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A Clinical Trial of Amitriptyline in Depressive Patients

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Introduction

Amitriptyline (Tryptizol) is an antidepressant drug which is related structurally to imipramine (Fig. 1). Its full name chemically is 5-(d-dimethyl-aminopropylidene)-dibenzo (a,d) (1,4) cyclo-heptadiene hydrochloride. Numerous uncontrolled trials to date (Ayd, Bennett) have reported success with this drug in the treatment of both endogenous and reactive depressions. Several reports (Ayd, Dorfman, Dunlop) have stressed the fact that agitation as a manifestation of depressive illness is frequently relieved. The purpose of this study was to assess the effect of the drug on depression in a controlled trial.

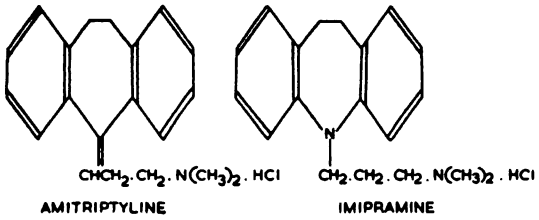

Fig. 1

Patients Studied

All cases of depressive illness, admitted to a special unit over a period of six months, that could fairly confidently be diagnosed as reactive or endogenous depression, were included in the trial. Patients were allocated to one of two groups by the chief pharmacist without the knowledge of the assessing clinician. Seventy female patients were included in the trial varying in age from 40 to 70, the average age being 57. For 47 of these patients this was their first admission to a mental hospital and for 13 their second admission. From the fact that they needed admission, it follows that all of the patients concerned were regarded as being severely depressed.

Method

The trial was double blind in structure. Tablets identical in appearance to the real drug were used as placebo. Only the chief pharmacist was aware which patients were receiving the real drug and which the placebo. One group of patients, containing 19 endogenous and 16 reactive depressions, received amitriptyline, while the other group containing 26 endogenous and nine reactive depressions received placebo tablets. At the beginning of treatment the patients' symptoms were noted and scored on a special chart recording the following items; depression, guilt, suicidal ideas, agitation, retardation, anxiety, feelings of paranoia or depersonalization, obsessional symptoms, hypochondriasis, appetite, weight loss and insomnia.

The patients were seen at weekly intervals over a four week period and the symptoms mentioned above reassessed to record improvement or lack of improvement. This was done by the same psychiatrist for each patient. Results at the end of four weeks were recorded as improved or not improved. "Improved" meant that the patient needed no further treatment and was considered fit for discharge or that she had reached a degree of recovery where she could be discharged on a maintenance dose of the drug. "Not improved" implied that the patient had shown no improvement or so little improvement that she needed further or alternative treatment such as E.C.T. or other antidepressant drugs. During the four week period some patients had their drug withdrawn and another treatment substituted if it was thought that they were not responding to treatment and that their condition was so serious that further delay would not be justified. This was recorded as a failure or "not improved". All patients on the trial received sodium amylobarbitone gr. 3 or 6 nocte.

Results

Taking both reactive and endogenous depressions together as a group (Table I), 35 patients received the drug and of these 22 were improved and 13 not improved. Thirty-five received the placebo and of these 11 were improved and 24 not improved. This is a statistically significant result in favour of the effect of the drug.

Twenty-five reactive depressions were included, of which 16 received the drug, and nine the placebo (Table III). Of the 16 who received the drug 13 were improved and three not improved. Nine received the placebo and three were improved and six not improved. This again is a statistically significant result in favour of the drug.

Where endogenous depression is taken separately the results are as follows (Table II). Nineteen received the drug and nine were improved while 10 were not improved. Twenty-six received the placebo, eight being improved and 18 not improved. These results, though in favour of the drug, do not reach statistical significance.

Table I.

All Depressions

	Not Improved	Improved	Total
Drug	13	22	35
Placebo	24	11	35
Total	37	33	70

$\chi^2 = 29{\cdot}25$. Highly significant (p much below ·001).

Table II.

Endogenous Depressions

	Not Improved	Improved	Total
Drug	10	9	19
Placebo	18	8	26
Total	28	17	45

$\chi^2 = 0{\cdot}678$. Not statistically significant.

Table III.

Reactive Depressions

	Not Improved	Improved	Total
Drug	3	13	16
Placebo	6	3	9
Total	9	16	25

Fisher's exact p is ·024, which is statistically significant.

Agitation as a manifestation of depressive illness, taken as a whole, was not shown to respond to the drug (Table IV).

Table IV.

Agitation in Depression (Endogenous and Reactive)

	Not Improved	Improved	Total
Drug	9	13	22
Placebo	12	11	23
Total	21	24	45

χ^2 0·210 $p < {\cdot}7 > {\cdot}5$ not statistically significant.

Nine patients who failed to respond to amitriptyline were given E.C.T. and 6 made a satisfactory recovery, while 13 who did not respond to the placebo were given E.C.T. and 11 made a good recovery.

In three cases side-effects which appeared when the drug was given at 50 mg. t.d.s. disappeared when the dosage was reduced to 25 mg. t.d.s.

Side-Effects

Side-effects were not very marked, despite the fact that the patients started off on a relatively high dosage of 50 mg. t.d.s. It must be admitted, however, that they were not questioned about them because it was felt that such knowledge might vitiate the double blind nature of the trial. The two main side-effects complained of were trembling of the hands (7) and tiredness (3). Three patients complained of dryness of the mouth, but so did three on the

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placebo tablets. One patient became hypomanic and this subsided when the drug was withdrawn and chlorpromazine substituted.

Discussion

The results of this trial suggest that amitriptyline is effective in the treatment of reactive depression to a statistically significant degree. In treating endogenous depression, although the results show that the drug produces better results than the placebo this did not reach statistical significance. Side-effects are not severe at therapeutically effective levels. Agitation as a symptom of depressive illness as a whole did not appear to be relieved. In the reactive depressive cases the impression was gained that the drug had a tranquillizing effect, and it would seem worthwhile to carry out a trial to compare the effects of amitriptyline with a tranquillizing drug such as chlorpromazine in such cases.

Summary

Seventy depressed patients, 45 endogenous and 25 reactive, were included in a double blind controlled trial to assess the value of amitriptyline in such cases. A favourable result to a statistically significant degree was seen in reactive depression. In endogenous depression the results, though in favour of the drug, did not reach statistical significance. Side-effects were not very marked at a dosage of 50 mg. t.d.s. A further trial to compare chlorpromazine with amitriptyline in hospitalized reactive depressive patients would seem worth while.

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