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Effect of ECT in Endogenous Depression: A Double Blind Comparison with Imipramine

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Abstract

In a double blind randomised trial, both ECT and imipramine produced equal and clinically significant improvements at the end of four weeks in endogenous depressives. The depression was assessed on the 17 item Hamilton rating scale for depression (HRSD) and was compared with its 6 item subscale. Whereas on the former scale ECT seemed superior only once, i.e., at the end of second week, with the latter scale, ECT seemed superior during all the first 3 weeks. Item analysis on the HRSD revealed significant differences with respect to the therapeutic effects of these two treatment methods.

Key words -
ECT,
Imipramine,
Hamilton Rating Scale for Depression (HSRD),
Item subscale
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Imipramine,
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6 Item subscale

The evidence in favour of the efficacy of ECT in depressive states seemed 'incontrovertible' [1] until the appearance of contradicting report by Lambourn and Gill [2]. While this study used unilateral brief pulse ECTs, three subsequent double blind studies [3], [4], [5] using bilateral sine wave ECTs have yielded positive results in favour of ECT. The results of these three studies warrant scrutiny with regard to the methods of assessment.

In the study by West [4] real ECT emerged as being superior, to placebo ECTs during all the first four weeks. Also the patients receiving placebo ECTs did not show any reduction in their depression scores. The assessment tool was Beck's depressive inventory. However Johnstone et al, [3] had observed that although real ECTs are superior to simulated ECTs, patients in the later group also showed considerable improvement on the depression scores. The assessment tool was Hamilton Rating Scale for Depression (HSRD) [6]. Likewise, in our study too [5] real ECTs seemed superior to imipramine only at the end of 2nd week as assessed on HSRD. Like in the earlier study [3] HSRD scores came down considerably in the initial weeks, even in the group not receiving ECT but only imipramine, thus narrowing the

difference.

The sensitivity of HSRD to measure the severity of depression has been questioned [7]. Bech et al, [7] have demonstrated that only six items of HSRD whereas twelve items of BDI (Beck's depressive inventory) withstand statistical tests to satisfactorily assess the global severity of depression. The 17 item HSRD - used in these two studies [3], [5] - has failed to differentiate degrees of depression adequately the different degrees of depression especially at more severe degree. Bech et al, [8], [9] have suggested that these six items of the HSRD which they have identified (Table - 3) are homogeneous and measure depression in the dimension of severity, while some of the items of the rejected eleven items may be measuring the drug side effect, nosology of depression etc. In a subsequent study Bech et al [9] have demonstrated that these six items can be more effectively used for measuring severity and changes in the degree of depression.

Other authors [10], [11], [12] concur with Bech et al. that the 17 item scale is less sensitive and that the 6 item scale may be used for measuring the severity of depression and changes in the severity. Thus we intended to re-examine our data [5] in the light of current criticisms on HSRD.

Patients and Methods

Thirty two endogenously depressed patients were entered into the trial after excluding any contraindications for ECT or imipramine. They were randomly allocated to receive either ECT + placebo or imipramine + placebo ECT, following informed consent. 24 patients (age range 22 to 66 years, Male :Female 11:13) however completed the trial and form the sample of this study. 11 patients received ECT + placebo, while 13 patients received imipramine + placebo ECT. These 2 groups were comparable with respect to relevant clinical variables, like age, sex, family and past history of affective illness and duration of illness. None of the patients chosen for the study had psychotic symptoms like hallucinations or delusions. None had received any treatment for the current episode excepting benzodiazepines, although even this was withheld during the study.

The patients in the ECT group received during each session one bilateral frontotemporal modified ECT, using 50 Hz sinusoidal current of 100 - 130 volts passed for a duration of 0.5 to 0.7 seconds (150-250 mgm of thiopentone, 20-30 mgm succinylcholine and 0.65 mgm of atropine). ECTs were administered on alternate days in the first 2 weeks and one each at the end of 3rd & 4th weeks. Following this the patients entered the maintenance ECT trial. Patients also received placebo capsules like in the imipramine group.

In the other group patients received 25 mgm capsules of imipramine, 3 per day in the first week and 6 per day in the following 3 weeks, they also received simulated ECTs (anaesthesia) in the manner described for the ECT group. No other psychotropic drugs were given to patients in both groups. Assessments were all double blind using HSRD 17 item scale. Patients were assessed at pretrial and at weekly intervals, at least 48 hours after the last ECT.

Analysis

Total doubled scores of HSRD were compared between the 2 groups using students' 't' test. Total scores of the 6 item subscale were similarly compared. Percentage improvement using these 2 scales, (this is the ratio of the difference between initial and weekly assessment score, to the initial score multiplied by 100) was calculated and Median test was applied. Mean scores of each of the items were

compared between the groups at each assessment, to identify the items which showed differential response to each of these treatment methods.

Results

The two groups did not significantly differ with respect to the means of total pretrial scores (Fig 1 & 2). At the end of 4 weeks both groups showed comparable degree of improvement as assessed either by 17 item HSRD or by the 6 item subscale (Fig. 1 & 2) and (3 & 4). However the results in the 2 groups differed in the first 3 weeks depending on the assessment procedure

- ***Mean ± SEM scores as assessed on the 17 item HSRD scale. Difference was statistically significant only at week 2 ($p < 0.05$)***
- ***± SEM scores as assessed on the 6 item subscale. The differences were statistically significant at week 1 ($p < 0.005$), week 2 ($p < 0.001$) and at week 3 ($p < 0.005$)***
- ***Average percentage improvement as assessed on 17 item scale***
- ***Average percentage improvement as assessed on 6 item subscale***

Using the 17 item HSRD the difference between the 2 groups reached statistical significance only at the end of second week in favour of ECT ($p < 0.05$), while using the 6 item subscale the differences between the two groups reached statistical significance, in favour of ECT at the end of all the first 3 weeks ($p < 0.005$, 0.001, 0.005 respectively in fig. 1 & 2). The proportion of patients who showed above-median-percentage improvements were significantly higher in the ECT group only at the end of third week $p < 0.01$) as assessed on the 17 item HSRD, whereas on the 6 item subscale the same proportion was significantly higher in the ECT group at the end of all the first 3 weeks ($p < 0.05$, 0.007 and 0.01 respectively - Table 1 & 2). The average percentage improvements which occurred in the two groups as assessed on the two scale is shown figure 3 and 4 and the effect of assessment procedure on the results is evident.

Table I - Median percentage improvement on 17 item HSRD scores

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Table II - Median percentage improvement and 6 item subscale

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When the individual 17 items of HSRD were analysed, some symptoms which had similar degree of severity between the groups in the initial weeks showed differences at later assessments (Table 3). ECT was superior to imipramine for 4 items of the subscale, whereas imipramine was superior to ECT for none of the 6 items.

Table III - Mean scores of the items of HSRD

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ECT. n = 11

Drug. n = 13

At a week IV, none of the items showed any difference between the groups. Items not mentioned did not show any differences at any assessments. Symptoms, 1, 2, 7, 8, 13 and psychic anxiety,

form the 6-item subscale [7].

Discussion

The differences between the two treatment methods as assessed by the 17 item HSRD, although significant in favour of ECT, are narrow. When assessed on the 6 item subscale the differences become more pronounced and appear in favour of ECT during all the first three weeks of assessment. Since the latter scale seems to measure depression in the dimension of severity [7] it appears that ECT markedly alleviates the severity of depression earlier than imipramine. Also greater number of patients improve at each week with ECT with regards the severity of depression.

The effects of drugs on other symptoms of depression viz., insomnia, tend to dilute the differences between the two treatments. This could have happened in the Northwick Park trial [4] wherein the authors stated the patients not receiving real ECTs also showed appreciable degree of reduction in the HSRD scores. It may be recalled here in this study the use of benzodiazepines could have reduced the scores on items like anxiety and insomnia and thus effecting a reduction in the total score. Thus an item analysis could have proved more informative. Secondly, when the individual items of HSRD were analysed the items which showed preferential response to ECT (Table 3) are some of the items of the subscaler suggested [7]. Item analysis point out distinct differences between the two treatment methods, ECT being clearly superior to four out of the six items of the subscale while the drugs being superior to apparently none of the six items. Despite the anxiolytic effect, imipramine failed to show superiority even on the item of psychic anxiety indicating that ECT had significantly alleviated this symptom also. The preferential response of the drug treated group on the scores of insomnia are well expected.

The study has thus pointed out some qualitative differences in the outcome of the two antidepressant treatment methods. ECT being relatively superior to imipramine or items which measure the depression in the dimension of severity and that greater proportion of patients improve with ECT with respect to severity during each of the first three weeks.

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