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Effect of Intravenous Alfentanil on Hemodynamic Changes in Anesthesia for Electroconvulsive Therapy

Hamid Khsoro-Zamiri,[1] Mohammad Shabani*[2]

1. Department of Anesthesiology, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Neuroscience, Neuroscience Research Center, Kerman University of Medical Sciences, Kerman, Iran

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*Corresponding author at:
Department of Neuroscience, Neuroscience Research Center, Kerman University of Medical Sciences, Kerman, Iran
E-mail:
shabanimoh@yahoo.com
shabani@kmu.ac.ir

Abstract

***Background*:** Electroconvulsive therapy is one of the therapeutic ways to treat several severe and threatening psychiatric disorders that may cause hemodynamic complications. This study was conducted to examine the effects of intravenous alfentanil on heart rate, mean arterial pressure, seizure duration, respiratory arrest, and recovery after electroconvulsive therapy (ECT).

***Materials and Methods*:** A total of 100 patients with psychiatric disorder were examined in a prospective randomized double-blind study. Alfentanil, thiopental, and succinylcholine were administered to 50 subjects, and the remaining subjects received normal saline, thiopental, and succinylcholine, in that neither the patient nor the injector was aware of alfentanil or normal saline in A and B coded syringes.

***Results*:** Two groups were not significantly different by age and sex. Average values of mean arterial pressure changes, immediately after ETC, were 5.41±1.9 and 32.29±2.7 in alfentanil and placebo groups, respectively. Mean values of heart rate changes, immediately after ECT, were 10.78±0.8 and 22.6±1.2 in alfentanil and placebo groups, respectively. Alfentanil significantly reduced heart rate and mean arterial pressure, after electroconvulsive. Alfentanil had no significant effect on seizure duration, respiratory arrest, and recovery.

***Conclusion*:** Alfentanil probably could be useful to reduce ECT-induced tachycardia and hypertension in high-risk patients without affecting seizure duration and treatment effects of ECT.

Introduction

Electroconvulsive therapy is a safe, effective, and fast therapeutic method for patients with major depression and other serious mental disorders [1]. Although, the exact mechanism of action of electroconvulsive therapy is elusive, but today it is taken to be a suitable and necessary method to alleviate disorders that respond less to medication, and to improve therapeutic responses. Despite appropriate therapeutic effects expected for electroconvulsive therapy, it seems to be associated with a series of adverse side effects. Electroconvulsive therapy is frightening due to the use of electricity and seizure induction [2]. It is also associated with increased heart rate and blood pressure [3], vegus stimulation, sever muscle cramps, arrhythmias, embolism, and apnea [4].

In order to reduce muscle cramps and avoid a possible dislocation of joints and fractures, patients are given anesthesia and muscle-relaxant injections. Profound cardiovascular and brain consequences are of other adverse side effects of ETC. Of the cardiovascular consequences of ECT, mainly due to autonomic nervous system activity, is depletion of the parasympathetic system (the tonic phase) for 5 to 10 seconds and the subsequent activity of the sympathetic system (clonic phase). First, bradycardia and hypotension, followed by tachycardia, hypertension, and arrhythmia (its peak wipes out one minute after ECT, and generally after 5-10 minutes), will occur [4]. Release of catecholamine, along with ECT-induced seizure and cardiovascular responses, during ECT, may be accompanied with several risks for patients, especially those with history of cardiovascular diseases [5]. In the previous studies, the effect of different medications such as phentermine, labtalol, lidocaine, trimethapan, etomidate compound, and alfentanil on hemodynamic changes caused by ECT, has been given attention [6-8].

In a study, conducted by Scholz et al., on the effect of alfentanil on cardiovascular responses, due to endotracheal intubation, they observed that alfentanil could reduce cardiovascular changes caused by endotracheal intubation in these patients [9]. Regarding ECT-induced hemodynamic changes and alfentanil-proven effects on reduction of hemodynamic changes during anesthesia and operative stress, this study was designed to investigate the effects of intravenous injection of alfentanil and thiopental sodium on heart rate, mean arterial pressure, and systolic and diastolic blood pressure compared with thiopental and placebo during ECT. In addition, the effect of alfentanil on post-ECT seizure duration, respiratory arrest, and recovery was studied.

Materials and Methods

This is a double-blind clinical trial study, in which 100 ECT-candidates, referring to psychiatric department of Shahid Beheshti Hospital in Kerman, was selected using convenience sampling. The inclusion criteria were as following: member of normal healthy human group I, ASA, 15-55 years old, without history of drug addiction (by asking from the patient and his/her family, and referring to the patient's profile), and without contraindications to ETC. Beforehand, approval from Ethics Committee of the University and informed consents from the patients were obtained. The subjects were divided into two equal groups, i.e. case and control. The variables investigated in this study included systole and diastole blood pressure, mean arterial pressure, arterial blood oxygen saturation, heart rate, seizure duration, apnea duration, recovery duration, age, and sex. In all cases under investigation, blood pressure, heart rate, and arterial blood oxygen saturation were measured as the basis, before undergoing ECT. None of the patients were received other premedication. Preoperative preparation procedure, including being NPO and receiving fluids based on body weight, was similar in all patients. Asthenia induction, in both groups, included 2.5 mg/kg thiopental, 5.0 mg/kg succinylcholine, and 0.5 mg atropine. Then, one of the groups received 10µg alfentanil (vial A) per kilogram of body weight, and the other group received equal volume of normal saline per kilogram of body weight (vial A) through intravenous injection. The blood pressure, heart rate, arterial blood oxygen saturation variables were measured and registered in respective checklist at 0, 5, and 10 minutes after ECT induction. Seizure, apnea, and recovery durations were attached to the checklist, as well. Data obtained from checklists were collected based on the variables and then the average of mean arterial blood pressure difference, heart rate, and arterial blood oxygen saturation differences, pre-ECT and at fifth and tenth minutes post-ECT in both groups were measured and compared. To analyze the results, SPSS-13 was utilized. After checking the normality, data were analyzed using K-S, Student's *t*-test, and χ^2 tests.

Results

The mean age was equal in both groups, and so there was no statistically significant difference between the groups in this regard. In addition, there was no significant difference in terms of gender distribution (Table 1). The average of mean arterial pressure was measured before ECT, and 0, 5, and 10 minutes after ECT in both case and control groups. Increase in the average of mean arterial pressure was lower in alfentanil groups than normal saline, immediately after it (p=0.038), (Fig. 1).

Then, the difference between the averages of mean arterial pressure before ECT and 0, 5th and 10th minute after it was measured and compared in both groups, and showed a significant different in all cases (p=0.01). The difference between the averages of heart rate before ECT and 0, 5th, and 10th minute after ECT was measured and compared in both groups. The result demonstrated significantly less increase in heart rate in alfentanil group than control group p=0.037 (Fig. 2). Then, the average of heart rate before ECT was compared with that of at 0, 5th, and 10th minutes after ECT, in both groups. The findings revealed a significant difference between the groups in that regard (p=0.006), figure 2. The arterial blood oxygen saturation values before ECT and 0, 5, and 10 minutes after it, in both groups, were not significantly different (Fig. 3). However, investigation into difference mean of arterial blood oxygen saturation before ECT and 0, 5, and 10 minutes after it showed a significant difference between the groups (p=0.045), in that alfentanil caused decrease in the difference mean of arterial blood oxygen saturation at that points of time (Fig. 3). In addition, no significant difference was seen in comparison between three variables, i.e. seizure, recover, and apnea durations in the groups under investigation.

Table 1. Comparison between the groups in terms of gender distribution (in percent) and mean age by injected substance

	Saline	Alfentanil
Male (percent)	50	49
Female (percent)	50	51
Age (year)	32±8	31±9

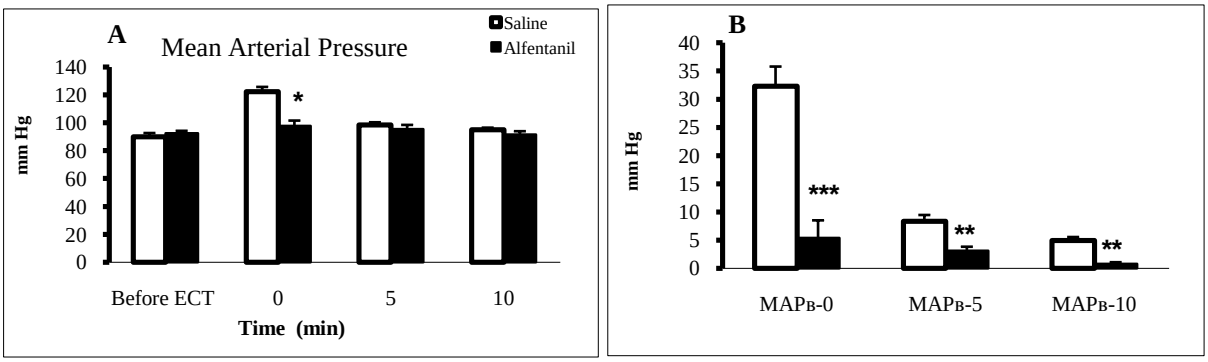

Figure 1. Comparison between the average (A) and mean arterial pressure difference (B) in the studied subjects by injection substance before and after ECT (0, 5, and 10 minutes after ECT). The results were reported in form of Mean±SEM
(MAP B-0, MAP B-5, and MAP B-10): mean arterial pressure difference before ECT and 0, 5, and 10 minutes after it), * presence of: significant difference with control group, p=0.038, **presence of: significant difference with control group, p=0.008, *** presence of: significant difference with control group, p=0.001

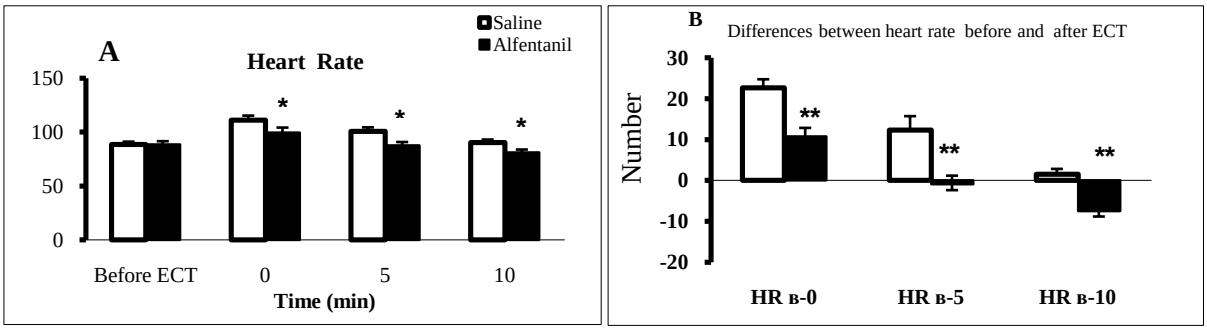

Figure 2. (A) comparison of the mean and (B) difference in heart rate before ECT and 0, 5, and 10 minutes after ECT by injected substance (HR B-0, HR B-5, and HR B-10): heart rate difference before ECT and 0, 5, and 10 minutes after it * presence of: significant difference with control group, p=0.037, ** presence of: significant difference with control group, p=0.006

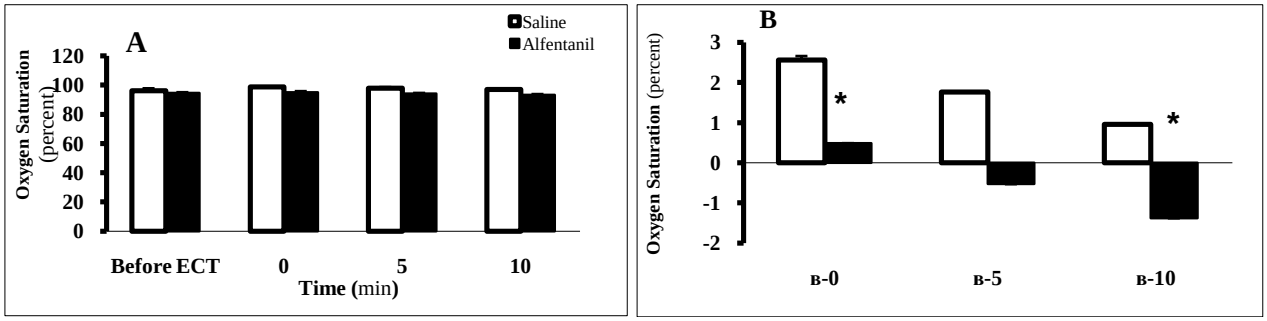

Figure 3. (A) comparison of the mean and (B) difference in arterial blood oxygen saturation before ECT and 0, 5, and 10 minutes after it in the studied subjects, by injected substance
* presence of: significant difference with control group, p=0.045

Discussion

In this study the effects of intravenous injection of alfentanil, along with thiopental, on the heart rate, mean arterial pressure, systole and diastole pressures, seizure duration, respiratory arrest, and recovery after electroconvulsive therapy were investigated. The results from this study showed a significant difference between the groups in terms of using alfentanil in measuring mean arterial blood pressure, heart rate, arterial blood oxygen saturation before ETC and 0, 5, and 10 minutes after it. However, no significant difference was observed between the groups in terms of seizure and apnea durations. In contrast to our study, Nguyen et al., reported no significant difference between the groups in hemodynamic parameters with respect to the use of alfentanil, along with propofol and methohexitone. However, the use of alfentanil in their study prolonged recovery and seizure durations [10]. Alfentanil is a synthetic opioid agonist (phenylpiperidine derivative) of fentanyl family, used in an anesthesia state, especially when hemodynamic stability in vital. Alfentanil has more rapid analgesic onset as well as shorter elimination than fentanyl [9]. It has been determined that alfentanil can be useful in reducing hemodynamic responses to intubation during surgery, for its contribution to cardiovascular sustainability. However, respiratory suppression effects of this medicine should be taken into consideration, its sedation and respiratory depression durations are far shorter than fentanyl and sufentanil [9]. Cardiovascular responses to ECT are due to autonomic nervous system action. Instant parasympathetic activity, causing transient bradycardia, followed by a sympathetic discharge resulting in increased hypertension and tachycardia levels, can be due to the responses from brain centers that are responsible for regulating the cardiovascular system, to ETC-induced pain and seizure [11]. Alfentanil is administered intravenously or epidurally. It also has rapid analgesic onset when it is administered intravenously. In addition, alfentanil is a potent mu and kappa opioid receptors agonist and can induce analgesia and reduce ECT-induced stress, by binding to mu-opioid receptors [12]. Therefore, in case of using it as premedication before ECT, it may reduce ECT-induced fear and stress, and also its subsequent hemodynamic changes which usually occur after ECT. In a study, Groenland et al. investigated the effects of etomidate-alfentanil on hemodynamic changes during ETC. They showed that etomidate-alfentanil can moderate hemodynamic changes such as ECT-induced heart rate, diastole blood pressure, and mean arterial pressure both before and after electrical stimulation. They also demonstrated that alfentanil prolongs apnea duration, while has no influence on seizure duration [8]. In a study by Van den Boek et al., the effect of alfentanil, along with etomidate, on seizure duration during anesthesia for ECT was investigated, showing no significant difference with placebo group [7]. In a study conducted by Akcaboy et al., the impacts of

remifentanil and alfentanil on seizure duration, stimulus amplitudes, and recover parameters were investigated. The results showed that mean seizure duration was longer in remifentanil-propofol and alfentanil-propofol. Moreover, recover parameters were similar in remifentanil and alfentanil groups; significantly different from propofol group [13]. Using high doses of alfentanil (25µg/kg per kg of body weight), Dinwiddie et al., observed that some patients experienced nausea and vomiting [14]. Whereas, in our study, using low alfentanil dose (10 µg/kg), none of the opioid-induced adverse side effects such as chest wall stiffness, respiratory depression, nausea, and vomiting were not observed. In case of using 2 mg alfentanil before anesthesia and endotracheal intubation onset, adrenergic responses of sympathetic system and hemodynamic changes would be reduced without causing any complication in the circulatory system [15]. Whereas, some studies have shown that injection of alfentanil to newborns does not have positive effect on reduction of hemodynamic changes during endotracheal intubation [16]. Regarding the results from comparing mean seizure duration in case and control groups, comparing recovery and seizure duration in them and equality of their means, moderating effect of alfentanil on hemodynamic parameters, and a little number of ECT-induced adverse side effects in low doses, it seems that alfentanil has no conflict with ECT therapeutic effects in psychiatric patients. In addition, it probably can be used as a safe and effective drug for controlling ECT-induced hemodynamic changes.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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