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EFFECT OF IMIPRAMINE AND ECT ON PLATELET MAO ACTIVITY IN DEPRESSIVES

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SUMMARY

Platelet monoamine Oxidase (MAO) activity was estimated in 30 depressed patients treated with Imipramine or ECT over a period of 5 weeks and pretreatment and post treatment values were compared. Imipramine and ECT caused significant reduction of platelet MAO, which after 7 days washout period comes to the pretreatment level while subjects clinical status remained unchanged. The percentage blockade in platelet MAO values by Imipramine and ECT was 51.40±13.43 and 34.73±24.27 respectively.

Tricyclic antidepressant drugs are generally considered to act effectively in the treatment of depression by increasing the functional levels of biogenic amines at specific brain receptor sites. Recently various studies, considering in vitro and in vivo effect of tricyclic on monoamines have appeared in the literature (Edwards and Burns, 1974; Roth and Gillis, 1974 a; Sullivan, 1977). These studies have demonstrated that inhibition of monoamine oxidase (MAO) plays a role in the clinical action of tricyclic anti-depressants.

Various hypotheses—neurochemical, neuroanatomical, neuroendocrinal and psychological have been propounded to understand the mechanism of action of electroconvulsive therapy (ECT) (Ottason, 1980; Miller, 1976; Weaver et al., 1976) but it is not possible to pin point a single mechanism of action. The present work is an endevaour in this area.

Indian literature is short of studies conducted in this specific area (Trivedi et al, 1988 b) and the ones reported are in Schizophrenics (Sen Gupta et al., 1981; Gupta et al., 1985; Trivedi et al., 1987, 1988 a).

Aim : to study the effect of treatment (Imipramine and ECT) and clinical response on monoamine oxidase activity in depressed patients.

Material and Methods

Thirty male depressed patients (according to ICD-IX- 296) and fulfilling research diagnostic criteria (Spitzer et al., 1978) and meeting predefined selection criteia were selected. These patients were randomly assigned to imipramine (Group A) or ECT (Group B) treatment.

Only those subjects were chosen for study who were between 17-60 yrs, had minimum of 17 score on Hamilton Psychiatric Rating Scale for depression (HRSD) (Hamilton, 1960), had haemoglobin not less than 10 gm%, had absence

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of major physical illness, papilloedema, glaucoma or prostratic hypertrophy, had no immediate danger of suicide and had not received ECT in the past 3 months.

Procedure

All the experimental group subjects were kept drug free for 7 days and score on HRSD was assessed on the day of starting treatment (day O).

Group A : The patients received tablet imipramine on a fixed dosage of 225 mg/day in divided dosage which was achieved within a week starting from 75 mg/day followed by 150 mg/day for next 3 days and 225 mg/day thereafter and continued till the end of 5 week study periods provided there were no serious side effects of imipramine which were assessed clinically.

Group B : Patients were given direct ECT; first 3 on alternate days starting from day one, and on every fourth day thereafter to a maximum of 10 at the end of 5 weeks treatment phase.

In both the above groups (A & B) the treatment was stopped at any assessment point at which clinical improvement occured i.e. HRSD score falls on or below 5 point. Subsequent to the completion of treatment, all the patients (Group A and B) were kept drug free of imipramine and ECT for seven days so as to abolish immediate effect of ECT and imipramine on platelet MAO.

Patients were assessed on Hamilton Psychiatric Rating Scale for Depression at the time of inclusion in the study, then at weekly interval and after 7 days of postreatment washout period. Blood was drawn at the bigining of study, then at the completion of the treatment and after 7 days of post treatment washout. Details regarding sample collection and estimation of Platelet MAO activity is given elsewhere (Trivedi et al., 1988 b).

Results

The mean age of the group was 40.3 years (range 24-57). In the Imipramine group (N=15) 2 patients had shown improvement after 3 weeks, 4 patients after 4 weeks and in 9 patients treatment was continued till 5 weeks. The mean duration of Imipramine treatment was 4.47 weeks. In ECT treatment group (N=15) 3 patients had shown improvement after 3 weeks, 5 patients after 4 weeks and in 7 patients the treatment was continued till 5 weeks. The mean duration of ECT treatment was 4.27 weeks.

Table 1. *Comparison of Hamilton Psychiatric rating scale for deperession (HRS-D) total scores in pretreatment, post treatment and post-treatment after washout period in E.C.T. and imipramine treated group of patients.*

	Pre-treatment (N=15)	Post-treatment (N=15)	Post treatment after washout (N=15)
	(A)	(B)	(C)
ECT treated group			
Mean	28.47	4.73	5.87
s.d.	4.41	4.09	4.80
Range	22–39	0–14	0–14
	(D)	(E)	(F)
Drug treated group			
Mean	28.26	5.00	5.07
S.D.	3.94	4.23	4.40
Range	22–36	0–13	0–13

Significant comparisons :

A Vs. B : $t=13.80$; d.f. $=14$; $p<0.001$
A Vs. C : $t=13.93$; d.f. $=14$; $p<0.001$
D Vs. E : $t=18.46$; d.f. $=14$; $p<0.001$
D Vs. E : $t=15.07$; d.f. $=14$; $p<0.001$

E. C. T. and Imipramine produced significant improvement in depression but there was no significant difference between the treatment modalities.

Table 2. *Comparison of platelet MAO values in E. C. T. and Imipramine treated group of patients in pretratment, post treatment and post-treatment after washout period.*

	E.C.T. treated Group (N=15)	Imipramine treated Group (N=15)
	(A)	(B)
Pre-treatment		
Mean	42.52	41.82
s.d.	21.20	21.68
Range	1.13—91.31	16.17—116.60
	(C)	(D)
Post treatment		
Mean	29.03	20.79
s.d.	18.05	15.45
Range	4.16—68.56	9.13—73.38
	(E)	(F)
Post treatment after washout period		
Mean	42.97	31.90
s.d.	26.85	20.67
Range	12.91—104.37	14.84—110.33

*MAO values were represented in n/mol/min/mg/protein), Significant comparisons :

B Vs D : $t=9.60$; d.f. $=14$; $p<0.001$
D Vs F ; $t=9.30$; d.f. $=14$; $p<0.001$
A Vs C : $t=2.96$; d.f. $=14$; $p<0.05$

There was significant decrease in mean post-treated platelet MAO values when compared to pretreatment values both in Imipramine and ECT group. There was again a increase in platelet MAO values at post treatment washout period which was significant in imipramine group and insignificant in ECT group. Thus, it is evident that Imipramine and ECT had reduced platelet MAO values in depressed patierts which tended to return more or less to pretreatment values.

Discussion

To study the effect of Imipramine and ECT on platelet monoamire oxidase activity of depressed patients, the pre-treatment and post-treatment monoamine oxidase values were compared and a signficant decrease was observed in post treatment period. The percentage blockade (decrease) of platelet monoamine oxidase activity was studied comparing the post-treatment after 7 days washout period values with that of post-treatment values. The pre-treatment values were not considered because in that period although patients were drug free for 7 days, the disease process i.e. depression was there, which could have caused a faulty interpretation as it has already been seen that platelet MAO is increased in depressed patients (Mann, 1979; Trivedi et al., 1988b). Whereas taking into account, the post-treatment (after 7 days washout period) values, the effect of depression on platelet MAO values was eliminated. The mean percentage blockade of MAO activity by Imipramine and ECT was found to be 51.40 ± 13.43 and 34.73 ± 24.27 respectively.

In vitro inhibition of the enzyme monoamine oxidase has also been reported in several animal studies (Roth and Gillis 1974, a & b). Sulivan et al. (1977) reported 40% decrease in platelet MAO activity in 11 male paients of primary depression after 3 weeks of treatment with imipramine or amitryptyline. Edwards and Burns (1974) reported in vitro inhibition of platelet MAO acti-

vity by amitryptyline. Roth and Gillis (1974 a) working on mitochondrial preparations of rabbit lung and brain observed that Oxidase deamination of tyramine, 5HT and bata-phenyle thylamine (PEA) was inhibited by imipramine. The same workers in another study (Roth and Gillis, 1974 b) determined the ability of several structurally related tricyclic antidepressant drugs to inhibit both the type A form of the MAO (5HT determination) and the type B form of the enzyme (PEA deamination). However, several reports challenge the proposal that tricyclic antidepressants affect MAO activity (Reveley et al., 1979; Davidson et al., 1978; Giller et al., 1980). Reveley et al. (1979) did not find any significant inhibition of platelet MAO activity in depressives treated by amitryptiline for 4 weeks. Thus, the present observation of significant inhibition of MAO activity by imipramine supports other workers observation of inhibition of both types of mitrochondrial MAO and suggests that 'imipramine inhibition' of the oxidative deamination of NE, 5HT, PEA and other biogenic amines may contribute to the clinical action of this drug. There has been very little work on the effect of ECT on MAO activity. The only human study, investigators could come across has been done by Mann (1979), who did not find any significant change in pretreatment and posttreatment values. However, Pryor and Otis (1970) and Pryor et al. (1972) working on animal brain MAO activity observed that multiple ECT causes increased enzyme activity persisting for several weeks.

A significant decrease in platelet MAO activity in post-treatment phase, as found in this investigation, supports the hypothesis of increased post synaptic activity of catecholamines after ECT (Grahame-Smith et al., 1978). There is still more research to go in establishing the exact mechanism of action of ECT.

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