Original Article

Comparison of Low Dose Propofol and Etomidate in Electroconvulsive Therapy a Double Blinded Randomised Controlled Crossover Trial

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Abstract

Background: Electroconvulsive Therapy is used for treatment of various psychiatric disorders and different anaesthetic agents were used earlier like Thiopentone, Methohexital, Ketofol and Propofol. Here we compare low dose Propofol and Etomidate with respect to motor seizure duration, seizure threshold, hemodynamic parameters, recovery characteristics and adverse effects. **Material and Methods:** After obtaining institutional ethical committee approval, 44 psychiatric patients of ASA grade 1 and 2 who required electroconvulsive therapy were included in the study. They were randomised by computer generated random number list into Group 1 and Group 2. In group 1 patients will receive Inj Propofol 1mg/kg in the first sitting[1P] and then Inj Etomidate 0.2mg/kg in the second sitting[1E]. In Group 2 patients will receive Inj Etomidate 0.2mg/kg in the first sitting[2E] and then Inj Propofol 1mg/kg in the second sitting[2P]. Effects of these drugs on seizure duration, threshold, hemodynamics, recovery characteristics and adverse effects were studied. **Results:** Seizure duration was higher when Etomidate [50± 11.49 s] was used compared to when Propofol was used [35.5± 9.05 s] which was statistically significant. Seizure threshold increased in the second sitting of electroconvulsive therapy compared to that in the first sitting irrespective of the drug used. Etomidate tends to have stable hemodynamics compared to Propofol. Propofol had early and smooth recovery as compared to Etomidate. **Conclusion:** Etomidate has advantage of longer seizure duration and stable haemodynamics. It may be useful in patients achieving subtherapeutic responses to electroconvulsive therapy. Propofol has rapid and smooth recovery, can be useful in elderly population.

Keywords: Electroconvulsive Therapy, Etomidate, Propofol.

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Introduction

Electroconvulsive therapy involves application of electric current to the human brain. It is used to treat certain psychiatric conditions like bipolar mood disorders, schizophrenia, catatonia, severe depression and suicidal tendency, mania, postpartum psychosis.[1,2] It is considered when rapid and robust clinical response is needed and in cases which are resistant to medical therapy. The general anaesthetic agent used is expected to have ideal characteristics like smooth induction, rapid recovery, minimal hemodynamic changes, achieve longer seizure duration, affordable and easily available.[3] Many intravenous anaesthetic agents were used like Methohexital, Thiopentone, Etomidate, Ketamine, Benzodiazepines and Propofol. Low dose Propofol causes longer seizure duration than higher doses of Propofol.[4] So, we compared low dose Propofol versus Etomidate in ECT.

Materials and Methods

After obtaining institutional ethical committee approval and informed written valid consent from the patients' attenders, 44 psychiatric patients of ASA grade I&II admitted with depressive disorder, schizophrenia, obsessive compulsive disorder, mania, catatonia and any other psychiatric disorder who required ECT from 8th January 2022 to 8th January 2023 were included in the study.

The patients were randomized by using a computer-generated random number list and randomly allocated in the ratio of 1:1 to one of the two study groups using coded and sealed opaque envelopes opened shortly before induction of anaesthesia. They were put into Group 1 and Group 2. In group 1 patients will receive Inj Propofol 1mg/kg in the first sitting(1P) and then Inj Etomidate 0.2mg/kg in the second sitting(1E). In Group 2 patients will receive Inj Etomidate 0.2mg/kg in the first sitting(2E) and then Inj Propofol 1mg/kg in the second sitting(2P).

The blinding was ensured by having the study drugs prepared and injected by an investigator who was not involved in collection of data. An independent observer, blinded to the type of drug being used, recorded the data. All the patients were kept fasting overnight. Benzodiazepines were stopped one day before the ECT.

Patient were wheeled into ECT room and intravenous cannula

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was secured. Baseline Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, SpO2 were recorded. Inj. Glycopyrrolate 0.2mg was given intravenously. Patients were mask ventilated with 100% Oxygen

Subgroup P patients received intravenous propofol 1mg/kg (10mg/ml iv preparation). Subgroup E patients received intravenous Etomidate 0.2mg/kg (2mg/ml iv preparation). Induction dose was considered adequate if loss of consciousness was achieved, confirmed by loss of responsiveness to verbal commands and loss of eyelash reflex.

Following this, manual blood pressure cuff was applied to the lower leg and inflated above systolic blood pressure to isolate the circulation of the foot to permit an accurate assessment of the motor seizure. Succinylcholine 0.5 mg/kg IV was administered to all the patients for neuromuscular relaxation.

When fasciculations subsided, bite block was inserted to prevent tongue bite. The psychiatrist was allowed to place bitemporal ECT electrodes on the forehead. A brief pulse stimulus of 0.7 s using a pulse of 70 Hz and 84 mC by Medica Brief pulse ECT machine BPE-2000 was given.

Motor seizure duration was recorded as the time interval between starting of the seizure episode till cessation of tonic-clonic motor activity in the isolated lower limb.Seizure threshold was measured as the lowest dose of stimulation which could elicit seizure activity clinically.

Subsequently, all the patients were ventilated with a face mask with 100% oxygen until the return of spontaneous respiration. All the patients were monitored for changes in HR, SBP, DBP, SpO2, and respiratory rate after the administration of study drug, after giving succinylcholine, then after ECT, at 1, 3, 5,7, 10 min, and then every 5 min throughout the procedure till shifting of the patient to post-anesthesia care unit (PACU).

Any side effects such as pain on injection site, fall in SpO2 below 90%, hypotension, i.e., fall in the MAP below 60 mmHg, nausea, vomiting, and myoclonus were noted.

Statistical analysis: Data was entered into Microsoft excel data sheet and analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was the test of significance. Continuous data was represented as mean and standard deviation. Independent t test was the test of significance to identify the mean difference between two groups. p value <0.05 was considered as statistically significant.

Results

Our study design is crossover study. 44 patients were considered. 2 groups of 22 patients each were made. In Group 1, patients received Inj. Propofol 1 mg/kg IV in the first ECT, then Inj. Etomidate 0.2 mg/kg IV in the 2nd ECT. In group 2 patients received Inj. Etomidate 0.2mg/kg IV in the first ECT and then Inj. Propofol 1 mg/kg in the 2nd ECT.

Table 1: Comparison of Group 1 and Group 2 according to age of patients

Age groups	Group 1	%	Group 2	%	Total	%
20-29yrs	9	40.91	9	40.91	18	40.91
30-39yrs	11	50.00	11	50.00	22	50.00
>=40yrs	2	9.09	2	9.09	4	9.09
Total	22	100.00	22	100.00	44	100.00
Mean age	30.82		31.55		31.18	
SD age	9.24		5.70		7.60	
P=1.00						

Mean age in group 1 is 30.82 ±9.24 years and 31.55±5.70 years in Group 2. There was no significant difference between different age groups and both groups were comparable [Table 1]. Both groups were comparable with respect to gender [Table 2].

Table 2: Comparison of Group 1 and Group 2 according to gender of patients.

Gender	Group 1	%	Group 2	%	Total	%
Male	11	50.00	14	63.64	25	56.82
Female	11	50.00	8	36.36	19	43.18
Total	22	100.00	22	100.00	44	100.00
Chi-square=0.8340, p=0.3610						

Table 3: Comparison of Propofol (1P+ 2P) and Etomidate (1E+2E) with Seizure threshold and Seizure duration by independent t test.

Variables	Groups	Mean	SD	SE	t-value	P-value
Seizure threshold	Propofol (1P+ 2P)	125.23	33.54	5.06	1.2365	0.2196
	Etomidate (1E+2E)	114.43	47.21	7.12		
Seizure duration	Propofol (1P+ 2P)	35.52	9.05	1.36	-6.9781	0.0001*
	Etomidate (1E+2E)	50.91	11.49	1.73		

Seizure threshold was higher with Propofol (125.23 ±33.54mC) than Etomidate (114.43±47.21mC), [Table 4, Figure1] but the results were statistically insignificant. Motor seizure duration with Etomidate (50.91±11.49s) was longer than that with Propofol (35.52±9.05s) [Table4, Figure1] and this difference was statistically significant with p value of 0.0001.

Seizure threshold in the 2nd ECT (134.95±39.12mC) was higher than that in the 1st ECT (104.70±37.61mC) irrespective of the drug used, this was statistically

significant with p value of 0.0004 [Table5, Figure2].

Table 4: Comparison of 1st ECT (1P+ 2E) and 2nd ECT (1E+2P) with Seizure threshold and Seizure duration by independent t test

Variables	Groups	Mean	SD	SE	t-value	P-value
Seizure threshold	1st ECT (1P+ 2E)	104.70	37.61	5.67	-3.6974	0.0004*
	2nd ECT (1E+2P)	134.95	39.12	5.90		
Seizure duration	1st ECT (1P+ 2E)	43.02	12.41	1.87	-0.1400	0.8890
	2nd ECT (1E+2P)	43.41	13.46	2.03		

Heart rate, oxygen saturation, systolic, diastolic and mean blood pressures were comparable in both the groups [Table 6-10].

Opening eyes after use of propofol (256.34±23.63s) was earlier than that after etomidate (269.95±25.01s), this difference was statistically significant with p value of 0.0103. Though obeying commands after propofol (438.68±27.51s) was earlier than that after etomidate (450.45±29.58s), this difference was statistically insignificant [Table 11, Figure3].

Table 5: Comparison of Propofol (1P+2P) and Etomidate (1E+2E) with Heart rate at different time points by independent t test

Time points	Propofol (1P+2P)		Etomidate (1E+2E)		t-value	p-value
	Mean	Std.Dev.	Mean	Std.Dev.		
Basal	87.95	11.94	88.68	12.50	-0.2791	0.7808
After induction	87.86	9.84	87.30	11.17	0.2532	0.8007
After SCh	99.48	14.31	96.48	12.50	1.0472	0.2979
At 1 min	99.32	10.52	96.45	11.26	1.2325	0.2211
At 3 min	98.89	9.95	96.45	11.84	1.0434	0.2997
At 5 min	95.86	11.73	93.59	11.32	0.9249	0.3576
At 7 min	92.82	9.70	91.27	11.40	0.6851	0.4951
At 10 min	89.95	10.75	89.55	11.30	0.1739	0.8623

Table 6: Comparison of Propofol (1P+2P) and Etomidate (1E+2E) with SBP at different time points by independent t test

Time points	Propofol (1P+2P)		Etomidate (1E+2E)		t-value	p-value
	Mean	Std.Dev.	Mean	Std.Dev.		
Basal	118.50	9.28	120.25	8.70	-0.9126	0.3640
After induction	110.41	11.14	114.00	11.22	-1.5066	0.1356
After SCh	123.91	8.42	124.41	13.71	-0.2061	0.8372
At 1 min	126.73	7.53	124.95	10.26	0.9240	0.3581
At 3 min	126.36	9.83	121.68	8.86	2.3469	0.0212*
At 5 min	122.73	11.40	118.86	8.82	1.7774	0.0790
At 7 min	121.36	10.13	120.09	6.91	0.6883	0.4931
At 10 min	120.18	9.04	120.00	8.45	0.0975	0.9226

Table 7: Comparison of Propofol (1P+2P) and Etomidate (1E+2E) with DBP at different time points by independent t test

Time points	Propofol (1P+2P)		Etomidate (1E+2E)		t-value	p-value
	Mean	Std.Dev.	Mean	Std.Dev.		
Basal	79.59	6.62	79.59	5.95	0.0000	1.0000
After induction	77.14	6.30	79.23	9.06	-1.2568	0.2122
After SCh	82.23	6.64	84.27	9.50	-1.1700	0.2452
At 1 min	82.95	3.89	83.00	5.34	-0.0456	0.9637
At 3 min	81.45	6.26	81.05	5.29	0.3312	0.7413
At 5 min	80.82	3.79	79.32	4.97	1.5908	0.1153
At 7 min	80.68	4.04	79.55	4.27	1.2820	0.2033
At 10 min	80.14	5.55	79.68	4.60	0.4182	0.6768

Table 8: Comparison of Propofol (1P+2P) and Etomidate (1E+2E) with MAP at different time points by independent t test

Time points	Propofol (1P+2P)		Etomidate (1E+2E)		t-value	p-value
	Mean	Std.Dev.	Mean	Std.Dev.		
Basal	92.56	6.94	93.14	6.13	-0.4182	0.6769
After induction	88.23	6.87	90.82	8.89	-1.5295	0.1298
After SCh	96.12	6.43	97.68	10.31	-0.8522	0.3965
At 1 min	97.55	4.17	96.98	6.59	0.4771	0.6345
At 3 min	96.42	6.80	94.59	5.83	1.3578	0.1781
At 5 min	94.79	5.48	92.50	5.82	1.8975	0.0611
At 7 min	94.24	5.35	93.06	4.57	1.1143	0.2683
At 10 min	93.48	6.14	93.12	5.16	0.3008	0.7643

Table 9: Comparison of Propofol (1P+2P) and Etomidate (1E+2E) with SpO2 at different time points by independent t test

Time points	Propofol (1P+2P)		Etomidate (1E+2E)		t-value	p-value
	Mean	Std.Dev.	Mean	Std.Dev.		
Basal	98.66	0.71	98.66	0.71	0.0000	1.0000

After induction	98.66	0.71	98.66	0.71	0.0000	1.0000
After SCh	98.68	0.71	98.68	0.71	0.0000	1.0000
At 1 min	98.64	0.72	98.64	0.72	0.0000	1.0000
At 3 min	98.61	0.72	98.61	0.72	0.0000	1.0000
At 5 min	98.66	0.71	98.66	0.71	0.0000	1.0000
At 7 min	98.64	0.72	98.64	0.72	0.0000	1.0000
At 10 min	98.66	0.71	98.66	0.71	0.0000	1.0000

Table 10: Comparison of Propofol (1P+2P) and Etomidate (1E+2E) with opens eyes in(s) and obeys commands in (s) by independent t test

Variable	Propofol (1P+2P)		Etomidate (1E+2E)		t-value	p-value
	Mean	Std.Dev.	Mean	Std.Dev.		
Opens eyes in(s)	256.34	23.63	269.95	25.01	-2.6248	0.0103*
Obeys commands in (s)	438.68	27.51	450.45	29.85	-1.9237	0.0577

In Etomidate group one patient had myoclonus exceeding 2 minutes which was terminated by Inj. Midazolam 2 mg IV. No other adverse effects were seen in this group. Whereas in the Propofol group 4 patients had pain on injection and 1 patient had nausea as side effects [Table 12].

Table 11: Side effects

	Myoclonus	Pain on injection	Nausea	Fall in SpO2 <90%	Fall in MAP <60 mmHg
Propofol	0	4	1	0	0
Etomidate	1	0	0	0	0

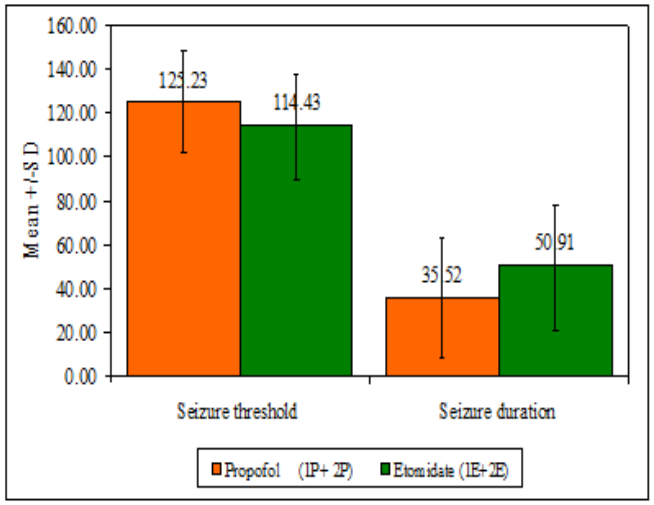

Figure 1: Comparison of Propofol (1P+ 2P) and Etomidate (1E+2E) with Seizure threshold and Seizure duration.

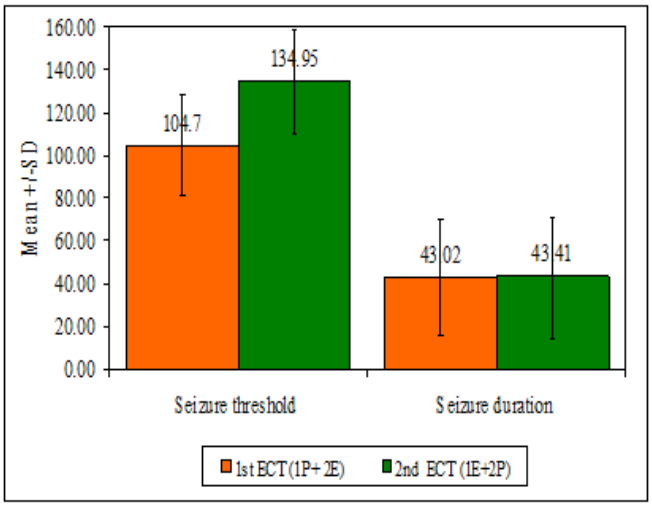

Figure 2: Comparison of 1st ECT (1P+ 2E) and 2nd ECT (1E+2P) with Seizure threshold and Seizure duration

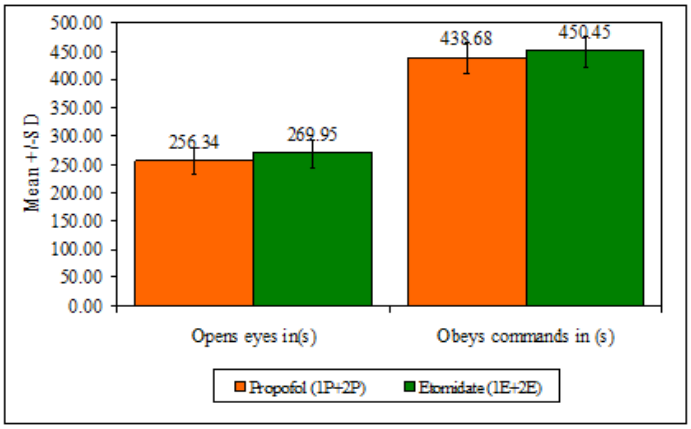

Figure 3: Comparison of Propofol (1P+2P) and Etomidate (1E+2E) with opens eyes in(s) and obeys commands in (s)

Discussion

ECT is mainstay of treatment in psychiatric conditions where immediate action is needed. It is useful in conditions refractory to medical line of management. Different anaesthetic agents have individual advantages and disadvantages. Many agents decrease the seizure duration which can hamper the efficacy of ECT. Here Propofol and Etomidate are compared. Motor seizure duration and seizure threshold was compared between that of Propofol and Etomidate. Seizure threshold was compared between the 1st ECT and the 2nd ECT irrespective of the drug used. Haemodynamic parameters, recovery parameters and side effects were compared between Propofol and Etomidate.

Motor seizure duration

Gazdag G et al,[5] showed that Etomidate (46.3±23.8s) was found to have significantly more seizure duration than Propofol (33.6±15.9s). In study conducted by Avramov MN et al,[6]

seizure duration with propofol was 32 seconds and with Etomidate was 44 seconds. Eranti S.V. et al,[7] noted that motor seizure duration with propofol was 17.32±8.59s and that with Etomidate was 31.93±29.07s. Tan et al,[8] demonstrated that motor seizure duration with Etomidate was 52.65s and that with Propofol was 24.55s. Graveland et al,[9] found that mean motor seizure duration with Etomidate was 46.1±14.4s and that with Propofol was 22.39 ±7.1s. Singh et al,[10] conducted a meta analysis and found that pooled motor seizure duration in Etomidate group was longer by 11.13s than Propofol group. Mir et al,[11] found that motor seizure duration in Propofol group was 27.6s and 56.5s in Etomidate group. Jindal et al,[12] demonstrated that mean motor seizure duration with etomidate (55.17 ± 19.06 s) was more, as compared to propofol (27.80 ± 17.33 s). In our study, motor seizure duration with Etomidate (50.91±11.49s) was more than that with Propofol (35.52±9.05s) and this difference was statistically significant with p value of 0.0001.

Seizure threshold

Patel A.S. et al,[13] found that mean final seizure threshold (mC) for Etomidate was 193.4±114.4 mC and that for Propofol was 384.0 ±195.7 mC. Eranti S.V. et al,[7] demonstrated that mean seizure threshold with propofol was 675.63 ±203.85 mC and that with Etomidate was 209.86 ±116.91 mC. Graveland et al,[9] found that mean seizure threshold with Propofol was 544.9 ± 237.6 mC and that with Etomidate was 227.6 ±130.4. Coffey et al,[14] demonstrated that the seizure threshold for first ECT was 55.0±26.3 mC and that for second ECT was 81.5± 51.4 mC. In our study, 125.23 ±33.54 mC was the seizure threshold associated with Propofol and 114.43 ±47.21 mC with Etomidate. In the first ECT, the seizure threshold was 104.70 ±37.61 mC and 134.95 ±39.12 mC in the second ECT. The seizure threshold increased in the subsequent ECT treatments.

Recovery Parameters

Avramov et al,[6] found that the time to open eyes after Propofol was 14±4 min and that after Etomidate was 16±6 min. The time to obey commands after Propofol was 19±6 min and that after Etomidate was 21±8 min. Mir et al,[11] demonstrated that the time to obey commands after Propofol was 7.1±0.32 min and that after Etomidate was 9.1±0.37 min. Jindal et al,[12] found that the recovery time after Propofol was 6.4±3.90 min and that after Etomidate was 7.17±2.38 min. In our study the time to open eyes with Propofol was 4.27±0.39 min and that after Etomidate was 4.5±0.42 min; The time to obey commands after Propofol was 7.31±0.46 min and that after Etomidate was 7.51±0.5 min.

Haemodynamic data

Avramov MN et al,[6] found that Propofol attenuates haemodynamic response to ECT better than Etomidate. Zahavi and Dannon et al,[15] noted a stable diastolic blood pressure in case of Etomidate and elevated DBP in case of Propofol. Mir et al,[11] concluded that Propofol was superior to Etomidate and Thiopentone with respect to haemodynamic changes. Jindal et al,[12] concluded that Etomidate has stable haemodynamics and is better than other anaesthetic agents in cases of coronary artery disease, myocardial ischaemia, hypovolemia, cerebral vascular disease, valvular heart disease and cardiomyopathy. In, our study SBP values, HR, DBP and SpO2 was comparable with both the groups.

Side Effects

Patel A.S. et al,[13] noted that in the Etomidate group of 36 patients, 6 patients had tachycardia, one had bradycardia, 3 patients had hypertension, 9 patients had tachypnoea and 3 patients had arrhythmia. In Propofol group of 29 patients, 7 patients had tachycardia, 6 had hypertension, 4 had hypotension, 5 had tachypnoea and 2 had nausea and vomiting as side effects. Tan et al,[8] found that, in the Etomidate group of 20 patients, 6 patients had myoclonus and 2 had pain on injection. In the Propofol group of 20 patients, 5 patients had pain on injection and 1 had abnormal movements. Jindal et al,[12] observed myoclonus in the Etomidate group with an incidence of 8.6% and no myoclonus was seen in Propofol group. In our study, in Etomidate group one patient had myoclonus exceeding 2 minutes which was terminated by Inj. Midazolam 2 mg IV. No other adverse effects were seen in this group. Whereas in the Propofol group 4 patients had pain on injection and 1 patient had nausea as side effects.

Conclusion

Seizure duration is significantly higher with Etomidate than Propofol in our study. So we can conclude that Etomidate is a better agent for those patients who have subtherapeutic ECT treatments with short seizure duration.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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