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d-AMPHETAMINE AS A PREDICTOR FOR RESPONSE TO IMIPRAMINE AND AMITRIPTYLINE[1]

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SUMMARY

Patients with endogenous depression fulfilling Feighner's criteria were included in the trial. All had pretrial scores above 20 on Hamilton's depression rating scale.

Drugs were divided into groups A and B. Group A comprised of placebo and d-amphetamine. It was found that all patients who improved with d-amphetamine also improved with tricyclics. Two who did not improve with d-amphetamine did not improve with tricyclics.

With the introduction of new anti-depressants and with different symptom complexes responding to different drugs, it is becoming increasingly difficult to choose the right anti-depressant for a particular patient. Various attempts have been made to find out predictors for response to anti-depressants. Clinical, biochemical and pharmacological predictors have been studied. Only a few studies of response prediction have appeared in the literature (Murphy *et al.*, 1978). Low baseline urinary excretion of 3 MHPG in depressives have been associated with good response to d-amphetamine (Fawcett *et al.*, 1972) and to imipramine (Mass *et al.*, 1972). The response with a one to two day trial of d-amphetamine has been noted to be a good predictor of response to imipramine and desipramine (Fawcett *et al.* 1971).

Although d-amphetamine is known to be a central nervous system stimulant, there is a wide variation in individual responses (Lasagna *et al.*, 1953, Tecce & Cole 1974, von Kammen & Murphy, 1975). If a one to two day administration of d-amphetamine can predict responses to anti-depressants which may otherwise require a 3 to 6 week trial, a more rational psycho-pharmacological approach to the treatment of depression could result rather than present day trial and error (Klein and Davis, 1969).

This study is an attempt to evaluate the usefulness of a three day trial of d-amphetamine as a predictor for response to tricyclic antidepressants and also to find out whether there is selective prediction for imipramine and amitriptyline.

MATERIAL AND METHOD

Subjects : Initially 17 patients (14 males, and 3 females) with endogenous depression fulfilling criteria of Feighner *et al.* (1978) for primary depression, in addition, one of the following were included in the trial :

(*a*) Family history of depression
(*b*) History of previous attack of depression
(*c*) Early morning insomnia
(*d*) Diurnal variation of mood.

All had scores above 20 on Hamilton Depression Rating Scale. None of them had been on any treatment prior to the trial. Their ages ranged from 22 to 52 yrs. All were admitted as inpatients at NIMHANS, Bangalore. During the first two days of their stay they were given

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placebo and investigated. Two of them showed remarkable improvement and were hence excluded from the study. One patient developed severe stereotype after starting on trial drug, and was excluded. Thus 14 patients were taken for the study.

Administration of drugs :

Drugs were divided into Groups A and B. Group A comprised of placebo and d-amphetamine (7.5 mg per capsule). Group B comprised of imipramine and amitriptyline. Patients were initially started on Group A drugs for the first three days, in a double blind manner. They were given 1 cap. at 8 a.m. and one at 2 p.m. For the next four weeks Group B drugs were given (double-blind) with graded increase in dosage starting from 75 mg to 225 mg. (1st week, 1 cap. h.s., 2nd week, 2 h.s., 3rd and 4th weeks, 3 h.s.).

Evaluation of Treatment :

Patients were rated on Hamilton Depression Rating Scale at the beginning of the trial, on the 1st and 3rd day of Group A use, and 2 weeks and 4 weeks after beginning Group B. Ratings on all occasions were done between 9 and 10 a.m.

Criteria for evaluating response :

50% reduction from the initial score was considered as good response. In evaluating response to Group A, 50% reduction in partial score (4 items on Hamilton Depression Rating Scale HDRS comprising depressed mood, work and interest, retardation, agitation) was used.

RESULTS

Fisher's Exact Probability test was used for finding statistical significance.

When Hamilton Depression Rating Scale was used to evaluate there was improvement in two of fourteen patients (Table 1). On the third day the same results were obtained.

On evaluation with partial scoring, i.e., on four items of HDRS as already mentioned—

(1) 1st day observation showed same results as with evaluation on all items of HDRS (Table 3).

TABLE 1—*Response to Group A as on H. D. R. S.*

	Placebo	d-amphetamine	Total	on Day 1 and Day 3 of use
Improved ..	..	2	2	
Not improved	6	6	12	p=0.3077
	6	8	14	N.S.

TABLE 2—*Response to Group B as on H. D. R. S.*

	Imipramine	Amitriptyline	Total
Improved ..	5	5	10
Not improved	2	2	4
	7	7	14

TABLE 3—*Response to Group A as evaluated with partial score on 1st day of use*

	Placebo	d-amphetamine	Total
Improved ..	..	2	2
Not improved	6	6	12
	6	8	14

TABLE 4—*Response to Group A as evaluated to partial scores on 3rd day of use*

	Placebo	d-amphetamine	Total	
Improved ..	..	6	6	p=0.009
Not improved	6	2	8	Significant.
	6	8	14	

(2) 3rd day observation showed improvement in 6 out of 8 patients who had been given d-amphetamine. This was statistically significant as compared to group A placebo (Table 4).

All patients who improved with d-amphetamine also improved with tricyclics. The two who did not improve with d-amphetamine did not improve with tricyclics. (Table 5).

TABLE 5—*Chart showing response to Group A and Group B drugs*

Serial number	Placebo	d-amphetamine	Imipramine or Amitriptyline
1.	N.I.		I
2.	—	I	I
3.	—	I	I
4.	N.I.	—	I
5.	—	I	I
6.	N.I.	—	I
7.	N.I.	—	I
8.	—	I	I
9.	N.I.	—	N.I.
10.	—	N.I.	N.I.
11.	—	I	I
12.	—	N.I.	N.I.
13.	—	I	I
14.	N.I.	—	I

Note : I Improved
NI Not improved

DISCUSSION

We found significant association, between response to d-amphetame and tricyclics when improvement was evaluated with partial scores. These results are consistent with the study of Fawcett and Siomopoulos (1971) and Von Kammen and Murphy (1978). Their studies also had limitations because of the small number of subjects.

Amphetamines have been used in the treatment of depression although their efficacy has not been consistently demonstrated. Amphetamine may have unpleasant side-effects, irritability, loss of sleep which may make the assessment of anti-depressant effect more complex.

This study shows the d-amphetamine can be used as a predictor for response to tricyclics. Selective prediction for imipramine or amitriptyline was not seen.

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