Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL11, ISSUE 02, 2020

Original research article

Comparative study of propofol versus ketamineas inducing agent on hemodynamic and seizure activity in modified electroconvulsive therapy

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Abstract

Introduction: Convulsive interventions have been used for treatment of different psychiatric illnesses since the 16th century and even today in the form of Electroconvulsive Therapy (ECT).[1] General anaesthesia is required for ECT and it is usually provided by a hypnotic agent. Considering the intravenous anaesthetics, it should provide a smooth and rapid induction, with minimal effects on seizure activity, rapid recovery and hemodynamic stability. The aim of this study was to compare the hemodynamic effects and seizure activity during Modified Electroconvulsive therapy with Propofol and Ketamine used as inducing agents.

Methods: The present study was a prospective, single blinded, randomized controlled and comprised of 60 psychiatric patients. The patients were randomized to receive either Propofol (group P) or Ketamine (group K) as an inducing agent 30 patients each. To compare the study groups, parametric data (like age, sex, weight) was analyzed by paired Student's t-test and non-parametric data was compared by chi square test.

Results: Ketamine caused significant rise in Heart rate (HR) and both systolic as well as mean arterial pressures at the time of induction, muscle relaxation and electrical stimulation as compared to propofol. Ketamine group had the significant more seizure duration than that of propofol group. Recovery time was less in propofol group but statistically was not significant.

Conclusion: use of ketamine has favourable effect on the seizure duration and may have clinical advantage but at the cost of unacceptable hemodynamic parameters. So, it must be used with vasoactive drugs to control rise in HR, Blood pressure.

Keywords: Propofol, Ketamine, Electroconvulsive therapy

Introduction

Convulsive interventions have been used for treatment of different psychiatric disorders since the 16th century and even today in the form of ECT [1]. Now a days, ECT has become an effective treatment option for many psychiatric illnesses, such as severe depression, bipolar disorder, and schizophrenia [2, 3]. ECT is a procedure of safe induction of a series of generalized epileptic seizures for therapeutic purposes, using brief-pulse stimulation techniques under anaesthesia and muscle paralysis [4]. The choice of anaesthetic agent may influence seizure, hemodynamic, and recovery parameters and even the cognitive functions after ECT [5]. Considering the intravenous anaesthetics, it should provide a smooth and rapid induction, with minimal effects on seizure activity, rapid recovery and hemodynamic stability and no pain on injection. Various types of anaesthetic agents are available, including Methohexital, Thiopental Sodium, Propofol, Benzodiazepines, Etomidate, Ketamine and Sevoflurane. Propofol has become a well-liked induction agent in ECT as it is associated with reasonable hemodynamic response to ECT and quick recovery with little nausea, although it causes increased seizure threshold and marked shortening of seizure duration [6, 8].

Ketamine has been used in ECT anaesthesia for decades and it has been suggested that ketamine possesses an advantage of the antidepressant and cognitive function preserving action along with seizure inducing property during ECT [9]. However, cardiotoxicity and induction of transitory psychotic episodes, and delayed recovery, are the main disadvantages of ketamine that make its use limited [9, 10].

The present study was designed to evaluate propofol as an induction agent for modified ECT and compare it with ketamine and the effect of these two agents on hemodynamic parameters and seizure duration.

Aim and Objectives: To study and compare the hemodynamic effects and seizure activity during

ISSN:0975 -3583,0976-2833 VOL11, ISSUE 02, 2020

Modified Electroconvulsive therapy (MECT) with Propofol and Ketamine used as inducing agents.

Material and Methods: The present study was a prospective, single blinded, randomized controlled study which was carried out in the department of Anaesthesiology, Mahatma Gandhi Insitute Of Medical Siciences, Sewagram, Wardha, after approval of the local institutional ethical committee FROM MAY 2013 TO 2015 April. In this study we compared the hemodynamic effects and seizure activity of Propofol and Ketamine used as an inducing agents in patients undergoing modified electroconvulsive therapy.

The study was comprised of 60 psychiatric patients. The patients were randomized to receive either Propofol (group P) or Ketamine (group K) as an inducing agent 30 patients each.The patients belonging to group P received inj Propofol 1.5 mg/kg IV and group K received inj. Ketamine 2 mg/kg IV, as inducing agents for general anaesthesia during the MECTs.

Inclusion criteria

Patient of either sex with age group 15-45 years

Patients with American society of anaesthesiologists (ASA) grades I and II

Exclusion criteria

- Relative refused to give consent
- Children below 15 years
- Patients undergoing ECT for the second time without any seizure on the previous ECT
- Patients with ASA grade III and IV
- Agitated patients requiring additional sedation

All patients were undergone pre-anaesthetic evaluation comprising of detail history taking, clinical examination. The current medications were recorded and continued throughout the trial. Informed written consent was taken from the patient and his/her responsible relatives or guardians.

The procedure was carried out in morning with all the patients fasting overnight, with no dental prosthesis, contact lenses, or any ornaments and wearing proper clothing. The procedure room was fully equipped with drugs necessary for the cardiopulmonary resuscitation, intubation and defibrillation. Monitoring of systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), ECG and haemoglobin oxygen saturation (SpO_2) were observed and recorded prior to induction and throughout the procedure. All patients received pre-anaesthetic medications with injection (inj.) Glycopyrrolate 0.2 mg IV and inj. Ondansetron 0.08 mg/kg IV before the start of procedure. All patients were pre-oxygenated with 100% oxygen for 5 minutes. Anaesthesia was induced with either Propofol (1%) at the dose of 1.5 mg/kg or Ketamine at the dose of 2 mg/kg. Then Succinylcholine was administered in dose of 0.5 mg/kg body weight.

All the patients were ventilated with 100% oxygen with face mask using Magill's circuit (Mapleson A circuit) till fasciculations subsided and muscle relaxation achieved.

A mouth gag (Oberto's mouth gag) was inserted inside the oral cavity separating tongue, teeth and buccal mucosa, to prevent any damage to the oral cavity during the procedure. The ECT electrode was applied to the head on both sides of the temporo-frontal regions (bi-temporal ECT). MECT was given using a pulse of 70 Hz of 0.8 msec duration with total stimulus time not exceeding 1.25 seconds, by BPE-591 machine, to all patients in the study. If required mouth gag was changed to Guedel's airway after the seizure activity subsided. Patients were ventilated with 100% oxygen till regaining of spontaneous respiration.

The HR, SBP, DBP, SpO_2 and ECG changes were recorded at different time intervals including, before induction of anaesthesia (T0), after administration of the study drug (T_i), after Succinylchline (T_S), after applying ECT (T_e), at one minute (T_1), at three minutes (T_3), at five minutes (T_5), at ten minutes (T_{10}) and at 15 minutes (T_{15}).

The duration of seizure activity was recorded in seconds by clinical method (tourniquet method) from the start of electrical impulse to the end of the clonic contraction using a hand held stopwatch.

The assessment of recovery was done on six criteria:

1. Establishment of spontaneous ventilation (R1)
2. When patient will be able to open eyes on command (R2)
3. Able to answer the questions (like where are you) i.e. orientation (R3)
4. Able to sit up (R4)
5. Ability to stand (R5)
6. Ability to walk from the recovery room (R6)

The assessment was done at frequent intervals and time was noted from induction to achieve these criteria.

Side effects during induction, during procedure and recovery were also noted like-

ISSN:0975 -3583,0976-2833 VOL11, ISSUE 02, 2020

During Induction: Discomfort on injection site, movement not due to light plane of anaesthesia, hypertonus, hiccough, flush, twitching, tremor, masseter spasm, cough, bronchospasm, laryngospasm and hypoxia.

During the procedure: Fracture of long bones, injuries to soft tissues of the oral cavity, bronchospasm, laryngospasm, hypoxia and cardiac arrest.

During recovery: Euphoria, withdrawal, headache, vomiting/ nausea, bronchospasm, flush, depression, restlessness, confusion, amnesia, myalgia, bronchospasm, laryngospasm and hypoxia.
Complications if occurred during study were treated as per standard line of management.
To compare the study groups, parametric data (like blood pressure, heart rate, and mean arterial blood pressure) was analysed by paired Student's t-test and non-parametric data was compared by chi square test.

Observations and Results
There were 22 and 28 patients with grade I ASA and 8 and 2 patients with grade II ASA in Group K and Group P respectively.
The age of patients ranged from 16 years to 53 years in group P while 17 years to 60 years in group K. The mean age was 32.23 years and 30.3 years in Group K and P respectively. P= 0.66, p>0.05.
The weight of patients ranged from 40-72 kg in Group K while 45-70 kg in group P. The mean weight was 57.06 kg and 57.33 kg in Group K and P respectively. p= 0.89, p>0.05.
Thus age and weight were statistically comparable.
In the present study, the number of male patients and female patients were 17 and 13 in group K while 14 and 16 in group P.
The group were statistically comparable as for sex ratio, as p value being 0.60 (p>0.05).

Table 1: Showing diagnosis in both the groups

Diagnosis	Frequency	Percent
Acute and transient psychosis	2	3.3%
Bipolar mood disorder	20	33.3%
Catatonic schizophrenia	2	3.3%
Mixed anxiety depression	1	1.7%
Paranoid schizophrenia	21	35.0%
Schizoaffective disorder	3	5.0%
Severe depressive disorder	6	10.1%
Severe depression with mental retardation	1	1.7%
Severe depression with psychotic symptoms	4	6.7%
Total	60	100.0%

Table 2: Showing the Mean HR in both the groups at different times

Time	Group P	Group K	P value
ToHR	77.20	74.03	0.469
TiHR	79.60	90.23	0.330
TsHR	90.27	100.73	0.307
TeHR	92.00	125.70	0.002
T_1HR	82.77	113.63	0.000
T_3HR	86.77	105.97	0.020
T_5HR	85.17	102.33	0.037
T_{10}HR	84.27	100.37	0.072
T_{15}HR	83.80	97.67	0.077

Figures in the parenthesis indicates Standard Deviation

The mean HR values for Te and T_1, T_3, T_5, T_{10}, T_{15} in group P were not significantly increased when compared to the pre-induction level. While, all these above values in group K, showed a significant increase when compared to the pre induction level and the maximum increase was seen at the Te.
The difference between the mean pulse rates for Te, T_1, T_3 and T_5 in both groups were statistically significant (p value < 0.05).

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Table 3: Showing Mean SBP in both the groups at different times

TIME	Group P	Group K	P value
ToSBP	112.60	115.73	0.543
TiSBP	105.17	136.70	0.003
TsSBP	123.57	147.53	0.034
TeSBP	131.03	161.97	0.018
T_1SBP	126.53	150.73	0.042
T_3SBP	117.70	142.50	0.009
T_5SBP	118.07	135.17	0.065
T_{10}SBP	117.30	132.40	0.049
T_{15}SBP	114.97	130.93	0.031

Figures in the parenthesis indicates Standard Deviation

The differences for values of mean SBP between the two groups at the interval of Ti, Ts, Te, T_1, T_3, T_{10}, T_{15} were statistically significant ($p< 0.05$) as shown in Table 3.

Table 4: Showing the Mean DBP in both the groups at different times

	Group P	Group K	P Value
ToDBP	71.20	77.80	0.141
TiDBP	69.70	94.17	0.001
TsDBP	80.93	104.37	0.007
TeDBP	86.60	110.57	0.007
T_1DBP	83.37	99.73	0.011
T_3DBP	77.50	96.63	0.010
T_5DBP	76.73	90.47	0.049
T_{10}DBP	77.47	89.83	0.060
T_{15}DBP	77.73	90.00	0.045

Figures in the parenthesis indicates Standard Deviation

The mean DBP showed statistically significant difference between the two groups for the values of Ti, Ts, Te, T_1, T_3, T_5, T_{15} ($p< 0.05$) as shown in Table 4.

Table 5: Showing the Mean Arterial BP (MAP) in both the groups at different times

	Group P	Group K	P Value
ToMAP	84.66	89.37	0.40
TiMAP	82.40	104.87	0.006
TsMAP	94.03	118.60	0.014
TeMAP	99.97	127.27	0.020
T_1MAP	99.87	117.63	0.033
T_3MAP	99.90	107.20	0.015
T_5MAP	99.90	105.10	0.061
T_{10}MAP	99.70	103.03	0.109
T_{15}MAP	99.27	101.77	0.073

Figures in the parenthesis indicates Standard Deviation

Just after induction (Ti) and muscle relaxation (Ts) the MAP in group P and in group K showed statistically significant difference with $p< 0.05$, as shown in Table 5.
Then the mean MAP in group P and group K showed statistically significant difference for the values of Ti, Ts, Te, T_1 and T_3, with $p< 0.05$, as shown in Table 5.

Table 6: Showing the Mean Seizure duration in both the groups

	Group k	Group p	P value
Seizure duration	25.43	17.47	0.024

The difference between the mean seizure duration of two groups was statistically significant with the p Value = 0.024 (<0.05), as shown in Table 6.

Table 7: Showing the Mean Recovery time in minutes in both the groups

Recovery	Group K	Group P	P value
Establishment of spontaneous ventilation(R1)	3.27	2.97	0.739
When patient was able to open eyes on command(R2)	6.23	6.17	0.600
Able to answer the questions i.e. orientation(R3)	9.77	9.20	0.740
Able to sit up (R4)	13.33	12.50	0.339
Ability to Stand (R5)	16.30	15.63	0.492

ISSN:0975 -3583,0976-2833 VOL11, ISSUE 02, 2020

Ability to walk from the recovery room (R6)	20.13	18.80	0.068

Figures in the parenthesis indicate the standard deviation

The two groups had no significant different in view of all these recovery times, as the p value was > 0.05 (Table 7). The recovery time was measured from the time as soon as the electrical stimulation was applied.

Among complications, in group P, six patients complained of pain and discomfort at the injection site, one suffered from the cough, one got headache and one suffered from confusion.

In group K, two patients had euphoria, one patient got headache and two suffered from confusion as complication.

Table 8: Showing distribution of complications in both the groups

Complications	Groups		Total	P value
	Propofol	Ketamine		
Present	9 (30.0)	5(16.7)	14 (23.3)	0.36
Absent	21(70.0)	25(83.3)	46 (76.7)	
Total	30 (50.0)	30 (50.0)	60 (100.0)	

Figures in the parenthesis denotes percentages) (x2 value 0.84 at df1)

30.0% patients had complications in group P as compared 16.7% in group K but statistically this difference was not significant (p value >0.05)

Discussion

There was no statistically significant difference between the two groups in age, sex ratio and ASA status.

Hemodynamic variability

In the present study, the HR was statistically significantly increased in the ketamine group compared to propofol group. The mean maximum rise in HR in group P above the baseline value was about 22% and 42% in group K, which was clinically significant.

According to one comparative study of propofol and ketamine in ECT, by Yalcin S *et al*, the induction HR was significantly decreased compared to baseline values in the propofol group and it was significantly increased at induction and at the 3rd, 5th, and 10th minute compared to baseline value in ketamine group [11]. In that study, HR at induction and 3rd minute of ECT was statistically significantly increased in the ketamine group compared to propofol group. In another study, by Wang X *et al*, propofol group had significantly lower maximal heart rates (101.5/min) compared to ketamine (130.2/min) [12]. Our results are comparable with these studies.

In the present study, the ketamine group showed significant increase in the values, at the time of induction, muscle relaxation, electrical stimulation, 1st, 3rd, 10th and 15th minute than propofol. In case of mean arterial pressure, When the two groups were compared, ketamine group had significant increase in mean arterial pressure at time of induction, muscle relaxation, electrical stimulation, 1st and 3rd minute than propofol group. In ketamine group, mean maximum rise in SBP from baseline was 28.55% and mean maximum rise in MAP was 29.88%. In propofol group, mean maximum rise in SBP from baseline was 14.07% while mean maximum rise in MAP was 15.58%. Thus blood pressure changes in the ketamine group went beyond the clinically relevant range (± 20%) from baseline. This difference was also statistically significant.

In the previous similar study, by Yalcin S *et al*, induction MAP values significantly decreased compared to baseline values in the propofol group [11]. While MAP at the 1st, 5th, and 10th minute in the ketamine group significantly increased compared to baseline values. MAP measured at baseline, at induction, and at the 1st, 3rd, 5th, and 10th minute after ECT were not statistically significantly different among the two groups. The observations in another study by Hoyer C *et al*, showed that in the ketamine group, 47.3% of the seizures resulted in postictal hypertension with systolic blood pressure over 200 mmHg, whereas the incident was lower in the etomidate (23.8%) and thiopental group (29.2), and lowest in the propofol (7.1%) group, with a significant difference [13].

Similarly, Okamoto N *et al*, found that there was significantly higher rate of hypertension in ketamine group as compared to propofol group [9]. In other study, by Wang X *et al*, the similar observation of higher rate of hypertension in ketamine group as compare to propofol group was found in results [12]. Our findings also match the observations in the above mentioned studies.

Seizure duration

The aim of ECT is to obtain generalized convulsions over 20 seconds. Reducing the duration of convulsive activity in the brain reduces the therapeutic efficacy [14].

In the present study, the mean seizure duration in the group P was 17.47 seconds and was 25.43 seconds in group K, showing a statistically significant difference between the two groups. In another study, by

ISSN:0975 -3583,0976-2833 VOL11, ISSUE 02, 2020

Hoyer C *et al*, ketamine anaesthesia in ECT had longer seizures [13]. On the other hand, lowest quality seizures were observed under propofol anaesthesia, corroborating previous findings [13]. In other previous comparative studies also, by Yalcin S *et al*, Okamoto N *et al* and Wang X *et al*, the ketamine group had the significant more seizure duration than that of propofol group [9, 11, 12]. Our study findings are similar to the above mentioned studies.

Recovery profile

In the present study, simple recovery test like ability of the patients response to vocal commands with opening eyes, able to answer question, ability to sit unaided, stand and walk from the recovery room were used.

The recovery time was less in propofol group than ketamine but statistically it was not significant. While in the past, a similar study by, Yalcin S *et al*, showed that the spontaneous breathing time in ketamine group statistically increased compared to propofol group, also eye-opening time and obeying-command time were significantly increased in the ketamine group compared to propofol group [11]. Our study findings match with findings of Yalcin *et al*.

Complications

During ECT, complications can occur at any stage during induction, during the application of electrical current or recovery.

In our study, during induction, some patients complained of severe injection pain, but this problem was solved by slower injection and the use of larger veins. 20% patients in group P complained of pain and discomfort at the injection site. Similarly, in previous studies, by Okamoto N *et al* and Wang X *et al*, 42% and 45% of patients respectively, in the propofol group suffered from pain at injection site, whereas none in ketamine group suffered from this [9, 12]. However one patient of group P suffered from the cough. On the other hand, Ketamine is known for its mechanism of suppressing N-methyl D-aspartate (NMDA) receptors which effectively suppresses coughing [15].

In the recovery period, 6.7% patients in the group K had euphoria and 3.3% patient in each group got headache as complication. 6.7%patients of group K and 3.3% from the group P suffered from the confusion as a part of complication. Similarly in other study, by Krystal AD *et al*, the percentage of patients with headache were 42% vs 50%, patients with nausea were 17% vs 25%, with brief delirium after awakening were 8% vs 17%, with prolonged delirium were 0% vs 8% and sense of fear upon awakening from anaesthesia were 0% vs 25% in the group p and k respectively [16]. In another study, 2 out of 30 patients in ketamine group had nausea and vomiting [11]. In a similar comparative study, by Okamoto N *et al*, the adverse events in the ketamine and propofol groups were headache (36% vs 40%), nausea (9% vs 15%), sense of fears with hallucinations upon awakening from anaesthesia (27% vs 0%), brief delirium within 1 hour after awakening (9% vs 15%), and prolonged delirium longer than 1 hour (0% vs 5%) [9].

Summary: An attempt has been made in our present work to study hemodynamic parameters, seizure duration and recovery parameter with use of either propofol or ketamine during modified ECT. In patients undergoing modified ECT, use of ketamine has favourable effect on the seizure duration and may have clinical advantage. But this comes at the cost of delayed recovery and unacceptable hemodynamic parameters. We recommend that if ketamine is considered as an induction agent during modified ECT, it must be used with vasoactive drugs to control rise in HR, BP. Further trials are however needed to support this recommendation.

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