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Original Research Article

EFFECTIVENESS OF THIOPENTONE AND PROPOFOL AS INTRAVENOUS INDUCTION AGENTS FOR MODIFIED ELECTROCONVULSIVE THERAPY: A COMPARATIVE STUDY

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Abstract

Background: To evaluate the comparative effectiveness of Thiopentone and Propofol as intravenous induction agents for modified Electroconvulsive therapy (ECT) by analyzing various parameters such as the onset of action, depth of anesthesia, muscle relaxation quality, seizure activity quality, and adverse effects. **Materials and Methods:** This prospective study involved 60 patients who met the inclusion criteria for modified ECT and were randomly assigned to either the Thiopentone group or the Propofol group, with 30 patients in each group. The ECT procedure was conducted in accordance with international standards approved by the institution. A brief pulse stimulus of 90-120 volts was applied for approximately 2 seconds to induce seizure. Induction time (defined as the time from intravenous anesthetic agent injection to the loss of eyelash reflex) and the quality of induction, seizure duration, side effects, and complications were recorded for both groups. Descriptive statistics were used to describe baseline participant characteristics. The collected data was statistically analyzed using the Chi-square test where appropriate, and a p-value of less than 0.05 was considered significant. **Result:** The study found a statistically significant increase in mean heart rate in the Thiopentone group compared to the Propofol group. Additionally, both systolic and diastolic blood pressure showed an increase from 1-2 minutes post ECT in both groups. However, at 2 minutes post ECT, the Thiopentone group showed a 40% increase in systolic blood pressure compared to a 9% increase in the Propofol group. **Conclusion:** Propofol is a safer choice of induction agent for ECT when compared to Thiopentone. Propofol provides better hemodynamic stability, faster induction, and a smoother and quicker recovery profile. Furthermore, Propofol has fewer post-ECT complications when compared to Thiopentone. Overall, these findings suggest that Propofol is a preferable induction agent for ECT when considering patient safety and efficacy.

INTRODUCTION

Electroconvulsive therapy (ECT) involves inducing seizures through the application of electrical stimulation in an anesthetized patient.[1] It is an established therapy used primarily to treat severe major depressive disorders with suicidal tendencies that have not responded to other forms of treatment. ECT also plays a crucial role in the treatment of other psychiatric conditions such as mania, catatonia, schizophrenia, and neuroleptic malignant syndrome.[2] The primary goal of ECT is to induce a generalized tonic-clonic seizure lasting at least 20-30 seconds. Another important measure of the clinical efficacy of ECT is the cumulative seizure time duration, which is the total duration of all seizure activities during the treatment period.[3] ECT is generally considered to be a safe procedure that is well-tolerated by patients. However, there are rare complications associated with ECT such as prolonged apnoea, dental injuries, cardiac ischemia, tongue laceration, and status epilepticus.[4,5] Additionally, ECT has been reported to cause significant changes in the autonomic nervous system (ANS) such as tachycardia and elevation in blood pressure, as well as arrhythmias such as sinus tachycardia, ventricular tachycardia, and premature ventricular contractions (PVC).[6-8] The crude form of ECT was first introduced in 1937 by Cerlett and Bini,

which did not involve the use of sedation, neuromuscular blockade, or supplementary oxygenation. However, over time, the clinical practice of ECT has evolved, and the use of anesthetics, muscle relaxants, and controlled ventilation with oxygen became more widespread. This led to the development of "modified ECT," which made the use of unmodified ECT unjustified and unethical. The introduction of these modifications also highlighted the pivotal role of anesthesiologists in the administration of ECT.[9] To ensure safe and effective anesthesia during ECT, it is crucial to use an appropriate anesthetic agent. Ideal anesthesia should provide rapid and smooth induction, rapid recovery, and transient effect on the autonomic nervous system (ANS). Several anesthetic agents are used for ECT, including Thiopentone, Propofol, midazolam, etomidate, and methohexitone. Thiopentone is an ultra-short-acting barbiturate that induces anesthesia smoothly with positive allosteric modulators activity at GABA and glycine receptors.[10] Propofol is a selective modulator of GABA and an intravenous sedative and hypnotic.[11,12] The aim of this study was to compare the effects of Thiopentone and Propofol on hemodynamic changes during ECT, as well as on seizure duration and recovery profiles.

MATERIALS AND METHODS

The present study was conducted at the Department of Anaesthesiology, D.Y Patil Hospital, D.Y. Patil University School of Medicine, Nerul, Navi Mumbai, for a period of 2 years (Oct 2016-Oct 2018). It was a prospective observational study with a sample size of 60 patients, randomly divided into two groups of 30 each, namely the Thiopentone and Propofol groups. Simple random sampling technique was used to select eligible patients, including adults between 18 to 65 years of age, diagnosed with major depressive disorder or bipolar disorder (ICD-10 code 296), with ASA status I & II, undergoing elective electroconvulsive therapies, and with normal clinical and laboratory investigations and stable hemodynamics. Patients who were unwilling to participate, had coagulation problems, injection site infection, allergy to study drugs, pregnant or breastfeeding, or with ASA status III and IV were excluded from the study.

Study Procedure

The study commenced after receiving approval from the institutional ethics committee and obtaining informed consent from eligible participants who were randomly assigned to either the thiopentone or propofol group, with 30 participants in each group. All participants were kept nil per oral and attached to monitors measuring ECG, pulse rate, NIBP, and SpO2 before the procedure. These monitors were checked at intervals of 1, 2, 5, and 10 minutes, as well as 30 minutes and 1 hour after the procedure. Prior to the procedure, all patients received a premedication of i.v. glycopyrrolate 0.2 mg and were preoxygenated for 3 minutes. General anaesthesia was induced using intravenous anaesthetic agents, with dosages of thiopentone at 2-3 mg/kg and propofol at 1-1.5 mg/kg, as per the allocated group, until the loss of eyelash reflex.

Following neuromuscular relaxation induced by intravenous succinylcholine (0.5-1 mg/kg), patients were ventilated with 100% O2 at a fresh gas flow rate of 4-6 l/min without the use of any inhalational agent. ECT was performed in accordance with international standards approved by the institution, using a brief pulse stimulus (90-120 volts MECT) for about 2 seconds to produce seizure. The study recorded the induction time (i.e., from the time of injecting intravenous anaesthetic agent to loss of eyelash reflex) and quality of induction, seizure duration, and any side effects or complications that arose in both the Thiopentone and Propofol groups.

Statistical analysis

Descriptive statistics like mean and standard deviation (SD) were used to describe baseline study participant parameters. Parametric tests were used to analyze parametric data if passed the tests of normality; if failed, then non- parametric tests were used for analysis. The data collected was statistically analysed using Chi-square test wherever applicable and the p value less than 0.05 was considered statically significant. The data analysis was performed using the GraphPad software.

RESULTS

The study compared the demographic parameters between the Thiopentone and Propofol groups [Table 1]. The mean age of the Thiopentone group was 32.6 ± 9.37 years, while that of the Propofol group was 37.3 ± 14.52 years, with no statistically significant difference between them (p=0.295). The mean weight of the Thiopentone group was 52.11 ± 11.70 kg, and that of the Propofol group was 53.79 ± 11.17 kg, with no significant difference between them (p=0.667). Out of the total 60 participants, 23 were males in the Thiopentone group, and 16 were males in the Propofol group, while 7 females were in the Thiopentone group, and 14 females were in the Propofol group. Ten patients in the Thiopentone group were on concurrent medication (antidepressants or antipsychotics), while 8 patients in the Propofol group were on concurrent medication. Only one patient in each group had pre ECT physical risk factors such as hypertension. The Thiopentone group received a mean dose of 76.20 ± 14.76 mg (range: 60-100 mg), while the Propofol group received a mean dose of 120 ± 28.30 mg (range: 100-200 mg).

[Table 2] displays the changes in heart rate before and after ECT in the two. There was no statistically significant difference between the groups in the heart rate before ECT (p=0.903). However, there was a statistically significant difference between the groups

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in the heart rate at the 2nd minute after ECT (p=0.043). No statistically significant difference was observed in the heart rate at 1st, 5th and 10th minute post ECT. There was an increase in heart rate from second minute onwards in both groups with a maximum increase by 5th minute, with the thiopentone group registering a higher heart rate than the propofol group.

The data presented in [Table 3] demonstrate the changes in systolic blood pressure in both groups. The baseline systolic BP was not significantly different between the two groups. However, both groups showed an increase in systolic BP after ECT administration. The increase was more pronounced in the thiopentone group compared to the propofol group. The data also reveal that there was a gradual increase in BP from the 2nd to 5th minute, with a statistically significant increase in BP observed in the thiopentone group compared to the propofol group. Therefore, it can be concluded that the two groups showed differential changes in SBP following ECT administration.

[Table 4] displays the changes in diastolic blood pressure (DBP) between the two groups. Similar to the SBP, the baseline difference in DBP between the two groups was not significant. Post-ECT administration, there was an increase in DBP in both groups. However, the increase in DBP was significantly higher in the thiopentone group compared to the propofol group. The maximum increase in DBP was observed around 1-2 minutes after ECT administration.

[Table 5] presents the ECT treatment and recovery parameters of both groups. The thiopentone group had a longer mean seizure duration compared to the propofol group, and the propofol group required a higher stimulus intensity than the thiopentone group, with a statistically significant difference between the two groups. Although the number of patients requiring re-stimulation was higher in the propofol group than in the thiopentone group, the difference was not statistically significant. The propofol group had a significantly faster rate of eye opening and obeying command compared to the thiopentone group. However, there were no significant differences observed in orientation between the thiopentone and propofol groups.

Table 1: Demographical Data of all study participants (n=30 in each group)

Parameter	Thiopentone	Propofol	Range	P value
Age (years) Mean ±/- SD	32.6 ± 9.37	37.3 ± 14.52	18-62	0.295
Weight (kg) Mean ±/- SD	52.11 ± 11.70	53.79 ± 11.17	29-85	0.667
Male	23	16	-	-
Female	7	14	-	-
Patients on concurrent medication (antidepressants or antipsychotics)	10/30	08/30	-	-
Patients with pre ECT physical risk factors such as hypertension	01/30	01/30	-	-
Dose of anaesthetic agent	76.20 ± 14.76 (Range: 60-100 mg)	120 ± 28.30 (Range: 100-200 mg)		
*Calculated using t-test. P-value < 0.05 considered statistically significant.				

Table 2: Changes in Heart rate before and after ECT (n=30 in each group)

Parameters		Mean ± SD		't' Value	p-value
		Group T	Group P		
Pre ECT		90.30 ± 9.38	90.50±8.36	0.44	0.903
Post ECT	1st min	95.88±8.80	94.28±9.5	0.50	0.676
	2nd min	108.81±6.99	95.38±9.72	0.14	0.043
	5th min	106.75±6.09	97.37±6.19	0.64	0.063
	10th min	105.38±89.25	89.25±7.03	5.287	0.04
*Calculated using t-test. P-value < 0.05 considered statistically significant.					

Table 3: Changes in SBP before and after ECT (n=30 in each group)

Parameters		Mean ± SD		't' Value	p-value
		Group T	Group P		
Pre ECT		127.63±11.97	125.33±10.68	0.55	0.59
Post ECT	1st min	137.77±13.07	128.77±14.85	2.220	0.002
	2nd min	154.1±24.5	138.9±23.1	2.570	0.008
	5th min	148.3±14.42	134.6±9.97	2.643	0.04
	10th min	130.40±7.58	126.43±9.15	1.988	0.06
*Calculated using t-test. P-value < 0.05 considered statistically significant.					

Table 4: Changes in DBP before and after ECT (n=30 in each group)

Parameters		Mean ± SD		't' Value	p-value
		Group T	Group P		
Pre ECT		81.07±7.68	84.67±6.77	1.34	0.185
Post ECT	1st min	98.1±11.45	90.27±9.3	2.03	0.047
	2nd min	92.43±7.63	83.47±6.75	3.36	0.001

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	5th min	86.47±6.74	81.4±6.81	2.01	0.049
	10th min	83.6±5.48	79.53±5.24	1.74	0.087
*Calculated using t-test. P-value < 0.05 considered statistically significant.					

Table 5: ECT treatment and recovery parameters of both groups (n=30 in each group)

Parameters		Mean ± SD		't' Value	p-value
		Group T	Group P		
ECT Treatment parameters	Mean seizure duration (sec) mean ± SD	41.79±11.7	29.59±8.97	12.2	0.004
	Max. Stimulus intensity (seizure threshold) mean ± SD	165±55.59	276±90.99	4.08	0.001
	No. of patients who required Restimulation	5/30	9/30	0.8789	0.3831
Recovery Parameters	Eye Opening (mins)	9.03±2.20	7.40±1.98	2.192	0.009
	Obey (mins)	11.5±2.74	10.10±1.68	1.974	0.006
	Orientation	14.20±4.35	12.25±1.92	1.853	0.08
*Calculated using t-test. P-value < 0.05 considered statistically significant.					

DISCUSSION

This is a prospective randomized study was conducted to compare Thiopentone versus Propofol with respect to hemodynamic parameters, seizure duration, recovery, complications and outcome in a mixed group of 60 depressed and maniac patients. Both the groups were matched by demographic and clinical variables.

The presents study found that the Thiopentone group had a consistent increase in mean heart rate from the 2nd minute onwards, which continued up to the 10th minute. On the other hand, the Propofol group had a peak mean heart rate around the 5th minute, after which it returned to baseline heart rate by the 10th minute. The difference in mean heart rate between pre ECT heart rate and peak heart rate was considerably higher in the Thiopentone group (16.08 beats/min) compared to the Propofol group (6.87 beats/min). These results are consistent with a study conducted by Boey et al, who observed a significant increase in heart rate in the Thiopentone group compared to the Propofol group.[13] The findings were also supported by Park et al, who noted that Propofol had a lesser impact on haemodynamic changes.[14] The study observed that the increases in the mean heart rate were significantly higher in group T compared to group P, and that Propofol use had a significant protective effect on the cardiovascular system as a whole.

The increase in SBP and DBP was observed in both groups from 1-2 minutes post ECT, with a higher increase in the Thiopentone group compared to the Propofol group. The Thiopentone group showed a 40% increase in systolic blood pressure at 2 minutes post ECT, while the Propofol group showed a 9% increase. The Thiopentone group also showed a higher increase in BP at 2nd, 5th, and 10th minute readings compared to the Propofol group. These findings are consistent with a study by Kadoi et al, which showed decreased end systolic area and fractional area change in the Propofol group compared to the Thiopentone group.[15] Similar observations were made by Boey et al, who also reported lesser increases in mean systolic and diastolic pressure in the Propofol group compared to the Thiopentone group.[13] Another study by Muiler et al demonstrated that the attenuation of hyperdynamic state with Propofol was more pronounced than with equipotent doses of thiopentone when given as a single bolus, which is consistent with the results of the present study.[16]

The dose of anaesthetics used for ECT has been found to have an impact on the degree of attenuation of haemodynamic responses after ECT. In this study, Propofol was administered at a dose of 1mg/kg. Other studies have reported different doses of Propofol. For instance, Fredman et al used a lower dose of 0.75mg/kg and reported improved haemodynamic stability, with a slight increase in post-ictal haemodynamic values above the pre-ictal values[17]. On the other hand, Mulier et al used a higher dose of 1.4mg/kg and reported that Propofol reduced systolic arterial blood pressure below the baseline values.[16]

The therapeutic efficacy of electroconvulsive therapy (ECT) depends on the mean seizure duration. The seizure must last for more than 20 seconds to have a positive effect. In this study, Thiopentone showed a significantly higher mean seizure duration of 41.79±11.7 seconds at a dose of 2.5mg/kg as compared to the propofol group (29.59±8.97 seconds). This finding is consistent with a previous report by Boey et al, which also demonstrated that the use of propofol was associated with significantly shorter motor and EEG seizure duration.[13] It should be noted that higher doses of propofol can reduce seizure duration to less than the acceptable therapeutic level, which is a duration of seizure longer than 20 seconds.[18]

The results of this study revealed that the propofol group required a higher stimulus intensity compared to the thiopentone group, and this difference was statistically significant. This finding is consistent with the results of a study conducted by Mitchell and Smythe, who reported a decrease in ACTH, prolactin, and cortisol levels in the propofol group compared to the thiopentone group. This decrease in hormone levels was attributed to the shorter mean seizure duration observed in the propofol group. Therefore, it can be inferred that the dose of anaesthetic used can influence the therapeutic efficacy of ECT by affecting the seizure duration and subsequent hormonal changes.[19]

In ECT, seizure threshold can vary significantly among subjects, with most individuals having a threshold above 150 mC, and only a few having very

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high thresholds ranging from 400 to 800 mC. In this study, the patients' seizure threshold was found to be within the range of 150 mC to 400 mC. The results of the study showed that patients in the propofol group required a higher mean stimulus intensity to achieve adequate seizures than those in the thiopentone group. Specifically, the mean stimulus intensity was 165 mC in the thiopentone group, while it was 276 mC in the propofol group.

The study evaluated the recovery characteristics of patients, which included eye opening, obeying commands, and orientation to time, place, and person. The mean duration of eye opening in the Propofol group was significantly shorter (7.40 minutes) than in the Thiopentone group (9.03 minutes) ($p<0.05$). The mean duration of obeying commands was also significantly shorter in the Propofol group (10.10 minutes) than in the Thiopentone group (11.5 minutes) ($p<0.05$). However, there was no significant difference in the mean duration of orientation to time, place, and person between the two groups, with the Propofol group showing a mean duration of 12.25 minutes and the Thiopentone group showing a mean duration of 14.20 minutes ($p>0.05$). The Propofol group showed earlier recovery characteristics than the Thiopentone group.

Similar findings were reported by Butterfield N et al and Gracia et al, who also observed earlier recovery with Propofol compared to Thiopentone.[20,21] However, in contrast to these studies, Matters et al reported that the more rapid recovery rates noted with Propofol in other procedures were not evident after electrically induced seizures.[22]

CONCLUSION

In conclusion, our study demonstrates that the use of Propofol as an induction agent for Modified ECT is a safer option when compared to Thiopentone, in terms of better hemodynamic stability, quicker induction with a smoother and faster recovery profile, and fewer post-ECT complications. This finding is particularly relevant for treating a large number of outpatients. Therefore, we recommend the use of Propofol over Thiopentone in Modified ECT procedures. It is important to note, however, that our study's limitation is its relatively small sample size.

REFERENCES

1. Boiteux J, Roubaud L, Gendelet N, et al. Indications for electroconvulsive therapy. Encephale. 1997; 23; 21-6.
2. Fink M. Electroconvulsive therapy update: recognizing and treating psychotic depression. Journal of Clinical Psychiatry. 2003; 64: 232 –4.
3. Dwyer R, McCaughey W, Lavery J, et al. Comparison of propofol and methohexitone as anaesthetic agents for electroconvulsive therapy; effects on haemodynamic response and seizure duration. Anesthesiology. 1989; 70: 412 – 7.
4. Abrams R. Electroconvulsive therapy. New York: Oxford Press, 1998.
5. Weiner RD, Coffey CE. Practical issues in the use of electroconvulsive therapy (ECT). Psychiatr Med. 1991;9(1):133-41
6. Jones RM, Knight PR: Cardiovascular and hormonal responses to ECT. Anesthesia. 1981; 36: 795–9.
7. O' Flaherty D, Hussain MM, Moore M, Wolff TR, Sills S, Giesecke AH: Circulatory response during electroconvulsive therapy. Anesthesia. 1992; 47: 563–7.
8. Arneson GA, Butler T. Cardiac arrest and electroshock therapy. Am J Psychiatry. 1961;177:1020–2.
9. American Psychiatric Association. Electroconvulsive Therapy: Task Force Report No. 14. Washington, DC: American Psychiatric Association; 1978.
10. Russo HI, Bressolle F. Pharmacodynamics and pharmacokinetics of thiopental. Clin Pharmacokinet. 1998;35(2):95-134.
11. Paul F. White. Propofol: Its Role in Changing the Practice of Anesthesia. Anesthesiology. 2008;109:1132-6.
12. G Trapani, C Altomare, G Liso, E Sanna, G Biggio. Propofol in anesthesia. Mechanism of action, structure-activity relationships, and drug delivery. Curr Med Chem. 2000;7(2):249.
13. Boey WK, Lai FO. Comparison of propofol and thiopentone as anaesthetic agents for electroconvulsive therapy. Anaesthesia. 1990 Aug;45(8):623-8.
14. Park HS, Lee JH, Lee KH. "Comparison of Propofol and thiopentone for electroconvulsive therapy - effects on haemodynamic changes and intraocular pressure. British Journal of Anaesthesia.1999; 14(3:2)
15. Kadoi Y, Saito S, Ide M, Toda H, Sekimoto K, Seki S, Takahashi K, Goto F. The comparative effects of propofol versus thiopentone on left ventricular function during electroconvulsive therapy. Anaesth Intensive Care. 2003 Apr;31(2):172-5.
16. Mulier JP, Wouters PF, Van Aken H, Vermaut G, Vandermeersch E. Cardiodynamic effects of propofol in comparison with thiopental: assessment with a transesophageal echocardiographic approach. Anesth Analg. 1991 Jan;72(1):28-35
17. Fredman B, Nathanson MH, Smith I, Wang J, Klein K, White PF. Sevoflurane for outpatient anesthesia: a comparison with propofol. Anesth Analg. 1995 Oct;81(4):823-8.
18. Fink, Max. Convulsive Therapy in Delusional Disorders. Psychiatric Clinics of North America. 1995; 18(2): 393–406.
19. Mitchell P, Smythe G, Torda T. Effect of the Anaesthetic agent propofol on hormonal responses to ECT. Biol psychiatry 1990; 28: 619-20.
20. Butterfield NN, Graf P, Macleod BA, Ries CR, Zis AP. Propofol reduces cognitive impairment after electroconvulsive therapy. J ECT. 2004 Mar;20(1):3-9.
21. García García E, Rosa Díaz J, Rodríguez Casas E, Echazabal Martínez, Raola Sánchez ME. Propofol versus thiopental in electroconvulsive therapy. Rev Cubana Med Milit 2007; 36(2).
22. Matters RM, Beckett WG, Kirkby KC, King TE. Recovery after electroconvulsive therapy: comparison of propofol with methohexitone anaesthesia. Br J Anaesth. 1995 Sep;75(3):297-300.

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