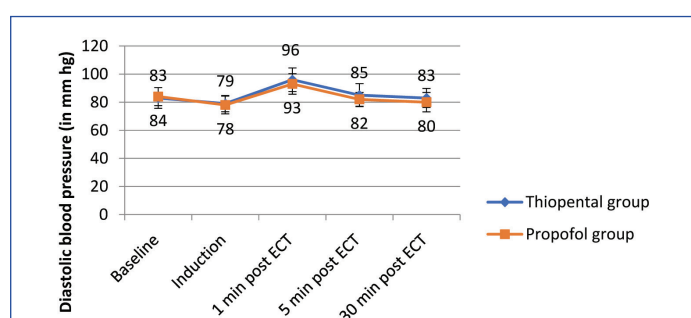
Baseline	Thiopental group (n=25)	Propofol group (n=25)	p-value
First time seizure occurrence, n (%)	21 (84%)	14 (56%)	0.03
Seizure duration, seconds	38±4.6	26±5.9	0.001

[Table/Fig-3]: Incidence and duration of seizure after ECT session.

The changes in systolic blood pressure, diastolic blood pressure, and heart rate from the baseline, induction, one minutes post ECT, five minutes post ECT, 30 minutes post ECT were recorded [Table/Fig-4-6]. There was no statistically significant difference found in either of the two groups. The time to eye opening in the thiopental group was 488.87±52.10 seconds while in the propofol group it was 476.57±43.68 seconds, difference was not statistically significant ( $p=0.37$ ) [Table/Fig-7]. No oxygen desaturation episodes and adverse effects related to anaesthesia were recorded in either group.



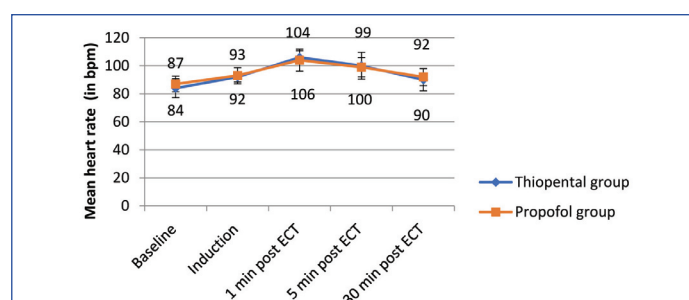
[Table/Fig-4]: Graph showing mean and standard deviations of systolic blood pressure of patients undergoing ECT.



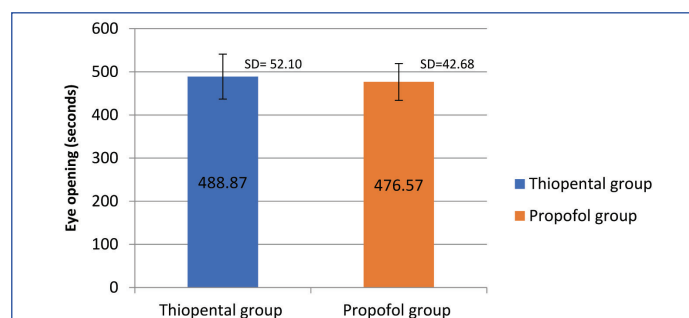
[Table/Fig-5]: Graph showing mean and standard deviations of diastolic blood pressure of patients undergoing ECT.

## DISCUSSION

In the present study, we compared thiopental and propofol as induction agents for ECT. Since both thiopental and propofol possess anticonvulsant activity, we used fentanyl as premedication to reduce the doses of the study drugs. In the present study, the authors found that the first occurrence of seizure activity was significantly higher in the thiopental group compared to the propofol group (84% vs 56%,  $p=0.03$ ), and the duration of seizures was significantly longer in the thiopental group than in the propofol group ( $38\pm4.6$  vs  $26\pm5.9$ ,  $p=0.001$ ). Similar results were reported in studies by Nuzzi M et al., Patil M et al., Manasa SS et al., and Gaddam NR et al., [16,18-20]. Nuzzi M et al., found seizure occurrence was significantly higher



[Table/Fig-6]: Graph showing mean and standard deviations of the heart rate of patients undergoing ECT.



[Table/Fig-7]: Graph showing mean and standard deviations of recovery time of patients following ECT.

in the thiopental group (81% vs 52%,  $p=0.023$ ) and also seizure duration significantly longer in the thiopental group (35 sec vs 11 sec,  $p=0.046$ ) [16]. Patil M et al., found that the mean seizure duration of the thiopental group was  $50.83\pm8.45$  seconds vs. the propofol group,  $34.70\pm8.68$  seconds; this difference was statistically significant [18]. Manasa SS et al., found that the mean seizure duration between thiopental and propofol (28.3 vs. 20.9 s) was statistically significant ( $p<0.01$ ) [19]. In a similar study conducted by Gaddam NR et al., they observed that the seizure duration was longer in the thiopental group ( $30.78\pm12.80$ ) compared to the propofol group ( $24.85\pm10.72$ ), although this difference was not statistically significant [20].

Haemodynamic parameters were comparable in both groups, which aligns with the findings of Nuzzi M et al., who also found no haemodynamic instability between both groups [16]. In a previous study by Martínez-Amorós E et al., the propofol group exhibited a statistically significant decrease in systolic and diastolic blood pressure compared to the thiopental group [11]. Cardiovascular parameters showed significantly attenuated changes in the propofol group versus thiopental, with markedly smaller increases in both systolic ( $14.74\pm12.83$  vs  $47.04\pm14.12$  mmHg,  $p<0.001$ ) and diastolic blood pressure ( $6.52\pm8.36$  vs  $28.52\pm9.94$  mmHg,  $p<0.001$ ) from initial to final ECT session [11].

Another study by Jarineshin H et al., also showed significantly lower systolic and diastolic blood pressure with propofol compared to thiopental [21]. The propofol group exhibited significantly lower systolic blood pressures immediately after seizure ( $138.8\pm17.85$  vs  $148.96\pm15.09$  mmHg,  $p<0.001$ ), at three minutes ( $124.52\pm12.5$  vs  $132.18\pm11.77$  mmHg,  $p<0.001$ ), and at five minutes post-seizure ( $118.06\pm12.19$  vs  $123.40\pm10.06$  mmHg,  $p=0.002$ ). Similarly, diastolic blood pressures were significantly lower in the propofol group at all post-seizure intervals ( $p<0.001$ ,  $p=0.006$ , and  $p=0.009$ , respectively) [21]. The haemodynamic stability observed in the present study may be attributed to the lower doses of thiopental and propofol used, compared to the study by Martínez-Amorós E et al., and Jarineshin H et al., [11,21].

Recovery time was statistically insignificant in both groups, which is similar to the study conducted by Bauer J et al., Nuzzi M et al., and Verma A et al., [13,16,22]. The use of fentanyl as a premedication in the present study likely allowed for lower doses of both thiopental and propofol, which may have contributed to a quicker return to



baseline cognitive function, thereby potentially equalising recovery times between the two groups during ECT. However, this contrasts with the studies by Butterfield NN et al., Shah PJ et al., Kayalha H et al., and Manasa SS et al., who observed earlier recovery with propofol compared to thiopental [19,23-25].

In a study by Butterfield NN et al., recovery time was significantly shorter after propofol (9.9±2.8 minutes) compared to thiopental (12.1±4.2 minutes) ( $p<0.05$ ) [23]. Recovery time, was also significantly shorter with propofol (4.56 minutes) compared to thiopental (6.6 minutes) in a study by Shah PJ et al., ( $p<0.05$ ) [24]. In another study by Kayalha H et al., the mean duration of recovery was shorter with propofol (9±3 minutes) compared to thiopental sodium (13±5 minutes) ( $p<0.05$ ) [25]. Similarly, Manasa SS et al., reported that recovery time was significantly shorter for propofol (311.5±58.6 seconds) compared to thiopental (467.0±72.2 seconds) ( $p<0.01$ ) [19]. In these studies, higher doses of both anaesthetic agents were used (propofol 1.5-2.5 mg/kg and thiopental 3-5 mg/kg) without opioid premedication [19,23-25]. Propofol facilitates faster recovery in ECT due to its rapid redistribution and metabolism, leading to a shorter elimination half-life as compared to thiopental. This results in swift clearance from the body and a quicker return of cognitive function. No episodes of oxygen desaturation, or adverse effects related to anaesthesia were recorded in either group, which is consistent with studies conducted by Verma A et al., and Nuzzi M et al., [16,22].

### Limitation(s)

The study only included ASA 1 or 2 patients, excluding those with more complex medical conditions who might respond differently to the anaesthetic agents. There was no analysis based on psychiatric diagnosis, which might affect seizure threshold and response to anaesthetics.

## CONCLUSION(S)

In the present study, thiopental appears to be a better choice than propofol for induction in patients undergoing ECT due to its association with a significantly higher occurrence of first-time seizure activity and longer duration of seizure activity compared to propofol. Importantly, both groups exhibited no haemodynamic instability, oxygen desaturation, or adverse events when used in conjunction with fentanyl. Additionally, recovery times were similar in both groups. However, anaesthetic selection should ultimately be individualised based on patient characteristics, co-morbidities, and treatment goals. Future research with larger sample sizes, across multiple centers, and incorporating psychiatric outcome measures would further strengthen these findings and help establish more definitive practice recommendations.

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- For any images presented appropriate consent has been obtained from the subjects. NA

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