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The Effect of Adjunctive use of Dexmedetomidine and Metoral with Thiopental on Hemodynamic Status, Agitation, and Patient Satisfaction in Patients with Mood Disorders after Electroconvulsive Therapy

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Abstract

AIM: The aim of our study was to determine the effect of adjunctive use of dexmedetomidine and metoral with thiopental on hemodynamic status, agitation, patient satisfaction, and duration of seizure in patients with mood disorders in electroconvulsive therapy (ECT).

METHODS: This study is a randomized, double-blind, clinical trial. Sixty patients (18–60 years) according to DSM5 criteria had mood disorder and were candidates for ECT. Patients were randomly divided into two groups of 30 each. One group received 5.0 μg/kg dexmedetomidine 10 min before induction of thiopental, and the other group received 5.2 mg intravenous metoprolol immediately before ECT. Patients' satisfaction, duration of seizure, and arterial oxygen saturation were evaluated.

RESULTS: The mean age of both groups was approximately 37 years with the majority of men. No significant difference was found between the two groups in terms of age and sex, blood pressure (BP), heart rate (HR), duration of seizure, and arterial oxygen saturation before ECT. The mean BP and HR in the recovery were lower in the dexmedetomidine group than in the metoral group. Arterial oxygen saturation percentage was not significantly different between the two groups. The recovery time in the dexmedetomidine group was longer than the metoral group ($p = 0.001$). Post-ECT satisfaction was found to be higher in the dexmedetomidine group than in the metoral group and the mean agitation score was found to be higher in the metoral group.

CONCLUSION: Both metoral and dexmedetomidine as adjuvants decrease the hyperdynamic responses of patients after ECT, whereas the effect of dexmedetomidine is more than metoral; on the other hand, neither dexmedetomidine nor metoral has any negative effect on seizure duration, but dexmedetomidine significantly prolonged recovery time as compared to metoral.

Introduction

Mood disorders, sometimes called affective disorders, consist of major depressive disorder (MDD), bipolar disorder, and other mood disorders. Patients with major depressive episodes are often referred to as MDD or unipolar. Patients with manic episode or both manic and hypomanic episodes are considered as bipolar disorder. A complete diagnostic evaluation must first be performed to treat patients with mood disorders and then a treatment plan can be implemented [1]. At present, existing treatments place particular emphasis on drug therapy combined with psychotherapy; however, the use of *electroconvulsive therapy* (ECT) may be the best and fastest approach in *treatment*-resistant depression, psychotic patients, those with suicidal thoughts, and pregnant mothers with severe depression or mania [2].

ECT is one of the most effective treatments for many diseases [3], which has been found to be a safe and effective choice for the treatment of mood disorders [4].

ECT causes seizures by electrical impulses of varying frequencies through electrodes placed on the scalp [5]. ECT has little risk and is one of the safe methods used for treatment under general anesthesia. The estimated risk of serious complications is about 1/1000, which is similar to general anesthesia for small medical procedures. One of the complications of electric shock is sudden parasympathetic release at the moment of electric shock, which anticholinergic drugs are often used to reduce this complication before an electric shock. Immediately after the parasympathetic release, the sympathetic system activates, increasing the patient's heart rate (HR) and blood pressure (BP), and even causes cardiac arrhythmias, such as fluttering sensation (palpitations) and atrial fibrillation [3]. Although ECT is a very safe treatment and has no absolute contraindication, both the physician and the patient must be aware of a number of side effects, such as cognitive impairment, which is rapidly resolved in most cases. Rarely, it causes seizures, short-term complications such as headaches, muscle aches,

nausea, vomiting, and fatigue [6]. Different drugs are applied to induce anesthesia in patients. The effect of anesthetic drugs during treatment with ECT is important in several respects including possible effects on patients' mental status, effects on seizure duration, as well as different effects of anesthetic drugs on maintaining cardiovascular stability in patients. In other words, a drug is more favorable for inducing anesthesia to produce longer seizures and at the same time a more stable cardiovascular condition. Various drugs are currently used for this purpose, including metoprolol, methohexital, propofol, and dexmedetomidine [7].

Dexmedetomidine is a selective α2 agonist that predominantly affects the locus ceruleus [8]. Dexmedetomidine attenuates central nervous system stimulation by reducing the release of presynaptic norepinephrine, causing sedative, more broadly, analgesic, anxiolytic, and sympatholytic effects without effect on the respiratory system.

The hypodynamic responses to ECT are associated with an acute increase in plasma epinephrine and norepinephrine concentrations [9]. The most common side effects of dexmedetomidine are due to its mechanism of action, including hypotension and bradycardia. Metoprolol (selective β1 blocker) is a common drug for reducing cardiac output, HR, and BP and its peak is 15–20 min after intravenous injection [10]. Therefore, both metoprolol and dexmedetomidine can be effective in controlling the hemodynamic symptoms of ECT [11]. To date, no comparable studies have compared dexmedetomidine and metoral in combination with anesthetics for ECT. Therefore, we decided to compare the effect of adding dexmedetomidine and metoral to thiopental on hemodynamic status, agitation, patient satisfaction, and duration of seizure in patients with mood disorders who were candidates for ECT.

Methods

This study is a double-blind randomized clinical trial which was performed on 18–60 years old patients with mood disorder referred to Amir Kabir Hospital in Arak, Iran. ECT candidates were randomly divided into two groups of dexmedetomidine and metoral using randomized complete block design and data were collected through checklist. If they had inclusion criteria, they were included in the study.

Inclusion criteria included: (1) All patients with mood disorders who are candidates for ECT, (2) having a form of informed consent, and (3) average age of 18–60 years. Exclusion criteria included: (1) All patients with cardiopulmonary arrest after induction of anesthesia during ECT, (2) all patients who need intubation after ECT due to prolonged apnea and respiratory failure, and (3) all patients who do not develop seizures during the ECT process.

In the present study, informed consent for participation in the research was completed for each patient. Patients were then placed on an ECT bed in a supine position and an intravenous line was inserted by a No. 20 *Angiocath*. Patients were given about 1–3 ml/kg of fluid before anesthesia as CVE. Necessary monitoring was performed for patients including HR, RR, arterial blood oxygen saturation, and NIBP.

For the purpose of blindness, the drugs were pre-prepared by the anesthesiologist responsible for the design and made available to the anesthesiologist resident who was unaware of the type of medication. In both drug groups (dexmedetomidine and metoral), the syringes were the same, the volume of the drug injections reached 10 cc. In Group A, 0.5 μg/kg intravenous dexmedetomidine was injected before anesthesia. For double blinding, the drug was reached to 10 ml with normal saline. Then, the anesthesia was induced by intravenous injection of 2–3 mg/kg thiopental and intramuscular injection of succinylcholine 0.5 mg/kg in both groups. At this stage, 0.5 mg intravenous atropine, a short-acting anticholinergic agent to reduce the effects of parasympathetic release at the moment of electric shock, was injected in both groups. After anesthesia and immediately before stimulation with ECT, 2.5 mg of metoral was injected for Group B to be at the peak of its effect at the time of sympathetic release, which occurs a few seconds after the shock, and during sympathetic effects of metoral. Ventilation was performed with 100% oxygen for all patients. After complete anesthesia, electric shock was applied bilaterally with the amount of energy required by the psychiatrist. Then, the data obtained from patients regarding hemodynamic symptoms, seizure duration, recovery time, agitation score, satisfaction, and arterial blood oxygen saturation were recorded by the resident in a questionnaire. Explanation that the agitation score was recorded as objective by the resident in the questionnaires after observing the patients. Subjective satisfaction was recorded by questioning patients. The questionnaires were completed by the psychiatry resident who was unaware of the type of medication.

Agitation score

1. Sleepy
2. Awake and peaceful
3. Irritable and noisy
4. Disconsolate noisy
5. Severe blenched or willing to wake up from bed or sitting on the bed and shrieking

Satisfaction score

1. Happy and peaceful
2. Without rumble and not bad satisfaction
3. Having no acquiescence or moderate satisfaction

4. Patient unsatisfaction and shows that patient does not like any same treatment

Calculation of the sample size

The sample size was 30 people in each group according to the following formula and 5 people in each group were considered for sample loss during the study.

$z_1-\alpha_2=1.96$ $z_1-\beta=1.28$ $n:\frac{\left(z_1-\alpha/2+z_1-\beta\right)^2(\delta_2+\delta_2)^2}{(\mu_1-\mu_2)^2}$

$\mu_1=33.2$ $\mu_2=29.2$

$\delta=4.7$ $\delta=3.9$

Data analysis

Data were statistically analyzed using the SPSS software version 19. Data were analyzed using t-test. ANOVA test, Chi-square, and the results were indicated as graphs and tables.

Ethical considerations

A written letter was received from university officials to introduce us to the research centers. A written letter was obtained from the respected authorities of the selected research centers. The purpose of the study was described for all research units and their written consent was obtained. All patients' information was kept confidential by the plan's administrator. In all stages of research, all Helsinki Research Ethics Statements and Research Ethics Committees were considered. Ethic code of IR.ARAKMU.REC.1397.044 was approved for this study. The registration code at the Iran Clinical Trial Center for this project is IRCT20141209020258N87.

Results

The addition of dexmedetomidine and metoral to thiopental in patients with hemodynamic status and duration of seizure was evaluated. According to Table 1, the mean age of both groups was approximately 37 years and the majority were male (70%). There was no significant difference between the two groups in terms of age, sex, hemodynamic parameters, mean arterial BP, HR, and oxygen saturation before ECT.

Table 1: Comparison of age and sex distribution of patients with mood disorders

Groups	Dexmedetomidine group	Metoral group	p value
Age	7.2 ± 8.37	1.1 ± 9.36	0.1
Sex (%)			
Male	7.70	8.68	0.2
Female	3.29	2.31	

Table 2 indicates mean BP, HR, and arterial oxygen saturation before shock therapy, and no significant differences were found between the two groups in mean BP, HR, and arterial oxygen saturation before ECT (p = 0.4, p = 0.6).

Table 2: Comparison of mean blood pressure, heart rate, and arterial oxygen saturation before ECT

Group	Dexmedetomidine group	Metoral group	p value
Mean arterial blood pressure before shock	9.2 ± 8.90	4.6 ± 3.92	0.4
Heart rate before shock	7.3 ± 8.100	2.5 ± 7.95	0.6
Arterial oxygen saturation before shock	6.4 ± 2.95	2.4 ± 1.94	0.4

ECT: Electroconvulsive therapy.

Comparison of mean BP, HR, and arterial oxygen saturation after ECT (recovery) is indicated in Table 3, there was a significant difference between the two groups in mean recovery of patients' mean BP and HR. The mean BP and HR of patients in the dexmedetomidine group were lower than that of the metoral group (p = 0.02, p = 0.01). However, no significant difference was found in arterial oxygen saturation in recovery (p = 0.4).

Table 3: Comparison of mean blood pressure and heart rate and arterial oxygen saturation after ETC (recovery)

Group	Dexmedetomidine group	Metoral group	p value
Mean recovery arterial blood pressure	1.4 ± 9.80	9.4 ± 6.86	0.02
Mean recovery heart rate	2.3 ± 3.80	3.6 ± 2.88	0.01
Mean arterial oxygen saturation recovery	1.5 ± 2.94	6.5 ± 1.92	0.4

ECT: Electroconvulsive therapy.

According to Table 4 and Figure 1, no significant difference was found between the two groups in terms of seizure duration (p = 0.08). However, there was a significant difference between the two groups in terms of recovery time (in min). Significantly, the recovery time was significantly longer in the dexmedetomidine group as compared to metoral group (p = 0.03).

Table 4: Comparison of duration of seizure and average duration of recovery in patients with mood disorders

Group	Dexmedetomidine group	Metoral group	p value
Duration of seizures (in s)	1.2 ± 4.27	3.4 ± 1.30	0.08
Duration of recovery (in min)	3.1 ± 8.15	2.3 ± 7.11	0.03

According to Table 5, a significant difference was found in satisfaction score between the two groups so that the level of satisfaction was found to be higher in the dexmedetomidine group than in the metoral group. In terms of post-ECT agitation score, the score of agitation was significantly higher in the

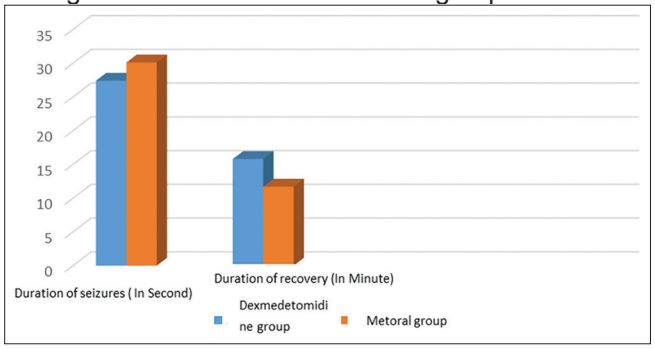

Figure 1: Comparison of duration of seizure and mean recovery time in patients with mood disorders

metoral group and agitation rate was higher in this group. (Score agitation in dexmedetomidine group was approximately 2), (p = 0.3).

Table 5: Comparison of satisfaction score and agitation score in patients with mood disorders

Group	Dexmedetomidine group	Metoral group	p value
Satisfaction score	98.0 ± 38.1	1.1 ± 67.2	0.3
Agitation score	85.0 ± 87.1	98.0 ± 41.3	0.3

Discussion

A complete diagnostic evaluation must first be performed to treat patients with mood disorders and then a treatment plan is implemented [12]. The current therapies focus on drug therapy with psychotherapy, however, in depressed patients, ECT may be the best and fastest treatment [13]. The impact of ECT has been indicated by various sources. Since the 1950s, there has also been a tendency to concurrent use of ECT and antidepressants to increase treatment success, it has been reported that ECT is 20–40% more effective than drug therapy [14]. The aim of this study was to compare the effects of the combination of dexmedetomidine and metoprolol with thiopental on hemodynamic status, agitation, and satisfaction after ECT in patients with mood disorder. The results of this study indicated that there was no significant difference in the duration of seizure between the two groups. Neither of the two adjuvants had a negative effect on the duration of seizures. The results of this study demonstrated that the hemodynamic parameters were more stable in the dexmedetomidine group than in the metoral group. Tachycardia and ECT-induced hypertension were inhibited in the dexmedetomidine group compared to the remifentanil group. There was a significant difference between the two groups in terms of satisfaction and agitation score; therefore, satisfaction was higher in the dexmedetomidine group than in the metoral group (score: 1). Agitation was higher in the metoral group and agitation score was higher in this group (agitation score in the dexmedetomidine group = 2).

Mason *et al*. (2013) compared the effect of dexmedetomidine and ketamine-propofol anesthesia combination before ECT with non-dexmedetomidine group. This study was performed on 40 patients who received ECT and it was found that adding dexmedetomidine was associated with increased seizure duration, decreased restlessness, increased satisfaction, and a decrease in BP and PR of the patients. In our study, dexmedetomidine also led to a significant decrease in BP and HR after ECT, and patients' agitation scores decreased in the dexmedetomidine group [15].

In the 2016 study by Aparna *et al*., 60 patients aged 18–60 years scheduled for ECT were evaluated.

The recipient group received dexmedetomidine (0.5 μg/kg) diluted to 10 ml with 0.9% saline or 10 ml 0.9% saline (control) 10 min before induction of anesthesia with thiopentone. The increase in MAP and HR was lower in the dexmedetomidine group compared to the placebo group. Mean agitation score was less in dexmedetomidine group and duration of convulsion was not different in both groups. In our study, dexmedetomidine also reduced BP, HR, and decreased post-ECT agitation [16]. In 2016, Aksay *et al*. retrospectively analyzed 7 patients who received 178 ECT sessions between 2011 and 2015. Their analysis revealed that the prevalence of post-ictal agitation was lower in dexmedetomidine recipients and it was suggested that adjunctive use of dexmedetomidine to S-ketamine in ECT may be promising for reducing agitation [1]. The results of our study were similar in relation to the reduction of agitation in the dexmedetomidine group.

In another study by Moshiri *et al*., in Iran in 2016, the effect of dexmedetomidine, alfentanil, and placebo on ECT candidate patients was evaluated that there was no significant difference between the three groups in terms of seizure duration, agitation score, and hemodynamic parameters. The recovery time was shorter in the control group compared to dexmedetomidine and alfentanil. The results of the mentioned study have shown that the use of both alfentanil and dexmedetomidine as adjuvants did not cause significant changes in the hemodynamic parameters and duration of ECT-induced seizures [4]. The results of this study were inconsistent with our findings, since in our study, both adjuvant drugs resulted in a decrease in BP and HR after ECT, whereas the decrease was higher in the dexmedetomidine group. In other words, the ECT-induced hyperdynamic changes were less in the dexmedetomidine group. The results of several studies indicate that dexmedetomidine completely reduces the ECT-induced hyperdynamic responses in recovery. While it has no specific effect on the duration of seizures or recovery. The results of our study also confirm precisely this and indicate that hemodynamic stability during recovery and reduction of ECT-induced hypodynamic responses to dexmedetomidine. In our study, the effect of dexmedetomidine in controlling patients' hyperdynamic responses was higher than that of metoral. Both drugs had no adverse effect on the duration of seizures. However, the recovery time was significantly increased in the dexmedetomidine group. It is important to note that agitation score was higher in the dexmedetomidine group than in the dexmedetomidine group, and patients' satisfaction with recovery was higher in the dexmedetomidine group.

Conclusion

Both dexmedetomidine and metoral as adjuvants lead to a decrease in the post-ECT

hyperdynamic response of patients. Whereas the effect of dexmedetomidine is greater than metoral, on the other hand, none of the dexmedetomidine and metoral drugs had a negative effect on the duration of seizure. Dexmedetomidine significantly prolongs recovery time compared to metoral and agitation was also enhanced by the use of metoral.

References

1. Aksay SS, Bumb JM, Remennik D, Thiel M, Kranaster L, Sartorius A, *et al*. Dexmedetomidine for the management of postictal agitation after electroconvulsive therapy with S-ketamine anesthesia. Neuropsychiatr Dis Treat. 2017;13:1389-94. https://doi.org/10.2147/ndt.s134751
   PMid:28579785
2. McDaniel WW, Sahota AK, Vyas BV, Laguerta N, Hategan L, Oswald J. Ketamine appears associated with better word recall than etomidate after a course of 6 electroconvulsive therapies. J ECT. 2006;22(2):103-6. https://doi.org/10.1097/00124509-200606000-00005
   PMid:16801824
3. Aksay SS, Bumb JM, Jank C, Biemann R, Borucki K, Lederbogen F, *et al*. Serum lipid profile changes after successful treatment with electroconvulsive therapy in major depression: A prospective pilot trial. J Affect Disord. 2016;18:85-8. https://doi.org/10.1016/j.jad.2015.09.037
   PMid:26426831
4. Moshiri E, Modir H, Bagheri N, Mohammadbeigi A, Jamilian H, Eshrati B. Premedication effect of dexmedetomidine and alfentanil on seizure time, recovery duration, and hemodynamic responses in electroconvulsive therapy. Ann Card Anaesth. 2016;19(2):263-8. https://doi.org/10.4103/0971-9784.179618
   PMid:27052067
5. Moy RJ, Le Clerc S. Ketamine in prehospital analgesia and anaesthesia. Trends Anaesth Crit Care. 2011;1:243-5. https://doi.org/10.1016/j.tacc.2011.08.002
6. Lisanby SH. Electroconvulsive therapy for depression. N Engl J Med. 2007;357(19):1939-45.
   PMid:17989386
7. Mohseni M, Ghanbari AS, Motazedi MA, Pournajafian A, Faiz H, Soleimani M, *et al*. Comparison of the effects of ketamine and thiopental on hemodynamic variables and duration of seizure in patients treated with electro-shock. Anesth Pain Acad Jihad. 2014;30:15-21.
8. Copeland J, Dillon P. The health and psycho-social consequences of ketamine use. Int J Drug Policy. 2005;16:122-31. https://doi.org/10.1016/j.drugpo.2004.12.003
9. Ibrahim L, Diazgranados N, Luckenbaugh DA, Machado-Vieira R, Baumann J, Mallinger AG, *et al*. Rapid decrease in depressive symptoms with an N-methyl-d-aspartate antagonist in ECT-resistant major depression. Prog Neuropsychopharmacol Biol Psychiatry. 2011;35(4):1155-9. https://doi.org/10.1016/j.pnpbp.2011.03.019
   PMid:21466832
10. Jiwanmall M, Joselyn AS, Kandasamy S. Intravenous clonidine as a part of balanced anaesthesia for controlled hypotension in functional endoscopic sinus surgery: A randomised controled trial. Indian J Anaesth. 2017;6(1):418-23. https://doi.org/10.4103/ija.ija_58_17
    PMid:28584352
11. Wijeysundera DN, Bender JS, Beattie WS. Alpha-2 adrenergic agonists for the prevention of cardiac complications among patients undergoing surgery. Cochrane Database Syst Rev. 2009;7(4):CD004126. https://doi.org/10.1002/14651858.cd004126
    PMid:19821319
12. Kranaster L, Kammerer-Ciernioch J, Hoyer C, Sartorius A. Clinically favourable effects of ketamine as an anaesthetic for electroconvulsive therapy: A retrospective study. Eur Arch Psychiatry Clin Neurosci. 2011;261(8):575-82. https://doi.org/10.1007/s00406-011-0205-7
    PMid:21400226
13. Hoyer C, Kranaster L, Janke C, Sartorius A. Impact of the anesthetic agents ketamine, etomidate, thiopental, and propofol on seizure parameters and seizure quality in electroconvulsive therapy: A retrospective study. Eur Arch Psychiatry Clin Neurosci. 2014;264(3):255-61. https://doi.org/10.1007/s00406-013-0420-5
    PMid:23835527
14. Grant IS, Nimmo WS, McNicol LR, Clements JA. Ketamine disposition in children and adults. Br J Anaesth. 1983;55(11):1107-11. https://doi.org/10.1093/bja/55.11.1107
    PMid:6639827
15. Mason KP, Robinson F, Fontaine P, Prescilla R. Dexmedetomidine offers an option for safe and effective sedation for nuclear medicine imaging in children. Radiology. 2013;267(3):911-7. https://doi.org/10.1148/radiol.13121232
    PMid:23449958
16. Aparna AB,Thatte S, Pranita AK. Dexmedetomidine in premedication to attenuate the acute hyperdynamic response to ECT: A randomised, double-blind, controlled study. South Afr J Anaesth Analg. 2016;22:180-4. https://doi.org/10.1080/22201181.2016.1244316