

PREDICTION OF RESPONSE TO TRICYCLIC ANTIDEPRESSANTS WITH A SINGLE INJECTION OF METHYLEAMPHETAMINE

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SUMMARY

Twenty five patients of endogenous depression fulfilling Feighner's criteria were selected for this study. It was found that the patients who improved with methylamphetamine responded to imipramine and those who did not improve with methylamphetamine improved with amitriptyline.

For the past decade a large variety of drugs has been found to be effective in the treatment of Depression. Their precise indicators however, are not yet clearly known.

There is therefore, a need for devising a method for the prediction of response to anti-depressant medication. There are different symptom complexes of depression which respond differently to different types of antidepressant medication currently available. Various clinical, bio-chemical and pharmacological predictors have been reported with only a few studies of response prediction appearing in the literature (Murphy *et al.*, 1978).

A current approach to depression is that of the "two disease model of depression" (Davis, 1976). According to this hypothesis there are at least two types of depression referred to as type A and type B which are distinct from each other as determined by certain parameters (Davis, 1976, Mass, 1975, 1978, Asberg *et al.*, 1973).

Type A

- (1) Low levels of MHPG
- (2) Positive response to imipramine
- (3) Brightening of mood with amphetamines

Type B

- (1) Normal levels of MHPG
- (2) Positive response to amitriptyline
- (3) No change of mood with amphetamines.

There is a wide variation in the central nervous system stimulant action of amphetamines (Lasagana *et al.*, 1953, Tecce & Cole 1974, Von Kamman & Murphy, 1978). If one intravenous administration of methyleamphetamine can predict response to antidepressants which otherwise require 3-6 weeks trial it would be a great advantage over the present trial and error method.

This study is an attempt to predict selective response to imipramine or amitriptyline on the basis of one intravenous injection of methyleamphetamine.

MATERIAL AND METHODS

This study was conducted on 25 patients treated at the Department of Psychiatry, R. N. T. Medical College & Associated Groups of Hospitals, Udaipur. They were suffering from endogenous depression fulfilling Feighner's diagnostic criteria for use in Psychiatric research for Primary Depression (Feighner *et al.*, 1972). Three patients who did not come for follow up

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were dropped from the study. All the patients had a score above twenty on Hamilton Depression Rating Scale.

The drugs were divided into two groups. Group I comprised of a Placebo (10 cc of 10% injection G.N.S.) and Injection methylamphetamine 20 mg/1.0 ml in 9 cc of GNS. Group II comprised of imipramine and amitriptyline tablets (25 mg/tab.).

Patients were rated initially on Hamilton Depression Rating Scal before treatment and Group I drugs were given slowly intervenously in a double blind manner. Patients were evaluated one hour after group I drug and 50% reduction in the partial score (4 items on Hamilton Depression Rating Scale of—depressed mood, work and interest retardation, agitation)—was used as a measure to evaluate the response to drugs of Group I (Quadri *et al.*, 1980).

Group II drugs were not started (double blind) with gradul increase in dose starting from 100 mg to 225 mg. Patients were rated on Hamilton Depression Rating Scale at the end of 2nd and 4th week of starting the Group II drugs.

RESULTS

Table 1 shows the response to Group I drugs as evaluated on partial scores of HDRS one hour after the use. Chi-Square with Yate's correction was used for finding statistical significance. Table (1) shows improvement in 9 out of 12 patients who had been given methyleamphetamine which is highly significant ($p < 0.01$).

Table 3 shows that 3 patients who did not improve with methylamphetamine improved with amitriptyline while out of 9 patients who improved with methyleamphetamine 6 patients who received imipramine improved whereas 3 patients who received amitriptyline did not improve.

Table 2 shows the response to tricyclics at the end of 4th week. 7 patients who did not improve with the tricyclics were

later given ECT.

It can thus be seen that patients who improve with methyleamphetamine respond to imipramine whereas patients who do not improve with methyleamphetamine improve with amitriptyline.

TABLE 1—Response to Group I drugs as evaluated on partial scores of HDRS 1 hour after the use.

	Inj. GNS 10%	Inj. Methyle- ampheta- mine	Total
Improved	..	9	9
Not-improved	10	3	13
	10	12	22

$X^2=9.78$, d.f.=1, $p < 0.01$

TABLE 2—Response to Group II drugs as evaluate ond HDRS at the end of 4th week.

	Imi- pramine	Amitri- ptyline	Total
Improved	9	6	15
Not-improved	3	4	7
	12	10	22

$X^2=0.08$, d.f.=1, N.S.

TABLE 3—Response to group I and group II drugs.

Response to Me- thyleamphetamine	Response to Imipramine		Response to Amitri- ptyline		Total
	I	NI	I	NI	
Improved	6	0	0	3	9
Not-improved	0	0	3	0	3
	6	0	3	3	12

NI=not improved, I=improved.

DISCUSSION

We found a significant association between response to methyleamphetamine and selective prediction of response for amitriptyline and imipramine. Similar studies have been reported by Fawcett and Siomopoulos (1971), Von Kammer and Murphy (1978), Quadri *et al.* (1980) using oral d-amphetamine which required 1-3 days for prediction of response to tricyclics. Our study has distinct advantages as we can not only predict the response just after an hour but also select the drug, IMIPRAMINE or AMITRIPTYLINE, which is likely to be effective. Our study also supports the two disease model of depression (Davis, 1976).

We agree that the number of patients in our study is small but similar limitations are present in the studies of Fawcett & Siomopoulos (1971), Von Kammer and Murphy (1978) and Quadri *et al.* (1980). Furthermore on extensive screening of literature we could not find any study using intra-venous methyl amphetamine as a predictor of response to tricyclic antidepressants.

Though the distribution of the patients to the two antidepressant drugs was a blind one it has so happened that not a single case of *no improvement* to methyleamphetamine category was given imipramine and all the three cases of this category (not improved to methyl amphetamine) were given amitriptyline.

We also agree that to come to a definite conclusion it is desirable that some patients of this category should be given imipramine and if they do not improve it can be definitely concluded that the responders to methyleamphetamine injection improve with imipramine and non-responders improve

with amitriptyline. Further work is needed in this direction.

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