Propofol and Ketamine in Electroconvulsive Therapy Anesthesia: A Randomised Controlled Study

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ABSTRACT

Introduction: Currently, the effects of combined anesthesia (propofol and ketamine) for patients with depressive disorder who have undergone electroconvulsive therapy (ECT) are unclear. Study aimed to evaluate the effect of ketamine, propofol, and ketofol on hemodynamic profile, duration of seizure activity, and recovery times in patients undergoing ECT.

Material and methods: Sixty patients who were scheduled for ECT treatment were enrolled. The study population was randomly assigned to receive one of three anesthetic agents: ketamine, propofol, or ketofol. The required total dose of the three agents was recorded. Mean arterial pressure (MAP), heart rate (HR), and oxygen saturation values were recorded at baseline, at induction, and at 1, 3, 5, and 10 min after the end of seizure.

Results: We found that both ketamine and ketofol have an increased mean seizure duration compared to propofol, ketofol had more favorable hemodynamic effects than ketamine and propofol, and ketamine was found to have longer recovery times compared to both propofol and ketofol.

Conclusion: We found that both ketamine and ketofol have an increased mean seizure duration compared to propofol.

Keywords: Anesthesia,Electroconvulsive Therapy, Ketamine, Propofol, Seizure.

INTRODUCTION

Electroconvulsive therapy (ECT), introduced by Cerlitti and Bini in 1937, is the induction of a generalised seizure by electrical stimulation of one or both cerebral hemispheres. It has become a highly sophisticated and precise procedure with passage of time. Initially, ECT was used to treat several types of psychiatric disorders and to calm disruptive inpatients in psychiatric wards, regardless of their diagnosis. In recent years, its use is restricted primarily to severe mental illnesses when there is an urgent need for treatment or secondarily after failure or intolerance to pharmacotherapy.[1, 2]

Administration of psychotropic medications or anesthetic agents during ECT is done to improve the therapeutic effect of ECT in depressive patients. The main objective of general anesthesia during ECT is to produce an unconscious state free from recall and muscle paralysis and the choice of anesthetic agent may influence seizure, hemodynamic, and recovery parameters and also cognitive functions after ECT. Ketamine, N-methyl-D-aspartate receptor antagonist has a quick, remarkable, and persistent antidepressive effect and exerts rapid beneficial effects in patients treated with ECT. But ketamine could induce various degrees of adverse effects such as cardiovascular system excitement, postanesthesia nausea and vomiting, and hallucinogenic activity.[2,3]

Propofol, an anesthetic agent, is alsoused in ECT, as it has not been shown to have an antidepressive effect. In addition, propofol, a potent anticonvulsant, might influence the quality of the induced seizure and hamper the effectiveness of treatment.[4]

The combination of ketamine and propofol, referred to by the portmanteau ‘‘ketofol,’’ is gaining reputation for various anesthetic procedures. Ketamine mitigates propofol-induced hypotension, and propofol mitigates ketamine-induced vomiting and recovery agitation.[5]

We carried out this study to evaluate the effect of ketamine, propofol, and ketofol on hemodynamic profile, duration of seizure activity, and recovery times in patients undergoing ECT.

MATERIAL AND METHODS

The period of study was from January 1 2019 to December 31 2019, after obtaining institutional ethical committee clearance and informed consent from the subjects. Sixty patients who were scheduled for ECT treatment were enrolled. The study population was randomly assigned to receive one of three anesthetic agents (ketamine, propofol, or ketofol). The study protocol we followed was based on the study of Yalcin et al (2012).[6]

Exclusion criteria

1. Presence of any serious physical disease, such as cardiovascular disease, cerebrovascular disorder, intracranial hypertension, respiratory tract disease, or severe fracture;
2. Presence of a foreign body, such as a pacemaker,

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intracranial electrode, or clips;
3. History of serious adverse effects related to anesthetics, for example, allergy; and a family history of reactions to the study drugs;

After premedication with intravenous atropine sulfate (0.25 mg), propofol (10 mg/ml), ketamine (10 mg/ml), or ketofol was administered slowly (20 mg/10 s) until the patient no longer responded to his/her name being called loudly and showed loss of the eyelash reflex. The required total dose of propofol, ketamine, or ketofol was recorded. Mean arterial pressure (MAP), heart rate (HR), and oxygen saturation values were recorded at baseline, at induction, and at 1, 3, 5, and 10 min after the end of seizure.

The duration of the motor seizure was defined as the time from the ECT stimulus to cessation of tonic–clonic motor activity in the 'isolated' arm. The time from the end of succinylcholine administration until spontaneous breathing, eye opening, and obeying commands was recorded. Probable side effects, including nausea, vomiting, bradycardia, tachycardia, respiratory depression, hypoxemia, and hypotension/hypertension were recorded immediately before premedication and subsequently at 5-min intervals for up to 20 min after electrical stimulus until the patient was discharged from the recovery unit to the psychiatry department. Respiratory depression was accepted as a respiratory rate of less than 10 breaths/min, hypoxemia was defined as peripheral oxygen saturation (SpO2) of 90% or less, bradycardia was defined as HR less than 50 beats/min, tachycardia was defined as more than 100 beats/min, hypotension was defined as MAP less than 60 mmHg, and hypertension was defined as MAP more than 120 mmHg.

RESULTS

We found that motor seizure duration in the propofol group was significantly decreased compared to other groups ($p<0.001$). Spontaneous breathing time in ketamine group was statistically increased compared to propofol group ($p = 0.001$). Whereas eye-opening time ($p<0.001$) and obeying-command time ($p<0.001$) were significantly increased in the ketamine group compared to other groups (Table 1). Regarding side effects, there were no statistically significant differences between groups (Table 2).

Mean total drug dosages for propofol, ketamine, and ketofol groups were, 91 ± 11 mg propofol, 86 ± 15 mg ketamine, 44 ± 12 mg propofol, and 45 ± 12 mg ketamine respectively. When MAP was compared among the three groups, both at baseline, at induction, and at different time intervals, we did not notice any statistically significantly difference.

Induction HR was significantly decreased compared to baseline values in the propofol group. In the ketamine group, HR was significantly increased at induction and at the 3rd, 5th, and 10th minute compared to baseline value ($p<0.001$). In the ketofol group, HR did not significantly change during the study. HR at induction was statistically significantly increased in the ketamine group compared to other groups.

DISCUSSION

When the seizure is inadequate, that is, short or unsuccessful the electrical stimulus is increased followed by potentiation of the side effects. When the therapy in itself is without effect the number of treatments is increased. Thus, there is a need to optimise each ECT treatment to lessen the energy and number of treatments.[4-6] In our study, we found that both ketamine and ketofol have an increased mean seizure duration compared to propofol, ketofol had more favorable hemodynamic effects than ketamine and propofol, and ketamine was found to have longer recovery times compared to both propofol and ketofol.

When compared to a propofol–fentanyl combination, a combination of propofol–ketamine for deep sedation for burns dressings on the ward was associated with fewer episodes of restlessness requiring further doses of sedatives.[7] Strayer RJ and Nelson (2008) showed that ketofol successfully produced deep sedation for prolonged pediatric orthopedic procedures in conjunction with regional analgesia.[8] Wang et al (2012) found that propofol combined with ketamine as an ECT anesthesia has no negative effects on the inherent antidepressant properties of ketamine. Moreover,

Incident	Propofol group (n = 20)	Ketamine group (n = 20)	Ketofol group (n = 20)	p (ANOVA)
Motor seizure (s)	31.2 ± 5.4	39.7 ± 3.7	36 ± 5.1	<0.001
Spontaneous breathing (s)	261 ± 12.8	273.4 ± 10.8	270.3 ± 7.8	0.001
Open eyes (s)	418.3 ± 19.2	543.7 ± 42.8	443.6 ± 31.7	<0.001
Obey commands (s)	516.7 ± 38.4	579.6 ± 36.9	520.4 ± 29.8	<0.001

Table 1: Seizure duration and recovery times of patients

Side effect	Propofol group (n = 20)	Ketamine group (n = 20)	Ketofol group (n = 20)	p (Chi square)
Nausea and vomiting (n)	0	1	0	NS
Bradycardia (n)	1	0	0	NS
Tachycardia	1	2	1	NS
Hypotension (n)	1	0	0	NS
Hypertension (n)	0	2	1	NS
Arrhythmia (n)	0	1	0	NS

Table-2: Side effects among groups

the combined anesthesia could reduce ketamine-mediated adverse effects. They concluded that propofol combined with ketamine has a rapid antidepressive effect and has reduced adverse effects compared with ketamine anesthesia in patients with ECT. Hence the combined anesthesia might be the first-choice anesthesia in patients with depressive disorder and ECT.[9]

Our data suggest that the use of ketamine and propofol in combination might be advantageous for hemodynamic stability and analgesia while decreasing recovery time by reducing the total amount of ketamine. Additionally, it is assumed that the sedative and antiemetic effects of propofol may counterbalance the nauseant and psychomimetic effects of ketamine. Some clinicians favor ketamine and propofol in combination over either agent alone for reasons of this potential balance of effects. Some authors argued that ketofol is a misleading concept, that it is nothing more than standard propofol sedation in which fentanyl analgesia is replaced with subdissociative ketamine, and they emphasize that there is no compelling evidence that ketofol reduces respiratory depression or produces sedation superior to either ketamine or propofol alone. They argued that it is not logical to administer two drugs and to have to anticipate the unique adverse effects of each when monotherapy works just as well and presents only one set of potential adverse events. They concluded that before ketofol can be recommended, it needs to be established that the combination offers a noticeable advantage over either agent alone.[9,10]

Etomidate or a 1 : 1 ketamine plus propofol combination may be the best method to achieve general anaesthesia in the ECT setting, especially if seizure duration is inadequate. Etomidate being supported by a meta-analysis and propofol : ketamine by randomised controlled trials, which is probably the most valuable scientific work on the subject at the moment.[10,11]

Ketofol, similar to ketamine, would provide cognitive function preserving effects more than propofol alone with fewer side effects and better recovery times than ketamine alone; attention might be focused on this in further studies.

Limitations

1. Absence of evaluating cognitive function-preserving and antidepressant effects of the drugs with long-term follow up,
2. Relatively small sample size and
3. Absence of anesthesiologists' and psychiatrists' satisfaction scores.

One should keep in the mind that generalizing data of the present study might not be appropriate because our results denote therapeutic responses of a population from the same geographic region and genetic origin; subjects from other geographic region(s) and genetic origin(s) might respond differently to study medications than did our study population.

CONCLUSION

Ketofol mixture is associated with a longer mean seizure time than propofol, and shorter mean recovery times than ketamine, with better hemodynamic stability without any important side effects in ECT anesthesia. Further studies investigating the optimal doses, cognitive function-preserving effect and antidepressant effects, and physician satisfaction scores should be elucidated.

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