IMIPRAMINE WITH ELECTRICAL TREATMENT IN DEPRESSION—A CONTROLLED TRIAL

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SINCE the introduction of anti-depressant drugs into general use in the psychiatric field, there have been several statements to the effect that such a drug administered concurrently with electrical treatment reduces the number of shocks required to achieve a satisfactory response. This has been claimed by Sargant (1961) but without experimental support. Dunlop (1960) has published a comparison between the number of electrical treatments given with the anti-depressant drug during a particular attack, and the number of treatments without the aid of a drug in an earlier attack in the same patient: however, comparison of treatments in the same group of patients at different times is unreliable because there may be other factors to account for the differences noted. A controlled trial is necessary to ensure that all factors are constant other than the one under consideration.

More important than the number of electrical treatments given is the high relapse rate which is found (Kiloh *et al.*, 1960). It is important to know whether an anti-depressant drug can reduce the likelihood of relapse. The present trial was carried out to provide information on these two points.

METHOD

In-patients suffering from a depressive illness warranting electrical treatment were selected for the trial. In general the criteria were depression, of moderate to severe intensity, with retardation or agitation, feelings of hopelessness and pessimism. After physical and psychiatric examination a decision was made as to suitability for inclusion in the trial. Once selected, the pharmacist allocated the patient randomly to one of two groups, unknown to the participating doctors. One group received imipramine 25 mg. t.d.s. for three days, increased to 50 mg. t.d.s. for the remainder of the stay in hospital. The second group received tablets identical in appearance but not containing a pharmacologically active constituent. After one week on the tablets, electrical treatment was commenced. This was given twice weekly, using an Ectron machine, (1 second duration shock), with modification by thiopentone and suxethonium bromide. The patient was seen in order to decide whether each treatment was necessary; judgment was based on the clinical condition of the patient, and no attempt was made to standardize the number of treatments. The patients were kept in hospital for seven to ten days following the last treatment.

After discharge, many of the patients attended a Follow-up Clinic at monthly intervals for six months. These patients were asked to continue taking tablets, which were supplied from the hospital to ensure continuity of treatment. Some patients continued on the same tablets that they had been taking while having electrical treatment, while others had their tablets changed from the

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inert to the active drug or vice versa. This was done randomly by the pharmacist and again without the knowledge of the doctors concerned: for the first month, 50 mg. t.d.s. of imipramine or the equivalent number of inert tablets were given and after that the dose was reduced to 25 mg. t.d.s.

Results

1. *In-patient Treatment*

Forty-three patients, of whom forty were female, participated in the trial. Three patients were withdrawn from the trial by the end of the first week; two had improved to such an extent that electrical treatment was not indicated and one had deteriorated so much that urgent electrical treatment was required; all were subsequently found to have received placebo tablets. Of the remaining forty patients, nineteen were found to have had imipramine and twenty-one were receiving inactive tablets. The two groups were found to be similar with regard to age, their means being 47·9 years (range of 28–71) and 49·0 years (range of 30–70) for the drug and placebo groups respectively (t=0·303 which is not statistically significant).

All patients responded satisfactorily to the course of treatment; the mean value of the number of treatments given to the "drug" group was 6·3 and to the "placebo" group, 7·0: t test (0·29) showed that the means did not differ significantly. To show that these figures did not result merely from the application of a standard course of six treatments, frequency distributions were drawn up for each group of patients (Table I).

TABLE I

Frequency Distribution of E.C.T.

No. of E.C.T.	No. of Patients: Drug Group	Placebo Group
3	2	0
4	3	5
5	3	2
6	3	2
7	2	5
8	1	2
9	4	0
10 or more	1	5
Total	19	21

The mean length of stay in hospital was also noted for the two groups. For the "drug" group it was 51·2 days and 48·6 days for the "placebo" group. There was no significant difference between the two means (t=0·49).

2. *Follow-up Treatment*

It was not found possible to follow up eight of the patients who participated in the in-patient study, owing to transport difficulties; of the remaining thirty-two patients, twenty-eight were followed up for the full six months, or until relapse occurred. Of the four patients who withdrew from the investigation before it was completed, two left the area and contact was lost; these were subsequently found to have been taking the placebo. The remaining two patients were both found to have been taking imipramine; one stopped this spontaneously and has remained well, whilst the other relapsed four months after discharge and was readmitted following a suicidal attempt.

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Of the twenty-eight patients who formed the subject of the follow-up study, twelve were subsequently found to have received imipramine and sixteen the placebo; of the former group, two patients relapsed and required further E.C.T. This may be contrasted with the placebo group, where eleven patients relapsed. (Table II).

TABLE II

Condition on Follow-up

Result	Imipramine	Placebo
Satisfactory	10 (83·3%)	5 (31·3%)
Relapse	2 (16·7%)	11 (68·7%)
Total	12	16

Of the patients who were taking imipramine in hospital, six continued it and remained well, whilst of the remaining eight patients who reverted to the placebo all but one relapsed. Eight of the patients who were given the placebo in hospital continued to take it during the period of the follow-up study and four relapsed, whilst a further six were changed on to imipramine and of these one relapsed. (Table III).

TABLE III

Effect of Changes in Treatment

In-patient Treatment	Out-patient Treatment			
	Imipramine		Placebo	
	Satisfactory	Relapse	Satisfactory	Relapse
Imipramine	5	1	1	7
Placebo	5	1	4	4
Total	10	2	5	11

DISCUSSION

There are two possible ways in which the addition of an anti-depressant drug during a course of E.C.T. may affect the outcome. In the first place, it may reduce the actual number of treatments given. The results of this controlled trial demonstrate that this is not so. It is true that the patients who were receiving Imipramine had on average slightly less electrical treatment, but even if this reached statistical significance there is no clinical advantage in reducing the number of E.C.T.s by such a small amount. This accords with the findings of Muller (1961) who used phenelzine, a mono-amine oxidase inhibitor, in a similar type of controlled trial. Providing that the difference in the number of treatments given is only of the order of one or two, in the majority of cases it is of comparatively little importance to either the patient or the doctor how many treatments are actually given. More important is the long term effect of the course of treatment, that is, the possibility of subsequent relapse. This is the second way in which an anti-depressant drug may be of importance. Muller (1961) found that phenelzine potentiated the effect of E.C.T. If imipramine given with E.C.T. potentiated its effect, one would expect to find a lower relapse rate in patients who had received imipramine in hospital and a placebo in out-patients, compared with those who had the placebo throughout the study. The number of cases is too small to show more than a tendency, but these results provide no evidence that the response is better in the former group. (Table III).

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The immediate response to E.C.T. is highly satisfactory, particularly when patients are carefully selected. Where adequate facilities for out-patient E.C.T. are available, it is permissible to admit patients to hospital for a short course of treatment designed to overcome the immediate depression and rely on a careful follow-up, with additional out-patient treatment when necessary to deal with relapse. This has been our policy in the past. The addition of anti-depressant medication following E.C.T. has made it even more satisfactory to implement this plan, since the likelihood of relapse is markedly reduced.

Summary

1. A controlled trial of electrical treatment with imipramine and with a placebo was carried out in hospital.

2. A number of patients who participated in the trial were followed up for six months as out-patients. They continued to receive imipramine or placebo.

3. There was no evidence either of a reduction in the number of electrical treatments required, or of a potentiation of its effect beyond the duration of the course.

4. The administration of imipramine markedly reduced the rate of relapse.

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References

Dunlop, E. (1960). *Dis. Nerv. Syst.*, **21**, 130.
Kiloh, *et al.* (1960). *J. Ment. Sci.*, **106**, 1139.
Muller, D. (1961). *J. Ment. Sci.*, **107**, 994.
Sargant, W. (1961). *Brit. Med. J.*, *i*, 225.

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