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Comparison of Pretreatment with Dexmedetomidine and Metoprolol on Attenuation of Hemodynamic Parameters and Emergence During Electroconvulsive Therapy

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ABSTRACT

Objective: To evaluate the effects of Dexmedetomidine and Metoprolol as a pretreatment regimen on hemodynamic parameters and emergence during ECT.

Study Design: Randomized controlled trial (ANZCTR Trial Id: ACTRN12623000539639)

Place and Duration of Study: Department of Anesthesia, CMH, Sialkot, Pakistan, from January 2021 to April 2022.

Methodology: All patients undergoing ECT at CMH were enrolled in this prospective study using a convenient sampling method and divided into three groups. The C Group included subjects not pretreated with any medication. Group-D received an injection of Dexmedetomidine 0.5 µg/kg diluted in 10 mL NaCl, infused intravenously over 10 minutes. Group-M received an injection of Metoprolol 1 mg diluted in 10 mL NaCl, infused over 2 minutes during preoxygenation. Heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded at baseline, then documented after drug administration at various time intervals

Results: This study performed statistical comparisons of heart rate, blood pressure, and post-procedure recovery parameters among three groups (Group-C, Group-D, and Group-M). Significant differences were found in heart rate, with Group-D and Group-M displaying significantly lower heart rates than Group-C at various time points after the intervention (p<0.001). Additionally, Group-D had significantly higher systolic blood pressure than both Group-C and Group-M after the intervention (p<0.001). Conversely, Group-M showed significantly lower diastolic blood pressure compared to Group-C and Group-D (p<0.05). Furthermore, post-procedure recovery parameters, including spontaneous respiration, eye opening, and obeying commands, occurred significantly faster in Group-D and Group-M compared to Group-C (p<0.001 for spontaneous respiration and eye opening, p=0.022 for obeying commands).

Conclusion: Metoprolol at a dose of 1 mg or Dexmedetomidine administered intravenously at a dose of 0.5 µg/kg are both effective methods for attenuating hemodynamic parameters during ECT. Dexmedetomidine causes a mildly delayed recovery, but it is better than Metoprolol in its ability to calm emerging agitation. This effect occurs without any change in seizure duration.

Keywords: Agitation, Attenuation, Dexmedetomidine, Metoprolol.

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INTRODUCTION

According to the WHO, there are more than 320 million depressed globally.[1] Though an estimated 790,000 people commit suicide each year due to depression, barely half of patients obtain an effective treatment. Electricity is directly administered to the scalp during electroconvulsive therapy (ECT) to cause a grand mal seizure. However, seizure duration has been demonstrated not to be a hallmark of treatment efficiency, as long as motor seizure duration lasts for more than 15 seconds,[2] contradicting the incorrect belief that a prolonged seizure is mostly useful. The major adverse effects of ECT can last for several weeks and include dizziness, muscular cramps, tiredness, and retrograde amnesia.[3,4] As a first-line therapy for TRD, ECT is the treatment of choice.[5] Generalized autonomic nervous system stimulation brought on by ECT first leads to bradycardia from parasympathetic nerve stimulation, which is quickly followed by more pronounced sympathetic stimulation, which causes temporary tachycardia and hypertension. These unpleasant stimuli are linked to sudden, unwelcome, and temporary alterations in the heart and blood vessels in the brain.

Patients who suffer from ischemic heart disease, hypertension, or cerebrovascular illness may suffer

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injury from the acute hyperdynamic reaction. However, the generalized tonic-clonic seizure may result in a variety of injuries, such as bone fractures or tongue bites, which are avoided by general anesthesia. Dexmedetomidine is a helpful anesthetic agent that is becoming more and more common during procedural sedation.[6] Dexmedetomidine is an alpha-2 selective agonist containing anxiolytic, sedative, sympatholytic, and analgesic properties that can lessen post-procedure anxiety in patients as well as attenuate the hyperdynamic response.[7] Presynaptic receptors in the central nervous system are inhibited, and peripheral norepinephrine release is decreased.[8]

Dexmedetomidine's attenuating efficacy as a premedication for ECT was demonstrated in some trials, although others found it to be non-significant. This might be as a result of variations in the anesthetic protocol and Dexmedetomidine dose used during ECT.[9] With a mortality rate of 0.03%, cardiovascular problems are the most common reason for death with modified ECT. Because of this, anesthesiologists always worry about minimizing hemodynamic alterations and promoting post-treatment recovery, which calls for the best pretreatment regimens. Unfortunately, little research on post-procedure recovery and emerging agitation is known, and no appropriate pretreatment regimen has been discovered. In order to increase the comfort and safety of modified ECT, a variety of medications are used as pretreatment regimens, including local anesthetics, ganglionic blockers, β-blockers, calcium channel blockers(nifedipine), α-2 agonists, direct vasodilators, and opiates.[10]

The goal of this study was to assess the cardiovascular effects of Dexmedetomidine (0.5 µg/kg) and Metoprolol (1.0 mg/kg) on the hemodynamic response during ECT in terms of mean HR, SBP, and DBP, as well as post-procedure recovery duration.

METHODOLOGY

From January 2021 to April 2022, a Randomized controlled trial (RCT).was conducted at the anesthesiology department at the Combined Military Hospital in Sialkot, Pakistan. Ethical approval was obtained from ERC vide letter number ERC/12/2021, dated 24th Dec 2021. Trial was registered with ANZCTR vide no: Trial Id: ACTRN12623000539639 dated 22 May 2023. All patients undergoing ECT in hospital were selected by a convenience sampling method. The sample size was calculated based on a reference study of Modh DB, *et al*.[11] A total of 102 patients participated in the study, who were randomly allocated into three groups of 34 each. Group-C (Control), Group-D (Dexmedetomidine), and Group-M (Metoprolol). Confidence interval of 95% 2D Standard Deviation, Power of 80 %, an error of 0.05, and *p*-value of< 0.005 was considered to be significant. (Figure)

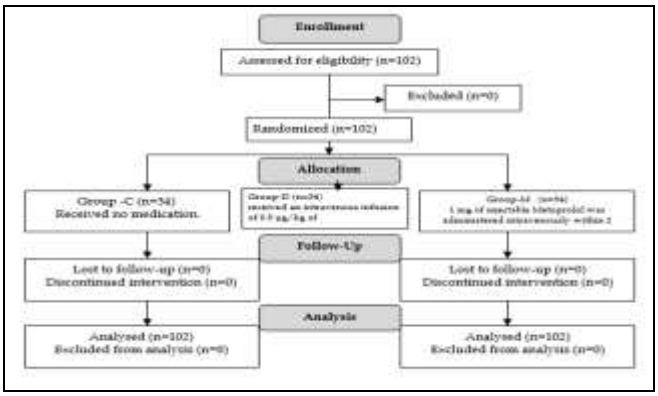

Figure: Patient Flow Diagram (n=102)

Inclusion Criteria: Both male and female patients aged greater than 18 years with ASA I and II were included in this study.

Exclusion Criteria: Children, individuals in the geriatric range, pregnant women, obese individuals, and those with known systemic illnesses or allergies were excluded.

The day before electroconvulsive therapy, patients underwent pre-anesthesia evaluations. Each patient had standard lab tests, an ECG, and a chest X-ray. For 10 hours before the procedure, patients were kept nil per oral. Patients in pre-op suites underwent clinical examinations, and Schiller multiparameter monitor data for HR, SBP, and DBP were recorded. Agitation scores were noted. The 20G IV cannula used to secure the IV line was employed to slowly administer the infusion. A premedication consisting of IV injections of Ondansetron 4 mg and Glycopyrrolate 0.2 mg was given to each patient 10 minutes before the ECT procedure. The Schiller multiparameter monitor was attached after the patient was placed on the table. SBP, DBP, and resting heart rate were recorded. In Group-D, patients received an intravenous infusion of 0.5 µg/kg of Dexmedetomidine diluted with normal saline to a maximum of 10 mL, administered over 10 minutes. Conversely, when preoxygenation began in Group-M, 1 mg of injectable Metoprolol was administered intravenously within 2 minutes, diluted

with normal saline to a maximum of 10 mL. For Group-C patients, no medication was given.

Heart rate, SBP, and DBP are reported as "P" hemodynamic parameters. Patients were preoxygenated with 100% oxygen for 3 minutes before induction with injections of propofol 1 mg/kg and succinylcholine 0.5 mg/kg. After one minute of induction, an oral soft bite block was applied, and a shock current for electroconvulsive therapy was administered. The same ECT shock treatment was given to all patients. The emergence and duration of tonic-clonic seizures served as proof of the ECT current's efficacy. Ventilation with 100% oxygen was maintained until satisfactory breathing was achieved. Following medication delivery, 1 min, 3 min, 5 min, and 10 min after an ECT shock, the following times were monitored and recorded: E1, E3, E5, and E10. The time for spontaneous breathing to return, the duration required for eye opening, resumption of spontaneous breathing, and the patient's level of agitation were used to measure post-op recovery following succinylcholine treatment. Patients were monitored for hypotension, bradycardia, arrhythmias, bronchospasm, nausea, vomiting, and other complications.

The data was coded before being entered into an Excel spreadsheet. Software. Statistical Package for the Social Sciences (SPSS) version 23:00 was used for the analysis. Calculated descriptive statistics were used. Using one-way ANOVA, the variables in all three groups were compared.The p value ≤ 0.05 was considered as signifiacnt.

RESULTS

In this study, the outcome measures of heart rate (HR), blood pressure (BP), and post-procedure recovery parameters were compared among the groups. The mean ages of participants in these groups were 41.85±12.67, 29.79±10.14, and 37.59±15.62 years, respectively as shown in Table-I. The average weights for Group-C, Group-D, and Group-M were reported as 63.08±8.21 Kg, 61.86±9.82 Kg, and 62.81±7.75 Kg, respectively. Gender distribution is given in Table-I.

Table-I: Demographic Data (n=102)

Characteristics	Group-C	Group-D	Group-M
Age (years) (Mean±SD)	41.85±12.67	29.79±10.14	37.59 ±15.62
Gender (M:F)	21:18	7:22	13:19
Weight (Kg) (Mean±SD)	63.08±8.21	61.86±9.82	62.81±7.75

Table-II shows the heart rate (HR) statistical comparability across all three groups. After the administration of drugs, notable changes were observed. In Group-D and Group-M, there was a significant reduction in the mean values of Heart rate. Conversely, no significant changes were noted in these parameters within Group-C, which served as the Control Group.

Baseline systolic blood pressure was significantly lower in Group-M compared to Group-C and Group-D, while at 3 minutes post-induction, Group-M had significantly lower systolic blood pressure than Group-C and Group-D. At 5 minutes post-induction, there were no statistically significant differences in systolic blood pressure among the three groups.(Table-III)

At the pre-induction phase, Group-D had significantly higher diastolic blood pressure than Group-C and Group-M, while at 1, 3, and 5 minutes post-induction, Group-M showed significantly lower diastolic blood pressure compared to Group-C and Group-D, as shown in Table-IV.

As shown in Table-V, Post-procedure recovery parameters, including spontaneous respiration, eye opening, and obeying commands, were significantly faster in Group-D and Group-M compared to Group-C (p<0.001, p<0.001, and p=0.022, respectively)

DISCUSSION

The current study determined that both Metoprolol at a dose of 1 mg or Dexmedetomidine administered intravenously at a dose of 0.5 µg/kg are effective methods for attenuating hemodynamic parameters during ECT. Literature has highlighted that appropriate anesthetic administration is crucial to a successful ECT. Anesthesiologists strive to achieve muscular relaxation with airway preservation, reduction of hemodynamic and cerebrovascular changes, prevention of psychological and physiological stress, and smooth and speedy recovery without losing the benefits of ECT. Anesthesiologists can achieve a balance between under- and over-sedation, as well as anticipate problems and lower consequences, by having a complete grasp of the ECT's physiology, mechanism, and systemic effects both before and after the treatment.[11]

The study's findings align with those of Parikh *et al.*, who observed that administering selective beta1 blockers decreased mean hemodynamic parameters. This decline may be due to the drug's negative

inotropic and chronotropic effects on the heart. Metoprolol, a selective β1 adrenergic receptor blocker, acts on the SA node and AV node to slow conduction velocity and prolong the refractory period in AV nodal conduction fibers, which may promote cardiac stability after ECT for sinus tachycardia and other arrhythmias. Due to its pharmacokinetic properties, the ultra-short-acting blocker Metoprolol provides the advantage of titrability, making it suitable for quick treatments such as ECT. However, like other selective beta1 antagonists, Metoprolol can cause bronchospasm, severe transient bradycardia, and hypotension, especially when given quickly or at higher doses, and may also shorten seizure duration.[12]

The study by Singh *et al.,* investigated the effectiveness of Dexmedetomidine, Esmolol, and their combination in mitigating the hemodynamic response to laryngoscopy and intubation in patients undergoing coronary artery bypass grafting (CABG).The study found that the combination of Dexmedetomidine and Esmolol provided superior control over heart rate (HR) and pulmonary artery pressures compared to either drug alone. Both drugs effectively reduced blood pressure. The findings are aligned with current

Table-II: Comparative Mean Heart Rate In Three Study Groups (n=102)

Mean Heart Rate (bpm)	Group-C (n=34)	Group-D (n=34)	Group-M (n=34)	*p*-Value
Baseline	82.82 ± 10.81	86.59 ± 15.67	90.34 ± 10.19	0.040*
Pre induction	85.67 ± 8.03	69.31 ± 9.93	85.31±10.79	< 0.001*
1 min	86.90 ± 24.21	73.83 ± 8.77	84.56±17.60	< 0.001*
3 min	92.72 ± 18.82	81.48 ± 9.52	83.13 ± 11.96	0.003*
5 min	94.44 ± 13.09	80.93 ± 7.95	87.41 ± 9.65	< 0.001*
10 min	-	-	90.69 ± 10.55	-

**indicates statistical significance at p ≤ 0.05 Test applied one-way ANOVA.Bpm – beats per minute*

Table-III: Comparative Means of Systolic Blood Pressure (mmHg) In Three Study Groups. (n=102)

Systolic Blood Pressure (mmHg)	Group-C (n=34)	Group-D (n=34)	Group-M (n=34)	*p*-Value
Baseline	134.62±12.77	135.59±8.98	123.84±8.95	< 0.001*
Pre induction	125.69±7.99	138.34±21.86	125.38±6.32	< 0.001*
1 min	143.90±19.96	148.03±7.69	139.84±19.61	0.184
3 min	141.85±19.45	145.76±19.31	130.25±15.27	0.003*
5 min	128.72±7.48	133.38±15.02	129.38±13.95	0.267
10 min	-	-	131.38 ± 10.70	-

**indicates statistical significance at p ≤ 0.05 Test applied one-way ANOVA.*

Table-IV: Comparative Means of Diastolic Blood Pressure (mmHg) In Three Groups (n=102)

Mean Diastolic Blood Pressure (mmHg)	Group-C (n=34)	Group-D (n=34)	Group-M (n=34)	*p*-Value
Baseline	82.26±15.28	87.21±7.66	83.03±7.06	0.171
Pre induction	77.51±7.75	90.97±15.26	80.88±8.17	< 0.001*
1 min	83.85±7.75	90.21±8.65	82.56±16.86	0.027*
3 min	91.62±19.95	90.72±11.71	80.72±8.59	0.005*
5 min	81.67±7.05	87.93±14.86	80.19±9.54	0.013*
10 min	-	-	83.00±4.43	-

**indicates statistical significance at p ≤ 0.05 Test applied one-way ANOVA.*

Table-V: Comparison of Post-Procedure Recovery Parameters (n=102)

Parameters	Group-C (n=34)	Group-D (n=34)	Group-M (n=34)	*p*-Value
Spontaneous Respiration (per min)	3.90±0.85	3.14±0.57	2.85±0.74	< 0.001*
Eye Opening (per min)	5.28±1.05	4.41±0.68	4.36±1.21	< 0.001*
Obeying Commands (per min)	8.15±1.69	6.83±1.97	7.19±2.43	0.022*

**indicates statistical significance at p ≤ 0.05 Test applied one-way ANOVA.*

study in terms of understanding the combination medicinal treatment. Although Esmolol and Metoprolol are both beta-blockers used to treat similar conditions.Esmolol is an ultrashort-acting beta-blocker, while metoprolol has a longer duration of action.[13]

A pilot study conducted by Fu *et al.*, suggests that Dexmedetomidine alone (0.5-1.0 microg/kg given intravenously) is not beneficial in controlling the acute hyperdynamic response after ECT. This endorsed the study objective of studying the benefit of combined therapy.[14]

Studies on combined premedication therapy with various drugs by Mizrak et al., and Moshiri *et al.*, have shown additional benefits in mitigating the agitation.[15,16] These studies have been well aligned with the objectives of the current study, with a difference in the choice of drugs. Over the next five years, significant advancements are anticipated in neuromodulation and drug development. These innovations aim to produce more tolerable versions of electroconvulsive therapy (ECT) and ketamine, enhancing patient care and treatment efficacy. It also accounts for a well-informed practice of monitoring cardiovascular response for ECT seizure evaluation.[17,18]

In the future, there should be more studies conducted to evaluate the effects of systemic diseases, such as hypertension and ischemic heart disease, as well as aging, on the efficacy of Dexmedetomidine and Metoprolol in reducing emergence agitation during electroconvulsive therapy for patients with treatment-resistant depression.

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CONCLUSION

Metoprolol at a dose of 1 mg or Dexmedetomidine administered intravenously at a dose of 0.5 µg/kg are both effective methods for attenuating hemodynamic parameters during ECT. Dexmedetomidine causes a mildly delayed recovery, but it is better than Metoprolol in its ability to calm emerging agitation. This effect occurs without any change in seizure length or the development of any complications.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

KM & MS: Data acquisition, data analysis, critical review, approval of the final version to be published.

MAA & BY: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MS & SS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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