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Research Article

COMPARISON ON EFFECT OF KETOFOL AND KETOFOL-DEXMEDETOMIDINE COMBINATION ON HYPERDYNAMIC RESPONSES TO MODIFIED ELECTROCONVULSIVE THERAPY AND THEIR ROLE IN AGITATION AND PATIENT'S SATISFACTION

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ABSTRACT

Objective: The aim of our study was to assess the anesthetic effect of combined ketofol-dexmedetomidine on hemodynamics, seizure duration, recovery characteristics, agitation, and patient's satisfaction following electroconvulsive therapy (ECT) in psychiatric patients.

Material and method: A total of 46 patients of the American Society of Anesthesiologists grade I and II were divided into 2 groups. Group A (ketofol group) patients were premedicated with injection glycopyrrolate 0.005 mg/kg IV. Group B (ketofol-dex group) patients were given 0.005 mg/kg IV glycopyrrolate and 0.5 μg/kg dexmedetomidine was infused intravenously over 10 min before induction of anesthesia. Both the groups were induced with injection ketofol for ECT and hemodynamic responses, motor seizure response, recovery profile, agitation score, and patient satisfaction score were observed.

Result: The demographic profile was comparable in both groups. Ketofol used was less in ketofol-dex group (81.96±9.26 mg) compared to ketofol group (104.78±10.92mg). Ketofol-dex group has a lower incidence of agitation (1.43±0.59 vs. 2.09±0.60), more patient satisfaction (1.35±0.57 vs. 2.04±0.71), and acceptable decrease in heart rate and blood pressure as compared to ketofol group without any significant side effects. Motor seizure duration was prolonged in ketofol-dex group (39.04±2.67 s) compared to ketofol group (35.04±2.95 s).

Conclusion: Dexmedetomidine is effective in attenuating acute hyperdynamic response to ECT without altering seizure duration and recovery from anesthesia, with the added benefit of decreasing post-ECT agitation with more patient satisfaction.

Keywords: Electroconvulsive therapy, Ketofol, Dexmedetomidine, Hyperdynamic responses, Agitation.

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INTRODUCTION

Electroconvulsive therapy (ECT) consists of programmed electrical stimulation of the central nervous system to initiate seizure. ECT is very effective for many psychiatric disorders, such as severe depression, schizophrenia, and bipolar disorder. The aim of general anesthesia during ECT is to provide amnesia and muscle paralysis to unconscious patient. ECT is associated with hyperdynamic responses due to increased concentrations of catecholamines [1]. To attenuate these, many pharmacological agents such as beta-blockers, calcium channel blockers, alpha2-agonists, direct-acting vasodilators, and local anesthetic are used.

The general anesthetic agents used for ECT should have rapid onset and emergence and they should not interfere with seizure activity and duration. With the use of propofol, cerebral and systemic hemodynamic responses are usually stable but because of its anticonvulsant effect, seizure duration tends to be shorter.

Ketamine has been a less preferred anesthetic agent because of concerns about the risk of excessive cardiovascular system response. However, it provides an earlier recovery after electroconvulsive therapy and has the potential to reduce retrograde amnesia. It also has antidepressive action, which accelerates the clinical response to ECT [2].

Ketamine and propofol (called "ketofol") when used in combination will decrease consumption and preserve hemodynamic stability while propofol relieves hallucinations associated with ketamine. They have opposing effects on the hemodynamic and respiratory systems. Their side-effects on these systems could be reduced by administering a combination of them at a lower dose.

Dexmedetomidine is a highly selective α2-adrenergic agonist and also has sedative, sympatholytic, and analgesic action. It has been considered a safe and effective adjuvant in anesthetic and analgesic preparation. It is effective in the management of emergence agitation after ECT [3].

The aim of our work was to study the anesthetic effect of combined ketofol-dexmedetomidine on hemodynamics, seizure duration, recovery characteristics, agitation, and patient's satisfaction following ECT in psychiatric patients.

METHODS

Here, we did a prospective observational study over 18-month duration. After getting approval from Institutional Ethical Committee, written informed consent was obtained from all the patients before ECT.

Patients of physical status I and II of both sexes aged between 18 and 60 years undergoing ECT were included in this study. Patients with serious physical diseases such as cardiovascular diseases, cerebrovascular disorder, intracranial hypertension, respiratory tract diseases or a previous fracture, glaucoma, arterial aneurysm, or cerebrovascular malformations were excluded from our study. Patients with the American Society of Anesthesiologists grade III and IV, with pacemaker, seizure history, pregnancy, and allergic to study drugs were also excluded from the study.

Sample size was calculated using Open Epi software version 3.0 in which we took reference from the mean and standard deviation of a total ketofol dose from the previous study by Shams and El-Masry [1]. Our level of significance was 5% and power of study was 80%. We obtained sample size of 23 for each group from all these calculations.

Data were expressed as mean±standard deviation (SD). Quantitative variables are presented as mean±SD and a t-test was used to compare significance between the two groups. Qualitative data were expressed as number (%) and analyzed using a Chi-square test. A $p<0.05$ was taken as significant and $p<0.001$ was taken as highly significant.

A total of 46 patients were divided into 2 groups. Group A (ketofol group) patients were premedicated with injection glycopyrrolate 0.005 mg/kg IV. Group B (ketofol-dex group) patients were given 0.005 mg/kg IV glycopyrrolate and 0.5 µg/kg dexmedetomidine was infused intravenously over 10 min before induction of anesthesia.

Table 1: Patient's satisfaction score

1	Pleased and calm
2	Patient without any complaint (satisfaction is not bad)
3	Patient has some complaints (middling quality of satisfaction)
4	Patient complained that the treatment was unpleasant

Table 2: Agitation score

1	Sleeping
2	Awake and calm
3	Irritable and crying
4	Inconsolable crying
5	Severe restlessness and disorientation

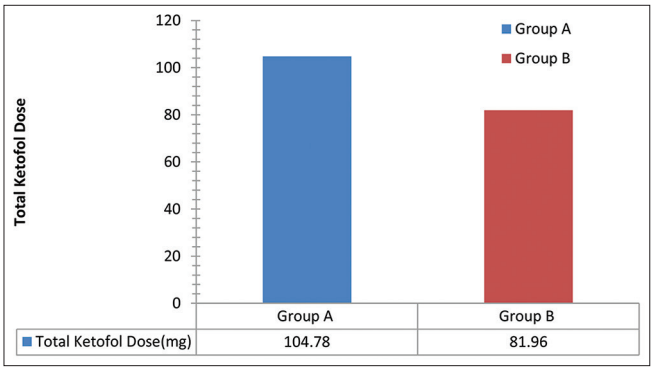


Fig. 1: Total ketofol dose in both the groups

All the patients were preoxygenated with 100% O_2, after which ketofol (1:1 mixture of 10 mg/mL ketamine and 10 mg/mL propofol in a 20 mL syringe) was given slowly (20 mg/10 s) until the patient did not respond to his/her name being called loudly and till the loss of eyelash reflex. The total dose of ketofol required was recorded. One arm was isolated by inflating the tourniquet to a pressure 20% more than systolic blood pressure (SBP) for visual confirmation of motor seizure duration. Succinylcholine in a dose of 0.5 mg/kg was administered after isolation of one arm and manual ventilation was performed with Magill circuit and face mask using 100% oxygen at flow rate of 8 L/min. A bite block was used to protect patient's teeth, lips, and tongue.

A suprathreshold electrical stimulus was given through bi-frontotemporal electrodes and ventilation was assisted with oxygen during the procedure.

Mean arterial pressure (MAP), heart rate (HR), and oxygen saturation were recorded at baseline, after induction, at the end of motor seizure, 5, 10, 20, 30, 40, and 50 min after that. The duration of motor seizure (time from electrical stimulation to the cessation of tonic-clonic motor activity) was recorded in the "isolated arm." The time from the end of succinylcholine administration until spontaneous breathing, eye opening, and obeying commands were recorded. Patients were looked for side effects until they were discharged from the post anesthetic care unit to the psychiatry department. Agitation score and patient's satisfaction scores were evaluated when the patient was completely awake after ECT with the reference from below.

RESULTS

We have done our statistical analysis by unpaired t-test for quantitative data and Chi-square test for qualitative data and $p>0.05$ considered insignificant, <0.05 considered significant, and <0.001 considered highly significant.

The demographic profile was comparable in the two groups. In both groups, male–female ratio was comparable.

When we compared ketofol dose in both the groups, total (mean) ketofol used was less in ketofol-dex group (81.96±9.26) compared to ketofol group (104.78±10.92 mg), which was highly significant ($p<0.001$).

Hemodynamic parameters

There was a significant decrease in pulse rate from the baseline after induction in Group B. At the end of motor seizure, pulse rate increased in both the group, but rise in Group A was significant compared to

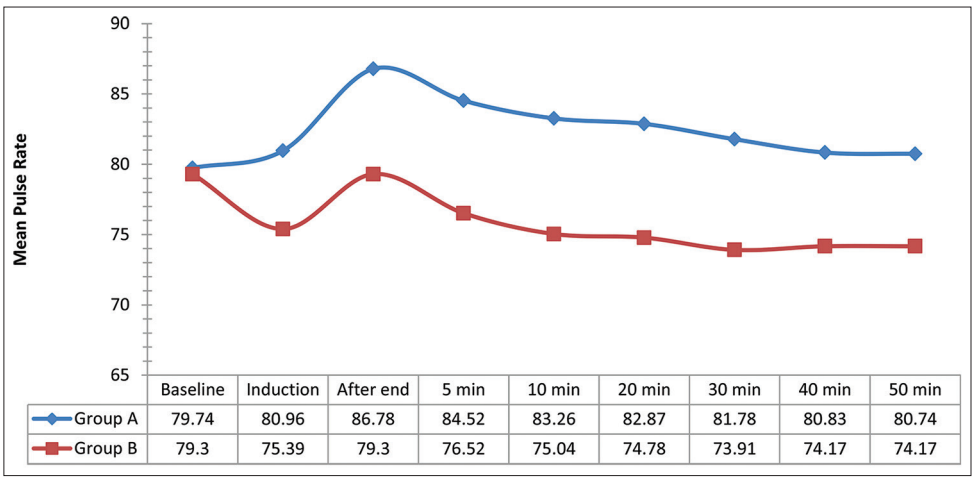
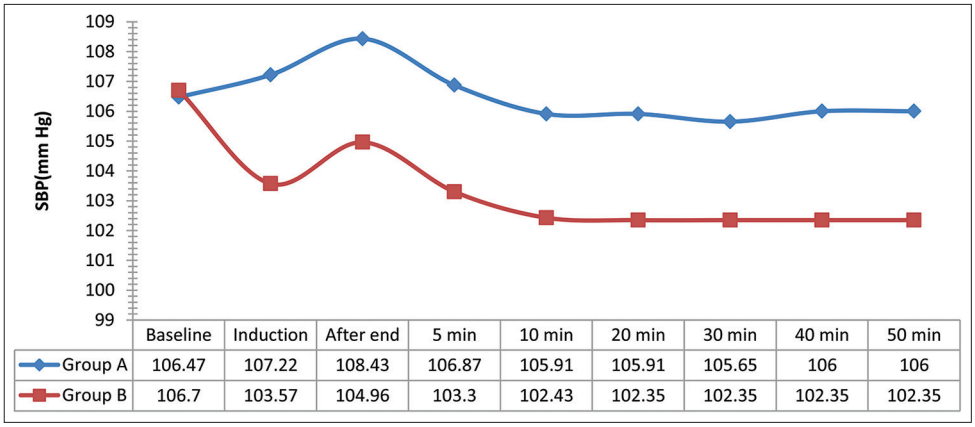
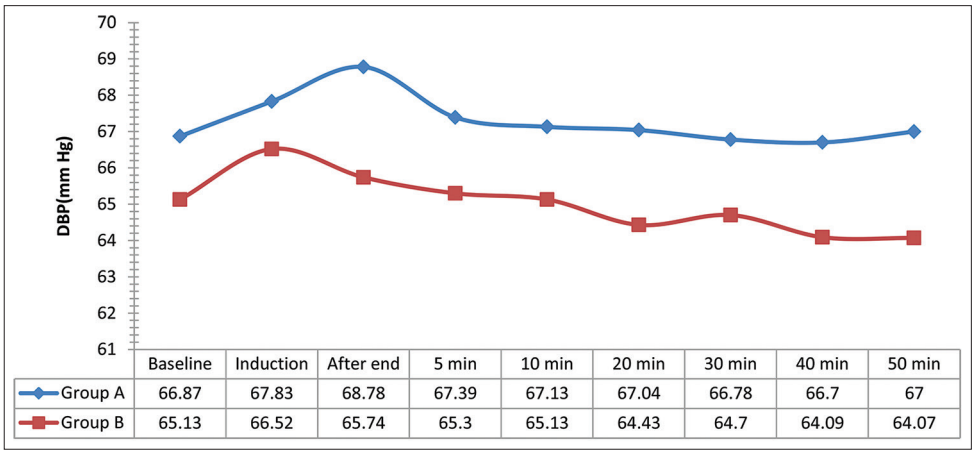


Fig. 2: Mean pulse rate in both the groups



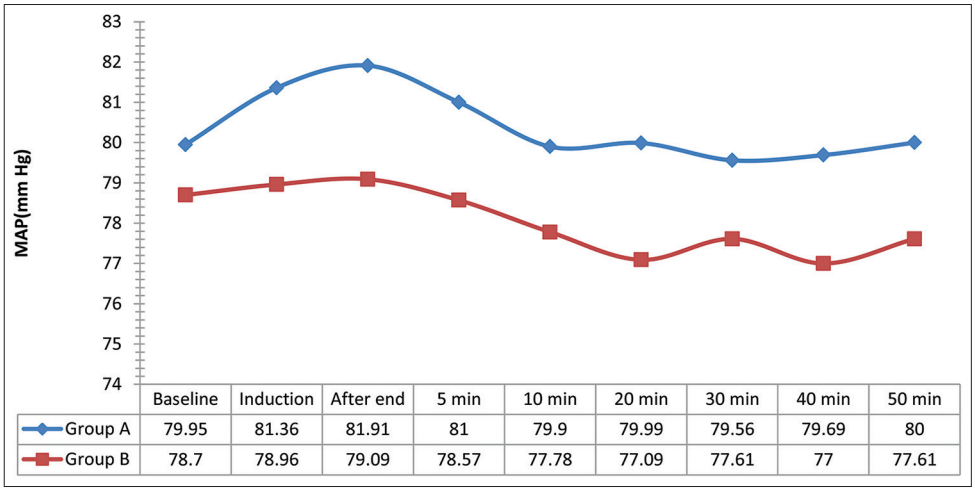
	Baseline	Induction	After end	5 min	10 min	20 min	30 min	40 min	50 min
Group A	106.47	107.22	108.43	106.87	105.91	105.91	105.65	106	106
Group B	106.7	103.57	104.96	103.3	102.43	102.35	102.35	102.35	102.35

Fig. 3: Mean systolic blood pressure in both the groups



	Baseline	Induction	After end	5 min	10 min	20 min	30 min	40 min	50 min
Group A	66.87	67.83	68.78	67.39	67.13	67.04	66.78	66.7	67
Group B	65.13	66.52	65.74	65.3	65.13	64.43	64.7	64.09	64.07

Fig. 4: Mean diastolic blood pressure in both the groups



	Baseline	Induction	After end	5 min	10 min	20 min	30 min	40 min	50 min
Group A	79.95	81.36	81.91	81	79.9	79.99	79.56	79.69	80
Group B	78.7	78.96	79.09	78.57	77.78	77.09	77.61	77	77.61

Fig. 5: Mean arterial pressure in both the groups

Group B and remained elevated till the end. In general, decrease in pulse rate in ketofol-dex group compared to ketofol group was highly significant ($p<0.001$).

There was a significant decrease in mean SBP (mm Hg) ($p<0.05$) in ketofol-dex group compared to ketofol group at the time of induction. After ECT, there was rise of SBP in both the groups which was not significant as compared to induction value. SBP in group B remained decreased till the end compared to Group A, which was significant ($p<0.05$).

Mean diastolic blood pressure remained not significant ($p>0.05$) at the time of induction. There was a significant decrease in mean diastolic blood pressure (mmHg) ($p<0.05$) in ketofol-dex group compared to ketofol group during ECT and thereafter.

There was a significant decrease in MAP (mmHg) ($p<0.05$) in ketofol-dex group compared to ketofol group at the time of induction. During ECT and thereafter MAP remained on the lower side in ketofol-dex group as compared to ketofol group. There was no difference in oxygen saturation among the groups.

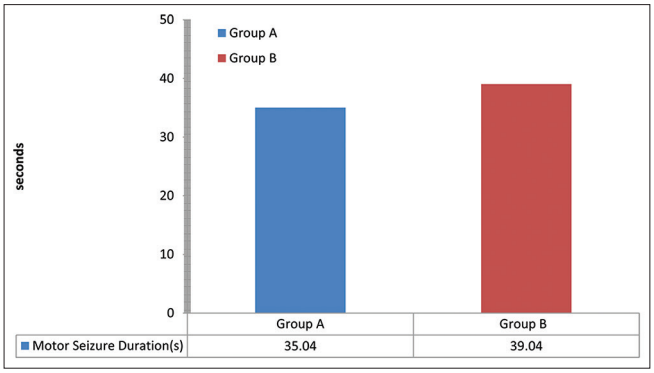


Fig. 6: Motor seizure duration in both the groups

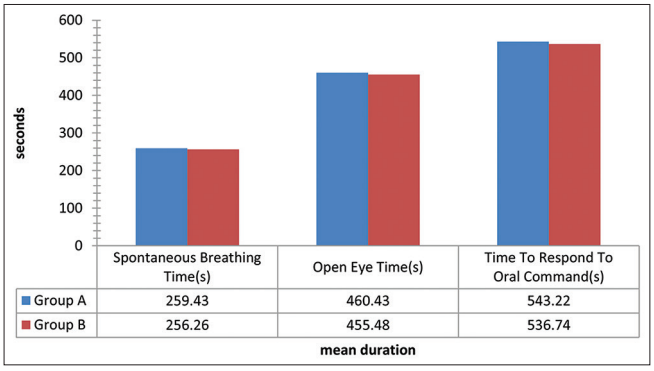


Fig. 7: Recovery parameters in both the groups

Motor seizure duration was prolonged in ketofol-dex group (39.04±2.67 s) compared to ketofol group (35.04±2.95 s), which was highly significant (p<0.001).

Spontaneous breathing time (259.43±42.5 s vs. 256.26±7.56 s), eye-opening time (460.43±11.63 s vs. 455.48±8.58 s), and time to response to verbal commands (543.22±10.15 s vs. 536.74±6.30 s) were not significantly higher in ketofol group (Group A) as compared to ketofol-dex group (Group B), respectively. These findings were comparable in both the groups.

Patient's satisfaction was significantly higher in ketofol-dex group (group B) compared to ketofol group (group A), as number of patients with satisfaction score 1 was significantly higher 70% (16 patients) in ketofol-dex group compared to 21.74% (5 patients) in ketofol group. Patient's satisfaction score was 1.35±0.57 in Group B as compared to 2.04±0.71 in Group A, which is highly significant (p<0.001).

The patients with agitation scores 1, 2, and 3 in ketofol group were 13.04%, 65.22%, and 21.74%, respectively, compared to ketofol-dex group where scores 1, 2, and 3 were 60.6%, 34.7%, and 4.35%, respectively. Thus, less agitation was seen in patients with ketofol-dex group compared to ketofol group. The mean agitation score in Group B was 1.43±0.59 as compared to 2.09±0.60 in Group A, which was highly significant (p<0.001).

None of the patients complained of awareness during anesthesia. Two patients in ketofol group and one patient in ketofol-dex group developed coughing. Headache occurred in two patients in ketofol group and none of the patients in ketofol-dex group developed headache. No patient experienced respiratory depression, hypoxemia, bradycardia, hypotension, or hypertension.

DISCUSSION

ECT is one of the most effective though less understood treatments for psychiatric illnesses. Anesthesia not only enables the ECT procedure but also has a great impact on electrophysiological and seizure parameters. Anesthesia improves ECT tolerability and efficacy.

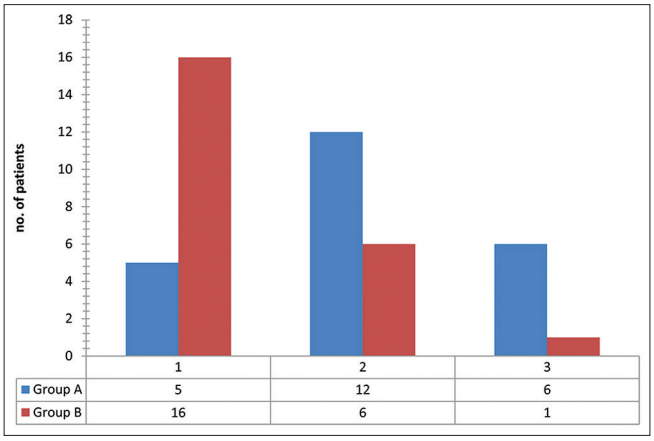


Fig. 8: Comparison of satisfaction score in both the groups

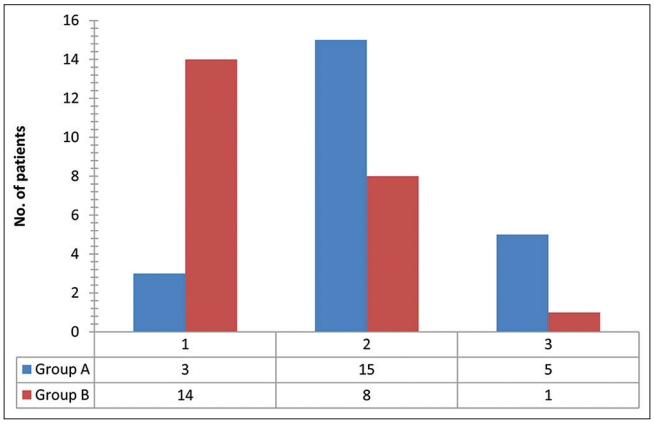


Fig. 9: Comparison of agitation score in both the groups

Ideal intravenous agents used for modified ECT should provide rapid onset, short duration of action, attenuation of adverse physiological effects of ECT, and rapid smooth recovery without adverse shortening of seizure duration.

Ketamine seems to be an appropriate induction agent for ECT due to preservation of cognitive function, antidepressant effect, seizure induction, and improvements of response in resistant depression to ECT. Okamoto *et al.* [4] showed that ketamine is useful in severe cases when the early antidepressant effect is needed. Mechanism of the antidepressant effect of ketamine is suppression of excitotoxicity and neuroprotective action due to NMDA antagonism. Delayed recovery, cardiac hyperactivity, and transient psychotic episodes are the main pitfalls of ketamine. It causes systemic release of catecholamines and inhibition of norepinephrine re-uptake at peripheral nerves and myocardium [1].

Propofol is considered one of the most popular anesthetic agents in ECT due to rapid recovery, minor hemodynamic response, and antiemetic effect.

Ketofol (ketamine+propofol) can give hemodynamic stability and analgesia. The total amount of ketamine required for ECT is reduced when ketofol is used as compared to ketamine alone. Ketofol also reduces the recovery time without any significant side effects. In addition, sedative and antiemetic effects of propofol may counterbalance the nausea and psychomimetic effects related to ketamine [1].

Dexmedetomidine is a potent α2-adrenergic agonist with unique properties of sympatholysis, sedation, and analgesia that make it an ideal agent for ECT to blunt the acute hyperdynamic response associated with it and its sedative effect reduces agitation and improves satisfaction in patients.

In our study, the total (mean) ketofol used was less in ketofol-dex group (81.96±9.26 mg) as compared to ketofol group (104.78±10.92 mg), which was highly significant (p<0.001). We observed that the use of dexmedetomidine prevented hyperdynamic responses during ECT. Motor seizure duration was prolonged in ketofol-dex group (39.04±2.67 s) compared to ketofol group (35.04±2.95 s), which was highly significant (p<0.001). Spontaneous breathing time, eye-opening time, and time to respond to verbal command were comparable in both the groups. Higher satisfaction and less agitation were seen in patients of ketofol-dex group as compared to ketofol group.

In 2017, Shams and El-Masry [1] and in 2019, Roopesh Kumar, Chavi Sethi, Prashasti Sexena, and Aman Singh [5] observed that ketofol-dex combination in ECT was associated with longer mean seizure duration, effective anti-depressant, less incidence of agitation, more patient satisfaction and acceptable decreases in blood pressure and HR when compared to ketofol alone.

In 2012, Erdogan Kayhan *et al*. concluded that ketofol provides better seizure quality than propofol. Hence, ketofol can be used as an alternative agent to increase the seizure quality and clinical efficiency of ECT [2].

In 2017, Sharan *et al*. studied the comparison of dexmedetomidine with propofol versus esmolol with propofol to attenuate hemodynamic stress responses after ECT. They observed that both dexmedetomidine and esmolol attenuate the hyperdynamic response to ECT without affecting the seizure duration, but when it comes to stable vitals, smooth emergence, and no adverse effect on recovery duration, dexmedetomidine has a more favorable response [6].

In 2018, Garg *et al*. observed that dexmedetomidine in a dose of 1 μg/kg attenuated the hyperdynamic response to ECT without affecting the seizure duration and had a more favorable response in view of smooth emergence with no adverse effects on recovery duration [7].

In 2024, Buddha *et al*. observed that duration of motor seizure was longer in KFD compared to KF (28.57±2.32 in KFD, 22.43±1.00 in KF with p<0.001) with a minimum acceptable hemodynamic fluctuation and reduced induction dosages of ketofol (54.07±3.11 in KFD, 81.30±2.36 in KF with p<0.001) [8].

Hence, adding dexmedetomidine premedication with ketamine-propofol induction (Ketofol-dex) has added benefit of anti-depressant effect following ECT due to improved seizure duration in a calm patient. Ketofol-dex combination has the advantages of lower incidence of agitation, more patient satisfaction, and acceptable decrease in HR and blood pressure when compared to induction agent alone without any significant side effects. In addition, dexmedetomidine also decreases intra-operative consumption of anesthetic agents and also decreases sympathetic tone, both of which are helpful for decreasing postoperative nausea and vomiting.

CONCLUSION

Thus, we can say that dexmedetomidine is effective in attenuating acute hyperdynamic response to ECT without altering seizure duration and recovery from anesthesia, with the added benefit of decreasing post-ECT agitation with more patient satisfaction.

FUNDING

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CONFLICTS OF INTEREST

No conflicts of interest.

AUTHOR'S CONTRIBUTION

All authors data collection, data analysis, and preparation of manuscript.

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