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Original Research Article

A Comparison of the Efficacy of Thiopentone, Propofol, and Admixture of Propofol and Ketamine (Ketofol) for Modified ECT Anesthesia

Meera Pandey[1], Akansha Jain[2], Ajay Singh[3], Sonali Tripathi[*], Amit Jain[4]

[1]Assistant Professor, Department of Anaesthesiology, SMBT Medical College, Dhamangaon, Nashik, Maharashtra, India.
[2]Assistant Professor, Department of Anaesthesiology, Chirayu Medical College, Bhopal, Madhya Pradesh, India.
[3]Assistant Professor, Department of Anaesthesiology, Bundelkhand Medical College, Sagar, Madhya Pradesh, India.
[*]Assistant Professor, Department of Anaesthesiology, Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India.
[4]Professor, Department of Anaesthesiology, Super Speciality Hospital, NSCB Medical College, Jabalpur, Madhya Pradesh, India.

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Corresponding author: Dr. Sonali Tripathi
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Abstract

Background: Electrically inducing seizures in patients during electroconvulsive therapy (ECT) has been proven to have therapeutic effects. The circulatory system may experience severe disruptions as a result of ECT, and cerebral blood flow and intracranial pressure may noticeably increase. Many anaesthetic medications may be used to affect these cardiovascular alterations. The two induction drugs for ECT that are most frequently used are thiopentone and propofol. Ketofol, a propofol and ketamine admixture has recently been tested in ECT.

Aims and Objectives: This study compared the efficacy of intravenous (IV) sodium thiopentone, propofol, and ketofol, used as IV anaesthetic agents in modified ECT, on the hemodynamic changes caused by the procedure, the length of the seizures, and the time it took for patients to recover.

Materials and Methods: Ninety patients between the ages of 18 and 60 with ASA grades I and II who were scheduled for ECT participated in this prospective, randomized controlled trial. Patients in group T received 3 mg/kg of thiopentone, patients in group P received 1 mg/kg of propofol, and patients in group K received an injection of Ketofol, which is a combination of 0.5 mg/kg of propofol and 0.5 mg/kg of ketamine. For the first thirty minutes, the hemodynamic and recovery parameters in both groups were assessed. Agitation scores, obeying to verbal commands, spontaneous eye opening timings, and seizure duration were also recorded.

Results: Following the administration of shock, there was a statistically significant difference in heart rate at 10 minutes and systolic blood pressure at 5 minutes between the Thiopentone group and the other two groups (p-values 0.008 and 0.011, respectively). The variations in seizure duration, the amount of time it took for the eyes to open spontaneously, and the ability to comply with vocal commands were not statistically significant ($p>0.05$). In comparison to groups P (1.64 0.48) and K (1.78 0.64), Group T had the highest mean agitation score (2.14 0.56) ($P=0.004$).

Conclusion: Thiopentone demonstrated inferior hemodynamic stability compared to propofol and ketofol, but similar seizure duration and recovery measures. Propofol and Ketofol can

therefore be employed as efficient induction drugs for ECT, despite the fact that propofol causes less agitation than Ketofol.

Keywords: Ketofol, Propofol, Seizures, Thiopentone, Hemodynamic, Electroconvulsive Therapy.

Introduction

A tiny electric current is sent through the brain of the sedated patient during ECT, a therapeutic method for psychiatric diseases. A convulsion occurs and is altered by muscle relaxants. Among other illnesses, ECT is a very safe and efficient way to treat serious depression and catatonia [1]. Yet, the general public, medical students, and even doctors have a lot of unfavourable attitudes and misconceptions [2].

Nonetheless, during anaesthetic management of ECT, there is still room for worry regarding the duration of anaesthesia, hemodynamic changes, induction and recovery time and features, interaction with antipsychotic medicines, effect on seizure duration, and post-ECT disorientation [3]. ECT may have unfavourable side effects, including bradycardia, hypotension, tachycardia, hypertension, and post-procedure headache, myalgia, and agitation [4].

Both thiopentone and propofol have been used frequently in ECT. Thiopentone's anti-convulsant function causes side effects that are unacceptable for ECT, including delayed recovery, an increased risk of arrhythmias, laryngospasm, a rise in seizure threshold, and a dose-dependent shortening of seizure duration [5]. Faster induction, easy recovery, and less post-procedural agitation are all advantages of propofol. Its hypotensive effect is helpful in preventing ECT-induced hypertension, but it also reduces seizure length in a dose-dependent manner, which is undesired in ECT. Ketofol, a ketamine and propofol combination is now being tested as an ECT induction agent. Propofol and ketamine's circulatory effects counteract one another to keep hemodynamic stability [6,7].

Thiopentone and propofol have been the focus of numerous research studies that compared their effectiveness as ECT induction agents. The efficacy of ketamine has already been evaluated during ECT. There has been limited research on the use of ketofol as an ECT inducing agent. To investigate the effects of intravenous (IV) Thiopentone, Propofol, and Ketofol employed as IV anaesthetic agents in modified ECT on ECT-induced hemodynamic alterations, seizure duration, and recovery parameters, the current study was conducted.

Material and Methods

90 adult patients participated in this prospective, double-blind and randomized study after receiving approval from the institutional ethical committee and obtaining informed consent from patients and their relatives.

Inclusion Criteria:

- Adult patients of either sex, with an ASA grade of I or II,
- Age range of 18 to 60 years
- Weights between 40 and 70 kg,
- Modified electroconvulsive treatment is scheduled.

Exclusion Criteria: Patients with history of uncontrolled hypertension, diabetes mellitus, thyroid dysfunction, valvular heart disease or bronchial asthma, pregnant and lactating mothers were debarred from the present study. Individuals having a history of food or drug allergies were also disqualified.

By using computerized randomization, all the patients were divided into three groups of 30 each.

Primary outcomes

- Comparison of hemodynamic stability.
- Comparison of seizure duration.

Secondary outcomes

- Spontaneous eye opening timings.
- Time to responding to verbal commands.
- Agitation scores.

The patient's and the patient's relative are informed and written consent was obtained. Before receiving ECT, patients were set aside NPO (nil per oral) for 6 hours while still being allowed to take their prescribed antipsychotics the day of the procedure. Using the sealed envelope approach, patients were randomly allocated into three groups of 30 each. Patients in group T received 3 mg/kg of thiopentone, patients in group P received 1 mg/kg of propofol, and patients in group K received an injection of Ketofol, which is a combination of 0.5 mg/kg of propofol and 0.5 mg/kg of ketamine. In order to prevent observer bias, patients were kept blinded using the sealed envelope approach and the observer anesthesiologist was also kept unaware about which medicine was administered to which patient. The anesthesiologist who administered the study medicines stopped participating in the study.

Intravenous cannulation was performed and a ringer lactate (RL) infusion began in the ECT Theater. Basic measurements have been taken, including heart rate (HR), mean blood pressure (MBP), systolic blood pressure (SBP), and diastolic blood pressure (DBP).

Glycopyrrolate injection (0.004 mg/kg) was administered as a premedication. The vital signs (BP, HR, and SPO2) were measured. After waiting for two minutes, the patient was administered the study medicine, and hemodynamic data were recorded. To track the length of the seizure activity, one of the upper limbs was isolated and the sphygmomanometer cuff was inflated to 100mmHg above the systolic blood pressure. After limb isolation, succinylcholine was administered at a dose of 0.75 mg/kg, and manual ventilation utilizing Bain's circuit and 100% oxygen at a flow rate of 8L/min was carried out. To prevent damage to the patient's oral cavity's structures, a biting block was applied. Bi fronto-temporal electrodes were used to deliver a supra-threshold electrical shock, and oxygen support was provided for ventilation. The length of the seizure, or the interval between shock delivery and the end of tonic-clonic motor activity in the "isolated" limb, was noted. At 0, 5, 10, 15, and 20 minutes following the administration of the shock, systolic (SBP), diastolic (DBP), mean (MAP), HR, and oxygen saturation (SpO2) were measured. 100% oxygen was used to ventilate the patients until spontaneous breathing resumed. We also observed how long it took for the eyes to open and how long it took for the subject to comply with spoken orders. Ondansetron 4 mg IV was given if patients complained of nausea or vomiting at all. Using an emergence agitation score, post-recovery agitation was assessed [8].

Statistical Analysis

Data presentation as mean ± SD (standard deviation) was used throughout the statistical study. The Chi-square test was used to assess the demographic data, and the analysis of variance test was used to determine whether the mean difference was statistically significant. The SPSS 17 programmer was used to calculate frequency and percentage. A "P" value of 0.05 or less was regarded as statistically significant, and a value of $P > 0.05$ as non-significant.

Result

The average age and weight of the participants in our study were 31.63 ± 10.19 years and 56.53 ± 12.50 kg, respectively,

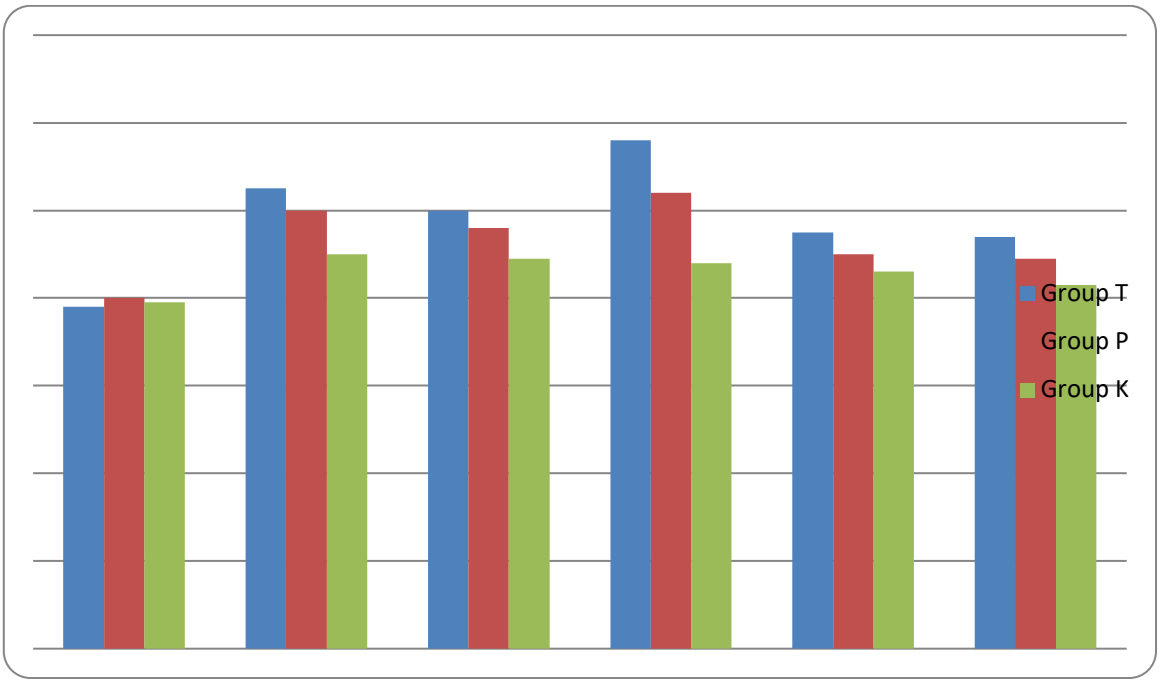
with a male:female ratio of 57:43%. Pre-operative (Baseline) vital signs (HR, SBP, DBP, and MAP) were comparable across all groups ($p > 0.05$). (Table 1).

Table 1: Comparison of the baseline (pre-induction) parameters between the three groups

Variable	Group-T	Group-P	Group-K	p-value
SBP (mmHg)	118.32±9.36	121.30±8.32	119.43±8.56	0.32(NS)
DBP (mmHg)	76.32±8.34	78.12±7.36	77.25±7.72	0.42(NS)
HR (bpm)	78.36±6.02	80.34±7.23	79.42±6.34	0.30(NS)
SPO2	98.01±1.02	97.23±0.98	97.67±0.99	0.21(NS)

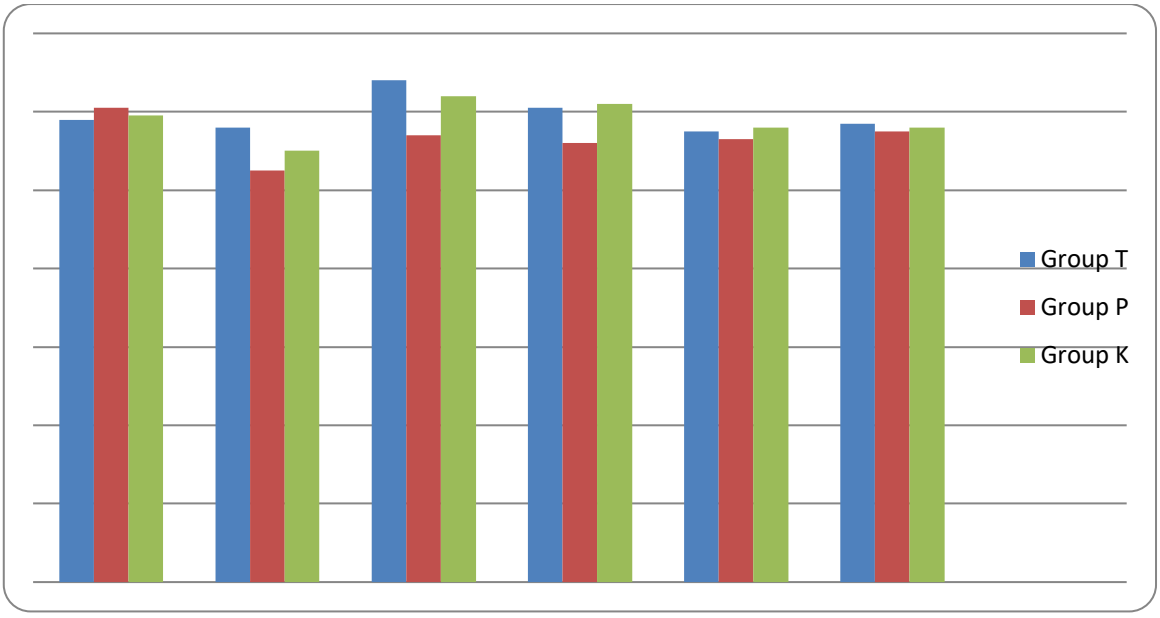
NS- Not Significant

HR augmented in all groups following premedication (Inj. Glycopyrrolate) administration. Once the shock was administered, greater heart rate acceleration was seen. In comparison to the Ketofol and Thiopentone groups, the percentage rise in heart rate was lower in the propofol group. The study groups' heart rates differed statistically significantly at 10 minutes after shock delivery, with group T displaying greater values than groups K and P ($p = 0.008$). **(Graph 1)**



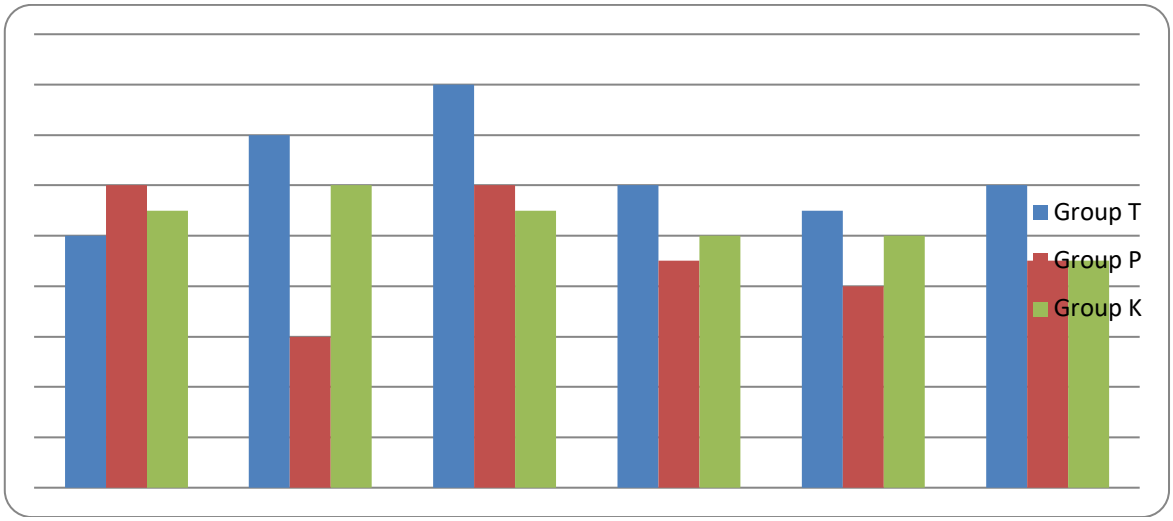
Graph 1: Comparison of mean heart rate at different time interval in three groups

After giving study medicine, statistically significant decrease in mean SBP was observed compared to baseline in Group *P* (4.84%), whereas Group K showed statistically insignificant decline (1.13%) and Group T showed insignificant rise in SBP (3.66%). All the study groups showed statistically significant increase in SBP after delivery of shock (*P* <0.05) There was statistically significant difference in SBP at 5 min after delivery of shock where group T showed higher value compared to group K and *P* ($p = 0.011$)



Graph 2: Comparison of systolic blood pressure (SBP) at different time interval between the three groups

After the study drug was administered and immediately following shock, there was a statistically significant difference in DBP, with group T having a larger value than groups K and P ($P < 0.05$).



Graph 3: Comparison of diastolic blood pressure (DBP) at different time interval between three groups

Although the difference was statistically insignificant, Group T had longer-lasting seizures (30.78 ±12.80) than Group P (24.85 ± 10.72) and Group K (25.88 ± 12.25), despite the fact that the variation was noted. Latency to spontaneous eye opening and time to comply with vocal cues were comparable across the three groups ($p = 0.431$ and $p = 0.265$, respectively). 10% of patients in the Ketofol group and 23.33% in the Thiopentone group had agitation scores more than 2. No patients in the propofol group had an agitation score of greater than 2. Group T had the highest mean agitation score (2.13 ± 0.57), which was statistically significantly different from Group P (1.63 ± 0.49) and Group K (1.77 ± 0.63) (P=0.003).

Table 2: Comparison of seizure duration and recovery parameters between the three groups

Variables	Group-T (Mean±SD)	Group-P (Mean±SD)	GroupK (Mean±SD)	p-value
Seizure duration (seconds)	38.77±12.80	24.85±10.73	25.89±12.26	0.127 (NS)
Spontaneous eye-opening time	5.07±2.38	4.21±2.82	4.81±2.68	0.432 (NS)
Time to obeying verbal commands	7.27±2.68	5.91±3.72	6.34±3.37	0.266 (NS)
Mean Agitation score	2.14±0.56	1.64±0.48	1.78±0.64	0.004 (HS)

Discussion

Generalized seizures that are triggered electrically are used in electroconvulsive therapy to treat the symptoms of psychiatric diseases like severe depression, mania, and schizophrenia. When a patient's reaction to pharmacotherapy is insufficient, it is also utilized as a backup treatment [11]. Anaesthetic drug use lessens the physical and psychological damage, but it also has side effects that can persist for hours after the treatment, including nausea, vomiting, dizziness, headaches, and drowsiness. Barbiturate anaesthesia may worsen the amnesic impairments established on by ECT for nonverbal information. Due to drowsiness, sleepiness, and psychomotor impairment caused by anaesthesia, falls and the risk of fractures have also been linked to this condition [12,13].

In order to achieve the desired therapeutic benefits, it is crucial to maintain the proper level of anaesthetic during the treatment and allow for an adequate seizure length. ECT is associated with hemodynamic instability, which can be problematic in cardiac patients and include bradycardia followed by tachycardia and hypertension. The optimal inducing substance must reduce hemodynamic instability produced on by ECT without shortening seizure duration. Thiopentone sodium, an ultra-short acting barbiturate, has an anticonvulsant effect that may shorten the length of seizures. Tendency of propofol to vasodilate improves hemodynamic stability during ECT, yet its powerful anticonvulsant impact also reduces seizure activity. Ketamine can cause behavioral or cognitive abnormalities, including post-procedural psychosis. On the other hand, its antidepressant effect aids in enhancing ECT's symptomatic results. Due to its less profound anticonvulsant activity during ECT, ketamine lengthens the duration of seizures [9-19]. However ketamine might worsen the tachycardia and hypertension after ECT [18,20].

Ketofol, a propofol and ketamine combination is a relatively recent induction drug being utilized in ECT. The combined actions of the two medications allow for a reduction in dosage of each whilst also achieving the desired effects of hypnosis, analgesia, and amnesia. Propofol and ketamine hemodynamically balance each other out; hence the combination is beneficial for preserving hemodynamic stability. When both medications are taken at the same time, propofol lessens the ketamine-related hallucinations.[21] When taken in conjunction with propofol, the convulsant effect of ketamine reduces the anticonvulsant effect of propofol, improving seizure duration [22].

To reduce their impact on seizure length during ECT, induction drugs are employed in slightly lower quantities. After an extensive literature search, we discovered that the typical induction dosages for thiopentone, propofol, and ketamine in ECT are 2–4 mg/kg, 0.75–2 mg/kg, and 0.7–2.8 mg/kg, respectively. In the current investigation, we employed 0.5 mg/kg of ketamine mixed with 0.5 mg/kg of propofol as ketofol, 3 mg/kg of thiopentone, and 1

mg/kg of propofol. These doses correspond to those that were applied in the experiments by Omprakash *et al* [15] and Erdogan *et al* [19] respectively.

In those induced with Thiopentone, a research by Shah *et al* [13] demonstrates a significant occurrence of gag reflex, coughing, and vomiting. In our investigation, no such effect was noticed. 20% of patients experienced pain upon injection with propofol, and 3.3% developed thrombophlebitis. Yet, in our investigation, there was no evidence of such negative effects at all.

In their trial with propofol and thiopentone, Manjula *et al* [17] found a substantial increase in heart rate at 1, 2, 3, and 10 min after ECT. Our findings agree with what they found. Ketofol and propofol were used in a study carried out by Erdogan *et al* [19]. Their research revealed a substantial increase in heart rate in the propofol group at T0 and T5, but the heart rate in the ketofol group was greater at T0 and decreased at T1 compared to baseline. The elevation in HR was not permanent since they did not take an anticholinergic premedication.

After the study drug was administered, there was a fall in SBP, DBP, and MAP in group P in our study. All three groups experienced a statistically significant rise in blood pressure after receiving the shock, while group P experienced the lowest percentage increase and group T the greatest. Moreover, BP levels in group P reverted to baseline faster than those of groups K and T.

In their trial with ketofol (0.5/0.5) and propofol (1mg/kg), Erdogan *et al* [19]. found that both study groups experienced an increase in SBP compared to baseline values. Nevertheless, when the two groups were compared, the propofol group experienced a lower rise (P 0.05). Thiopentone, propofol, and etomidate were compared by Mir *et al* [23] as ECT induction agents. According to their research, SBP increased following shock delivery for the first two minutes before trending downward. In the thiopentone group, the variability was significant statistically. The propofol group displayed a lower rise than the initial value. In their trial using propofol (1.5mg/kg), etomidate (1.5mg/kg), and ketofol (ketamine 0.8mg/kg + propofol 1.5mg/kg), Jaitawat *et al* [24]. couldn't identify any statistically significant variation in SBP from baseline at any time interval. This is contrary to our findings. They may have attributed to this disparity by using larger doses of ketamine and propofol in their trial.

Erdogan *et al* [19]. discovered that the Ketofol group displayed significantly greater DBP values throughout all time periods compared to their baseline readings (P = 0.001). Ketofol group DBP values were found to be greater than propofol group DBP values at T0, T1, T3, and T5 (P 0.029). After shock delivery for 2 minutes, Mir *et al* [23] saw a statistically significant increase in DBP in all groups (P 0.05). Nonetheless, the thiopentone group's increase was statistically significant. Our study's findings concur with those of these two studies.

According to research, ECT-induced seizures that last less than 25 seconds have little therapeutic value [26]. The mean seizure length across all participants in our research was 25 s. Our research is consistent with observations made by Manjula *et al* [17]. and Erdogan E*et al* [19]. Propofol group seizures lasted less time than ketofol group seizures, according to Saban Y *et al* [25]. (P 0.01). When making ketofol, they employed a larger amount of ketamine. The ketofol group may have experienced longer-lasting seizures as a result of this. In their investigation, Hashemet *et al* [27]. found that the thiopentone group's seizure duration was longer than the propofol group's (P = 0.001). They may have observed anything different from our study because they used

a larger dose of propofol and a lower dosage of thiopentone in their investigation.

In any of the three groups, we did not observe a statistically significant variation in the recovery metrics. Erdogan and co. Similar recovery values were also discovered by Saban Y *et al* [25] and Bodkhe *et al* [28] in the groups ketofol/propofol and propofol/thiopentone, respectively. In contrary, Jaitawat *et al* [24] found that the propofol group had a shorter time to obey vocal directions than the ketofol group did. The ketofol group received larger doses of propofol and ketamine, which could have contributed to a slower rate of recovery. From 3.23% to 18% of post-ECT delirium cases have been documented [21]. There aren't many research that compare the effects of different induction agents while looking at post-ECT agitation. While propofol has the lowest incidence of post-procedure agitation, thiopentone and ketamine have been linked to increased agitation. In their investigation, Butter field *et al* [29]. found that propofol minimised cognitive deficits in the early stages of recovery following ECT compared to thiopentone anaesthesia. Our findings support their research. Propofol balances off the effects of ketamine in ketofol. As a result, agitation is less common and less severe compared to when treated with ketamine alone. 8.6% of participants in the ketofol group had an agitation score of greater than 2, according to Tarek *et al* [30]. These results are consistent with what we found.

Limitations

The electroencephalogram (EEG), which was not utilized in our study, should ideally be employed during ECT to assess seizure duration. In addition, we were unable to use BIS monitoring to determine the level of anaesthesia. It would have been better to use an induction agent dose to achieve a similar level of anaesthesia in the trial, which would have allowed for a more accurate assessment of hemodynamic parameters.

Conclusion

Propofol (1 mg/kg) and Ketofol (a combination of Propofol 0.5 mg/kg + Ketamine 0.5 mg/kg) were shown to have higher hemodynamic stability and reduced post-procedural agitation in the current investigation when compared to Thiopentone (3 mg/kg). So, so although propofol is linked to less post-procedural agitation than ketofol, it may be inferred that both drugs can be successfully used to induce patients for ECT.

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