Original Article

Propofol and Thiopentone as Anaesthetic Agents in Electroconvulsive Therapy and Effect of Clonidine as Premedicant

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DOI:10.37821/ruhsjhs.5.1.2020.17-23

ABSTRACT

Introduction: The present study was conducted to compare Propofol and Thiopentone as an anaesthetic agent for modified electroconvulsive therapy (MECT) and effect of Clonidine as an adjunct with respect to seizure duration, haemodynamic changes, recovery profile, and cognitive side effects.

Methodology: A prospective randomized comparative study was done on 120 patients of American Society of Anaesthesiologist (ASA) physical status I/II, scheduled for modified ECT. Induction was done with Thiopentone 2.5-3 mg/kg in group T and Propofol 1-1.5 mg/kg in group P. In group TC and PC, patients were given Thiopentone 2.5-3 mg/kg and Clonidine 0.5 mcg/kg and Propofol 1-1.5 mg/kg and Clonidine 0.5 mcg/kg, respectively, after randomization by computer generated random number table. Injection Succinylcholine 0.5 mg/kg was given for neuromuscular relaxation. Patients were ventilated with 100% oxygen with Bain circuit and mask. Modified ECT was given by trained psychiatrist. Outcome variables included seizure duration, haemodynamic changes, recovery profile, and cognitive side effects. The effect of Clonidine on hemodynamic response of ECT when given intravenously in small dose of 0.5 mcg/kg was also studied.

Results: The mean seizure duration in groups T, P, TC, and PC was 41.2±6.2, 33.8±3.8, 38.5±2.9, and 34.4±3.4 seconds, respectively ($p<0.0001$). Propofol seems superior to Thiopentone in attenuating the physiological response to ECT with minimal haemodynamic changes. Modified Aldrete score at 30 minutes were comparable in all the groups. The mean score on Mini-Mental State Examination (MMSE) was superior in Propofol Clonidine group.

Conclusion: Propofol in the dosage of 1.0-1.5 mg/kg body weight reduces seizure duration, but it provides superior haemodynamic stability, smooth and early recovery, and less cognitive impairment in comparison to Thiopentone with advantage of antiemesis. Use of Clonidine as an adjunct to Thiopentone and Propofol improves haemodynamic stability.

Keywords: Anaesthetic agents, electroconvulsive therapy, premedicant.

INTRODUCTION

Modified electroconvulsive therapy (MECT) is a safe, established, and one of the most effective treatment modalities for various psychiatric ailments like severe and drug resistant depression and mania, schizophrenic patients with affective disorders, suicidal drive, delusional symptoms, inanition, and catatonic symptoms.[1,2] The American Psychiatric Association recognizes no absolute contraindications to ECT.

Many anaesthetic techniques have been evolved over the years to improve comfort and safety of ECT.[3] Since only a brief period of unconsciousness is required, anaesthetic agent providing rapid and smooth induction, short duration of action, causing no shortening of seizure duration, and a rapid recovery profile would be an ideal anaesthetic agent for MECT. Thiopental, Etomidate, and Propofol are being used routinely for ECT anaesthesia. ECT is frequently associated with cardiovascular complications such as hypertension and tachycardia. Clonidine decreases the stress-induced sympatho-adrenal responses to painful stimuli and improves haemodynamic stability during general anaesthesia.[4]

This study was designed to compare the effect of Thiopentone sodium and Propofol as an induction agent for ECT anaesthesia with respect to haemodynamic changes, seizure duration, clinical effects, recovery profile, and cognitive side effects. The effect of adding Clonidine to these induction agents attenuating the acute hyperdynamic response of ECT, when given intra-venously in a small dose (0.5 microgm/kg body wt.) was also studied.

METHODS

This prospective, randomized, and comparative study was conducted for a period of one year after obtaining approval from Institutional Ethics Committee and written informed consent from patients and relatives. 120 patients were recruited according to American Society of Anaesthesiologist (ASA) physical status I and II of age group 18 to 60 years who were scheduled for MECT. Patients suffering from schizophrenia, acute psychosis, manic depressive psychosis, and depression were included. Patients with anticipated difficult airway, history of cardiopulmonary, renal, hepatic, endocrinal disorder, drug allergy, and epilepsy were excluded from the study. Patients with modified Mini Mental scale less than 9 for both recent and immediate memory were also excluded.

All the patients were randomly allocated into four groups of 30 each using computer generated randomization table. Group allocated were kept in sealed brown opaque envelopes. Groups T, P, TC, and PC were administered Thiopentone (2.5%) 2.5 -3 mg/kg, Propofol (1%) 1- 1.5 mg/kg, Thiopentone with Clonidine 0.5 mcg/kg, and Propofol with Clonidine 0.5mcg/kg, respectively.

All the patients were screened thoroughly in pre-anaesthetic clinic one day prior to MECT. Routine investigations like complete haemogram, urine analysis, and ECG were performed for every patient and specific investigations like blood sugar, blood urea, serum creatinine, LFT, serum electrolytes, blood gas analysis, chest X-ray, and pulmonary function test were performed whenever necessary. Memory assessment was done on two occasions using Mini Mental State Examination scale (MMSE)**.** Pre ECT-memory assessment was done on the morning of ECT**.** Post ECT memory assessment was done 3 hours after ECT was given using same scale.

All the patients were kept nil per orally for six hours before procedure and allowed to continue respective antipsychotic treatment till the day of procedure. On entering ECT room, IV line was secured and monitoring of baseline pulse, non-invasive blood pressure (NIBP), SpO2, respiratory rate, and ECG was done by using multipara monitor and the psychiatrist was allowed to place Bi-temporal ECT electrodes on forehead. All the patients were premedicated with injection Glycopyrrolate 0.2 mg I.V. and preoxygenated for three minutes. General anaesthesia was induced with intravenous anaesthetic agent as per the group allocated and adequacy of depth of anaesthesia was assessed by loss of eyelid reflex. Then injection Succinylcholine 0.5 mg/kg was given and muscle relaxation was assessed by drooping of lower jaw. Once adequate neuromuscular relaxation was obtained, Guedel's airway was inserted to prevent tongue bite and modified ECT was given by trained psychiatrist. A brief pulse stimulus of intensity 750 milli amperes was given for 1.8 milli seconds to produce seizure using microchip controlled brief pulse, sine wave ECT machine. Effective joules delivered were noted. Subsequently, all the patients were ventilated with 100% oxygen till the establishment of spontaneous

Table 1: Demographic profile and pre ECT MMSE score

Parameters	Group T	Group P	Group TC	Group PC	p value
Age (years) (Mean±SD)	28.1±6.4	29.1±6.7	26.7±5.6	27.8±6.1	0.5
Weight (kg) (Mean±SD)	58.7±5.6	59.1±6.0	57.5±5.7	60.0±4.5	0.3
ASA I/II (Median)	19/11	18/12	20/10	19/11	0.33
Pre ECT MMSE Score (Mean±SD)	26.5±1.5	26.0±1.2	26.6±1.0	26.1±0.9	0.21

$p<0.05$: Significant

Table 2: Mean dose of stimulus given and duration of seizure

Variable	Group T	Group P	Group TC	Group PC	p value
Dose of stimulus (Joules)	43.1±4.8	42.1±6.6	43.2±7.2	39.7±5.4	0.07 (NS)
Seizure duration (Seconds)	41.2±6.2	33.8±3.8	38.5±2.9	34.4±3.8	Overall 0.0001

$p < 0.001$ Highly significant, NS: Non significant

respiration. Monitoring of pulse, NIBP, SPO2, ECG changes was done after every 1 minute for 5 minutes, and then at interval of 5 minutes up to 30 minutes. Besides haemodynamic monitoring, seizure duration, side effects, and complications were also noted in all four groups. Duration of recovery (cognitive, orientation, and neuro-muscular co-ordination) was recorded from injection of intravenous anaesthetic agent to time taken to obey verbal commands, opening of eye, ability to sit unaided. Patients were sent out of observation area only after achieving modified Aldrete score more than 9.

Measurement of seizure duration: Measurement of seizure duration was done by using "tourniquet technique". A tourniquet was cuffed in an isolated arm before the administration of dose of Succinylcholine and convulsive movements of the distal arm, around which tourniquet was set to block the distribution of muscle relaxant, were noted using stop watch.

Scoring systems: Following scales were used-Mini Mental Scale for examination of memory,[5] Ramsay sedation scale and modified Aldrete scale were used for discharge criterion.[6]

Statistical analysis was done using SPSS version XVII. Quantitative data which had Gaussian distribution were analysed using Student t test or ANOVA, whichever was applicable. Quantitative data which had Non-Gaussian distribution were analysed using Mann Whitney test or Kruskal-Wallis H test, whichever was applicable.

RESULTS

All four groups were comparable with respect to patient's age, weight, ASA physical status, and pre ECT MMSE score (Table 1).

Mean dose of stimulus given was comparable among all four groups; decrease in duration of seizure was highly significant in group P and PC as compared to Thiopentone group ($p < 0.001$) (Table 2).

There were no significant difference in post ECT MMSE score between T and P groups and T and TC but significant differences were observed between T and TC and P and PC groups (Table 3). The discharge criteria were comparable among the four groups Post ECT modified Aldrete score is given in Table 4.

The haemodynamic characteristics are shown in figures 1 and 2. There was increase in heart rate from baseline in group T for initial three minutes, but no compensatory increase in heart rate was seen in group P. Addition of oral Clonidine resulted in better stabilisation of heart rate

Table 3: Post ECT MMSE score

Post ECT MMSE Score	Group T	Group P	Group TC	Group PC	p value
20	4	–	2	–	Overall
21	2	–	3	–	0.000 (S)
22	3	1	4	3	T v/s P
23	6	10	12	12	0.437 (NS);
24	9	12	6	9	T v/s TC
25	6	7	3	6	0.210 (NS); T v/s PC
Mean ± SD	23.1±1.5	22.8±1.33	23.5±0.92	23.9±0.85	0.018 (S);
SEM	0.28	0.24	0.16	0.14	P v/s PC 0.001 (S)

$p < 0.001$ Highly significant, NS: Non significant

Table 4: Post ECT modified Aldrete score at 30 minutes

Score	Group T	Group P	Group TC	Group PC	p value
9	16	20	14	20	0.58 (NS)
10	14	10	16	10	
Mean ± SD	9.4±0.5	9.4±0.5	9.3±0.4	9.4±0.5	
SEM	0.09	0.09	0.08	0.08	

NS : Non significant

during ECT. Mean arterial pressure (MAP) increased maximally in group T for initial 5 minutes as compared to other three groups, group P showed a minor increase with rapid normalisation within 2 minutes post ECT. There was significant stabilisation of MAP in group TC, while no post ECT increase in MAP was observed in group PC.

DISCUSSION

ECT is one of the most effective non-pharmacological treatment modalities in the dual fields of depression and psychosis. Typical response to ECT consists of generalised autonomic nervous system stimulation, release of catecholamines, transient tachycardia, hypertension, and occasional cardiac arrhythmias. The peak heart rate (HR), systolic blood pressure (SBP) values occur 3-5 minutes after applying electrical stimulus.[7] This increase in HR and SBP may be due to concomitant release of epinephrine and norepinephrine. Clonidine, being selective alpha-2 adrenoceptors, may cause inhibition of sympathetic outflow and potentiation of parasympathetic nervous activity.[8] It improves intraoperative haemodynamic stability and reduces the anaesthetic requirement.[7]

In the present study, increase in heart rate from baseline was seen in Thiopentone group for initial three minutes, but no compensatory increase in heart rate was seen in Propofol group. Our results are in accordance with previous studies.[9-12] Addition of oral Clonidine resulted in better stabilisation of heart rate during ECT; it is similar to previous study.[13,14.] Other studies[15,16] where dexmedetomidine was used as premedication agent have also shown similar results.

Mean arterial pressure (MAP) increased maximally in Thiopentone group for initial 5 minutes as compared to other three groups, Propofol group showed a minor increase with rapid normalisation within 2 minutes post ECT. This is in line with previous studies[9-11,17,18] but different from results obtained in another study.[19] Addition of

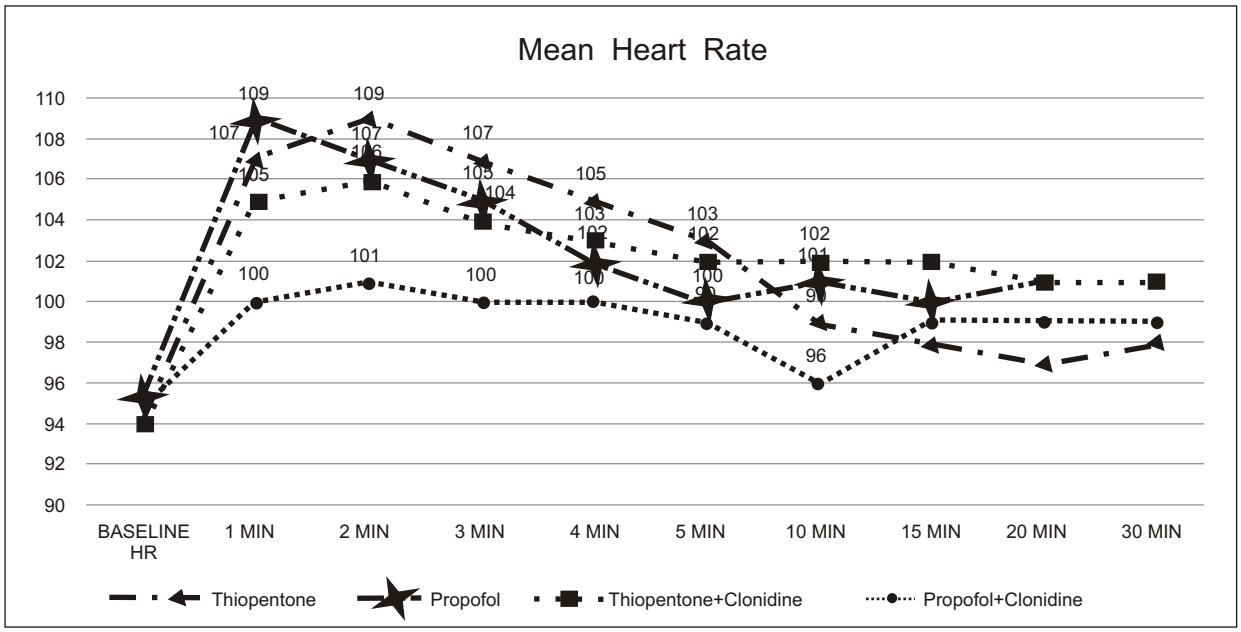

Figure 1: Comparison of mean heart rate among groups.

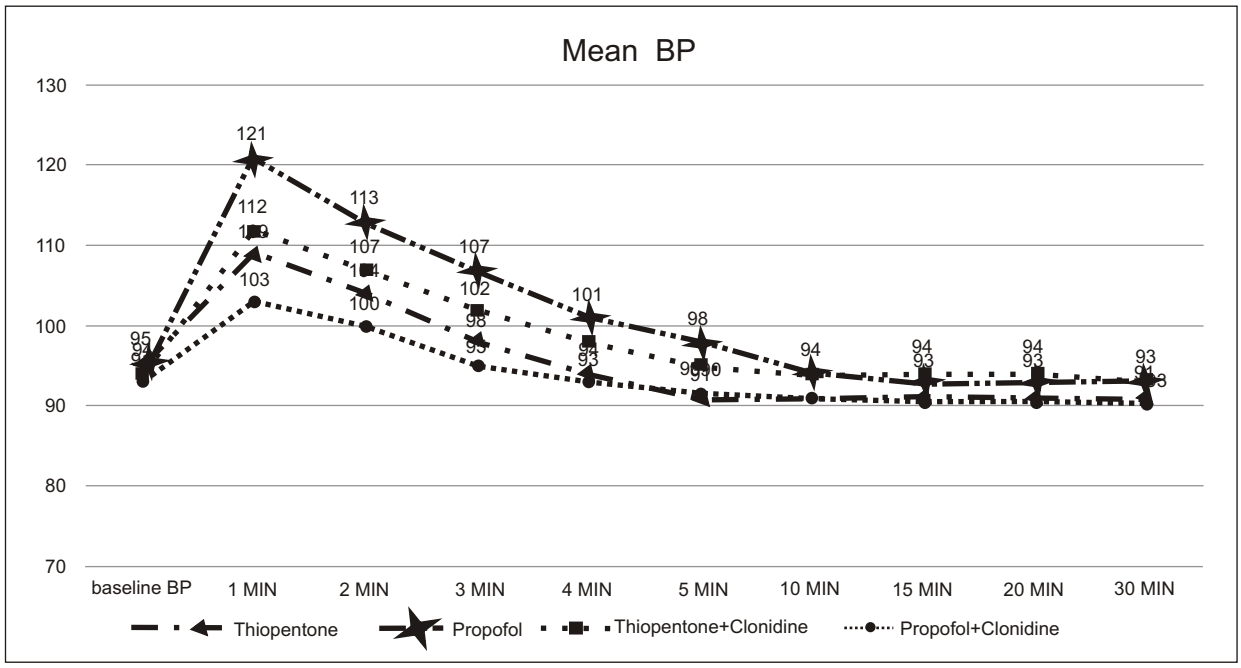

Figure 2: Comparison of mean blood pressure among groups.

Clonidine to Thiopentone resulted in significant stabilisation of MAP, while no post ECT increase in MAP was observed in Propofol Clonidine group, as Clonidine affects blood pressure in a complex fashion after systemic absorption because of opposing actions at multiple sites.[7, 8] In the nucleus tractus solitarius and locus ceruleus of the brain stem, activation of post synaptic alpha2 adrenoreceptors reduces sympathatic drive. Moreover, it also activates nonadrenergic imidazoline preferring binding sites in lateral lenticular nucleus, thereby producing hypotension and antiarrythmogenic effect. We did not find any study regarding use of intravenous Clonidine with Thiopentone in ECT anaesthesia, but previous studies showed improved haemodynamic response when oral Clonidine was used as premedication.[13, 14]

The duration of seizure activity lasting for > 25 seconds in single session or a maximum of 210 seconds of cumulative duration leads to good therapeutic outcome.[20] In the present study, the mean seizure duration was significantly shorter in Propofol group as compared to Thiopentone group. Elevation of seizure threshold after Propofol administration may be a reason for the lower seizure duration. Our results are in accordance with previous studies.[9,12,17,18,21] However, other studies[10,11,19] did not found statistically significant decrease in seizure duration with use of Propofol. No effect on seizure duration was noted when Clonidine was used as an adjuvant to Thiopentone and Propofol. This is in accordance with study conducted by W Fu et al.[13]

Though seizure duration was shorter in Propofol group, yet it was sufficient for generating favourable response. Our better results may be due to use of advanced brief pulse machine, with the therapist delivering optimized electric current doses. Rosa et al[22] also concluded that no difference in responses was seen if higher mean electric charge was used and that Propofol offered a better recovery profile.

Impairment of cognitive function continues to be main limiting factor for ECT's use, it is most severe during the post- ictal period.[23] In this study, no significant difference in cognitive function between Thiopentone and Propofol group was found as MMSE score before and 3 hours after ECT was comparable. This finding differs from previous studies[21,24,25] as they observed reduced cognitive impairment with Propofol. An important finding of this study was that combination of Clonidine and Propofol gave the best post ECT cognitive function scores as compared to Propofol or Thiopentone alone. It may be explained by more stable haemodynamic response in this group. Perhaps no study has been carried out till date for studying effects of Clonidine on cognitive functions, this field deserves further research to reach conclusive inference.

Post ECT recovery time was statistically comparable among all four groups, however response to verbal command, ability to sit and walk unaided were better in Propofol group, this is in consonance with previous studies.[10,11,17,18,24] No adverse effect on recovery profile was observed by use of Clonidine. W Fu et al [13] also reported that clonidine in small doses of 0.2 mg to 0.3 mg did not produce any residual sedation.

About 30% patients complained of pain at the site of injection in Propofol group as compared to 3.33% in Thiopentone group. Propofol is known to cause pain on injection which can be attenuated by using 1% lidocaine or by using better available formulations. Nausea was more with Thiopentone (23.3%) as compared to Propofol (3.33%). The antiemetic properties of Propofol can be beneficial while applying ECT as a day care procedure. Arrhythmias occurred in 6% patients in Thiopentone group only but were transient and resolved spontaneously. Arrhythmias were observed by Rompton in 19% of their patients, but no premedication was used in their study.[26]

CONCLUSION

This study concluded that Propofol in the dosage of 1.0-1.5 mg/kg body weight reduces seizure duration but it provides superior haemodynamic stability, smooth and early recovery, and less cognitive impairment in comparison to Thiopentone with advantage of antiemesis. So, it can be used safely for modified ECT in ASA grade I and II patients without compromising therapeutic outcome. Use of Clonidine as an adjunct to Thiopentone and Propofol improves haemodynamic stability.

Conflict of interest: None

Financial support: None

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