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The Effect of Atropine on Post-ECT Bradycardia in Patients with Major Depressive Disorder

Hassan Farashbandi,[1] Vahid Emdadi,[2] Hassan Haghshenas,[1] Vahid Khaloo,[3] Mohsen Kianpoor*[4]

1. Department of Psychiatry, Research Center for Psychiatry and Behavioral Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Psychiatry, Shiraz University of Medical Sciences, Shiraz, Iran
3. Anesthesiologist, Ebn-e-Sina Hospital, Shiraz, Iran
4. Department of Psychiatry, Zahedan University of Medical Sciences, Zahedan, Iran

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*Corresponding author at:
Department of Psychiatry, Zahedan University of Medical Sciences, Zahedan, Iran.
E-mail:
rcpsych1@sums.ac.ir

Abstract

***Background*:** Electroconvulsive therapy (ECT) is utilized for treatment of a range of psychiatric disorders including major depressive disorder (MDD). One of the major complications in using ECT is cardiovascular problems i.e., bradycardia. The present study was designed to investigate the effect of atropine on the pulse rate (PR) of the patients under treatment with ECT.

***Materials and Methods*:** In this randomized clinical trial, 30 patients with diagnosis of MDD who received atropine before ECT treatment (control group) were compared with 30 patients with the same diagnosis without receiving atropine (experimental group) under ECT treatment. Both groups received ECT under the same term and condition. The PR of the patients were recorded 7 times (twice before anesthesia and ECT and 5 fixed one min intervals immediately after receiving ECT); for 10 sessions of treatment with ECT (3 times a week). The results were analyzed using repeated measure analysis of variance. The PR under 50 was the cut off point for differentiating the patients suffering from bradycardia and those without it.

***Results*:** Slight increment in PRs for experimental group (patient who did not receive atropine) in contrast to control group were observed, but it did not reach a statistically significant level. The gender (male/female) did not have different PR. The age of the patients and initial PR (regarded as co-variances) did not show significant effect on PR for total sample.

***Conclusion*:** There seems to be not necessary to use atropine treatment for depressed patients receiving ECT.

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Introduction

Electroconvulsive therapy (ECT) is a remarkably effective treatment method in a large numbers of psychiatric and non-psychiatric disorders [1-7], particularly major depressive disorder [8]. Nevertheless, using this method is associated with various complications. The most critical complications are cardiovascular ones, out of which, bradycardia is the most significant [9]. Atropine is an anticholinergic agent which, in ECT centers is used routinely as a selective agent to prevent complications of electrical stimulus that is significant increase in parasympathetic activity leading to bradycardia and frequent asystoles, which can be prolonged [10-12]. Nevertheless, there are various and sometimes contradictory comments in literature about using of atropine and other anticholinergic agents such as glycopyrolate as premedication before ECT [13-15]. Glycopyrolate has the advantage of not passing the blood brain barrier, and as a result producing less post-ictal delirium, but atropine has been reported to provide more protection against bradycardia and asystole [16]. So far, no study has been conducted about using atropine as a pretreatment to prevent bradycardia caused by ECT or not, although it is routinely used in centers providing ECT in Iran. As it was mentioned, there are different ideas about this problem in ECT centers. Some anesthesiologists administer atropine before ECT based on the articles supporting use of atropine in all patients before ECT and other groups perform ECT without atropine as premedication with regards to the fact that routine atropine premedication is not recommended due to detrimental effects on myocardial work and demand [14, 17, 18].

There are also evidences that made many centers not to use atropine as premedication because of adverse effects. For example Maixner et al. refused using combination of atropine and neostigmine due to several adverse effects including urinary retention and incontinence, fecal incontinence, worse postictal delirium, and more bradicardia and hypotention, it means that atropine could not prevent the complications [19].

These two different and somehow preferential approaches were the reason why the authors decided to carry out a controlled study on the effect of atropine as a premedication before ECT on the heart rate-which has been considered as a simple index of cardiovascular function to determine the necessity of using or not using

atropine, so that the practitioner can use the treatment method in psychiatric patients in a better and safer way.

Materials and Methods

In this double blind randomized controlled study, performed in Ebn-e-Sina Psychiatric hospital, we selected, 30 hospitalized patients, as the target (experimental) group who received ECT without atropine and 30 others, as control group, received ECT with atropine. The physician who measured PR was blind to the groups that patients were assigned. All the patients had diagnosis of major depressive disorder (MDD) according to criteria of the diagnostic and statistical manual of mental disorders-IV-R.

The exclusion criteria for sampling in this study were: 1- Aged patients (over 45 years) in whom, compared to younger ones, the probability of undiagnosed physical illnesses are higher. 2- Patients having the history of drug abuse except smoking. 3- Those that had other psychiatric disorders other than major depression, except personality disorder. 4- Pregnant ladies. 5- Patients having clear physical problems. 6- Patients in whose using drug list there was no tricyclic antidepressants (TCA), to neutralize the comparative drug effect on the heart beats (according to the treating psychiatrists, consumption of these drugs was necessary and we could not discontinue them because of medical ethics). 7- Patients using other psychiatric or non-psychiatric drugs, except TCA, selective serotonin reuptake inhibitors (SSRI), risperidone and short-acting benzodiazpines, such as oxazepam or lorazepam. It is to note that the use of one TCA in the routine therapeutic dose was necessary for all patients.

All the patients were selected, with regards to exclusion criteria, randomly, as they entered to receive ECT (one assigned to experimental group and the next one assigned to control group). Before entering into the study, the subject and purpose of the study and its details were explained to each patients or his/her guardian in a simple language and a consent form was given to be signed. Prior to ECT, all patients received succinylcholine (5 mg/kg) and thiopental (3-5 mg/kg) for anesthesia. Before the injection of anesthetic agents, the patients of target group received 5 mg intravenous atropine while 5 mg normal saline was injected intravenously to each one of the control group patients. Throughout the study we followed all the patients attentively, that is, any incidence of new psychiatric problems, any physical illness or any change in their treatment process, was carefully watched. In case of loss of patients (patient refusal to continue ECT) or emergence of any physical disease during hospitalization or medication changes during treatment except what was considered permissible for research, the case was replaced with another appropriate one. In the present study the pulse rate of each patient was measured by pulse oximetry during 10 sessions of ECT, 7 times in each session, that is, before anesthesia, before (45 seconds after anesthetics infusion), after (1 min) ECT and 5 times with 5 min intervals after inducing ECT. To compare the two groups at different times of measurement and controlling individual variables, the data were analyzed using SPSS-13, statistical formulas, *t*-test and analysis of variance. The total eligible patients for the period of this study were 68 patients among them 8 patients were dropped due to discontinuation of ECT according to patients' refusal to continue ECT or emergence of any physical disease during hospitalization or medication changes during the course of hospitalization and couldn't be replaced due to deadline of study.

Results

The mean age of experimental group (30 patients) was 30.8±3.41 years of whom 14 were male and 16 were female. The mean age of control group (30 patients) was 27.7±1.17 years from which 12 were women whereas 18 ones were men.

A "Repeated Measures Analysis of Variance" was used. In this analysis PRs were regarded as dependent variable (seven times of measurement, before and after ECT). Gender (male-female) and groups (experimental-control) were independent variables. The age of patients was entered as co-variance, in order to control this confounding variable. The means and standard deviations (SD) of PRs for the two groups and male and female are represented in table 1. The PRs are recorded twice before anesthesia and 5 times after ECT with one minute intervals.

The results of repeated measures analysis of variance showed that gender (male-female) did not have different PRs. The interaction between group and gender was also not significant. The groups (experimental and controls) did not showed significant PRs difference. The age of the patients as covariance did not have effect on PRs. A fluctuation was observed in PRs of both groups during ECT (at the time of anesthesia inducing up to the fifth minute after ECT); however, the results showed the groups were not different in this aspect.

Table 1. Means and standard deviations (SD) of pulse rate for groups

PR Measured	Control male (N=18) Mean±SD	Control female (N=12) Mean±SD	Experiment male (N=16) Mean±SD	Experiment female (N=14) Mean±SD
1st	100.1±26.6	100.7±10.8	95.5±11.5	99.7±13.1
2nd	100.6±9.87	108.7±11.8	100.3±8.08	102.2±8.81
3rd	100.4±11.6	111.2±15.0	95.6±7.79	98.4±13.9
4th	100.4±9.17	107.7±13.14	98.1±9.83	100.1±11.9
5th	102.2±7.42	105.1±9.82	101.5±9.92	101.1±8.70
6th	120.6±8.04	104.6±9.12	103.6±9.18	103.3±8.60
7th	117.5±7.78	116.7±8.42	106.7±7.38	106.7±8.97

Final statistical analysis was carried out using an independent *t*-test to compare initial PR of groups. The results are presented in table 2. This finding indicates that there was no basic heart rate difference between the patients of experimental and control groups at initial phase.

Table 2. Mean±SD of pulse rate measured in initial phase

Group	No.	Mean±SD
Experimental Basic PR	30	97.47±12.26
Control Basic PR	30	100.36±21.45

Discussion

The results of present study showed that injecting atropine did not affect the PRs of patients. Wyant and McDonald who could not show a clear bradycardia during ECT, reported that, this phenomenon had been seen only in one case out of 39 patients during 297 times of ECT [20], but they had not focused on the heart beats of patients during ECT and immediately after that when there is the probable peak of the highest risk of bradycardia.

In a study that was conducted by Rasmussen et al., the effect of ECT on HR, cerebral oxygenation and the adjusting role of glycopyrrolate (an anticholinergic drug) against these effects were studied [21]. In this study, out of 17 patients who received ECT without glycopyrrolate, 15 ones (87%) showed bradycardia and reduction in brain oxygenation and in 8 patients who had received glycopyrrolate before ECT, the heart rate was maintained in the range 78 beats per min (94-40 beats per min). Also, no reduction of brain oxygenation was seen in such patients. Regarding the small numbers of subjects, vague patient selection and methodology leading to such results, this study will be in question strongly.

Although anticholinergic agents (such as atropine) has been routinely used before ECT to reduce or eliminate parasympathetic effect of ECT, some sources, such as Royal college of psychiatrist's ECT handbook [22] have recommended to use such agents in patients suffering from hypodynamic heart diseases and those who are susceptible to long term asystole during ECT and not to be used in patients having hyperdynamic conditions, such as hypertension and tachycardia.

Mayur et al., in a study on the effect of atropine premedication on rate-pressure product (RPP), which is a clinical indicator of myocardial oxygen demand and calculated by the heart rate multiplied by the systolic blood pressure, showed that atropine leads to a higher increase in the mount of RPP compared with placebo [23].

Referring to such finding, they recommended avoiding prescription of atropine prior to ECT except when the threshold of the seizure is determined. No remarkable effect of RPP influencing the clinical condition of patient was seen in the next studies. The results of the present study showed that, generally, PR increases during ECT, whereas, receiving and not receiving of atropine has no effect on adjustment and intensity of this phenomenon. Since PR in the present study and RPP in Mayur's study [23] were considered as the main indexes for evaluation of heart function, this can be one of the reasons of differences in the results. The most important factors leading to the different results of 2 studies are the small number of sample (30 patients in 2 groups with 15 people), and lack of control on the altering factors, particularly medications with some effects on heart beats and blood pressure. In the presents study this effect was minimized, although for more precise results, more comprehensive, sufficient samples are required in our study as well.

In a study conducted by Bouckoms et al. [24], it was found out that atropine caused elimination of ECT parasympathetic effects, in such a manner that led to HR increase and reduction of dropped beat numbers and premature arterial beats. So the researchers of this study suggested that these effects could be useful for patients with hypodynamic condition, such as those with bradycardia, bradyarhythmia and hypotension problems. On the other hand, since atropine increases cardiac activity, they suggested not prescribing atropine for patients with hypertension, tachycardia and ischemic heart disease prior to ECT. Although the aim of the present study was not arrhythmias caused by ECT and the effect of atropine on them, it did not confirm the results of the above-mentioned study on the effect of atropine on HR of patients. No difference was observed between prescription and not prescription of atropine on patients HR receiving ECT.

In the present study it was shown that no significant bradycardia emerges during ECT (from the time of induction of anesthesia up to five minutes after ECT). Regarding the results of the present study, users of ECT are recommended to avoid routine prescription of atropine in patients receiving ECT and use it for the patients suffering from a remarkable and long term bradycardia during ECT.

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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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