Effect of adding dexmedetomidine or remifentanil to thiopental in patients with mood disorder candidate for electroconvulsive therapy

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Abstract

Electroconvulsive therapy (ECT) is one of the appropriate treatments for many neuropsychiatric patients, especially those with mood disorders. Short-term complications of ECT include agitation and postictal. In this study, we compared the addition of dexmedetomidine or remifentanil to thiopental as the main anaesthetic used in ECT. In this double-blind randomised clinical trial, 90 patients with mood disorders (candidates for ECT) were divided into two groups based on their therapy: dexmedetomidine or remifentanil. In the first group (DG), patients were slowly injected intravenously with 0.5 μg/kg dexmedetomidine before induction of anesthesia. In the second group (GR), 100 μg of remifentanil was slowly injected intravenously.In addition, we collected demographic information such as respiratory rate, heart pulse rate, seizure time, mean of arterial blood pressure, recovery duration and the oxygen arterial saturation recorded after recovery. Data obtained were analysed by use of statistical software, SPSS-23. The mean age of both groups was approximately 37 years with the majority being men. There was no significant difference between the two groups in terms of age and sex, blood pressure, heart rate, duration of seizures and arterial oxygen saturation before ECT. The mean blood pressure and heart rate in the recovery group were lower in the dexmedetomidine group than in the remifentanil group and the hemodynamics in the dexmedetomidine group were more stable. The recovery time in the dexmedetomidine group was longer than that of the remifentanil group ($p = 0.001$). Both groups had approximately the same satisfaction and the rate of agitation after ECT was the same. Both remifentanil and dexmedetomidine as adjuvants lead to a decrease in patients' post-ECT hyperdynamic responses. In our study, we demonstrated that the effect of dexmedetomidine is greater than remifentanil. On the other hand, neither dexmedetomidine nor remifentanil had a negative effect on seizure duration, but dexmedetomidine significantly prolonged recovery time, when compared to remifentanil.

Key Words: Mood disorder, Electroconvulsive therapy (ECT), Dexmedetomidine, Remifentanil

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Psychiatric illnesses are common health problems due to the disability and functional impairment they cause. The burden of psychiatric illnesses in developing countries causes many problems and imposes high costs on the health system.[1] Results from recent research indicate a high prevalence of mood disorder in society.[2] Electroconvulsive therapy (ECT) has been recognised as a safe and effective choice for treatment of mood disorders.[3,4] ECT causes seizures by electrical stimulation at various frequencies, that is run through electrodes placed on the scalp.[5] 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 rapidly resolves in most cases), the rare occurrence of seizures, short-term complications such as headaches, muscle pain, nausea, vomiting, and fatigue.[6] ECT typically induces transient hypertension (HTN) and immediate tachycardia after stimulation, which may result in severe hyperdynamic responses in patients treated with ECT.7 One of the short-term side effects of ECT is postictal agitation,[5] which causes motor dysfunction, poor response to verbal materials, and disorientation. The overall incidence of this complication during ECT is about 12%.[8] The choice of anesthetic for ECT depends on its effect on hemodynamics, duration of seizures and recovery parameters.[9] Therefore, there are a wide range of drugs prescribed to reduce acute hemodynamic changes due to cardiovascular

complications associated with ECT. Remifentanil is a short-acting opioid with a potent analgesic effect. Remifentanil has been shown to be effective in lowering blood pressure and heart rate (HR) when used as an adjuvant in anesthesia.[7] The opioid acts by reducing the dose of anesthetic agents and usually improves the response to stimulation.[10] Dexmedetomidine is a selective α2 agonist that predominantly affects the locus coeruleus.5 Dexmedetomidine attenuates central nervous system (CNS) stimulation by reducing presynaptic norepinephrine release, causing sedative effects. More broadly, the drug leads to analgesic effects, anxiolytic, and sympatholytic effects without affecting the respiratory system. The hyperdynamic responses to ECT are associated with an acute increase in plasma epinephrine and norepinephrine concentrations.[4] The most common side effects of dexmedetomidine are due to its mechanism of action, including hypotension and bradycardia. Therefore, both remifentanil and dexmedetomidine can be effective in controlling ECT-induced hemodynamic symptoms.[10] The aim of this study was to compare the effects of dexmedetomidine and remifentanil in the treatment of mood patients who had undergone ECT. We examined the effect of the drugs on the hemodynamic status, duration of seizures, as well as agitation and recovery time in patients.

Materials and Methods

Ethical considerations

This study was approved by the Research Ethics Committee of the Arak University of the Medical Science. The Code of Ethics was: IR.ARAKMU.REC.1396.298, and the study was approved on the 26 Jul, 2018. The registration code at the Iran Clinical Trial Center for this project is IRCT20141209020258N90. Procedures were conducted in accordance with the Declaration of Helsinki for human studies of the World Medical Association.

Setting and procedure

This study was a randomised, double-blind clinical trial that was performed on patients who were considered to be mood disorder candidates for ECT (18-55 years old), referred to the Amir Kabir Hospital, Arak, Iran. Demographic characteristics such as heart pulse rate, seizure time, mean of arterial blood pressure, recovery duration and the arterial saturation oxygen recorded by monitoring after recovery were collected through use of checklists. All patients were classified as either being grade I (normal healthy patient) or grade II (patient with mild systemic disease), in accordance with the American Society of Anesthesiologists (ASA) classification system. A series of inclusion and exclusion criteria were established for this randomized controlled trial study. Individuals who satisfied the inclusion criteria were invited to take part in the study. Informed consent was obtained from each participant who was deemed eligible to participate in the study and accepted invitation.

Inclusion criteria were:

- Patients with mood disorder who were candidates for ECT, having informed consent.
- Age range from 18 to 55 years.
- No underlying renal, hepatic, cardiac and pulmonary diseases.
- Patients who were not psychotic except for mood disorder.
- Patients who did not have contraindication for ECT.
- No head trauma.

Exclusion criteria included:

- All patients who required intubation after ECT due to respiratory distress and prolonged apnea
- Patients who do not have seizures after receiving ECT.

In this study, 90 patients who were mood disorder candidates for ECT were randomly divided into two groups: dexmedetomidine (GD) and remifentanil (GR). The division was equal, with both the GD andG R groups each having 45 patients. Patients were then placed on an ECT bed in a supine position and an intravenous angiocath 20 was inserted. Patients were given about 1-3 ml / kg of fluid prior to anesthesia as compensatory intravascular volume expansion (CVE)**.** Then, necessary monitoring was performed, including (HR), respiratory rate (RR**),** arterial oxygen saturation, and non-invasive blood pressure (NIBP)**.** In the first group (GD), patients were treated with 0.5 μg / kg dexmedetomidine (volume reached to 5 cc) intravenously and slowly before induction of anesthesia. In the second group (GR) (100 μg of remifentanil, intravenous therapy (IV)) was injected. Patients in both groups were anesthetized with 2–3 mg / kg thiopental sodium, 0.5 mg / kg succinylcholine and 0.5 mg atropine.

Table 1: *Comparison of mean blood pressure, heart rate and arterial oxygen saturation before shock therapy*

Cardiovascular parameter	Dexmedetomidine group	Remifentanil group	*p*-value
Mean arterial blood pressure before shock	90.8 ± 2.9	92.5 ± 3.8	$p = 0.4$
Heart rate before shock	100.8 ± 3.7	101.9 ± 4.6	$p = 0.6$
Arterial oxygen saturation before shock	95.2 ± 4.6	94.9 ± 3.8	$p = 0.4$

Table 2: *Mean blood pressure, heart rate and arterial oxygen saturation during recovery after shock therapy*

Cardiovascular parameter	Dexmedetomidine group (DG)	Remifentanil group (RG)	*p*-value
Mean arterial blood pressure	80.9. ± 4.1	92.4 ± 4.92	$p = 0.02$
Average heart rate	80.3 ± 2.3.80	108.2 ± 5.108	$p = 0.001$
Mean arterial oxygen saturation	94.2 ± 5.1	93.8 ± 4.93	$p = 0.40$

Data analysis

All data obtained from the questionnaires were analyzed using SPSS-23 statistical software, t-test and Analysis of Variance (ANOVA). After anesthesia, the patients were re-hyperoxygenated and transferred to recovery. Questionnaires including demographic data, duration of seizure, hemodynamic status of patients, recovery time, agitation score and satisfaction score were completed for each patient, and descriptive statistics including mean and percent was used.

Results

The mean age distribution in the dexmedetomidine group was 37.8 ± 2.7 years and in the remifentanil group 36.9 ± 1.1 years. The mean age was approximately 37 years in both groups. t-test analysis showed that there was no statistically significant difference between the two groups ($p = 0.1$). Frequency distribution in the dexmedetomidine group was 70.7% for males and 29.3% for females and for remifentanil group 71.9% for males and 28.1% for females. There was no significant difference between the two groups ($p = 0.2$).

Comparison of mean blood pressure, HR and arterial oxygen saturation before shock therapy in patients with mood disorders (ECT candidates) in the two groups of dexmedetomidine or remifentanil were evaluated in Table 1. As can be seen, all *p* values were greater than 0.05. Thus indicated that there was no significant difference between the two groups in mean blood pressure, HR and arterial oxygen saturation before ECT.

Results differed for the post-ECT comparisons between the GD group and the GR group. There was a significant difference between the two groups in the mean blood pressure and HR in the recovery group, which was significantly lower in the dexmedetomidine group than in the remifentanil group ($p = 0.02$, $p = 0.001$). In other words, the hemodynamics of patients in the dexmedetomidine group was more stable. However, there was no significant difference in arterial oxygen saturation between the GD and GR group in recovery ($p = 0.4$) (Table 2 and Figure 1). Statistical comparison was also performed between the groups with regards to seizure duration and duration of recovery. It was found that there was no significant difference between the two groups in terms of duration of seizures (in seconds) ($p = 0.08$), although the duration of seizures was somewhat longer in the remifentanil group; but this difference was not significant. There was a significant difference between the two groups in terms of recovery time (in minutes) and the recovery time was significantly longer in the dexmedetomidine group than in the remifentanil group ($p = 0.01$) (Figure 2 and Table 3). The comparison of satisfaction score and agitation in patients with mood disorders, in the two groups of dexmedetomidine and remifentanil, was also evaluated. There was no significant difference between the two groups in terms of satisfaction and agitation. ($p = 0.4$, $p = 0.1$) (Table 4).

Discussion

ECT is one of the appropriate treatments for many neuropsychiatric patients, especially mood disorders.[11]

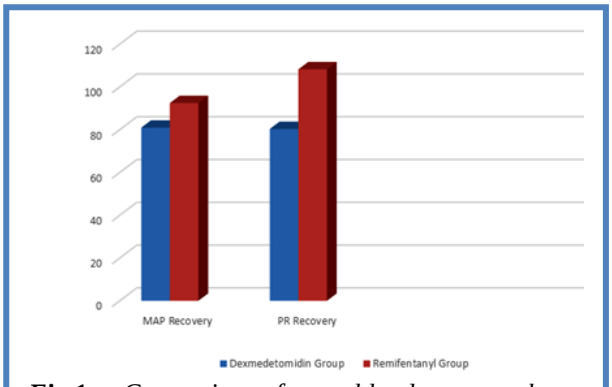

Fig 1. *Comparison of mean blood pressure, heart rate and arterial oxygen saturation after recovery of shock therapy*

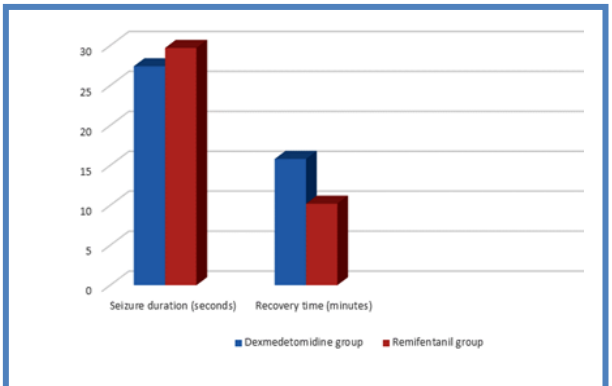

Fig 2. *Comparison of mean blood pressure, heart rate and arterial oxygen saturation after recovery of shock therapy*

Table 3. *Duration of seizures and mean duration of recovery*

Group	Dexmedetomidine (DG)	Remifentanil (RG)	*p*-value
Duration of seizures (sec)	27.4 ± 2.1	29.7 ± 2.3	$p = 0.08$
Duration of recovery (min)	15.8 ± 1.3	10.2 ± 2.4	$p = 0.01$

Table 4. *Satisfaction and Agitation Scores*

Score	Dexmedetomidine (DG)	Remifentanil (RG)	*p*-value
Satisfaction	98.68 ± 0.1	84.71 ± 0.1	$p = 0.4$
Agitation	85.78 ± 0.1	92.86 ± 0.1	$p = 0.1$

The short-term effects of ECT can be attributed to patients' postictal agitation.[12] Due to these side effects and to reduce hemodynamic changes, the use of two adjuvants such as remifentanil or dexmedetomidine along with thiopental can lead to hemodynamic stability and reduction of agitation in patients after ECT.[13] The results of our study are in line with the results of previous studies. One example is the study by Recart et al. 2003 in the United States.[7] This study examined the effect of remifentanil on blood pressure in patients. In comparison with the control group after ECT, it was significantly reduced. However, remifentanil had no adverse effect on the duration of seizures (with different periods). Also, the recovery time was not affected by remifentanil, and the final finding indicated that remifentanil did not adversely affect recovery and seizure duration but prevented post-ECT HTN, a serious ECT complication.[7] The results of this study were consistent with our study that in our study remifentanil as a thiopental adjuvant led to a decrease in blood pressure and HR (this decrease was acceptable); but had no effect on seizure duration and recovery. In another study conducted in China Li et al. 2016,[14] investigated the effect of low dose dexmedetomidine on hyperdynamic ECT responses. They indicated that HR and mean arterial blood pressure in the dexmedetomidine group were significantly decreased compared to the control group, while the duration of seizure, recovery time and spontaneous breathing were similar to those in the control group and did not have a negative effect in dexmedetomidine (2 μg/mg). Dexmedetomidine significantly reduced post-ECT headache and agitation.[14] The results of our study were also consistent with this study in that dexmedetomidine significantly decreased blood pressure and HR after ECT, and patients' agitation score decreased in the group where dexmedetomidine was administered. Salehi et al. 2008.[15] in a study on ECT candidates compared dexmedetomidine, esmolol and lignocaine drugs. They concluded that esmolol and dexmedetomidine significantly decreased mean arterial blood pressure and HR after ECT, compared with control and lignocaine groups. On the other hand, the effect of dexmedetomidine and esmolol on seizure duration was less than that of lignocaine. The overall conclusion of the study was that dexmedetomidine (in various combinations) and esmolol, can significantly improve cardiovascular response in patients after ECT, while not having a negative effect on the duration of seizure.[15] The results of this study are consistent with our study, because in our study, dexmedetomidine also reduced HR and blood pressure and decreased cardiovascular responses in patients, with no effect on seizure duration and recovery. In a study in Turkey, Bzthidsefo 2008 investigated the effect of dexmedetomidine on the reduction of ECT-induced hemodynamic response.[16] The author found that the duration of seizure and recovery time in the dexmedetomidine group did not change, whereas dexmedetomidine significantly reduced the ECT-induced hyperdynamic response and decreased blood pressure and HR during recovery.[16] Those results are also consistent with our study because we here show dexmedetomidine reduced the blood pressure and HR of the patients in recovery and controlled the hyperdynamic responses induced by ECT in the patients. Furthermore, it had no negative effect on the duration of seizure and recovery time. Results from numerous studies indicate that both remifentanil and dexmedetomidine decrease the ECT-induced hyperdynamic responses in recovery, while they have had no specific effect on duration of seizure or recovery. The results of our study also confirm exactly this and suggested stabilising hemodynamics in patient recovery and reducing ECT-induced hyperdynamic responses. However, the effect of dexmedetomidine in controlling the patients' hyperdynamic responses was more than remifentanil. 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 the agitation score was reduced in both groups. Furthermore, no difference was found between groups with regards to patient satisfaction in recovery, and there was a similar result for satisfaction scores in both groups.

In conclusion, our study found that both remifentanil and dexmedetomidine were capable of reducing the hyperdynamic responses of patients after ECT and that both has clinically relevant effect on seizure duration. In deed, we showed that dexmedetomidine significantly prolongs recovery time compared to remifentanil. It is hoped that these findings may guide therapies involving the use of ECT for patients with moods disorders.

List of acronyms

ANOVA - Analysis of Variance
CNS - central nervous system
CVE - compensatory intravascular volume expansion
DG - Dexmedetomidine group
ECT - Electroconvulsive therapy
HR – heart rate
HTN - transient hypertension
IV - intravenous therapy
NIBP - non-invasive blood pressure (
RG – Remifentanil group
RR - respiratory rate

Authors contributions

All authors participated in designing the study, analyzing the literature, collecting and analyzing data and writing the paper, that was finally approved by all of them.

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Conflict o f Interest

The authors declare no competing interests.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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