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Comparative Study to Evaluate the Effect of Inj. Labetalol and Inj. Esmolol in Attenuating Hemodynamic Response after Electroconvulsive Therapy

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ABSTRACT

Electroconvulsive therapy is useful in treatment of acute and medicated-resistant chronic depression and mania. To compare the effects of Esmolol & Labetalol to attenuate hemodynamic responses after electroconvulsive therapy. 90 patients aging 15 – 60 years were randomly divided into 3 groups of 30 people each. Group 1 received Inj. Normal saline i.v., Group 2 received Inj. Esmolol 1 mg/kg i.v. and Group 3 received Inj.labetalol 0.25 mg/kg i.v. Heart rate and Blood pressure was measured 1 minute after administration of test dose , electroconvulsive shock was applied after 2 minutes of test drug . Patients were observed for vitals and cardiac arrhythmias. The difference in mean heart rate and blood pressure were statistically significant 3 minutes after electroconvulsive therapy ($p<0.05$) with Esmolol, but statistically insignificant ($p>0.05$) at 5-10 min. The mean heart rate and blood pressure at 1 minute and 3 minutes after electroconvulsive therapy in Labetalol was statistically insignificant ($p>0.05$); but after 5 and 10 minutes were found to be statistically significant ($p<0.05$) Esmolol is effective in attenuating the hemodynamic response to electroconvulsive therapy in first 3 minutes whereas Labetalol is effective in attenuating the response in the period from 3 -10 minutes.

Keywords: Esmolol , Labetalol , electroconvulsive therapy, hemodynamic response

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INTRODUCTION

Electroconvulsive therapy (ECT) is a useful modality in the treatment of acute and medicated-resistant chronic depression and mania. [1] ECT was introduced in 1934. [2].

Before 1963, the ECTs were “unmodified” i.e. without the use of any drugs and oxygen. Beginning in 1963 the treatment was coined as “modified” by the use of intravenous anaesthetic agents, neuromuscular blockade and assisted or controlled ventilation with oxygen enriched air. [3]

Significant transient hypertension and tachycardia occurs during electroconvulsive therapy. [4]

Patient with co-existing disease like hypertension, coronary artery disease may develope complications like disturbance of heart rhythm, pulmonary edema, left ventricular failure, myocardial infarction and cardiac arrest. [5]

Attempts to modify these responses by various drugs e.g. ganglion blockers & potent vasodilators, barbiturates Opioids, Nicardipine, Urapidil, Diltiazem have been tried. None of this pharmacologic approaches has proved entirely satisfactory

The present study was designed to evaluate comparison between Inj. Esmolol i.v. and Inj. Labetalol i.v. to attenuate hemodynamic responses after electroconvulsive therapy

MATERIALS AND METHODS

This study was approved by ethical committee of B.J Medical college.

In this comparative study, 90 patients belonging to ASA group I & II who underwent electro convulsive therapy were included. In this study outdoor -patients and indoor patients of either sex, aged between 15 to 60 years were selected and written informed consent taken.

1) PATIENT SELECTION AND DESCRIPTION

a) Study design:- Comparative study
b) No. of total patients:- 90
c) Inclusive criteria:-
- Adults patients (age 15-60 yrs), both sex.
- Patients undergoing electro convulsive therapy
- Patients who have given written informed consent
- NBM patients
- ASA status I & II

d) Exclusive criteria:-
- Heart rate < 50 beats/min.
- Systolic blood pressure < 90 mmHg.

- Diastolic blood pressure < 50 mmHg.
- A-V block > First degree.
- H/O of bronchospasm, bronchial asthma.
- H/O of drug allergy or idiosyncrasy to ß-agonist.
- H/O of P.V.D, M.I. within 6 months.
- Impaired hepatic and renal function.
- Pregnant woman.
- Sick sinus syndrome.

Pre - operative evaluation of these patients was done in the morning on the day of application of electro convulsive therapy. All patients were normotensive and all patients were investigated hematological, biochemical and radiological. E.C.G & chest x-ray were also carried out. Weight of patient was recorded

Inj. Glycopyrolate and Inj. Ondansetron i.v. are given to the patient and time are noted.

2) Method

In the electro convulsive room, 18G cannula was placed in the vein, Blood pressure cuff and cardio scope was applied to the patient. ECG monitor and SpO_2 probe were applied to the patient.

After stabilization period of 5 minutes, H.R., S.B.P., D.B.P and SpO_2 were measured as baseline parameters and recorded as reading "0".

Patient was initially pre-oxygenated with 100% oxygen for 2 minutes and then induced with Inj. Propofol 1-2 mg/kg i.v. and Inj. Succinylcholine – 0.5 mg/kg. Test drugs were given i.v. Time of induction and time of test drug was noted.

90 patients undergoing G.A. were randomly divided into 3 groups of 30 each.

Group 1 received Inj. Normal saline i.v.
Group 2 received Inj. Esmolol 1 mg/kg i.v.
Group 3 received Inj. Labetalol 0.25 mg/kg i.v.

H.R. and B.P. was measured 1 minute after administration of test drug. An oral soft bite block was placed and electroconvulsive therapy shock current was applied after 2 minutes from the time of administration of test drug. Time of ECT shock was noted.

All the patients were given the electrical shock current with a pulse of 60 – 80 Hz of 0.75 msec duration with total stimulus time of 1.25 – 2.5 seconds for each ECT. A brief pulse constant current ECT apparatus using bilateral stimulation was used to deliver electrical stimulus via electrodes placed on patient's forehead. The effectiveness of ECT current was verified by appearance of tonic – clonic seizures.

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Controlled or assisted ventilation was continued with 100% oxygen until adequate respiration returned. H.R., S.B.P., D.B.P. and SpO_2 were measured at 1 min., 3 min., 5 min. and 10 min. after ECT shock and recorded as "A", "B", "C" and "D" respectively; whereas baseline vitals and vitals after 1min of administering drugs were recorded as "O" and "X" respectively.

Patients were observed for hypotension, cardiac arrhythmia, skin rash, bronchospasm during anesthesia period and post-operatively.

OBSERVATION AND RESULTS

The present study was carried out in the department of anaesthesiology, Civil hospital, Ahmedabad in 90 patients from 11/04/2012 to 14/10/2012. The data collected were analysed and studied comparatively.

There were no significant differences between groups in age, sex or weight distribution. [Table 1, 2, 3]

Effect on heart rate: as compared to control group, esmolol was effective in blunting the rise in HR in the immediate period (1 minute and 3 minute) after ECT but not effective in the later period (5 – 10 minutes later); whereas labetalol was able to blunt the rise in HR at 5-10 minutes but not effective in immediate period (1 and 3 minutes) [table 4]

Effect on systolic BP: as compared to control group, esmolol was effective in blunting the rise in systolic BP in the immediate period (1 minute and 3 minute) after ECT but not effective in the later period (5 – 10 minutes later); whereas labetalol was able to blunt the rise in systolic BP at 5-10 minutes but not effective in immediate period (1 and 3 minutes) [table no 5]

Effect on diastolic BP: similar to HR and systolic BP esmolol blunted the rise in diastolic BP in immediate period (1 and 3 mins) and labetalol in later periods (5 and 10 mins) [table no 6]

P value < 0.05 were considered statistically significant
P value > 0.05 were not considered as statistically significant

Complications noted: only 1 patient had bradycardia in Esmolol group, but did not required anticholinergic drug. Hypotension was noted in 3 patients in Esmolol group and in 2 patients in Labetalol group and treated with 100% oxygen and IV fluids.

DISCUSSION

Electroconvulsive therapy (ECT) is an important modality in the treatment of depression, especially in severe cases resistant to pharmacological therapy. Central Nervous system seizure activity rather than electrical stimulus is responsible for the beneficial effect of ECT but the exact mechanism of the therapeutic effects is not yet understood. [6]

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ECT is often associated with significant hypertension, tachycardia and an increase in cardiac output. After the application of electrical current, a brief parasympathetic discharge occurs within 10 to 15 seconds with the tonic phase of the seizure which is followed by sympathetic discharge of 10 to 12 seconds caused by epinephrine and nor-epinephrine release. Plasma epinephrine increases to 15 times normal levels and plasma nor-epinephrine peaks can become 3 times. [7, 8] Sinus tachycardia and arterial hypertension may develop.

Table – 1 – Age Distribution of cases

Age in years	No. of Patients.		
	Group – I (Control)	Group – II (Esmolol)	Group – III (Labetalol)
15 – 24	9	8	5
25 – 34	9	10	8
35 – 44	9	7	12
45 – 54	3	3	4
55 – 64	0	2	1

Table – 2 – Sex Distribution

Sex	No. of Patients.		
	Group – I (Control)	Group – II (Esmolol)	Group – III (Labetalol)
Male	12	15	18
Female	18	15	12

Table – 3 – Weight Distribution

Weight (Kg)	No. of Patients.		
	Group – I (Control)	Group – II (Esmolol)	Group – III (Labetalol)
40 – 49	0	1	3
50 – 59	11	11	13
60 – 69	17	11	9
70 – 79	02	07	5

Table – 4 – Heart rate Changes (mean +- SD)

Time Category	Group – I (Control)	Group – II (Esmolol)	Group – III (Labetalol)	P-value	
				Esmolol (Group – 2)	Labetalol (Group – 3)
O	79.46 – 7.66	79.46 – 11.01	86.1 – 13.18	-	-
X	86 – 6.24	72.4 – 13.01	84.2 – 18.2	0.001	0.611
A	94.83 – 6.23	78.1 – 13.88	100 – 13.4	0.001	0.060
B	102.73 – 5.9	81.13 – 14.8	98.6 – 13.6	0.001	0.137
C	87.86 – 5.7	89 – 9	81.7 – 11.9	0.56	0.014
D	88.93 – 5.88	87 – 8.8	82.8 – 11.59	0.322	0.013

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Table – 5 – Systolic Blood Pressure Changes (mean +- SD)

Time Category	Group – I (Control)	Group – II (Esmolol)	Group – III (Labetalol)	P-value	
				Esmolol (Group – 2)	Labetalol (Group – 3)
O	128.2 – 8.86	125.8 – 12.8	128.4 – 17.53	-	-
X	107.86 – 12.47	108.7 – 13.9	107.6 – 14.5	0.79	0.95
A	140.46 – 10.07	123.9 – 14.6	135 – 18.6	0.001	0.164
B	132 – 12.64	123.1 – 14.3	122 – 14.4	0.014	0.005
C	131.6 – 10.02	134 – 16.5	113 – 10.3	0.49	0.001
D	129.26 – 9.81	127.4 – 15.03	113.6 – 9.5	0.57	0.001

Table – 6 – Diastolic Blood Pressure Changes (mean +- SD)

Time Category	Group – I (Control)	Group – II (Esmolol)	Group – III (Labetalol)	P-value	
				Esmolol (Group – 2)	Labetalol (Group – 3)
O	82.8 – 6.23	78.73 – 9.84	79.93 – 8.18	-	-
X	86.4 – 7.32	68.2 – 10.1	67. – 6.49	0.001	0.001
A	92.5 – 6.45	77.73 – 10.35	89.9 – 7.37	0.001	0.151
B	93.46 – 6.57	81.46 – 9.57	77.9 – 8.55	0.001	0.001
C	89.93 – 7.49	78.33 – 11.63	74.7 6.81	0.001	0.001
D	88.33 – 6.98	90 – 9.4	73.9 – 6.02	0.43	0.001

Table – 7 – Complications

Complications	No. of Patients.		
	Group – I (Control)	Group – II (Esmolol)	Group – III (Labetalol)
Nausea & Vomitng	2	1	1
Hypertension	9	1	0
Hypotension	0	3	2
Bradycardia	0	1	0
Tachycardia	3	0	1

Studies have shown that the concentration of epinephrine decrease towards normal values 10 minutes after ECT and norepinephrine levels remain increased for twice as long. These hemodynamic changes produce an abrupt increase in myocardial oxygen consumption.[7,8] Therefore it may be beneficial to administer a short acting beta-blocker or a mixed alpha-beta-blocker to blunt the catecholamine stress response.

A cardiovascular mortality rate of 0.03% has been reported with ECT. [9] In patients with pre-existing cardiovascular disease, the acute hemodynamic response to ECT may increase the risks of myocardial ischemia and infarction and even cardiac rupture. Although rare cardiovascular complications are the main cause of death during ECT with a mortality rate of 0.03% of patients treated and 0.0045% of individual ECT treatments.[9, 10 11] This is higher than the often quoted overall anaesthetic mortality of 1:10,000.[12]

Many pharmacological methods have been used in an attempt to blunt the hemodynamic effect of ECT. These include many hypertensive drugs given by various routes (including trimethaphan, nitroprusside, nitroglycerin, propranolol, alprenolol, esmolol, labetalol, clonidine, dexmedetomidine, urapidil and nicardipine)

The ideal agent for attenuating the hyperdynamic response of ECT would be convenient, easily available, easy to prepare and administer, rapid acting, brief, non-toxic and have minimal or no side effects. [9, 13, 14]

Matthew B Weinger & his colleagues evaluated effectiveness of pretreatment regimens [esmolol (1.0 mg/kg), fentanyl (1.5µg/kg), labetalol (0.3 mg/kg), lidocaine (1.0 mg/kg) and saline solution (control)] to prevent the cardiovascular and neuroendocrine response to electroconvulsive therapy. They found that pretreatment with esmolol and labetalol had significantly reduced the hemodynamic response to ECT, compared with fentnyl, lidocaine or saline solution. Compared with saline solution (control), pretreatment with labetalol, fentanyl or lidocaine significantly reduced seizure duration and increase the frequency with which a second electrical stimulus was required. In contrast, esmolol pretreatment did not significantly affect seizure duration. [15]

Castelli I & Steiner LA (1995) studied the comparative effects of esmolol and labetalol to attenuate hyperdynamic states after electroconvulsive therapy. They compared the effects of five pretreatment (no drug; esmolol 1.3 or 4.4 mg/kg; or labetalol 0.13 or 0.44 mg/kg) in 18 patients with at least one cardiovascular risk factor. They found that there were significant peak increase in SBP and HR recorded 1 min after the seizure in control group. Comparable reduction (by approximate 50%) in these peak values were achieved after esmolol (1.3 mg/kg) or labetalol (0.13 mg/kg) and cardiovascular responses were nearly eliminated after the same drugs in doses of 4.4 and 0.44 mg/kg respectively. SBP values were lower after labetalol 10 min after the seizure, but not after esmolol. [16]

In the present study, ninety patients undergoing electroconvulsive therapy treatment were randomly divided into three groups with thirty patients in each group. Patients received either Esmolol (1 mg/kg), Labetalol (0.25 mg/kg) or Normal Saline (placebo) intravenously just after induction with propofol. Electroconvulsive therapy shock current was applied after 2 minutes from the time of administration of test drug. The baseline heart rate and blood pressure were recorded. Hemodynamic parameters before and after drug therapy and after the ECT current application were recorded at different time intervals (1 min, 3 min, 5 min, 10 min after ECT).

We have found that 1 mg/kg of Esmolol was effective in blunting the rise in mean HR and systolic BP up to 3 minutes and the mean diastolic BP up to 5 minutes. Kovac et al have found that 100 and 200 mg bolus doses of Esmolol significantly blunted the maximum increase in heart srate and mean arterial pressure following ECT in comparison to placebo. They also noted that there was significant difference in HR between the 100 mg esmolol dose and placebo for up to four minutes post-ECT and up to 18 minutes post-ECT for the 200 mg dose. This coincides with

our finding that a lower dose like 1 mg/kg of Esmolol is effective in blunting the rise in HR and BP after ECT for first 3-5 minutes.

A higher dose like 200 mg bolus of Esmolol may be effective in blunting the response for longer period but as Kovac at al have found that 200 mg dose also caused a slightly shorter duration of seizure, a lower dose was considered to be better for ECT. Shrestha S & his colleagues found that esmolol was effective in blunting the hemodynamic response after ECT stimulus in the first three minutes after application of the electrical current, whereas Labetalol was effective after 5 minutes onwards till 10 minutes.

Check. Y. Sum found that Esmolol hydrochloride was an ultra-short acting, ß1 selective adrenergic receptor blocker with a distribution half – life of two minutes and an elimination half-life of 9 minutes. Esmolol appeared quite suitable for use during a short –lived stress such as tracheal intubation or ECT.

MacCarthy EP and Bloomfield SS found that Labetalol was an andrenergic receptor blocking agent with mild alpha 1 – and predominant beta – adrenergic receptor blocking actions (alpha: beta blockade ratio of 1:7 for iv and 1:3 for oral administration).

Onset of action of IV Labetalol was 2 – 5 minutes with peak effect at 5 – 15 minutes. These pharmacokinetics of these drugs make it suitable for use during indication to blunt the stress response to ECT which can occure up to 10 – 15 minutes after the application of the stimulus, as it may take 10-20 minutes for the level of epinephrine and norepinephrine to come down to its normal level after ECT.

In our study, we found that a dose of 1 mg/kg of esmolol was effective in attenuating the hemodynamic response to ECT in the first 3 minutes which coincides with the onset time and the peak onset time of the drug. We also found that 0.25 mg/kg Labetalol was not effective in blunting the rise in mean HR, mean systolic and mean diastolic pressure in the first 3 minutes but effective after 3 – 5 minutes after ECT and up to 10 minutes, which coincides with the onset time and the peak onset time of the drug.

SUMMARY AND CONCLUSION

The present study was carried out to compare Esmolol and Labetalol to attenuate hemodynamic responses after electroconvulsive therapy.

Ninety patients undergoing electroconvulsive therapy treatment were randomly divided into three groups with thirty patients in each group. Patients received either Esmolol (1 mg/kg), Labetalol (0.25 mg/kg) or Normal saline (Placebo) intravenously just after induction with propofol. Electroconvulsive therapy shock current was applied after 2 minutes from the time of administration of test drug. All the patient were normotensive and belonging to ASA I or II.
It was observed that rise in HR, SBP, DBP in Esmolol treated patients were much lower as compared to control group in the immediate period (1 and 3 minute after ECT). While Labetalol

was found to be effective in blunting the rise in mean HR, mean systolic and mean diastolic pressure after 3-5 minutes after ECT and up to 10 minutes.

So we concluded that a dose of 1 mg/kg of Esmolol is effective in attenuating the hemodynamic response to ECT in the first 3 minutes whereas Labetalol is effective in attenuating the response in the period from 3 -10 minutes

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