Organic Article

Effect of Premedication with Oral Clonidine on Hemodynamic Response during Electroconvulsive Therapy

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Abstract

Background: Electroconvulsive therapy (ECT) is the most effective treatment available for the acute treatment of depression in patients who do not respond to medications. It is generally used as a second line treatment for many psychological disorders, mainly major depression and schizophrenia where medication is not effective. ECT is often associated with some complications such as hypertension, tachycardia arrhythmia and even myocardial infarction. Various methods have been used for prevention or control of these cardiovascular side effects.

Aim: The aim of this study was evaluating the effect of oral clonidine (0.3 mg) with control group to know the effect of oral clonidine on hemodynamic response during ECT.

Methods and Material: This prospective randomized crossover clinical trial was performed on 25 patients aged 20-50 years, weight 50-70 kg with ASA I and II who were candidates for ECT. Prior to ECT, each patient received oral doses of clonidine (0.3 mg) or a placebo 90 minutes before ECT. Baseline Heart rate, systolic, diastolic and mean arterial pressures were noted just before securing the intravenous cannula. The same parameters were noted after induction, immediately after seizure cessation following delivery of the electric shock and at 1 minute interval for 10 minutes. Statistical Analysis: Data was analyzed by ANOVA test (analysis of variance). P < 0.05 was considered statistically significant.

Results: Attenuation of maximum rise in the heart rate and mean arterial pressure by clonidine (0.3 mg) was evident and statistically significant when compared with control group.

Conclusion: Oral clonidine (0.3 mg) decreases the acute hypertensive response after electroconvulsive therapy; however, this antihypertensive effect was achieved by decreasing the blood pressure before the electrical stimulus.

Keywords: Electroconvulsive therapy, hemodynamic response, oral clonidine

Introduction

Electroconvulsive therapy (ECT) is the most effective treatment available for the acute treatment of depression in patients who do not respond to medications. The efficacy of ECT has also been well documented in mania and some forms of schizophrenia. It has also been used successfully in treating the motor and psychiatric symptoms of Parkinson’s disease.

The aim of ECT is to produce a grand mal seizure. It is the seizure rather than the electrical stimulus which is responsible for the therapeutic effect. However, it has potential complications such as neuromuscular injury, tooth fracture, tongue injuries, or bone fractures. Fractures or dislocations have frequently been associated with unmodified direct ECT in the past, so it has now been modified with anesthesia. The seizure also causes wide spread physiological changes, particularly affecting the cardiovascular and the nervous system. These are most commonly a transient period of hypertension and changes in the heart rate (HR), which can be hazardous as many patients who require ECT are elderly and have cardiac and cerebrovascular diseases. These cardiovascular changes may be altered using various preanesthetic agents with anesthetic drugs and convulsions can be reduced by the usage of muscle relaxants.

A preanesthetic medication forms an integral part of anesthetic management and is universally administered before any type of anesthesia. The ideal premedicant should be effective particularly affecting the cardiovascular and the nervous system.

Access this article online

Quick Response Code:
Website: www.aeronline.org
DOI: 10.4103/0259-1162.186599

How to cite this article: Deganwa ML, Sharma R, Khare A, Sharma D. Effect of premedication with oral clonidine on hemodynamic response during electroconvulsive therapy. Anesth Essays Res 2017;11:354-8.
and pleasant to be taken orally, have sedative, anti-anxiety, analgesic, anti-emetic, and antisialogogue properties and should not impair cardiovascular stability or depress the respiration. $\alpha_2$ adrenergic agonists attenuate stress-induced sympathoadrenal responses to painful stimuli, improve intraoperative hemodynamic stability, and reduce anesthetic requirements during surgery. Clonidine is centrally acting $\alpha_2$ adrenergic agonist with well-characterized antihypertensive properties.

$\alpha_2$-adrenoceptor agonists are mainly used as antihypertensive agents but have many properties of ideal premedicant and also beneficial effects on hemodynamics during stressful conditions such as laryngoscopy and endotracheal intubation.

This study was undertaken to observe and evaluate the effectiveness of 0.3 mg oral clonidine as a premedicant for its usefulness in attenuating the hemodynamic response to ECT. Oral clonidine was used, keeping in mind, its cost effectiveness and the ease of administration.

**Materials and Methods**

After approval from Institutional Ethics Committee and written informed consent of the patients, total 25 patients were selected for the study. Each patient received oral doses of clonidine (0.3 mg) or a placebo 90 min before a standardized anesthetic technique according to a randomized, double-blind, cross-over study design.

Normotensive patients of the American Society of Anesthesiologists Class I and II between 20 and 50 years age with body weight 50–70 kg were included in the study.

The exclusion criteria included patients having compromised renal status, pulmonary status (e.g., chronic obstructive pulmonary disease, bronchial asthma) and cardiac status (e.g., heart block II degree and above, hypertension, cardiac failure, patients on beta blockers), history of cerebrovascular accidents, arrhythmias, patients with known sensitivity to clonidine, and patients on antihypertensive medication. Preanesthetic evaluation was done thoroughly. The required investigations were done in all patients which included hemoglobin, urine examination for albumin, sugar and microscopy, standard 12-lead electrocardiogram, X-ray chest, blood sugar, blood urea, and serum creatinine.

Each patient received an oral dose of clonidine (0.3 mg) or a placebo 90 min before ECT. Noninvasive mean arterial blood pressure (MAP), electrocardiogram, HR, and oxygen saturation values were recorded before administering any intravenous (IV) medications and at 1-min intervals for 10 min after the ECT treatment. The blood pressure cuff was placed on the same arm at each ECT session in a given patient.

All patients received glycopyrrolate 0.1 mg IV before each treatment. Subsequently, they were induced with thiopentone 4–7 mg/kg IV administered over 10–15 s. After the loss of eyelash reflex, blood pressure cuff applied to the upper limb was inflated to isolate the arm and permit accurate measurement of the motor seizure duration. After confirming, the patient could be ventilated, injection suxamethonium 1.0 mg/kg IV was given for muscle relaxation. Patients were ventilated with 100% $O_2$ until fasciculations subsided.

As soon as the patient was relaxed, a mouth prop was inserted, and a bitemporal ECT was administered by the psychiatrist. The magnitude of the electrical stimulus was maintained at a constant level during every ECT session performed on each patient. The mouth prop was changed to Guedel’s airway after the seizure and ventilation were assisted with the face mask and 100% $O_2$ until the return of spontaneous respiration. The patient was observed for 10 min in the ECT room and later was monitored in the recovery room for an hour.

**Statistical analysis**

Statistical analysis was performed with the SPSS version 17 (SPSS Inc., Chicago, Illinois, USA) and MSXL. Analysis of variance test was used for blood pressure and HR comparison between all study groups at different times. $P < 0.05$ was considered to be statistically significant.

**Results**

In this study, 25 patients with different age groups, weight, and different psychiatric illness were chosen randomly, who received more than three successive modified ECT. The mean weight of the patients was 59.5 kg, and the mean age was 35.5 years [Figures 1 and 2].

Compared with the control group, significant differences were found in the baseline hemodynamic values in both groups. The pre-ECT treatment HR and MAP values were significantly lower in the Group B (clonidine) compared with the Group A (control). In addition, the maximum changes in both HR and MAP after the ECT stimulus were smaller in the Group B (clonidine) compared with the Group A (control) [Figures 3 and 4, Tables 1 and 2].

![Figure 1: Age distribution](image-url)
The mean seizure duration in Group B (clonidine) was 29.84 ± 5.437 seconds, as compared to 34.68 ± 6.243 seconds in Group A (control) [Figure 5 and Table 3].

**D**iscuss**i**on

ECT has a well-established role in the management of patients who have not responded to psychopharmacological treatment. Many studies documenting the efficacy of ECT for depressive illness have been published, finding ECT superior to medications in the treatment of patients with severe depressive illness, particularly those with psychotic and suicidal symptoms.

The procedure itself consists of programmed electrical stimulation of the central nervous system to initiate seizure activity. Regarding hemodynamic effects, seizure activity causes an initial parasympathetic discharge, later followed by sympathetic discharge. Death during ECT has been ascribed to cardiac problems involving both vagal and ectopic mechanisms. The ECT seizure causes widespread physiological changes due to autonomic stimulation. Bradycardia followed by tachycardia usually occurs along with hypotension followed by hypertension. It has been shown that during ECT, the rate pressure product can reach very high levels with ECG changes of myocardial ischemia. This is by far the most important indication for attenuation of hemodynamic response to ECT.

With the introduction of IV anesthetic agents, neuromuscular blockade and assisted or controlled ventilation with 100% O₂ in 1963, the ECT Treatment was modified. Use of IV anesthetic agents has brought a new dimension to ECT regarding patient comfort as well as amnesia during the procedure.

Many methods such as the use of inhalational anesthetic agents, lidocaine, opioids, direct acting vasodilators, and...
In this study, there was a significant difference in the HR at 3 min before the premedication between Group A (control) and Group B (0.3 mg clonidine). However, variation in HR was noted in each group at different time. There was increased in HR (maximum) by 27% (97 ± 12–124 ± 13) in Group A as compared to 19% in Group B (76 ± 12–91 ± 16) at 2 min following ECT. Attenuation of the maximum rise in the HR by clonidine is evident and statistically significant in Group B when compared with Group A (control). However, the mean maximal differences in HR from the baseline values were statistically significant in Group B when we compared to control. Even a similar study done by Sargazi et al. showed similar findings that clonidine was a better drug to attenuate rise in HR comparing it to control group, but in other studies Arineshin et al. and Fu et al. found no significant differences in HR values among the all study groups from control group.

There was a significant difference in the MAP at 3 min before the premedication between Group A (control) and Group B (0.3 mg clonidine). After the application of the electric shock, there was a rise in the MAP of approximately 20 mm Hg (100.2–119.8 mm Hg) in the Group A (control) as compared to Group B rise was 13 mm Hg (86.7–100.6 mm Hg) at 2 min following ECT. Attenuation of the maximum rise in the mean blood pressure by clonidine is evident and statistically significant in Group B when compared with Group A. However, the mean maximal differences in MAP from baseline in Group B were significantly less than Group A.

A similar study done by Sargazi et al. showed similar findings. Their conclusion based on the results was that oral clonidine, by attenuation of stress and pain reactions, causes stabilization of hemodynamics especially HR after ECT and they also suggested using this drug as premedication for patients who are candidates for convulsion therapy (ECT), especially those with abnormal cardiac stability.

Arineshin et al. found that mean systolic and diastolic blood pressures after ECT were significantly lower in clonidine group (P < 0.05), but there was no significant difference between HR after ECT in the two groups. Hence, they concluded that according to these results, clonidine can be used as premedication before ECT.

A similar study done by Albaalbaki et al. showed less hemodynamic changes and decrease of arrhythmia on taking the drugs in comparison with placebo and of the two drugs that they compared, propranolol was found to be more effective in the prevention of hemodynamic changes after ECT.

Fu et al. did a similar prospective, randomized, placebo-controlled, cross-over study to assess the effects of four different oral doses of clonidine (0.05–0.3 mg) on the acute hemodynamic response to ECT. The MAP values after ECT were significantly increased above the prestimulation values in all five study groups. Clonidine produced a dose-related decrease in MAP values before ECT stimulation irrespective of the baseline blood pressure, with P < 0.01. The peak MAP values after ECT stimulation were also decreased in a dose-related fashion, with P < 0.01. The peak MAP values in the large-dose clonidine groups were significantly decreased compared with the placebo and the small-dose clonidine groups. However, the mean maximal changes in MAP from
the prestimulation values were similar in all five study groups, ranging from 29 to 44 mm Hg. These data suggest that clonidine decreases the peak MAP value after ECT by decreasing MAP immediately before the ECT stimulus.

In another study, Rasmussen et al.\(^{[17]}\) have shown that after the electrical stimulus, there is a vagally mediated shorted lived bradycardia following sympathetically mediated tachycardia and rise in blood pressure. The initial bradycardia was not noticed in any of the patients in our study. Premedication with IV glycopyrrolate could have aborted that phase in our study.

ECT causes sympathetic system stimulation leading to hypertension and tachycardia immediately following the application of electrical stimulation. Severe elevation in blood pressure and HR would increase cardiac workload, thus predisposing individuals to myocardial ischemia and also arrhythmias in susceptible patients. The incidence of such cardiovascular complication is expected to on the rise. As there is an increase indication of ECT. In patients with secondary depression with comorbid illness, from our study, we find that attenuation of the accompanying cardiovascular changes can be achieved more effectively by giving oral clonidine before ECT. Clonidine caused a significant decrease in frequency of tachycardia in study group without producing hypertension or any undesirable effects. Clonidine preserves HR component of hemodynamic variability about desired level by balancing sympathetic to parasympathetic tone in healthy adult patients. Oral clonidine decreased the peak MAP after ECT without altering the duration of seizure activity. Therefore, data suggest that oral clonidine 0.3 mg given 90 min before ECT may be useful in preventing the acute hemodynamic responses after the procedure. However, this antihypertensive effect was achieved by decreasing the blood pressure before the electrical stimulus.

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**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.