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Original Article

STUDY OF HAEMODYNAMIC STATUS AFTER ANTICHOLINERGIC PREMEDICATION DURING ELECTROCONVULSIVE THERAPY - A COMPARATIVE STUDY BETWEEN ATROPINE AND GLYCOPYROLATE.

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ABSTRACT

Electroconvulsive therapy (ECT) is a highly successful treatment for severe depression and some other psychiatric disorder. 70%-80% patients respond to pharmacological therapy and at least 50% who do not respond to antidepressants do respond favourably to ECT. ECT is quicker, safer and more effective and has fewer side effects than drug therapy. ECT needs general anaesthesia; therefore interactions between psychotropic drugs, ECT and anaesthetic agents can occur. ECT is often associated with acute hyperdynamic response. CNS stimulants on the other hand may prolong seizure, also dysrrhythmias and elevate haemodynamic responses. Initial vagal responses immediately after application of current may lead to bradycardia and salivation, which may cause laryngospasm, bronchospasm and airway obstruction. There may be even asystole and hypoxic episodes. To prevent possible asystole, bradycardia and airway obstruction during ECT, atropine as premedication can be considered.

Atropine premedications produces anticholinergic mediated tachycardia, which is in addition to intense sympathetic response after ECT stimulus that contributes to greater myocardial workload. On the other hand, glycopyrolate is a long acting muscarinic antagonist five to six times as potent as atropine. It does not cross blood brain barrier, placenta and eye. It controls secretions with doses that don't cause marked changes in heart rate. Its effect on blood pressure is less than atropine. Atropine crosses blood brain barrier and thus affecting CNS. Our present study was performed to compare haemodynamic status after anticholinergic premedication with atropine and glycopyrolate during ECT. This study was randomized, prospective study. 90 patients for ECT, age 15-50 years, ASA grading I&II, and receiving antipsychotic therapy with major depressive illness were randomly selected by blind envelop method and divided into three groups of 30 patients each. Group-I received atropine, group-II received glycopyrolate and group-III received no premedication. Results of the study showed that anticholinergic premedication is not essential for safe and effective ECT therapy, if at all needed glycopyrolate is the therapy of choice.

Key words: *ECT; Atropine premedication; glycopyrolate*

INTRODUCTION

Electroconvulsive therapy is an effective treatment for severe depression and different psychiatric disorder. ECT is performed under general anaesthesia; therefore interaction may occur between psychotropic drugs, ECT and anaesthetic agents utilised.

ECT is usually associated with hyperdynamic responses eg. tachycardia, hypertension and dysrrhythmia. CNS stimulation may also prolong seizure. Initial vagal discharge just after ECT application may lead to bradycardia and increased salivation, which may cause laryngospasm, bronchospasm and airway obstruction. Even asystole and hypoxic episodes may occur. To prevent possible asystole, bradycardia and airway obstruction during ECT, atropine premedication may be considered[1]. Routine atropine premedication during ECT has been recommended[2], who claimed that the risk benefit

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analysis favours the use of anticholinergic. Though a report by the Royal College of psychiatrists recommended avoiding atropine premedications during ECT[3].

Cardiovascular changes occur consistently during ECT. Acute rises, albeit transient, occur in heart rate and arterial pressure and hence rate, pressure product (RPP), an index of myocardial O---$_2$ consumption. During modified ECT, a reduction in arterial O_2 saturation can occur even after adequate ventilation. An increase in RPP during ECT can create an imbalance between myocardial O_2 supply and demand. Treatment variables, such as ECT laterality (bilateral vs. unilateral) and anaesthetic agents (thiopental vs. methohexital) do not differentially reduce heart rate or arterial pressure after ECT[4]. Stimulus laterality may not offer a means of controlling cardiovascular responses during ECT. Other strategies aimed at reduction of heart rate and arterial pressure include pretreatment with nifidipine, labetalol or esmolol. Although these methods are effective in attenuation of the cardiovascular response, they are usually reserve for patient with compromised cardiac function.

Atropine premedication produces anticholinergic mediated tachycardia. This effect in addition to intense sympathetic response after ECT stimulus can potentially contribute to greater myocardial workload.

On the other hand, glycopyrolate is a long acting muscarinic antagonist 5 to 6 times as potent as atropine. As it is positively charged quaternary amine it does not cross blood brain barrier (BBB), placenta and eye. It is possible to control secretions with doses that don't cause marked changes in heart rate. It has less effect on blood pressure. Atropine tertiary amine are neutrally charged and can cross blood brain barrier, thus affect CNS.

There are reports that atropine could compromise cardiac stability[5] and for this reason current 'guidelines from Royal college of psychiatry recommend avoiding atropine during ECT[6].

In Bangladesh, some institutes use atropine premedication and some institutes (e.g. BSMMU) don't at all during ECT. No comparative study between two groups has been undertaken in our country. So, present study has been undertaken to compare haemodynamic effects of anticholinergic premedication.

MATERIALS AND METHODS

Approval of the ethical clearance committee of BSMMU was duly undertaken before carrying out the study. The clinical study on haemodynamic changes with premedication on ECT a comparison between atropine, glycopyrolate and control group was carried out in the department of Anaesthesia, Analgesia and Intensive Care Medicine collaboration with department of Psychiatry, BSMMU, Dhaka. Study comprised of 90 patients requiring ECT. They were recruited and grouped randomly over 90 patients, 30 patients in each group. The purpose of the study were clearly explained to each of the subject's legal guardian and recruited only after they had given written consent.

Selected patients were either sexes, between 15-50 years and ASA grading II & I. Those who were below 15 & above 50, raised ICP, with ICSOL, IHD, recent stroke, bone fracture, pregnancy, ASA grade III, IV and V and recent ingestion of food were excluded. Patients were divided into three groups, 30 in each group. Group-I- atropine premedication, group-II- glycopyrolate premedication and group-III- without premedication. All the above groups received TPS 2mg/kg, suxamethonium 0.5mg/kg and IPPV (Intermittent positive pressure ventilation) with 100% O_2.

METHODS:

After recruitment patients were randomly divided into three groups. Randomization was done using card sampling. According to card numbers, patients were grouped I, II and III. Group-I received atropine, group-II received glycopyrolate and group-III received no premedication, through an IV canula in the cephalic vein of forearm. Patients were assessed the day before ECT for G/A fitness. Patient was nil by mouth and no premedication was given the night before ECT. Anaesthesia was induced with thiopental 2mg/kg and suxamethonium 0.5mg/kg. Intermittent positive pressure ventilation with 100% O_2 using mask from Bain circuit was maintained from cessation of respiration until action of suxamethonium was dissipated as evidenced by disappearance of twitching. Cardiovascular monitoring (systolic and

diastolic blood pressure) was performed using automated cardiac monitor (Datex-Ohmeda) and heart rate by ECG lead II, and SPO_2 was continually displayed by using SPO_2 probe.

ECT was administered using a constant current bi-directional brief pulse. After seizure was over intermittent positive pressure ventilation with 100% O_2 was provided until resumption of spontaneous and regular breathing. The product of heart rate and corresponding systolic blood pressure regarded as RPP (Rate Pressure Product) was calculated. Cardiovascular recording was made before anaesthesia (just before administration of premedication), before stimulus application (45 second after injecting the premedication and just before stimulus application) and five times at 1 min. interval after the stimulus. Hypotension was defined as a systolic blood pressure less than 100 mmHg and less than 80% of base line blood pressure. Treatment option was kept for hypotension associated with bradycardia with rapid infusion of Ringer's lactate and atropine (0.3-0.6 mg IV). Treatment option was also kept for atropine induced tachycardia with small dose of thiopental (100 mg) or diazepam (0.1 mg/kg) may be given slowly to control convulsion. In study parameter A) Efficacy parameter were- pulse rate, non-invasive arterial pressure (systolic and diastolic), SPO_2 by pulse oximeter and ECG lead II tracing. B) Safety parameter – dysrrhythmias-bradycardia, tachycardia, ventricular ectopics and asystole, nausea, vomiting and salivation.

STATISTICAL ANALYSIS

Data were expressed as mean ± standard deviation. Data were analysed statistically using ANOVA, chi-square, and student's t test as appropriate with the help of SPSS version 6.0. P value less than 0.05 were considered significant.

OBSERVATIONS AND RESULTS

Demographic data (Table-I)

Observations of the present study were analysed in the light of comparison among groups. All results were expressed as mean ±SD. The studied groups became statistically matched for baseline for pulse (beat/min.) (p=0.33), baseline systolic blood pressure in mmHg (p=0.3), baseline diastolic blood pressure in mmHg (p=0.63) and baseline SPO_2.

HAEMODYNAMIC CHANGES:

1. Changes in pulse rate (beat/min.): (Fig.1 & 2)

Pulse rate was significantly higher in group-I during premedication (107±8beats/min) compared with group-II (91±10beats/min) and group-III (88±9beats/min) showing (p<0.05).

Pulse rate was significantly higher in group-I during induction (105±8beats/min) as compared with group-II (93±10beats/min) and group-III (91±11 beats/min) showing (p<0.05).

Pulse rate was significantly higher in group-I at three minute (91±9beats/min) compared with group-II (82±7 beats/min) and group-III (84±12 beats/min) showing (p<0.05).

Pulse rate was found significant at 4 minute (p=0.001) and 5 minute (p=0.001).

Table I

Characteristics of subjects

Variables	Group-I n=30	Group-II n=30	Group-III n=30	t-value	p-value
Age in year	34.75±4.90	334.45±5.66	34.40±5.68	0.215	0.837
Weight in Kg	62.95±6.09	63.88±9.48	64.83±9.45	0.455	0.628
Height in cm	155.42±3.42	155.20±4.68	156.20±4.88	0.729	0.468

Values were expressed as mean ± SD. Between groups analysis were done by ANOVA, values were expressed as significant df P< 0.05 (CI - 95%). * Indicate significant

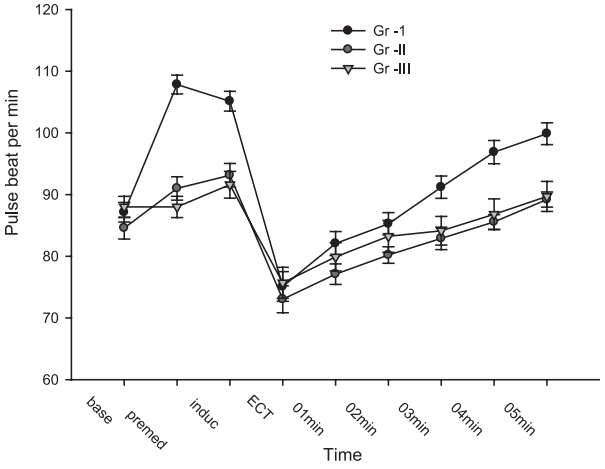

Fig.-1 : *Changes in Pulse Rate in different times.*

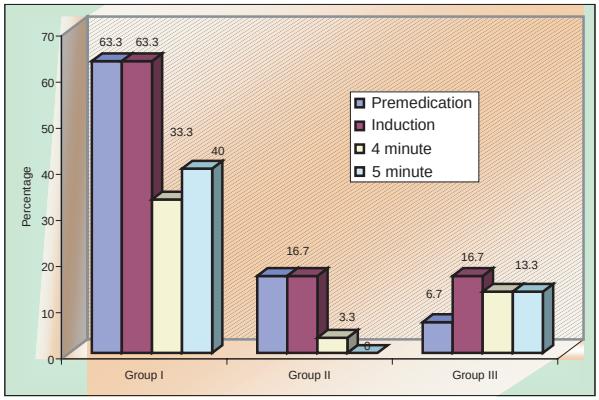

Fig 2: *Bar diagram showing the Tachycardia during different times among the three studied groups*

Incidence of tachycardia was found as follows- highest percentage (63.3%) of tachycardia occurred during premedication in group-I, followed by (16.7%) in group-II and only 6.7% in group-III. Difference was statistically significant ($p<0.05$) between group-I vs. group-II and the difference between group-I and group-III was also significant statistically during premedication. Similar statistically significant difference was found at induction and at 5 minute.

2. Changes in systolic blood pressure (mmHg)

The systolic blood pressure was significantly higher at premedication in Group-I (124 ± 19mmHg) as compared with group-II (111 ± 14 mmHg) and group-III (107 ± 9 mmHg) showing ($P<0.05$).

The systolic blood pressure was significantly higher at induction in Group-I (123 ± 18 mmHg) as compared with Group-II (114 ± 12 mmHg) and Group-III (116 ± 12 mmHg) showing ($P<0.05$).

The systolic blood pressure was significantly higher at 3 minute in Group-I (116 ± 13 mmHg) as compared with Group-II (108 ± 9 mmHg) and Group-III (110 ± 11 mmHg) showing ($P<0.05$).

Systolic blood pressure was also significantly higher at 4 min and 5 min in Group-I as compared with Group-II and Group-III as shown in Table-II.

Table II

Changes in Systolic blood pressure in different groups

Parameters	Group-I	Group-II	Group-III	F	P Value
Base line systolic blood pressure	109.67 ± 16.24	104.33 ± 13.11	107.33 ± 9.80	1.209	0.303
Systolic blood pressure in premedication	124.33 ± 19.73	111.50 ± 14.03	107.33 ± 9.80	10.358	0.001*
Systolic blood pressure at induction	123.33 ± 18.54	114.50 ± 12.96	116.17 ± 12.01	3.223	0.053
Systolic blood pressure during ECT	98.50 ± 13.46	93.63 ± 6.81	100.33 ± 13.64	2.607	0.079
Systolic blood pressure in 01 minute	107.17 ± 12.01	100.93 ± 9.96	105.17 ± 12.42	2.291	0.107
Systolic blood pressure in 02 minute	113.33 ± 12.62	104.00 ± 8.03	106.83 ± 12.56	5.403	0.006*
Systolic blood pressure in 03 minute	116.83 ± 13.29	108.83 ± 9.62	110.50 ± 11.99	3.882	0.024*
Systolic blood pressure in 04 minute	120.83 ± 13.84	111.90± 10.12	113.50 ± 11.15	4.881	0.009*
Systolic blood pressure in 05 minute	124.00 ± 13.98	114.33 ± 10.41	113.83 ± 11.04	6.941	0.001*

Values were expressed as mean ± SD. Between groups, analysis were done by ANOVA, values were expressed as significant df $P< 0.05$ (CI - 95%). * Indicate significant

Table III

Changes in diastolic blood pressure in mmHg in different groups.

Parameters	Group-I	Group-II	Group-III	F	P value
base line diastolic blood pressure	72.17 ± 10.80	70.77 ± 8.24	70.00 ± 7.19	0.459	0.633
diastolic blood pressure in premedication	86.00 ± 12.35	76.17 ± 9.16	70.00 ± 7.19	20.344	0.001*
diastolic blood pressure at induction	88.50 ± 12.47	79.33 ± 9.63	74.50 ± 8.02	14.504	0.001*
diastolic blood pressure during ECT	70.83 ± 12.67	67.33 ± 12.51	69.17 ± 11.75	0.606	0.547
diastolic blood pressure in 01 minute	76.33 ± 11.59	69.67 ± 8.09	74.03 ± 11.54	3.099	0.050
diastolic blood pressure in 02 minute	80.33 ± 9.46	73.13 ± 6.27	75.83 ± 10.91	4.801	0.011*
diastolic blood pressure in 03 minute	82.63 ± 8.37	74.63 ± 6.56	75.00 ± 5.72	12.587	0.001*
diastolic blood pressure in 04 minute	84.33 ± 7.96	76.17 ± 6.91	76.67 ± 5.47	13.379	0.001*
diastolic blood pressure in 05 minute	85.67 ± 7.28	78.33 ± 6.86	77.50 ± 5.53	13.903	0.00*

Values were expressed as mean ± SD. Between groups analysis were done by ANOVA, values were expressed as significant if P< 0.05 (CI - 95%). * Indicate significant

3.Changes in diastolic blood pressure (mmHg)

The diastolic blood pressure was significantly higher at premedication in group-I (86 ± 12 mmHg) as compared with Group-II (76 ± 9 mmHg) and Group-III (70 ± 7 mmHg) showing (P<0.05).

Diastolic blood pressure was significantly higher at induction in Group-I (88 ± 12 mmHg) compared with Group-II (79 ± 9 mmHg) and Group-III (74 ± 8 mmHg) showing (P<0.05).

Diastolic blood pressure was significantly higher at 3 minutes in Group-I (82 ± 8 mmHg) as compared with Group-II (74 ± 6 mmHg) and Group-III (75 ± 5 mmHg) showing (P<0.05).

Diastolic blood pressure was also found significantly higher at 4 min and 5 min as shown in Table III.

4. Rate pressure Product (RPP)

The base line mean ± SD value of RPP was 9485 ± 176 in Group-I, 8748 ±213 in Group-II and 9416 ± 165 in Group- III (P=0.214). There was no significant difference between the groups.

The mean ± SD value of RPP immediately after premedication was 13376 ± 132, 10104 ± 312 and 9424 ± 265 in Group-I, Group-II and Group-III respectively (P<0.05). They showed marked difference between the 3 groups.

The mean ± SD of RPP at induction were 12987 ± 265 in Group-I, 10623 ± 241 in Group-II and 9764 ± 134 in Group-III respectively were significant (P<0.05).

The mean ± SD of RPP at post ECT 2 minute, 3 minute, 4 minute and 5 minutes are significant and P<0.05 as shown in Figure-6.

5. SPO_2 changes are shown in Table-IV

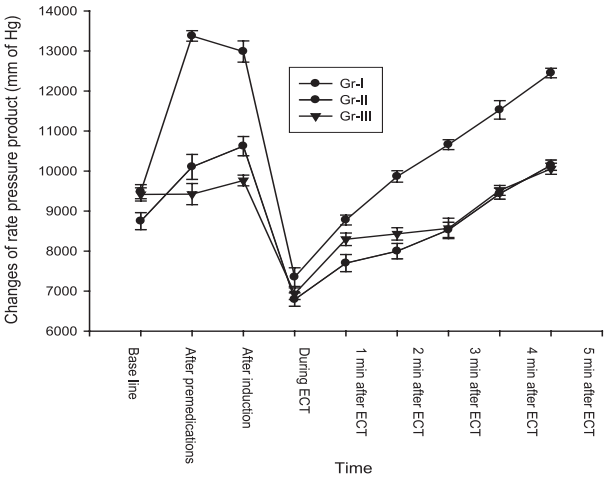

Fig.-3: *Effect of electroconvulsive therapy (ECT) on the product of heart rate and systolic arterial pressure (RPP) in patients who received atropine (Group-I), Glycopyrrolate (Group-II) and Control (Group-III) those who did not.*

Table IV

Changes in SPO_2 in different groups

Parameters	Group-I	Group-II	Group-III	F	P Value
Base line SPO_2	95.77 ± 1.19	96.20 ± 1.03	95.90 ± 1.06	1.226	0.298
SPO_2 in premedication	97.30 ± 0.84	97.67 ± 0.76	95.90 ± 1.06	32.566	0.001*
SPO_2 at induction	96.70 ± 2.02	97.60 ± 0.81	97.10 ± 0.80	3.397	0.037*
SPO_2 during ECT	96.37 ± 1.75	93.13 ± 2.11	93.00 ± 2.12	27.224	0.001*
SPO_2 in 01 minute	96.10 ± 1.32	96.13 ± 1.43	95.97 ± 1.27	0.129	0.878
SPO_2 in 02 minute	97.40 ± 0.93	97.60 ± 0.77	97.60 ± 0.86	0.547	0.580
SPO_2 in 03 minute	98.20 ± 0.61	98.37 ± 0.49	98.27 ± 0.58	0.664	0.517
SPO_2 in 04 minute	98.67 ± 0.55	98.87 ± 0.57	98.77 ± 0.43	1.110	0.333
SPO_2 in 05 minute	99.13 ± 0.68	99.17 ± 0.53	99.20 ± 0.48	0.101	0.903

Values were expressed as mean ± SD. Between groups, analysis were done by ANOVA, values were expressed as significant is P< 0.05 (CI - 95%). * Indicate significant

Table V

Perioperative complications in three studied groups.

	Group I (n=30)		Group II (n=30)		Group III (n=30)		Total (n=90)		c^2	P
Complications	n	%	n	%	N	%	n	%		
Nausea	3	10.0	1	3.3	0	0.0	4	4.4	3.662	1.160
Vomiting	2	6.7	1	3.3	0	0.0	3	3.3	2.068	0.355
Salivation	0	0.0	0	0.0	2	6.7	2	2.2	4.090	0.129
Bradycardia	0	0.0	0	0.0	2	6.7	2	2.2	2.022	0.363

Values were expressed as frequency with percentage over column total. Data were analysed by Pearson chi-square test. Values were expressed as significant if p (<0.05(CI – 95%).

Intra operative complications like nausea, vomiting, salivation, bradycardia, ectopic beat and asystole were observed in three groups. Bradycardia and salivation was not observed in-group I and II. Nausea and vomiting was not observed in group III. Ectopic beat, ST-change and asystole were not found in all groups. 4(4.4%) had nausea, 3(3.3%) had vomiting, 2(2.2%) salivation and 2(2.2%) had bradycardia of the three groups. No statistical significant (p>0.05) difference was found in the three study groups (Table-V).

No treatment was required for bradycardia in-group III as BP and SPO_2 was normal.

Vomiting and salivation were managed with suction, O_2 inhalation and lateral position of the patients and no other measure were needed as airway and SPO_2 was normal.

DISCUSSION

The mortality associated with ECT is low, it has been given variously as 1:10,000[7] or 5:70,000treatments[8] as 0.0036 percent[9]. Many of the reported deaths have occurred not during the convulsion itself but some times as late as 20 minutes after completion of the procedure[10].

No specific information about cause of death has been known. All that is known is that some fatalities have been shown as having been due to myocardial infarction[11]. It has been postulated that this may have been the result of increased cardiac work during shock with damage occurring perhaps slowly after rather than during convulsion[12]. Pretreatment anxiety may have been responsible for some deaths[13]. Cause of late death in literature mentioned fat embolism, a rupture duodenum, hemorrhage in the internal capsule and into thyroid as well as multiple fractures with pulmonary oedema[14]. It is doubtful whether any of these causes of death can be influenced by atropine in one way or the other.

Wide variety of studies had shown that there were a wide variety of attitudes towards premedication with atropine. There were those who give no atropine, either because it was not required in their estimation[15], while others considered it essential [16]. There were studies that complete atropinization with 1.5 to 2.0 mg IV [17]. Administration of atropine 0.4 to 6.5 mg even subcutaneously is quite common[18].

The side effects of anticholinergics manifest principally in the cardiovascular and central nervous system. During ECT initial vagal discharges may lead to bradycardia with decreased systolic blood pressure followed by sympathetic nervous stimulation and an increased heart rate and systemic blood pressure. These changes are undesirable if the patient has ischaemic heart disease. Patient receiving antipsychotics have adrenergic effect and hence tachycardia. Patient receiving further anticholinergic have additive sympathetic activity, which is undesirable. The most common cause of death due to ECT is myocardial infarction and cardiac dysrrhythmia.

Atropine has recently been shown to relax the lower esophageal sphincter, a some what unaccepted finding[19], and thus its omission may indeed be beneficial in the results of presence of the combination of succinylecholine and muscle contractions from electric shock.

CONCLUSION

Under the condition of present study it was concluded that anticholinergic premedication is not essential for safe and effective electroconvulsive therapy, if at all needed, glycopyrrolate is the drug of choice.

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