Comparison between sodium thiopentone, propofol and etomidate as an induction agent for modified electroconvulsive therapy

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Abstract

Introduction: Electroconvulsive Therapy is a well-established psychiatric treatment in which seizures are electrically induced in anaesthetized patients for therapeutic effects.

Material & Methods: This study was carried out after clearance from the ethical committee. 150 cases were in this study, divided into three equal groups (n=50). Group A was received Propofol 1%, group B received Etomidate, group C received Sodium Thiopentone 2.5%. They were compared as regards induction time, seizure duration, hemodynamic effects, recovery from anaesthesia & immediate side effects.

Result: Induction was quicker in Propofol group i.e. 44.3 /5.02 s than in Etomidate 52.54 / 5.21 s and 50.16 / 5.68 s. Seizure duration was significantly higher in Etomidate 29.34/ 6.99 s compared to Propofol 19.4/ 7.51 s & Thiopentone 24/ 6.99 s. Though significant rise in HR, SBP, DBP and MAP was observed in all 3groups following ECT; but the rise was least in Propofol group. Significantly faster recovery was observed with Propofol. Immediate side effects were not significant in the three groups.

Conclusion: Propofol seems to be superior to Etomidate and Sodium Thiopentone when used as an induction agent for modified ECT.

Keywords: ECT, propofol, etomidate, thiopentone

Introduction

Electroconvulsive therapy (ECT) is a well – established psychiatric treatment in which seizures are electrically induced in anaesthetized patients for therapeutic effects. The use of electroconvulsive therapy to provoke seizures was described in 1938 and was performed without Anaesthesia for almost 30 years [1]. The aim of electroconvulsive therapy is to provide a Grand Mal Seizure; it is a seizure rather than the electrical stimulus, which is responsible for its therapeutic effect. ECT is a simple procedure, performed on a highly diverse patient population, most often used as a treatment for severe Major Depressive disorders with suicidal tendencies, not responding to treatment and is also used in the treatment of Mania, Catatonia, and Schizophrenia[2,3].

This technique has replaced pharmacologically produced seizure therapy. The efficacy of ECT in alleviating acute depression is dependent on the duration of induced seizure. Electroencephalographic (EEG) seizure duration lasting from 25 to 50 seconds is found to produce the optimal antidepressant response. Initially, lack of adequate anaesthesia or muscle relaxation during ECT lead to bone fractures, dislocation of joints, biting of tongue, and tearing of muscle fibers [4]. In addition, lack of knowledge about the dose parameters for electrical stimulation leads to more adverse cognitive effects [5]. ECT can produce severe disturbances in the cardiovascular system, mostly a transient period of hypertension and changes in the heart rate [6]. When an electrical current is applied to the brain, the resultant EEG spike and wave activity is accompanied by generalised motor seizure and an acute cardiovascular response, which results in marked increase in cerebral blood flow and intracranial pressure [7]. The hemodynamic response to ECT can produce myocardial ischemia and even infarction, as well as transient neurological ischemic deficit, intracerebral haemorrhages and cortical blindness.

Due to trauma caused to patient physically and psychologically with unmodified direct ECT in the past, it has now been modified with anaesthesia [8]. These cardiovascular changes may be altered using various anaesthetic drugs and the violent muscular contractions occurring during the convulsions can be reduced by the use of muscle relaxants.

Sodium Thiopentone is a barbiturate that is used for General Anaesthesia, for the treatment...
Of ischemic brain injury, and for the treatment of neurosurgical situations such as high intracranial pressure [9]. Its effects on the cardiovascular system are a decrease in the mean arterial blood pressure and a decrease in cardiac output. Significant side effects of Sodium Thiopentone are laryngeal spasm and respiratory depression. Benign allergic skin reactions are common, but serious allergic reaction is rare.

Propofol causes a rapid and smooth entry into unconsciousness and is linked to rapid regaining of consciousness. Common side effects are cardiovascular depression, pain during injection, bradycardia, and apnea in the minutes after injection. Respiratory and cardiovascular function might be slightly depressed by Etomidate in an insignificant manner. It can cause adrenal suppression for a few hours and a decrease in the production of adrenocortical hormones such as cortisol. Additional side effects are nausea and vomiting during recovery from Anaesthesia, myoclonic activity, and pain during injection.

Material and Methods
After obtaining approval from the Institutional Ethical Committee along with written and informed consent, 150 adults of either sex belonging to American Society of Anaesthesiology (ASA) Class I & II posted for ECT, aged 18 to 60 years, willing to give consent were enrolled for this study. Patient’s refusal, allergic to study drug or any other substances, history of cardiovascular, renal and liver diseases and pregnancy were excluded from the study. Adequate NBM Status and valid informed consent was confirmed then patient was shifted to procedure room. Electrocardiogram, pulse oximeter, and non-invasive blood pressure were attached and baseline reading (0 reading) of vital parameters were recorded, this was followed by intravenous cannulation using 20G/22G cannula, and were premedicated with IV Glycopyrrolate 0.2 mg. The patients were assigned to one of the following group:

Group A - Propofol 1% - 1.5 mg/kg
Group B - Etomidate - 0.2 mg/kg
Group C - Thiopentone 2.5% - 5 mg/kg.

Patients were preoxygenated with 100% oxygen for 3 min. General anaesthesia was induced with IV anaesthetic agent as per the group allocated, till loss of eyelid reflexes. IV Succinylcholine 0.5 mg/kg was administered to all patients for neuromuscular relaxation. When fasciculations subsided and adequate neuromuscular relaxation was obtained, an adequate sized bite block was inserted to prevent tongue bite. A brief pulse stimulus (Medicad Machine) for about 1-2 s, frequency 70 Hz was given to produce seizures. Seizure duration was monitored by observation method. Subsequently, all the patients were ventilated with face mask with 100% oxygen at rate of 14-18 breaths per minute until spontaneous breathing returned and patient recovered from the state of anaesthesia. All the patients were monitored for changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and SpO₂ at basal level, 1 min, 2 min, 3 min, 5 min,10 min, 20 min, and 30 min after ECT. Duration of recovery were recorded from injection of anaesthetic agent to time taken to obey vocal commands such as opening of eyes, obey simple commands. The data collected was entered in the master chart. The result were analyzed statistically by percentage, mean, standard deviation, Chi-square test, unpaired t test,

ANNOVA test.

Results
The results are formulated in various sections:

Table 1: Age wise distribution of study participants in group A, B & C.

| Variables   | Group | N  | Mean | SD  | p-value |
|-------------|-------|----|------|-----|---------|
| Age (years) | A     | 50 | 31.69| 10.12|
|             | B     | 50 | 33.64| 10.04|
|             | C     | 50 | 31.76| 10.26|
| Total       |       | 150| 32.37| 10.11|

Graph 1: Age distribution of study participants in group A, B & C.

Table 2: Weight wise distribution of study participants in group A, B & C.

| Variables | Group | N  | Mean | SD  | p-value |
|-----------|-------|----|------|-----|---------|
| Weight (Kgs) | A     | 50 | 52.11| 6.99 |
|            | B     | 50 | 53.73| 8.55 |
|            | C     | 50 | 52.00| 7.48 |
| Total      |       | 150| 52.40| 7.28 |

Graph 2: Weight distribution of study participants in group A, B & C

Table 3: Gender wise distribution of study participants in group A, B & C.

| Gender | Group | Total |
|--------|-------|-------|
| Female | A     | 25    |
|        | B     | 28    |
|        | C     | 18    |
|        | Total | 71    |
|        | p-value | 0.121 |
| Male   | A     | 25    |
|        | B     | 22    |
|        | C     | 32    |
|        | Total | 79    |
|        | p-value | 0.55  |
| Total  |       | 50    |
|        |       | 50    |
|        |       | 150   |
|        | p-value | 0.803 |
Graph 3: Gender wise distribution of study participants in group A, B & C.

Table 4: ASA classification of participants among study group A, B & C.

| ASA Grade | Group | A  | B  | C  | Total |
|-----------|-------|----|----|----|-------|
| I         |       |    |    |    |       |
|           | I     | 46 | 47 | 44 | 137   |
|           |       | 92.0% | 94.0% | 88.0% | 91.3% |
| II        |       | 4  | 3  | 6  | 13    |
|           | II    | 8.0% | 6.0% | 12.0% | 8.6%  |
| Total     |       | 50 | 50 | 50 | 150   |
|           |       | 100.0% | 100.0% | 100.0% | 100.0% |
| p-value   |       |    |    |    | 0.5546|

Graph 4: ASA classification of participants among study group.

Table 5: Comparison of mean heart rate among study participants

| Heart Rate | Group | N  | Mean | SD  | p-value |
|------------|-------|----|------|-----|---------|
| 0 min(Baseline) | A | 50 | 91.78 | 16.31 | 0.575 |
| 0 min(Baseline) | B | 50 | 91.80 | 17.67 |
| 0 min(Baseline) | C | 50 | 88.58 | 18.68 |
| Total 0 min(Baseline) | | 150 | 90.72 | 17.53 |
| 1 mins | A | 50 | 95.00 | 19.02 | 0.47 |
| 1 mins | B | 50 | 98.82 | 17.17 |
| 1 mins | C | 50 | 99.48 | 18.30 |
| Total 1 mins | | 150 | 97.76 | 18.10 |
| 2 mins | A | 50 | 102.34 | 22.81 | <0.05 (A vs B & C) |
| 2 mins | B | 50 | 109.00 | 17.27 |
| 2 mins | C | 50 | 112.68 | 14.30 |
| Total 2 mins | | 150 | 108.01 | 18.84 |
| 3 mins | A | 50 | 100.98 | 18.57 | <0.05 (A vs B & C) |
| 3 mins | B | 50 | 107.52 | 18.54 |
| 3 mins | C | 50 | 110.72 | 16.46 |
| Total 3 mins | | 150 | 106.40 | 17.85 |
| 5 mins | A | 50 | 98.40 | 17.00 | 0.015(A & B vs C) |
| 5 mins | B | 50 | 100.18 | 20.26 |
| 5 mins | C | 50 | 108.30 | 15.24 |
| Total 5 mins | | 150 | 102.29 | 17.54 |
| 10 mins | A | 50 | 94.18 | 14.98 | 0.26 |
| 10 mins | B | 50 | 95.94 | 14.73 |

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Comparison of mean heart rate in group A, B and C.

### Table 6: Comparison of Systolic blood pressure (SBP) among the study participants in Group A, B & C.

| SBP | Group | N   | Mean  | SD   | p-value |
|-----|-------|-----|-------|------|---------|
|     | Baseline |     |       |      |         |
|     | A      | 50  | 115.66| 8.77 | 0.73    |
|     | B      | 50  | 116.72| 10.78|         |
|     | C      | 50  | 117.16| 9.50 |         |
|     | Total  | 150 | 116.51| 9.67 |         |
|     | A      | 50  | 120.30| 12.11| 0.028   |
|     | B      | 50  | 123.02| 10.06|         |
|     | C      | 50  | 126.52| 12.40|         |
|     | Total  | 150 | 123.28| 11.52|         |
|     | A      | 50  | 133.88| 13.99| 0.0004  |
|     | B      | 50  | 141.72| 17.21|         |
|     | C      | 50  | 147.58| 12.48|         |
|     | Total  | 150 | 141.06| 14.56|         |
|     | A      | 50  | 128.78| 15.76| <0.01   |
|     | B      | 50  | 145.12| 15.97|         |
|     | C      | 50  | 147.90| 18.47|         |
|     | Total  | 150 | 140.60| 18.69|         |
|     | A      | 50  | 120.68| 10.16| <0.01   |
|     | B      | 50  | 126.54| 12.73|         |
|     | C      | 50  | 130.64| 12.23|         |
|     | Total  | 150 | 125.95| 11.70|         |
|     | A      | 50  | 115.92| 8.10 | <0.05   |
|     | B      | 50  | 120.76| 9.43 |         |
|     | C      | 50  | 119.70| 8.03 |         |
|     | Total  | 150 | 118.79| 8.74 |         |
|     | A      | 50  | 112.68| 16.01|         |
|     | B      | 50  | 117.28| 7.67 |         |
|     | C      | 50  | 117.22| 8.51 |         |
|     | Total  | 150 | 115.73| 11.50|         |
|     | A      | 50  | 113.14| 6.68 | 0.071   |
|     | B      | 50  | 113.86| 8.11 |         |
|     | C      | 50  | 115.74| 8.71 |         |
|     | Total  | 150 | 114.25| 7.90 |         |

Comparison of Diastolic blood pressure (DBP) among the study participants in group A, B & C.

### Table 7: Comparison of Diastolic blood pressure (DBP) among the study participants in Group A, B & C.

| DBP | Group | N   | Mean  | SD   | p-value |
|-----|-------|-----|-------|------|---------|
|     | 0 min (Baseline) |     |       |      |         |
|     | A      | 50  | 73.64 | 7.07 | 0.505  |
|     | B      | 50  | 74.20 | 8.98 |         |
|     | C      | 50  | 75.54 | 8.83 |         |
|     | Total  | 150 | 74.46 | 8.32 |         |
|     | A      | 50  | 75.10 | 7.97 | <0.0001|
|     | B      | 50  | 77.86 | 9.68 |         |
|     | C      | 50  | 84.24 | 9.48 |         |
|     | Total  | 150 | 79.06 | 8.99 |         |
|     | A      | 50  | 83.18 | 10.89| <0.01   |
|     | B      | 50  | 90.40 | 7.99 |         |
|     | C      | 50  | 95.72 | 9.81 |         |
|     | Total  | 150 | 89.77 | 10.87|         |
|     | A      | 50  | 81.18 | 9.55 | <0.0001|
|     | B      | 50  | 91.08 | 9.80 |         |
|     | C      | 50  | 98.10 | 12.98|         |
|     | Total  | 150 | 90.12 | 10.77|         |
|     | A      | 50  | 76.50 | 7.89 | <0.01   |
|     | B      | 50  | 83.60 | 10.42|         |
|     | C      | 50  | 84.32 | 8.38 |         |
|     | Total  | 150 | 81.47 | 9.58 |         |
|     | A      | 50  | 74.28 | 7.63 | 0.089  |
|     | B      | 50  | 76.36 | 6.76 |         |
|     | C      | 50  | 77.56 | 8.00 |         |
|     | Total  | 150 | 76.07 | 7.35 |         |
|     | A      | 50  | 72.48 | 6.29 |         |
|     | B      | 50  | 74.64 | 6.67 |         |
|     | C      | 50  | 75.72 | 8.24 |         |
|     | Total  | 150 | 74.28 | 7.20 |         |
|     | A      | 50  | 72.34 | 6.09 | 0.071  |
|     | B      | 50  | 72.70 | 7.20 |         |
|     | C      | 50  | 74.66 | 7.88 |         |
|     | Total  | 150 | 73.23 | 7.12 |         |
Table 8: Comparison of Mean arterial pressure (MAP) among the study participants in group A, B and C.

| MAP (0 min) Baseline | Group | N  | Mean | SD  | p-value  |
|---------------------|-------|----|------|-----|----------|
|                     | A     | 50 | 87.40| 6.76|          |
|                     | B     | 50 | 88.02| 8.73|          |
|                     | C     | 50 | 89.10| 8.57|          |
|                     | Total | 150| 88.17| 8.05| 0.568    |
| 1 min               | A     | 50 | 91.54| 13.87| <0.01 (A & B vs C) |
|                     | B     | 50 | 96.00| 9.01 |          |
|                     | C     | 50 | 98.02| 10.05|          |
|                     | Total | 150| 95.18| 11.55|          |
| 2 min               | A     | 50 | 99.72| 10.85| <0.01 (all groups) |
|                     | B     | 50 | 106.88| 10.14|          |
|                     | C     | 50 | 112.68| 9.41 |          |
|                     | Total | 150| 106.43|11.40|          |
| 3 min               | A     | 50 | 96.76| 10.58| <0.01 (all groups) |
|                     | B     | 50 | 106.98| 17.38|          |
|                     | C     | 50 | 113.90| 14.20|          |
|                     | Total | 150| 105.88|15.89|          |
| 5 min               | A     | 50 | 90.78| 7.58 | <0.01 (A vs B & C) |
|                     | B     | 50 | 97.04| 15.81|          |
|                     | C     | 50 | 98.40| 9.21 |          |
|                     | Total | 150| 95.41| 11.84|          |
| 10 min              | A     | 50 | 88.06| 6.76 | <0.0001 (A vs B & C) |
|                     | B     | 50 | 92.98| 6.94 |          |
|                     | C     | 50 | 95.22| 7.65 |          |
|                     | Total | 150| 92.08| 7.11 |          |
| 20 min              | A     | 50 | 86.30| 5.37 | 0.33     |
|                     | B     | 50 | 86.82| 12.84|          |
|                     | C     | 50 | 88.96| 8.37 |          |
|                     | Total | 150| 87.36| 9.38 |          |
| 30 min              | A     | 50 | 85.60| 5.25 | 0.24     |
|                     | B     | 50 | 86.14| 6.47 |          |
|                     | C     | 50 | 87.88| 8.86 |          |
|                     | Total | 150| 86.54| 7.04 |          |

Graph 7: Comparison of Diastolic blood pressure (DBP) among study participants in group A, B and C.

Graph 8: Comparison of Mean arterial blood pressure (MAP) among study participants in group A, B & C.

Table 9: Comparison of mean induction time, seizure duration and anaesthesia duration in study participants between group A, B and C.

| Variables          | Group | N  | Mean | SD  | p-value    |
|--------------------|-------|----|------|-----|------------|
| Induction Time     | A     | 50 | 44.30| 5.02| <0.01 (A vs B & C) |
|                    | B     | 50 | 52.54| 5.21|            |
|                    | C     | 50 | 50.16| 5.68|            |
|                    | Total | 150| 49.00| 6.32|            |
| Seizure Duration   | A     | 50 | 19.40| 7.51| <0.01 (all groups) |
|                    | B     | 50 | 29.34| 6.99|            |
|                    | C     | 50 | 24.00| 6.99|            |
|                    | Total | 150| 24.25|8.20|            |
| Anaesthesia Duration| A   | 50 | 10.20| 2.75| <0.01 (A & B vs C) |
|                    | B     | 50 | 11.16| 2.49|            |
|                    | C     | 50 | 17.28| 4.11|            |
|                    | Total | 150| 12.88|4.47|            |
Table 10: Comparing side effects between group A, B and C.

| Side effects      | Group | N   | frequency | Percentage |
|-------------------|-------|-----|-----------|------------|
| Pain on injection | A     | 50  | 5         | 35.71%     |
|                   | B     | 50  | 0         | 0%         |
|                   | C     | 50  | 0         | 0%         |
| Total             | 150   | 5   | 35.71%    |            |
| Myoclonus         | A     | 50  | 0         | 0%         |
|                   | B     | 50  | 5         | 35.71%     |
|                   | C     | 50  | 0         | 0%         |
| Total             | 150   | 5   | 35.71%    |            |
| Cough             | A     | 50  | 0         | 0%         |
|                   | B     | 50  | 0         | 0%         |
|                   | C     | 50  | 4         | 28.57%     |
| Total             | 150   | 4   | 28.57%    |            |

Fig 12: Side effects

Result

- No significant difference was seen in the mean age, mean weight, gender wise distribution and ASA grading of the patients in the 3 groups.
- There was increase in heart rate after ECT in all the three groups, maximum rise was seen at 2 min interval after ECT, maximum increase was seen in group receiving Thiopentone, minimum in Propofol group which was statistically significant.
- SBP, DBP & MAP increased after ECT in all the three groups. Maximum rise was seen in Thiopentone group, minimum in Propofol group.
- Induction time was least in Propofol group compared to Etomidate and Thiopentone group. The mean induction time in group A, B and C was 44.30 +/- 5.02 s, 52.54 +/- 5.21 s and 50.16 +/- 5.68 s respectively. This was statistically significant in group A as compared to group B & C (P<0.01; A vs B & C).
- The mean seizure duration in group A, B and C was 19.40 +/- 7.51 s, 29.34 +/- 6.99 s and 24 +/- 6.99 s respectively. This was statistically significant in all groups. Seizure duration was maximum in group receiving Etomidate.
- The anaesthesia duration was minimum with Propofol.
- In group receiving Propofol pain on injection was observed in 5 patients as compared to none in Etomidate group & Thiopentone group. The incidence of myoclonus was high in Etomidate group i.e. 5 patients as compared to none in the other two groups. In Thiopentone group cough was observed in 4 patients and none in the other two groups.

Discussion

Electroconvulsive therapy is one of the most widely recognised, accepted & most effective treatment modality for various psychiatric illness. April 2013 saw the 75th anniversary of the first use of electroconvulsive therapy, making it the oldest surviving physical treatment in psychiatry.

In the present study, the demographic data i.e. mean age, gender distribution, mean weight, ASA grade was statistically significant. Studies conducted by Omprakash TM et al [10], Kumar A et al [11], Premendran B et al [12], Mir AH et al [13] showed similar results as our study.

Increase in the heart rate, SBP, DBP & MAP after ECT was observed in all 3 groups. It was statistically significant. Propofol showed minimum increase in all the 3 parameters. Propofol blunts sympathetic response, the lower heart rate in propofol has been attributed to resetting of baroreflex to allow lower heart rate at lower arterial pressures. Boey WK et al [14], Saito S et al [15], BP Manjula et al [16], Mir AH et al [17] showed similar results in their studies.

Mean seizure duration was significantly shorter with Propofol. Maximum duration was with Etomidate. Though studies show significant reduction in seizures duration with propofol, efficacy or therapeutic outcome was not affected. Studies by Duria U et al [17], Mir AH et al [13] were in concurrence with our study.

Mean duration of Anaesthesia was least in Propofol, had significantly earliest & smooth recovery (<0.01) followed by Etomidate and Thiopentone. Rosa MA et al [18], Premendran B et al [12] showed results concurrent with our study.

Propofol had pain on injection as the main side effect, Etomidate had myoclonus and Thiopentone had cough as side effects. Studies conducted by Patil AP et al [19], Donthu B et al [20], Mir AH et al [19] showed similar results. These studies are in concurrence with our study.

Thus, our study showed that propofol has least time for induction, provides stable hemodynamics, takes less time in recovery from anaesthesia. Etomidate has maximum seizure duration.

Conclusion

Propofol as an induction agent had a smooth rapid induction, comparable hemodynamic stability, reduced duration of seizure activity without affecting the efficacy of electroconvulsive therapy, faster recovery and minimal side effects after recovery.

Thus, Propofol seems to be superior to Thiopentone Sodium and Etomidate when used as an induction agent for Modified Electroconvulsive Therapy.

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