

COMPARISON OF PROPOFOL AND THIOPENTONE FOR MODIFIED ELECTROCONVULSIVE THERAPY

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Abstract

Background: This study was designed to compare Thiopentone and Propofol for Modified Electroconvulsive therapy (ECT) in terms of hemodynamic stability, seizure activity & recovery profile. **Materials and Methods:** 30 consented patients took part in this study with every patient receiving a total of six treatments. It was a randomized crossover study with 15 patients receiving Thiopentone in the first three treatments and Propofol in the next three treatments, while the other 15 received Propofol in the first three treatments and Thiopentone in the next three treatments. Hemodynamic parameters recorded were systolic blood pressure, diastolic blood pressure and pulse rate. Seizure activity was studied by seizure duration and quality of seizure in terms of tonus and clonus during seizure. Recovery was assessed by time for eye opening and time to sit unaided (both from the time of induction), quality of walking after 20 minutes of induction (graded on a five-point scale), and score in the questionnaire after thirty minutes of induction. **Result:** Pain on injection was the only side effect, significantly more with Propofol. The fall in blood pressure with induction was significant with both the agents. Increase in the blood pressure after ECT was also significant with both the drugs, but this rise was higher with Thiopentone. The increase in pulse rate was also significantly less with Propofol. The early return of hemodynamic variable towards the baseline values was significantly higher with Propofol. The mean duration of seizure in our study was 35.9 ± 2.1 secs with Thiopentone and 28.5 ± 2.25 with Propofol. Thus even though, Propofol was associated with a shorter duration of seizure as compared to Thiopentone, the resultant duration of seizure was significant for the therapeutic efficacy of ECT. There was no significant difference in the quality of seizure between the two drug groups. Comparison of recovery profile also did not reveal a significant difference between the two drug groups. **Conclusion:** We conclude that Propofol gives better hemodynamics, clinically significant seizure duration and similar recovery profile as compared to Thiopentone.

INTRODUCTION

ECT is a commonly used treatment for severe mental health conditions, such as depression and schizophrenia. The use of general anesthesia is necessary during ECT to induce controlled seizure and when used, it is termed as Modified ECT. Modified ECT necessitates the use of an appropriate anaesthetic that would produce a smooth as well as rapid induction and a quick recovery. It also mandates that there be an attenuation of the physiologic effects of ECT. Profound autonomic responses have been well documented as a result of both, the electric shock and the seizure. With the

application of stimulus there is an initial period of vagal reactivity followed by sympathetic hyperactivity.^[1-3]

Multiple drug regimens have been suggested to blunt these autonomic responses, but unfortunately these drugs have been associated with a decrease in the seizure duration. Seizures lasting less than twenty seconds are generally without any therapeutic benefit.^[2]

It is feared that in comparison to other available intravenous anaesthetic agents, Propofol has more potent anticonvulsant effects and this might decrease the seizure duration to less than required duration of at least 20 seconds.^[3-2] However the use of a minimally hypnotic dose of Propofol was associated

with a seizure duration that was comparable to hypnotic doses of methohexital. Studies have also shown that even though the seizure duration with Propofol is consistently shorter, the Hamilton Rating Scale for depression had improved to a similar degree as compared to methohexital.^[4]

Thus, although Propofol gives better hemodynamic stability and a superior recovery profile compared to Thiopentone, decrease in the seizure duration caused by it has been much talked about as a disadvantage. Considering the amount of work done on this topic, and the questions arising on the efficacy of Propofol as an anaesthetic agent for ECT, this study was done to compare it with more commonly used Thiopentone in our setup.

MATERIALS AND METHODS

The study was a prospective, randomized, crossover design, conducted by Department of Anesthesiology and Critical Care, involving 30 consented patients who were scheduled to undergo E.C.T in the department of Psychiatry at Jawaharlal institute of Post Graduate medical education and research (JIPMER), Pondicherry during the year 2003 - 2005.

Inclusion Criteria

ASA 1 or 2 patients, Age group >15 yrs or < 60 yrs and new cases with no previous ECT. Exclusion criteria included ongoing treatment with Carbamazepine, Aminophylline, Diltiazem, and Labetalol, patients requiring additional sedation on the day of ECT and history of ECT in the past

All patients underwent a pre-anesthetic evaluation and were assessed for fitness as well as for inclusion and exclusion criteria. A questionnaire was asked to the patients during the pre-anaesthetic evaluation and the score out of ten was recorded. Informed consent was taken. Randomization of the drug to be given first was also done during pre-anesthetic evaluation using sealed envelope technique. Thus, half of the patients received Propofol during the first three treatments and Thiopentone during the remaining three treatments while the other half had received Thiopentone during the first three treatments and Propofol during the next three treatments.

The medications which patients were receiving were recorded and kept unchanged throughout the study period. E.C.T was carried out in the morning after an overnight fast. Once the patient was shifted in the ECT room, base line blood pressure, pulse rate, were recorded. Intravenous access was secured in one of the upper limbs and the opposite upper limb was isolated by tying a tourniquet for the measurement of seizure duration. To attenuate the vagal stimulation, Atropine 0.3mg i.v was given one minute before induction.

After preoxygenation with 100% oxygen for 3 min, either Thiopentone (2.5 mg/kg), or Propofol (1.0 mg/kg), was given to the patients over 20 sec through an indwelling intravenous cannula. Induction was considered achieved if the eye lash reflex was lost

with in 30 secs, otherwise additional agent was given and titrated as necessary, and the dose was recorded for the next treatment. Same dose of the induction agent was used in the next treatment and criterion for induction was also kept same. If in case patient showed signs of light anesthesia in the next (or the second) treatment the dose was titrated for that sitting and this dose was given in the third treatment. Induction time was recorded from the time of giving the induction agent till the loss of eyelash reflex. After induction, systolic & diastolic blood pressure and pulse rate were recorded. During induction, occurrence of any adverse effect like, pain on injection, movement due to light anesthesia, hyper tonus, hiccough, bronchospasm, masseter spasm, cough & laryngospasm were also noted.

A tourniquet was tied to the upper limb after induction, and was inflated to 50 mmHg above the systolic blood pressure to measure the duration of unmodified seizure using the isolated arm technique. Succinylcholine 0.5 mg/kg was then administered. Once the fasciculations were over or if 60 secs had passed after giving succinylcholine, four breaths were given with 100% oxygen via a face mask. Bite block was inserted and bilateral ECT was given by the Psychiatrist. The settings and the position of the electrodes was decided by the Psychiatrist.

Recording of systolic & diastolic blood pressure, and pulse rate was done at one minute and five minutes after the cessation of seizure. Duration of seizure was recorded from the time of application of electric shock till the cessation of seizure in the isolated limb. Quality of seizure was graded as follows

Tonus

- Good -Facial muscle contraction with mild movement of fingers and toes
- Moderate: - Contraction of Facial muscles, shoulder and limbs
- Poor: - Severe contraction of all the muscles, including back.

Clonus

- Good: - Movement of facial muscles and platysma, with slight movement of fingers and toes
- Moderate: - Above plus movement of limbs
- Poor: - Severe movement of all muscles including back

After the seizure was over, ventilation was maintained with 100% oxygen using face mask and Bain's circuit till the return of spontaneous breathing. Four recovery parameters were studied

1. The time to open eyes on command
 2. Time to sit unaided
- Both the Parameters were recorded from the time of induction
3. Patient's ability to walk 10 meters after 20 minutes of induction. This was graded as

- No impairment
- Slight impairment: body sway
- Moderate impairment: one or two staggers only
- Severe impairment: constantly staggering

- Unable to stand
 - Refusal to cooperate
4. Questionnaire answered by the patient during pre op evaluation was repeated after 30 min of induction. Questionnaire consisted of the following:-
- What is your name?
 - What is your date of birth?
 - Do you know where you are?
 - Do you know what city you are in?
 - What is the name of your country?
 - Do you know the month?
 - Do you know the year?
 - Do you know the day of the week?
 - Do you know the date today?
 - Why are you here?

The score out of ten was recorded and compared with the score during the pre anaesthetic evaluation. During recovery occurrence of adverse effects like headache, vomiting, bronchospasm, flush, restlessness, confusion, nausea &, laryngospasm was noted.

The statistical package employed by us was Statistical package for social scientists (S.P.S.S. 13.0). Statistical analysis was performed using the paired 'T' test for numeric variables – induction time, seizure duration, hemodynamic parameters and questionnaire score. Incidence of side effects was analyzed by Fisher's exact test. Grading of walking and quality of seizure were analyzed using Wilcoxon sign rank test and sign test. Period effect was analyzed for the seizure duration. Statistical significance was assumed when $P < 0.05$.

RESULTS

Thirty patients were included in this study with 18 being females and 12 Males.

Mean age of the patient's population was 27.8 and weight was 55.8 kgs. Thirteen patients were diagnosed with catatonia, two with endogenous depression, one with manic psychosis, one with paranoid schizophrenia, four with psychosis, and nine with severe depression.

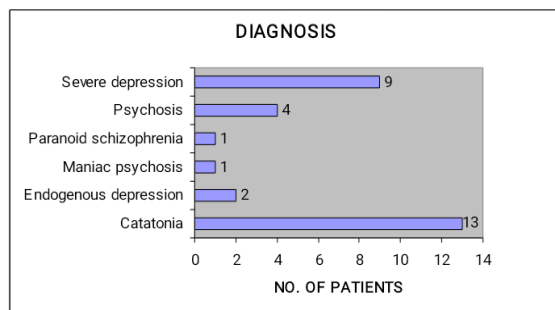


Figure 1: Indication for ECT

Mean induction time with Propofol in all the treatments was 36.5 ± 2.86 seconds while that with Thiopentone was 29.6 ± 2.07 seconds. This difference was statistically significant (<0.05). Mean dose of

Thiopentone required was 3.35 ± 1 mg/kg, and that of Propofol was 1.45 ± 0.56 mg/kg.

Statistical difference was noted only in the incidence of pain on injection and was significantly (P value 0.006) more with propofol (30%) than with thiopentone (8.8%).

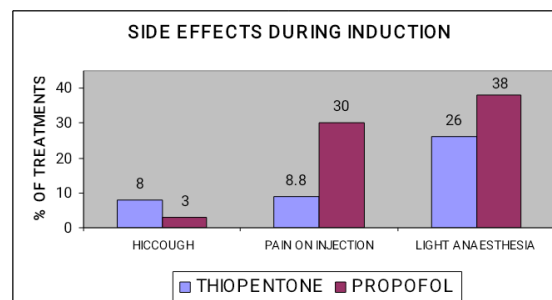


Figure 2: Side effects during induction

Hemodynamic parameters were comparable at baseline and induction readings, but there was a statistically significant difference in readings at one minute and five minutes after the ECT.

Base line systolic blood pressures were 117.4 ± 1.3 mmHg and 117.6 ± 1.4 mmHg with Thiopentone and Propofol respectively. The rise in systolic blood pressures after ECT was significant among all the treatments with thiopentone and propofol at one minute. At five minutes after ECT systolic blood pressure measurements with propofol were not significantly different from the base line values (in the first and second treatment). Thus, the trend of return to pre-anaesthetic measurements was early with propofol. This trend was not seen in with thiopentone. These differences were statistically significant (P value <0.05).

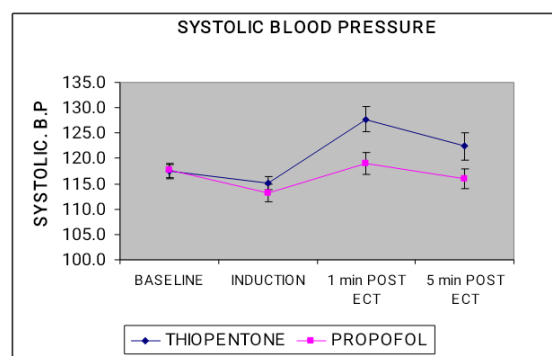


Figure 3: Systolic Blood Pressure

Baseline diastolic blood pressure and diastolic blood pressures after induction were comparable in both the groups being 77.4 ± 1.5 mmHg with Thiopentone and 78.8 ± 1.2 mmHg with Propofol. The diastolic blood pressures were significantly higher (P value <0.05) in Thiopentone group at both one minute and five minutes after the E.C.T. The difference in the diastolic blood pressure at induction and at one minute after ECT was analyzed. Similarly, the difference in diastolic blood pressure at induction and at five minutes was also analyzed. The rise in diastolic blood

pressures after ECT was significant in all the treatments with thiopentone and propofol at one minute. At five minute after ECT diastolic blood pressure measurements with propofol were not significantly different from the base line values in all the treatments. The rise in diastolic blood pressure from induction was significantly higher with Thiopentone at both one minute and five minutes after ECT. These differences were statistically significant.

Baseline pulse rate and pulse rate after induction were comparable in both the groups being 77.4 ± 10.2 mmhg with Thiopentone and 78.8 ± 2.3 mmhg with Propofol. The pulse rates were higher in Thiopentone group at both one minute and five minutes after the E.C.T. The rise in pulse rate from induction was significantly higher with Thiopentone at both one minute and five minutes after ECT. Propofol showed a return to baseline values at five minutes. This was not seen with Thiopentone. These differences were statistically significant (P value < 0.05).

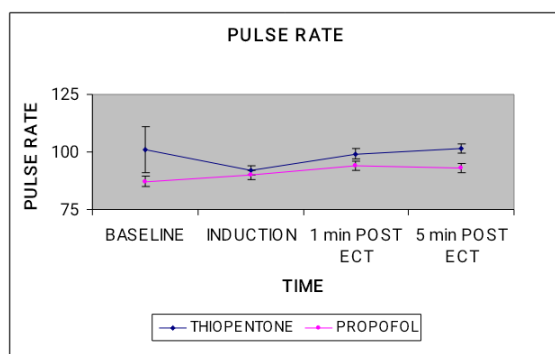


Figure 4: Pulse Rate

Seizure activity was studied as a) seizure duration and b) quality of seizure in terms of tonus and clonus during the seizure. Mean duration of seizure was 35.9 ± 2.1 seconds with Thiopentone and 28.5 ± 2.25 seconds with Propofol. This difference was statistically significant. There was no significant difference found in the seizure duration between first, second and the third treatments within the group.

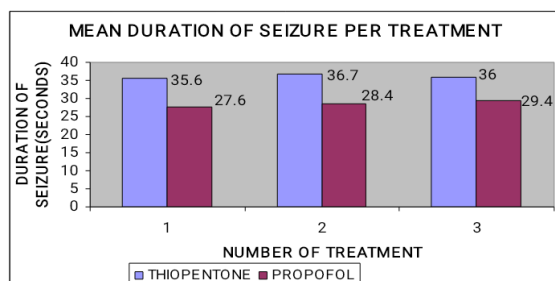


Figure 5: Mean Duration of Seizure Per Treatment

Quality of tonus was better with Thiopentone in 20% of the patients while with Propofol it was better in 23% of the patients. Rest 57 % of the patients had similar quality of tonus with Thiopentone as well as Propofol. Quality of clonus was better with Thiopentone in 20% of the patients while with

Propofol it was better in 30% of the patients. Rest 50 % of the patients had similar quality of clonus with Thiopentone as well as Propofol. Although this difference was not statistically significant, Propofol gave better seizure tonus in 3% of the patients and better seizure clonus in 10% of the patients.

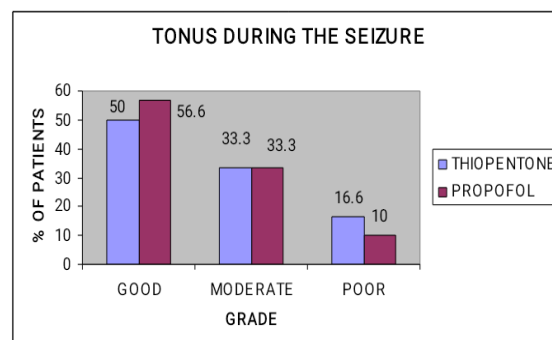


Figure 6: Tonus During Seizure

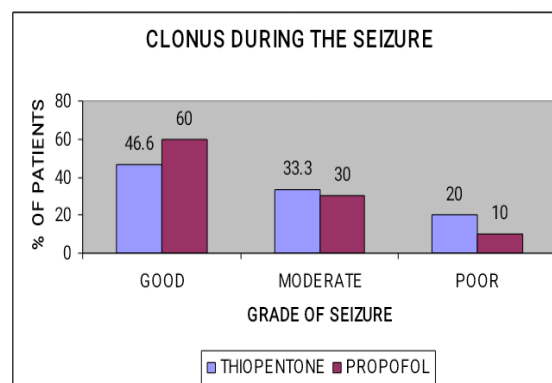


Figure 7: Clonus During Seizure

Recovery profile was studied with four parameters 1. Time for eye opening 2. Time for sitting, 3. Time for walking 10 & 20 minutes after ECT and 4. Response to questionnaire.

Mean time taken to open the eyes after induction was 8.1 ± 0.27 minutes and 9.6 ± 0.3 minutes, with Thiopentone and propofol respectively. This difference was not statistically significant. Mean time taken from induction to sit unaided was 12.9 ± 0.53 minutes and 12 ± 0.38 minutes with Thiopentone and Propofol respectively. This difference also was not statistically significant. Walking after ECT was graded; with 44% of the patients walking equally well with both thiopentone and propofol. 33% of the patients did better with Propofol while 23% of the patients did better with Thiopentone. Although this difference was not statistically significant, recovery was slightly better in the Propofol group.

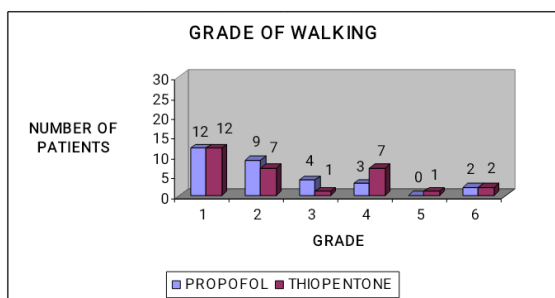


Figure 8: Grade of Walking

There was no statistical difference in the score of questionnaires between the two drug groups.

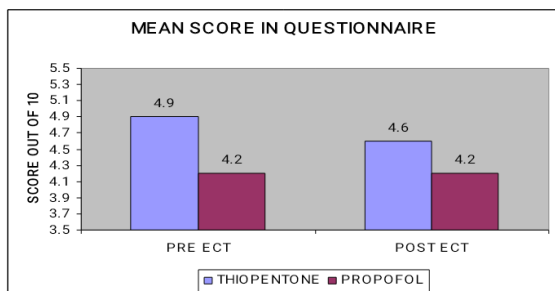


Figure 9: Mean Score in Questionnaire

DISCUSSION

In this study, we compared Thiopentone and Propofol as induction agents for ECT. Since electrically induced seizures produce effective amnesia, it is only imperative to provide hypnosis for the muscle paralysis in the event of a missed or incomplete induced seizure. Since the dose of induction agent inversely affects the duration of seizure duration, a minimal dose of induction agent should be used for ECT.^[4]

Avramov et al,^[4] had observed that Propofol, at doses of more than 1 mg/kg leads to 35 -45% decrease in the ECT induced seizure duration. Further as seizure duration of < 20 seconds is generally without any therapeutic benefit, it was decided by us to use 1 mg/kg as the dose of Propofol, similarly equipotent dose of Thiopentone (2.5 mg/kg) was used.^[2]

Mean doses of both the agents were comparable to the ones finally used by Boey et al,^[5] Mean induction time were comparable to the induction time for Propofol mentioned by Rolly et al when Propofol is given in 20 seconds (mean $\pm$ SD – 34.7 $\pm$ 8.6 secs)^[6]. Movement due to light anaesthesia was not significantly different between the two drug groups in our study. This difference was comparable to the incidence mentioned by Boey et al.^[5]

The increase in blood pressures after ECT was significant among all the treatments with Thiopentone and Propofol at one minute after ECT. At five minutes after ECT blood pressure measurements with propofol showed a trend of return to baseline values. Increase in pulse rate after ECT was also statistically significant in both the groups at one minute, but return towards the baseline at five

minute was significantly more with Propofol. Although this increase was statistically significant it was not of clinical significance as the blood pressures were below the range for them to be classified as hypertension. When the blood pressures were compared among Thiopentone and Propofol, they were significantly higher among Thiopentone treatments at one minute and five minutes and suggest that hemodynamics are better controlled with Propofol as compared to Thiopentone.

These findings were similar to those mentioned in the earlier studies.^[6-12] Significant fall in blood pressures after induction with both the agents was also mentioned by Boey et al,^[5] and Boysen et al.^[7,8]

Boey et al,^[5] had reported that the increase in systolic and diastolic blood pressures and the heart rate after ECT were significantly higher with Thiopentone as an anaesthetic agent as compared to Propofol. Wells et al had reported a return of cardiac output and hemodynamic variables to preanaesthetic values after ECT over two minutes when methohexital was used as an induction agent^[1]. Although we did not record the variables at two minutes, the return of blood pressures and pulse rates to baseline values was more in Propofol treatments, but at five minutes after ECT. Shigeru et al, had reported an increase in the middle cerebral artery flow after ECT and this increase was higher with Thiopentone as compared with Propofol.^[11] Thus to avoid cerebrovascular complications in high-risk patients which might arise during ECT, use of propofol as an anesthetic agent may be a better alternative to Thiopentone.^[3,13]

The mean duration of motor seizure in our study was 35.9 $\pm$ 2 secs with Thiopentone and 28 $\pm$ 2.5 secs with Propofol which was far above this value. A seizure duration of 25 secs has been suggested for maintaining the efficacy of ECT.^[14,15] Although Propofol, significantly reduced the seizure duration as compared to Thiopentone, the mean duration was clinically significant for the therapeutic efficacy of ECT. This difference in seizure duration between Thiopentone and Propofol was similar to that found in other studies, although the absolute values were different.^[7,8,10,16,17]

Seizure duration is affected by patient characteristics,^[23] drugs, their dosage, inspired oxygen concentration, and pattern of ventilation.^[13,18-20] In our study patients was not hyperventilated and 100% oxygen was used to ventilate. Drug dose was also kept minimal. Thus, these factors were excluded from influencing the seizure duration.

When period effect was analyzed by us using unpaired 't' test, no effect of it was found on the seizure duration hence it could be concluded that the decrease in seizure duration found with Propofol was statistically significant.

We did not find a statistically significant difference between thiopentone and propofol in terms of quality of seizure. Boey et al,^[5] had reported better quality of seizure with Propofol. We are not sure of the reasons for this difference. There might be other factors which play important role in determining the quality

of seizure, like voltage used, dose of relaxant, and the time elapsed after giving the relaxant before ECT is delivered.

The second edition of The ECT Handbook of the Royal College of Psychiatrists gives importance to the pattern of electroencephalographic (EEG) seizure rather than to the duration for measuring seizure adequacy.^[21]

Matters et al,^[22] had reported an insignificant difference in the psychomotor recovery after ECT for the drug type, when Methohexitone and Propofol were compared. Friedman et al,^[23] reported that the awakening times were similar between Propofol and Methohexital for ECT.

The recovery profile in our study also showed no difference between Thiopentone and Propofol.

In a prospective study comparing Propofol and Thiopentone, Patil et al,^[24] had similar observations except for faster emergence profile with propofol.

In another study, Mir et al,^[25] compared Propofol, Thiopentone and Etomidate and their results were similar to our results suggesting better hemodynamic and adequate seizure duration with propofol. They also observed Etomidate giving the longest duration of seizures.

CONCLUSION

With the observations we have gathered we conclude that

- The increase in blood pressure and pulse rate after ECT is less with Propofol as compared with Thiopentone
- Duration of seizure during ECT with Propofol is clinically significant
- Quality of seizure during ECT is not different with Thiopentone or Propofol as induction agents
- Recovery profile after ECT is similar with both Thiopentone and Propofol.

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