A CLINICAL COMPARISON OF PHENELZINE AND ELECTRO-CONVULSIVE THERAPY IN THE TREATMENT OF DEPRESSIVE ILLNESS

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THE mono-amine oxidase inhibitors, of which phenelzine ("Nardil") is one example, were introduced for the treatment of depressive illness as a result of the observation that iproniazid, which is a mono-amine oxidase inhibitor, produced euphoria and increased mental alertness in some tuberculous patients to whom it was given. Trials of iproniazid in mental illness were carried out (Loomer *et al.*, 1957; Cesarman, 1959), but it was found to be very liable to give rise to side-effects, being particularly toxic to the liver. Other less toxic mono-amine oxidase inhibitors such as phenelzine, which is chemically related to iproniazid, were later developed.

The mode of action of the mono-amine oxidase inhibitors in depressive illness is uncertain; the various theories were well summarized in an annotation in the *British Medical Journal* (1959), the conclusion being as follows: "At all events it is clear that until we know more about the normal physiological functions of amines in the body only tentative interpretations are possible." From the point of view of the clinician, whatever the mode of action of these new drugs, what matters is whether or not they have in fact a beneficial effect when used in depressive illness, and it should be possible to ascertain this by means of controlled clinical trials. Unfortunately, it is very difficult in depressive illness to justify the use of a placebo group when a known effective treatment—electro-convulsive therapy—is available, and in the present trial it was therefore decided to compare the results of treatment by phenelzine with those of E.C.T. Clearly, if any new drug is developed which can be shown to be as effective or more effective than E.C.T., the latter will soon be abandoned.

EXPERIMENTAL DESIGN

All the patients included in the trial were from one female acute admission ward. Inclusion in the trial was governed by the decision of the consultant psychiatrist, who considered firstly (*a*) that the patient's illness was depressive in type, and secondly (*b*) that electro-convulsive therapy would normally be indicated. The patients were then randomly allocated on admission to either the phenelzine or the E.C.T. group. Before treatment commenced, each patient was tested on the nine "depressive" scales found by Foulds and Caine (1959) to be valid with respect to the diagnosis of depressive illness in women; these test scales were derived from McCall's (1958) breakdown of the Minnesota Depression Scale.

Table I shows the pre-treatment scores of the E.C.T. and phenelzine groups on these nine depression scales, and the mean ages of the two groups. The Mann-Whitney "U" test (Siegel, 1956) was applied to these data, and showed that there

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was no significant difference between the two groups with respect to age and eight of the nine test scales. (The E.C.T. group on one of the scales showed slightly more "guilt" than the phenelzine group prior to treatment.) The two groups were thus closely matched on essential variables prior to treatment.

Table I

Pre and Post-Treatment Mean E.C.T. and Phenelzine Scores on Nine "Depression" Scales and Levels of Significance for these

	Mean Scores Prior to treatment E.C.T.	Phenelzine	Mann-Whitney U Test; U Values and levels of significance	Mean Scores following treatment E.C.T.	Phenelzine	Mann-Whitney U Test; Values and levels of significance
Age	43·8	51·3	135; not significant			
Scales Used						
1. Depression ..	37·2	35·6	170; not significant	24·7	32·6	82; $<·01>·001$
2. Affective-Face Validity (A.F.V.) ..	8·2	7·6	150; not significant	5·1	6·3	116; $<·05>·025$
3. Functional-Face Validity (F.F.V.) ..	5·0	4·7	139; not significant	2·6	4·4	72; $<·001$
4. A.F.V. plus F.F.V.	13·2	12·3	155; not significant	7·7	10·5	100; ·01
5. Health Face Validity (H.F.V.)	3·1	3·3	149; not significant	1·5	2·6	83; $<·01>·001$
6. Functional Component (F.C.)	1·9	2·0	135; not significant	1·0	1·7	66; $<·001$
7. Health Component (H.C.)	1·7	1·8	131; not significant	·9	1·4	90; $<·01>·001$
8. Self-Criticism ..	8·2	7·9	177; not significant	6·9	7·4	150; not significant
9. Guilt Scale	2·8	2·2	103; ·025	2·1	2·0	138; not significant

Results

There were 38 patients who completed the trial, which was concluded rather earlier than originally planned because it soon became apparent that phenelzine was inferior to E.C.T., and in view of this it did not seem justifiable to continue the trial any longer. Eighteen patients were treated with E.C.T. and twenty with phenelzine. The clinical psychologist who tested the patients on the nine depressive scales before treatment began retested them on the same scales one month after the commencement of treatment, being unaware of the type of treatment which had been given. Several patients originally included in the trial did not complete the month's treatment, and were therefore not included in the final assessment group of 38 patients: four patients originally included in the E.C.T. group responded rapidly to this treatment and left hospital before one month and did not attend for re-assessment, and in four patients on the phenelzine group the drug had to be discontinued because of deterioration in the mental state, and deterioration of behaviour necessitated discontinuation of treatment in one patient in the E.C.T. group. (None of these patients was included in the final assessment, but their inclusion would have made the result even more strikingly in favour of E.C.T.)

As indicated in Table I, E.C.T. was shown to be significantly superior to phenelzine in no less than seven of the nine scales; in the remaining two scales—"Self-criticism" and "Guilt", although the superiority of E.C.T. did not reach levels of statistical significance, examination of the mean scores will nevertheless show that a greater decrease in symptomatology occurred in response to E.C.T. than in response to phenelzine.

Side-Effects

E.C.T. was given three times weekly and the total number of treatments was determined by the response, being usually 6 to 8. There were the usual symptoms

of transient headache, confusion, and memory impairment, but no serious side-effects. Phenelzine was given in a dose of one tablet (15 milligrammes) three times daily, increasing after one week to two tablets three times daily; however, three patients developed marked oedema of the lower limbs on the higher dosage scheme, and this was therefore discontinued. The mechanism of production of this oedema was not obvious—in two there was evidence of myocardial degeneration on the E.C.G., and symptoms of early cardiac decompensation (though there was no oedema before treatment with phenelzine commenced), but in the third patient the E.C.G. was normal, as were the plasma proteins, and there was no clinical evidence of cardiovascular disease. In all three cases the oedema responded to reduction of dosage and the use of chlorothiazide. One patient on phenelzine developed mild postural hypotension, and one developed a transient skin rash.

Summary and Conclusions

A clinical trial is reported in which a comparison was made between the effects of electro-convulsive therapy and phenelzine ("Nardil") in the treatment of depressive illness. Patients were randomly allocated to one or other treatment, and were assessed on a nine-point rating scale for depression before and after one month of treatment. The two groups were closely matched before treatment, but assessment after one month showed that improvement in the patients treated with E.C.T. was far greater than that in the patients treated with phenelzine. Side-effects were few and unimportant with both methods of treatment.

It is concluded that phenelzine is much inferior to electro-convulsive therapy in the treatment of depressive illness.

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