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Research Article

COMPARISON OF ETOMIDATE AND PROPOFOL AS INDUCTION AGENTS IN MODIFIED ELECTROCONVULSIVE THERAPY

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ABSTRACT

Objective: The aim of the study was to compare the effects of induction agents Propofol and Etomidate on hemodynamic parameters (Heart rate, Systolic Blood Pressure, Diastolic Blood pressure, and mean arterial pressure) in modified electroconvulsive therapy (ECT).

Methods: It was a prospective, randomized, and double-blinded study. The present study was conducted in the Department of Anaesthesiology at our tertiary care multispeciality referral hospital, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun. A total of 80 adult patients in the age group 20–50 years belonging to American Society of Anesthesiologists physical status I and II were included in the study. They were randomly allocated to Group I (Propofol) and Group II (Etomidate), with 40 patients in each group. The duration of the study was September 2018–February 2020.

Results: Both Etomidate and Propofol have been proposed as good induction agents to be used for ECT, but each has its own merits and demerits. Propofol leads to a significantly shorter seizure duration as compared to Etomidate. Propofol has the advantage of having rapid and smooth recovery as compared to Etomidate. Recovery criteria in terms of return to spontaneous respiration, consciousness, and fully responding were statistically significant between the two drug groups ($p<0.001$).

Conclusion: Propofol has the advantage of having rapid and smooth recovery as compared to Etomidate. Minimum side effects were seen in both groups. Subseizure was seen with the Propofol group more than Etomidate. Hence, we conclude that Etomidate is a better induction agent as compared to Propofol in modified ECT.

Keywords: Electroconvulsive therapy, Cerebral hemispheres, Seizure, Etomidate, Propofol.

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INTRODUCTION

Cerlitti first described electroconvulsive therapy (ECT) in 1938 [1]. It is the process that induces a widespread seizure by electrical stimulation of the cerebral hemispheres [2]. Historically, it was used to treat a variety of psychiatric diseases as well as to quiet down unruly psychiatric patients, regardless of their condition. Its most common indication in recent years has been to treat severe or medication-resistant depression, mania, catatonia, and schizophrenia [3].

The precise method of action is uncertain, although it is thought to cause a global tonic-clonic epileptic seizure that rewires brain activity [4]. For over 30–35 years, an "unmodified" approach was used, in which the patient received no muscle relaxant or anesthesia during the treatment.

This method resulted in musculoskeletal issues in up to 40% of the participants. Various advancements were made to the process in the 1950s and 1960s to increase patient safety, reduce side effects, and achieve better results [5].

During the technique, an electrical current is given to the brain transcutaneously through two electrodes that are either bilaterally or unilaterally positioned. Bilateral ECT is more prevalent and preferred when clinical recovery must be completed as quickly as possible. Unilateral ECT is administered to the non-dominant hemisphere and has minimal cognitive side effects.

The overall goal of both procedures is to cause a broad seizure with distinct electroencephalography abnormalities. The ideal seizure duration is similarly unknown in the literature. It has been proposed that seizure durations that are either short (10 s) or too lengthy (>120 s) may diminish clinical efficacy.

The goal of this study is to compare the effects of various anesthetic agents used in ECT to recommend the best anesthetic agent in terms of hemodynamic stability, seizure duration, and recovery. Many intravenous anesthetics, including methohexital, thiopental, Propofol, ketamine, and sometimes inhalational drugs, are used to induce anesthesia. The optimum anesthesia for ECT should control hemodynamic alterations and problems while simultaneously providing appropriate amnesia and muscular relaxation. Although these are necessary prerequisites, the level of anesthesia should not be so deep that it unduly suppresses seizure activity, which is the treatment's purpose.

METHODS

It was a prospective, randomized, and double-blinded study. The present study was conducted in the Department of Anaesthesiology at our tertiary care multispeciality referral hospital, Shri Mahant Indresh hospital, attached to Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, which is a constituent college of Shri Guru Ram Rai University, Dehradun.

Inclusion criteria

The following criteria were included in the study:

- Adult patients with severe major depressive disorders with suicidal tendency, bipolar disorders, not responding to treatment, mania, catatonia, and schizophrenia
- American Society of Anesthesiologists (ASA) Grade-1 and 2
- The age group of 20–50 years of either sex.

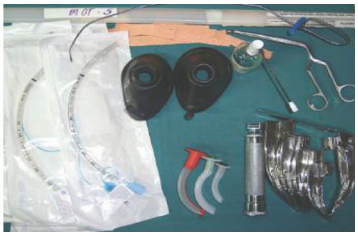
Exclusion criteria

The following criteria were excluded from the study:

- Patient's refusal
- Patients with a baseline heart rate (HR) <60 beats/min, baseline systolic blood pressure <100 mm Hg, and those with electrocardiography (ECG) abnormalities
- Patients with H/O chest pain/palpitations/syncope
- Patient responding to medical treatment
- ASA Grade 3 and 4
- Pregnant females
- Patient with hyperkalemia
- Patients with any known allergy.

Instruments required

- Anesthesia work station (Drager Fabius plus) with circle absorber
- Multipara monitor for NIBP, SPO_2, HR, and ECG
- Face Mask of appropriate size
- Resuscitation types of equipment (Laryngoscope with Macintosh blade, Ambu bag) in case of emergency



- A total of 80 patients, between the age group 20–50 years, belonging to ASA physical status I and II were included in the study
- Patients were randomly allocated to two groups – Group I and Group II (with a total of 40 patients in each group)
- The opaque and sequentially numbered sealed envelopes were stored in the pre-operative room
- Randomization of the patients to one of the two treatment arms was done
- Each patient picked up an envelope that contained a folded card. Those marked with "A" indicated randomization to receive 1% 1.5 mg/kg Inj. Propofol (I) and those marked "B" received 0. 2 mg/kg Inj. Etomidate (II)
- In the blinding process, the patient, as well as the anesthetist, was not aware of the drug used. The drug was not labeled as both of them were of the same color. Finally, it was given by some other anesthetist to the patient, and further readings were noted
- Group-(I): Comprising of 40 patients who received in. Propofol (iv) 1% 1.5 mg per kg as an induction agent
- Group-(II): Comprising 40 patients who received in. Etomidate (iv) 0.2 mg per kg as an induction agent
- The premedication, induction agent, and muscle relaxant to facilitate the procedure were standardized for both groups
- Intravenous cannulation was done with an 18G cannula after shifting the patient into the waiting area of the operation theater and was connected to a drip of ringer lactate solution
- The patient was connected to non-invasive blood pressure monitors, pulse oximeter probes, and electrocardiographic leads. All patients were pre-oxygenated with 100% oxygen for 3 min
- Premedication was done within. Midazolam 0.02 mg/kg, NJ. Glycopyrrolate 0.2 mg and in. Ondansetron 0.1 mg/kg and inj. Fentanyl 2 mcg/kg slowly intravenously, just before induction
- A general anesthetic agent was induced as per the group allocated till loss of eyelid reflex
- IV succinylcholine 0.5 mg/kg was administered to all patients for neuromuscular relaxation.

Motor seizure duration was seen and noted in both groups in seconds. It was recorded by the psychiatry team and was noted by the isolation limb method.

The recovery criteria were compared between the two groups. In this criteria, three parameters were recorded (in minutes):

- Return of spontaneous respiration: It was noted as the time when the patient's own respiratory efforts started coming
- Consciousness: It was noted when the patient became aware and started responding to one's surroundings
- Fully responding: It was noted when the patient started following all commands and was fit to be shifted to post-anesthesia care unit.

In the end, side effects of both the groups, if any, were also noted.

Ethical consideration

The research procedure followed was accordance with the approved ethical standards and study was approved by Institutional Ethics Committee. A written consent was taken from all potentially eligible subjects.

Statistical analysis

The data were analyzed using Statistical Package for the Social Sciences [version 20.0]. Parameters were recorded and data collected and analyzed using standard statistical methods, that is, Student's t-test and Chi-square test, as appropriate. Serial analysis of variance (ANOVA) was used to see the rate of change in hemodynamic stability. The statistical test was considered significant at $p<0.05$.

RESULTS

A total of 80 adult patients in the age group 20–50 years belonging to ASA physical status I and II were included in the present study. They were randomly allocated – to a Group I (Propofol) and Group II (*Etomidate*), with 40 patients in each group.

Patient demography

The demographic profile of patient in the both groups was similar with regard to age (p=0.709), sex (p=0.488), weight (p=0.066), height (p=0.068), Body mass index (p=0.032), and ASA grade (p=0.799) (Table 1).

Demographic profile

Table 1: Number and percentage of patients

Variables	Group I	Group II	p
Age (years)	30.325±13.43	31.45±13.33	0.709
Sex (male/ female), n (%)	27/13 (67.5/32.5)	23/17 (57.5/42.5)	0.488
Weight (kg)	65.78±7.43	62.65±7.57	0.066
Height (cm)	166.05±4.46	167.98±4.11	0.068
BMI (kg/m^2)	23.86±2.52	22.16±2.11	0.032
ASA (I/II), n (%)	30/10 (75.0/25.0)	29/11 (72.5/27.5)	0.799

BMI: Body mass index, ASA: American Society of Anesthesiologists

Distribution of different psychiatric disorders in both the groups

In both groups, the number of patients undergoing ECT for various diagnoses is depicted in the Tables below. Maximum patients who underwent ECT in the propofol group had bipolar disorder (25%), and in the etomidate group, the maximum number of patients had bipolar disorder (27.5%) and manic disorder (27.5%).

Distribution of different psychiatric disorders in both the groups

In both groups, the number of patients undergoing ECT for various diagnoses is depicted in the tables. Maximum patients who underwent ECT in the propofol group had bipolar disorder (25%), and in the etomidate group, the maximum number of patients had bipolar disorder (27.5%) and manic disorder (27.5%).

Effect on the hemodynamics

Repeated measures ANOVA was applied to determine the effect of both induction agents on various hemodynamic parameters across the

Table 2: Distribution of different psychiatric disorders in both the groups

Psychiatric disorders	Propofol (n=40), n (%)	Etomidate (n=40), n (%)
Bipolar disorder	10 (25)	11 (27.5)
Depressive disorder	8 (20)	7 (17.5)
Catatonia	5 (12.5)	1 (2.5)
Psychosis	3 (7.5)	1 (2.5)
Manic disorder	6 (15)	11 (27.5)
Schizophrenia	5 (12.5)	7 (17.5)
Dissociative disorder	3 (7.5)	2 (5)
Total	40 (100)	40 (100)

pre-ECT, ECT, and 30 min post-ECT time frames within and between the groups. The two inducing agents differ significantly in their effects on HR and systolic blood pressure (SBP) across the nine-time points (baseline till 30 min post ECT). Profile plots are given in Fig. 13 (HR) and Fig. 14 (SBP).

Effect on the hemodynamics (HR, SBP, diastolic blood pressure [DBP], and arterial oxygen saturation [SPO_2]) with induction agents Propofol and Etomidate from pre-ECT, during ECT till 30 min post-ECT time intervals.

HR

The mean HR in both groups was compared statistically in the baseline reading (p=0.1312). In the pre ECT period, that is, after induction, the increase in mean HR was seen in both groups. An increase in HR was more in the first group as compared to the second group, which was statistically significant (p=0.014). The maximum increase in HR was at 3 min following ECT, which was statistically non-significant in both groups (p=0.5255). This depicts that the change in HR caused by the drug during the procedure was similar. The HR at 30 min following ECT dropped to a lower level than the initial baseline HR in both groups (Table 4 and Fig. 15).

Seizure duration

In the case of seizure duration, the distribution of the two groups was comparable. On comparing, it was found statistically significant. In Group 1, the seizure duration was 29.15±9.95, while that of Group II was 47.33±15.19 (p<0.001).

Recovery criteria

Recovery criteria in terms of return to spontaneous respiration, consciousness, and fully responding were statistically significant between the two groups. The mean time to return to spontaneous respiration in Group I was 13.67±1.86, while that of Group II was 22.85±3.93 (p<0.001). In Group I, the meantime to regain consciousness was 15.75±1.81 as compared to Group II was 26.43±4.18 (p<0.001). At fully responding criteria, the mean was18.17±2.57 and 29.75±4.69 in Groups I and II, respectively (p<0.001).

Fatigue was noted in two patients in Group I and one patient in Group II. Similarly, weakness was noted in one patient in Group I and none in Group II, along with amnesia, which was found in two patients. Two patients in Group I had complaints of nausea, and in Group II, five patients had nausea. Twice the number of patients (four patients) exhibited sub-seizure as compared to Group I, where no sub-seizure was noted.

However, no statistically significant differences were observed in any of the adverse reaction profiles between the two groups.

DISCUSSION

ECT has developed into a widely recognized but frequently controversial treatment modality in psychiatric practice. Since the introduction of seizure therapy in 1934, the treatment process has undergone

Table 3: Effect on the hemodynamics

Variables	Mean±SD								F	p	Partial *et a*^{2}
	Pre-ECT	At ECT	1 min	3 min	5 min	8 min	10 min	20 min	30 min			
HR												
Propofol (n=40)	90.35±11.53	92.55±10.49	95.68±10.44	106.33±11.51	95.15±10.82	88.50±9.16	89.93±10.49	85.88±8.93	82.58±9.95	3.182$^{\#,a}$	0.002**	0.040
Etomid ate (n=40)	83.35±13.05	86.10±12.48	91.15±9.88	104.68±11.63	91.35±6.92	81.75±7.71	77.03±9.23	85.75±9.68	81.10±9.61			
SBP												
Propofo (n=40)	121.28±16.64	113.68±16.32	109.05±22.00	136.08±18.88	120.95±11.04	119.85±10.37	120.25±12.19	119.98±11.09	123.05±12.50	6.167	0.001**	0.073
Etomid ate (n=40)	121.70±17.26	123.10±13.99	124.00±11.51	126.90±14.19	121.30±10.07	127.80±14.35	117.8±14.30	121.48±14.13	118.40±11.06			
DBP												
Propofol (n=40)	75.20±10.88	71.38±10.74	68.05±14.55	82.13±12.20	77.15±10.99	76.03±10.56	74.78±11.26	73.18±10.08	72.83±10.50	1.491$^{\#}$	0.230	0.019
Etomid ate (n=40)	75.15±11.38	77.10±10.08	80.15±8.12	80.70±7.47	75.48±7.83	80.13±8.50	73.58±14.45	78.13±10.02	73.80±9.70			
SpO_2												
Propofo (n=40)	99.95±0.32	99.83±0.38	99.93±0.27	99.98±0.16	99.90±0.38	99.93±0.27	99.95±0.22	99.83±0.45	99.93±0.27	0.548$^{\#}$	0.750	0.007
Etomid ate (n=40)	100.00±0.00	99.80±0.46	99.93±0.27	100.00±0.00	100.00±0.00	99.93±0.35	100.00±0.00	99.93±0.27	100.00±0.00			

*p<0.05 levels (two tailed), **p<0.01 levels (two tailed), $^{\#}$Greenhouse-Geisser sphericity correction values, ^{a}Baseline HR and BMI was used as covariate. HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SpO_2: Arterial oxygen saturation, ECT: Electroconvulsive therapy, SD: Standard deviation

Table 4: Heart rate

Time	Group I	Group II	p
Baseline	88.16±10.96	84.23±11.89	0.1312
Pre-ECT	92.55±10.49	86.10±12.48	0.014
At 1 min	95.68±10.44	91.15±9.88	0.0512
At 3 min	106.33±11.51	104.68±11.63	0.5255
At 5 min	95.15±10.82	91.35±6.92	0.0651
At 8 min	88.50±9.16	81.75±7.71	0.0006
At 10 min	89.93±10.49	77.03±9.23	<0.0001
At 20 min	85.88±8.93	85.75±9.68	0.9504
At 30 min	82.58±9.95	81.10±9.61	0.5006

ECT: Electroconvulsive therapy

Table 5: Seizure duration

Time	Group I	Group II	p
Seizure duration (s)	29.15±9.95	47.33±15.19	<0.001

Table 6: Recovery criteria comparison between two groups (sec)

Time	Group I	Group II	p
Return to spontaneous respiration (min)	13.67±1.86	22.85±3.93	<0.001
Consciousness (min)	15.75±1.81	26.43±4.18	<0.001
Fully responding (min)	18.17±2.57	29.75±4.69	<0.001

Table 7: Side effects comparison between two groups (mean±SD)

Side effects	Group I, n (%)	Group II, n (%)
Fatigue	2 (5)	1 (2.5)
Weakness	1 (2.5)	0
Amnesia	2 (5)	0
Nausea	2 (5)	5 (12.5)
Sub seizure	4 (10)	0
Total	11 (27.5)	9 (22.5)

many changes that, while enhancing its efficacy and safety, have also complicated evaluation. Beginning in 1963, the treatment was modified by the use of intravenous anesthetic agents, neuromuscular blockade, and assisted ventilation with 100% oxygen.

The objective of the study was to evaluate the different effects of anesthetic agents used in ECT to suggest the preferred anesthetic agent in terms of better hemodynamic stability, adequate seizure duration, and recovery. The ideal anesthetic agent required for ECT should control the hemodynamic changes and related complications and also provide good amnesia and muscle relaxation along with adequate seizures.

There are similar studies that are suggestive of Etomidate as a more hemodynamically stable anesthetic. Jindal *et al*., in his study "Etomidate versus Propofol for Motor Seizure Duration during Modified ECT," took a sample size of a total of 70 patients aged 18–65 years which were randomly allocated using a computer-generated random number list into two groups – Group A: Propofol (1%)–1.0 mg.kg−1 and Group B: Etomidate 0.2 mg.kg−1 as an intravenous induction agent (75). Intraoperatively, motor seizure duration, induction time, and hemodynamic parameters, and at the end of the procedure, recovery parameters were assessed. He concluded that Etomidate had the advantage of longer seizure duration and stable hemodynamics. Mean motor seizure duration with Etomidate (55.17±19.06 s) was longer as compared to Propofol (27.80±17.33 s), and the difference was highly significant (p<0.001). Among hemodynamic parameters, there was a significant increase in HR (p=0.016) and a significant fall in mean arterial pressure (p=0.005) after induction with Propofol as compared to Etomidate. In his study, motor seizure duration was longer with Etomidate as compared to Propofol, and the difference was statistically significant (p<0.001), similar to the present study.

Zahavi and Dannon *et al*., in their study, also found stable hemodynamics with Etomidate as opposed to an elevation in blood pressure with other treatment groups (Propofol and Thiopental) [6]. DBP remained stable in the Etomidate group, as opposed to an elevation after treatment in the other groups (p=0.016). In the present study also, hemodynamics were stable with Etomidate. Similar results were contemplated in studies conducted by Aggarwal *et al*. also published a study on patients undergoing ECT comparing Propofol and Etomidate, which showed a significant decrease in MAP and a significant increase in HR from baseline to induction in the Propofol group as compared to the Etomidate group [6].

Erdil *et al*. have observed a more stable hemodynamic response with Propofol in comparison with Etomidate in their study evaluating patients with major depressive disorder and recommended the use of this agent in ECT anesthesia [7]. Gazdag *et al*. have found better hemodynamic effects of Propofol in comparison with Etomidate in their study comparing Etomidate and Propofol in patients with schizophrenia and depression [8].

The differences between these studies and ours may be caused by different characteristics (age, diagnosis, doses, groups, number of patients, etc.) of the patient populations. The Propofol group recovered faster than the Etomidate group in our study.

In a retrospective study comparing Etomidate (n=36) with Propofol (n=29), seizure duration was significantly shorter with Propofol, although total charge used and increase in charge between first and last treatments were both significantly longer; ECT course length was also significantly longer, requiring on average an extra two treatments with Propofol [9].

In our study, in the case of seizure duration, the distribution of the two groups was comparable.

We also observed that the mean seizure duration with the Propofol group was 29.15±9.95 s. Moreover, in the case of the Etomidate group was 47.33±15.19 s, which was comparable to the study conducted by Avramov *et al*. [10] Similar results were obtained by Bauer *et al*. [11] Mean seizure duration was found to be significantly significant (p<0.0001).

In our study, fatigue as a side effect was reported in two cases of the Propofol group and a single case of the Etomidate group. Weakness was reported in a single case in the Propofol group and none in the Etomidate group, while nausea was seen in two cases in the Propofol group, and five cases were found in the Etomidate group, respectively. No significant difference was noted in the adverse reaction profile between study groups (p=0.352). Similar side effects were seen with Etomidate and Propofol in a study by Aggarwal *et al*. [6] Jindal *et al*. found that in the Propofol group, the incidence of nausea and vomiting was 2.9% compared to 5.7% in the Etomidate group (p=0.555) [12].

CONCLUSION

In our study, we found that both the induction agents, Propofol and Etomidate, have individual advantages over one another. Etomidate has a better hemodynamic profile with fewer changes in HR, systolic blood pressure, DBP, and means arterial pressure compared to the Propofol group. It also has the advantage of providing a longer seizure duration. Etomidate was also found to be more effective in augmenting sub-therapeutic seizures. It can be a useful alternative for patients achieving suboptimal therapeutic responses to ECT. Propofol has the advantage of having rapid and smooth recovery compared to Etomidate. Minimum side effects were seen in both groups. Subseizure was seen with the Propofol group more than Etomidate. Hence, we conclude that Etomidate is a better induction agent than Propofol in modified ECT.

AUTHORS CONTRIBUTION

Contribute equally.

CONFLICTS OF INTERESTS

In my interest.

AUTHORS FUNDING

None.

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