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Original Article

COMBINED HALOPERIDOL AND ELECTRO CONVULSIVE THERAPY IN THE TREATMENT OF SELECTED CASES OF MANIA

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ABSTRACT:

Objective: To compare efficacy of combined haloperidol and electro convulsive therapy (ECT) in the treatment of Mania in selected cases who are resistant to medication alone and are severely ill.

Design: Two groups of 20manic patients received eight ECT sessions either actual or simulated, in a double blind controlled study. All patients received 30mg of Haloperidol daily until the sixth treatment and subsequently dose of anti-psychotic medication was adjusted for individual patient according to level of improvement.

Setting: Department of Psychiatry Jinnah Hospital, Lahore.

Results: Forty patients were included in the study between 1st July 1999 and 30th June 2000, the two groups did not differ significantly in any of the sociodemographic variables or any clinical variables as rated on Mania Rating Scale (MRS)[4] and Brief Psychiatric Rating Scale (BPRS)[19] before intake into the study and severity of index episode. At the end of eight sessions although 17 patients in the ECT group had made a complete recovery, in the simulated ECT group only one had recovered. Significantly more patients (16) in the simulated ECT group required an increase in anti-psychotic medication compared with the ECT group (two patients) ($P < 0.05$, Fisher's Exact Probability Test).

Conclusion: The results indicate that the group receiving the combination of Haloperidol and ECT did significantly better than the other group in severely disturbed patients. It is not recommended as routine procedure as modern antimanic drugs are affective in mania.

KEYWORDS: Mania, Electro Convulsive Therapy, Haloperidol.

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INTRODUCTION

One of the authors of this study (SIH) conducted a study[1] in which it was proved that ECT causes temporary impairment of memory which completely disappears within one week.

Published reports on the use of electro convulsive therapy (ECT) in the treatment of mania are not common, despite more than half a century of its use. There were contradictory reports of its efficacy before pharmacotherapy began to be used. Although some psychiatrists judged ECT to be as effective for mania as it was for depression, others considered it to be less so.[2,3,4] Early investigators also felt that manic patients required more frequent therapy,

usually multiple, daily treatment at the beginning of the course and that a larger course of treatment was needed compared with that required by most depressed patients.[5,6,7] Studies evaluating the efficacy of ECT in mania have been reported.[8,9,10,11] Contemporary treatment of manic episodes relies heavily on the use of lithium salts, neuroleptics or anticonvulsant drugs, by contrast, the role of ECT in mania has gained little attention.[12,13,14]

The use of anti psychotic drugs has become widespread, to combine such drugs with ECT has also become common practice.[15,16] This treatment modality has been the focus of research in psychotic disorders, especially schizophrenia but has not been reported as frequently in manic disorder.[17,18,19,20]

In a developing country such as Pakistan this is a prospective, double blind, controlled study, using standardized rating instruments, to evaluate the role of ECT combined with Haloperidol in mania in severely disturbed and resistant cases.

PATIENTS AND METHOD

Forty-two manic patients attending the Deptt. of Psychiatry were enrolled in the study. Two patients dropped out because of deterioration in their clinical condition. The remaining forty patients were evaluated. The inclusion criteria were: -

a. Fulfillment of DSM-IV (American Psychiatric Association 1994)[4] diagnostic criteria for a manic episode and were unmanageable.
b. Age of onset of the first episode to be between 20 and 40 years.
c. A minimum score of 20 on the Mania Rating Scale (MRS)[5] which is severely disturbed mania.
d. No lithium or any other prophylactic treatment.
e. No ECT in the last six months.
f. Patients who had failed to respond to high doses of modern effective antimanic drugs.

The sample consisted of an experimental group and a control group, both of 20 patients independently diagnosed to have severe and resistant mania by the investigators. The experimental group consisted of patients who received eight bilateral, modified ECT sessions and a fixed daily dose of 30 mg of Haloperidol until six sessions had been given. After the sixth session, the dose of Haloperidol was either modified or was replaced by another neuroleptic according to the severity of illness of each patient. The control group consisted of patients who received eight simulated ECT sessions and the same dose and schedule of neuroleptic drugs as the patients in the experimental group.

At intake, sociodemographic and clinical profiles were recorded by interviewing patients and their relatives. The patients were also rated on MRS[5] and the Brief Psychiatric Rating Scale (BPRS).[20] The method and course of treatment were explained to patients and their relatives and consent was obtained for both ECT and anaesthesia. The patients were then randomly allocated to one of the two treatment groups. The patients and their relatives were blind to this allocation.

Anaesthesia was given by thiopentone sodium (150-300) mg). Modified ECT at 110V for 0.6s using bilateral fronto-temporal leads and sinusoidal current, was given to the ECT group three times per week.

Patients in the simulated ECT group were similarly anaesthetized and electrodes were placed on the forehead but no electric shock was administered. Each patient and their relatives were interviewed before each block of two actual or simulated ECTs, that is, before the third, fifth and seventh sessions, and finally at least 24 hours after the eight sessions. Following t he interview, all patients were rated again on MRS and BPRS. Any extra medication used was also noted. Anticholinergic agents for extra pyramidal symptoms, nitrazepam for night sedation and intravenous diazepam to control acute excitement were used whenever necessary.

Patients whose scores fell below 6 on MRS and remained so for at least one week after completion of eight actual or simulated sessions were considered to have recovered and took no

further part in the study. For those who did not recover, a follow-up assessment was done every two weeks in the first month and every four weeks in the next two months. During this period, patients were maintained on neuroleptics and other necessary drugs and were carefully monitored. At every follow-up, patients were rated on MRS and BPRS, and those whose scores fell below 6 on MRS and thus maintained for at least one week were considered to have recovered and consequently took no further part in the study.

Parametric variables were analysed by coefficients of correlation, unpaired t-test and repeat measure analyses of variance (ANOVA). Non-parametric variables were analysed by X2 tests and Fisher's exact probability tests. Patients whose symptoms were not controlled by the treatment strategy were dropped from the study. It is important that combination of ECT and haloperidol was given to selected, resistant and unmanageable patients of mania.

RESULTS

The two groups did not differ significantly in any of the sociodemographic variables (age, sex, marital status, occupation, education, religion, or any clinical variables (family history of mental illness, past history of affective disorder, mean duration of index episode before intake into the study and severity of the index episode as rated on MRS and BPRS. In the total sample of 40 patients, however, it was found that those who had a family history and past history of affective disorder had a more severe manic episode at index evaluation than those who did not have positive histories.

At the end of eight sessions, although 17 patients in the ECT group had made a complete recovery, in the simulated ECT group only one had recovered.

When serial scores of patients in both groups were analysed on repeat measure ANOVAs, the results showed that there was a significant main affect for group ($F1,38=7.31$, $P<0.01$) indicating that overall, at the four points of assessment, scores in the ECT group were significantly less than scores in the simulated ECT group.[21,22]

There was a significant main effect for time ($F4, 112=218.19$, $P<0.0011$) indicating that both groups improved significantly across time; Scheffe's multiple comparison test revealed that significant improvement was observed from the first rating after the baseline assessment, that is, after the second session.

There was a significant group and time interaction ($F 4,112=29.6$, $P<0.001$) indicating that the ECT group improved at a significantly faster rate than the simulated ECT group; this difference in the rate of improvement was also observed after the second session (Scheffe's test). Details of serial scores on MRS are given in Table-I.

TABLE-I

Mania rating scale scores in the study groups during treatment

Time of evaluation	*ECT (n=20)*		*Simulated (n=20)*	
	Mean	*S.D.*	*Mean*	*S.D.*
At intake	25.53	3.88	23.46	1.59
After 2nd ECT	18.80	4.21	21.08	1.48
After 4th ECT	13.08	4.77	19.46	1.50
After 6th ECT	6.93	5.15	18.73	2.46
After 8th ECT	4.6	4.91	42.13	4.18

Repeat measure ANOVA
Significant main effect for group: F 1,38=7.31, P<0.1
Significant main effect for time: F 4, 112=218.19, P<0.001
Significant time and group interaction: F 4, 112=29.6 P<0.001

Although both groups were matched on overall severity of mania (as rated on MRS), at the time of intake, patients in the ECT group had significantly higher scores on four items, namely verbal and motor activity, mood and sleep disturbance. At the end of six actual or simulated sessions, that is, until the drug doses were held constant, the scores on all four items, along with four others i.e. hostility, self-esteem, conduct and work, had significantly reduced in the ECT group compared with the simulated ECT group[23,24]

Only three patients in the ECT group did not recover completely by the end of eight sessions. These three patients did not differ significantly on any sociodemographic or clinical variables compared with the rest of the patients in the group. The average Haloperidol equivalent dose per patient until recovery was 30 mg per day.

In the simulated ECT group, of the 18 patients who were followed up after the completion of simulated session, nine recovered completely after two weeks, another five after four weeks and the remaining four after eight weeks. All patients required an increase in the dose of neuroleptics to achieve clinical recovery. In this group, the average daily Haloperidol equivalent dose was 60mg.

Significantly more patients (16) in the simulated ECT group required an increase in antipsychotic medication compared with the ECT group (two patients) ($P<0.05$, Fisher's exact probability test).

No significant relationship was found between any of the sociodemographic variables and improvement of mania with ECT. Among the clinical variables, only high scores on disturbance of sleep and disruption of work (on MRS) were found to be significantly associated with improvement at the end of treatment with ECT.[25]

DISCUSSION

This study demonstrated that, in the two groups of manic patients comparable for age, sex, duration and severity of illness, the group receiving the ECT-Haloperidol combination showed significantly greater and faster improvement than the simulated ECT Haloperidol group, although patients in both groups improved significantly over the study period.

This improvement was noticed from the second session. Although almost half the patients recovered completely after six session, most had recovered fully after eight. We therefore conclude that minimum of six to eight ECT sessions on alternate days are required for the control of acute manic excitement in combination with a moderate dose of neuroleptics.

When individual manic symptoms were considered, it was noted that ECT had a substantial ameliorative effect on all the manic symptoms (recorded on MRS).

Another important finding is that the number of patients in the ECT group who required additional medication, both of dose and duration, is significantly fewer than in the simulated ECT group.[14,17] Distressing side effects such as extra pyramidal symptoms are one of the major limitations of intensive neuroleptic therapy. Our findings indicate that at least for short-term remission of manic episodes, the risk of such side effects can be minimized by combining ECT with a moderate dose of neuroleptic in selected unmanageable patients.

Our findings also demonstrate that a combination of ECT and a moderate dose of a neuroleptic is extremely effective in rapidly aborting an acute episode of mania.[3,6,18] This shortens the hospital stay and is thus cost effective. These considerations are important in Pakistan, where health resources are scarce. This finding is also compatible with other studies conducted in a similar way on schizophrenia, where it has been shown that combined ECT and neuroleptic therapy enhance the rate of improvement over either treatment alone.[10,11,13] Empirically, ECT in mania is generally recommended either when the illness is very severe or is resistant to an intensive course of pharmacotherapy. Our results highlight the fact that ECT can only be recommended for very selected manic patients. It is not to be used in routine cases of mania as they are very much manageable with modern antimanic medication.

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