

AWARD PAPER

Electroconvulsive Therapy in Lorazepam Non-Responsive Catatonia

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ABSTRACT

Aim: To compare the efficacy of electroconvulsive therapy (ECT) with risperidone in the treatment of lorazepam non-responsive catatonia. **Materials and methods:** Inpatients with non-affective catatonia (n=18) non-responsive to at least five-day trial of lorazepam (6-8 mg/day) were randomised into two groups in a double blind randomised design. Written informed consent was obtained. Four were dropped from the trial as they were found to have depressive catatonia. One group received true ECT (thrice weekly, n=8) plus oral placebo while the other received sham ECT plus risperidone (4-6 mg/day). Bush-Francis Catatonia Rating Scale (BFCRS) was administered twice weekly to assess improvement in catatonic symptoms over a period of three weeks. The two groups were compared using two-way RMANOVA. **Results:** BFCRS scores reduced markedly over treatment course and this reduction was more profound in the ECT group (p=0.035). Shorter the duration of illness greater was the response (lower scores of BFCRS). **Conclusions:** Superior clinical efficacy of ECT over neuroleptics in catatonia is confirmed by this randomized clinical trial.

Key words : Electroconvulsive therapy, catatonia, risperidone.

INTRODUCTION

Catatonia is a syndrome of motor abnormalities in association with disorder of mood, behaviour or thought (Mahendra, 1981). Catatonia is both a symptom and diagnosis by itself. It is a medical emergency. A detailed review of organic conditions producing catatonia is described elsewhere (Ahuja, 2000). Functional illnesses, which produce catatonia, include mood disorder (mania and depression), schizophrenia and/or dissociation. Rarely it can be a manifestation of other psychiatric illness such as obsessive-compulsive disorder (Jagadeeshan et al, 2002). Benzodiazepine, particularly lorazepam, is the treatment of choice in functional catatonia (Greenfield et al, 1987; Bush et al, 1996a; Payce et al, 1999). Nearly 70-80% of the patients improve within 48-

72 hours of lorazepam trial (6-8mg/day). Electroconvulsive therapy (ECT) is an alternative form of treatment in catatonia. ECT is found to be useful in lorazepam non-responsive catatonic patients (Rohland et al, 1993; Bush et al, 1996a). Catatonic symptom in severe depression also had a good prediction to ECT response (Abrams, 1997; Joseph, 1999). Many psychiatrists consider catatonia as a subtype of schizophrenia and have therefore used neuroleptic drugs with success (Joseph, 1999). Other agents used in the treatment include amobarbital, lithium and carbamazepine (Abrams and Taylor, 1976; Abrams, 1997). However their use is limited in clinical practice. There are also no comparative trials with these agents in the treatment of catatonia. This study compared the efficacy of ECT over antipsychotic drug - risperidone

in lorazepam non-responsive non-affective catatonia.

MATERIALS AND METHODS

Subjects

Drug naive inpatients (n=68) with a diagnosis of non-affective functional catatonia were considered for the trial. The clinical diagnosis (ICD-10; WHO, 1992) was made based on the detailed history obtained from patient's relatives and previous records. All patients received a trial of lorazepam (6-8mg/day PO or i.v. for a maximum period of 5-days). Fifty patients (73.5%) responded to treatment. Those not responding (having at least two catatonic signs; n=18) were considered for the study. None of the patients had any history suggestive of underlying organicity. None had received ECT in the past. Basic investigations (complete haemogram, biochemistry, serum electrolytes and urine examinations) were normal. The clinical diagnosis in lorazepam non-responsive patients was confirmed independently by another psychiatrist (GK) during the study period by clinical interview. Nine received a diagnosis of schizophrenia, five had psychosis NOS while the rest four had depressive catatonia. Depressive catatonic patients were excluded from analysis. Thus the final sample consisted of 14 patients (3 females). The mean±SD age of the sample was 23.8±4.1 years (range 20-47 years). They were randomised into one of the two groups (GK). One group received true ECT plus placebo (ECT group; n=8) while the other received sham ECT plus risperidone (risperidone group; n=6). Lorazepam was stopped in all patients before entering the study. The study was for a period of three weeks.

Consent for the study was obtained from the spouse or a nearest family member and also from the patient during the study period when he was able to provide consent. The psychiatry department at National Institute of Mental Health and Neurosciences, Bangalore approved the study protocol.

Treatment

Patients in ECT group received bilateral

modified ECT prescribed thrice weekly until clinical improvement was maximum and maintained for at least one week. Threshold was assessed at first ECT session using titration method and in subsequent sessions marginally suprathreshold doses (60mC + threshold) administered. Thiopentone (4mg/kg body weight), succinylcholine (1mg/kg body weight) and atropine (0.6mg) were used for modification. Cuff method was used to record motor seizure duration and computerized EEG was used for recording cerebral seizure at all ECT sessions. These patients also received oral placebo given in BID doses. No psychotropic medications were administered during the study period except in one for agitation (lorazepam 2mg at night). After the completion of the study period patients were started on risperidone (4-6mg/day).

Patients in risperidone group received oral risperidone in BID doses, 2mg per day (day-1) and that was increased to 4 to 6mg over two to four days until patient developed subtle extrapyramidal symptoms (EPS). Sham ECT was administered at thrice weekly ECT using intravenous thiopentone (4mg/kg body weight). The BP cuff was tied in the right leg and the EEG electrodes were applied over the scalp in sham ECT patients too.

Rating scales

In lorazepam non-responsive patients (n=18), the clinical diagnosis was confirmed by clinical interview (ICD-10; WHO, 1992) by another psychiatrist (GK) at baseline and during the study period.

Patients were evaluated for catatonic signs severity using Bush-Francis Catatonia Rating Scale (BFCRS; Bush et al, 1996b) administered before ECT (baseline) and twice weekly thereafter. Another psychiatrist (GK) administered BFCRS on the fifth day of lorazepam treatment. Patients who had no or only one catatonic sign on BFCRS were termed 'responders'. Those who had more than one were termed 'non-responsive' and continued in the trial.

Psychopathology was assessed once every week using Positive and Negative Syndrome Scale (PANSS; Kay et al, 1987). PANSS was not administered at baseline (as formal

interview was not possible). Scores were available in only eight patients at the end of one week and for all patients at the end of second and third week.

Columbia side-effect checklist (Sackeim et al, 1987) for ECT-induced side effects and Simpson-Angus rating scale (Lejoyeux et al, 1993) for risperidone-induced extrapyramidal side effects were administered once every week in all patients. A single psychiatrist (GNS) administered all the above rating scales through out the study period. He was blind to randomisation.

Statistics

Fisher's test was used to compare the demographic and clinical characteristics of the patients between the ECT group and risperidone group. The diagnostic agreement between the two raters in 18 patients was assessed by Kappa. The interrater reliability on baseline BFCRS score was measured by intraclass correlation. Two-way RMANOVA was used to compare the BFCRS scores between the ECT group and risperidone group over three-week period. Similarly PANSS scores available at the end of second and third week were compared between the two groups using two-way RMANOVA.

RESULTS

All subjects (n=14) completed the 3-week study period. The demography and clinical data of the ECT and risperidone groups are given in Table-1. The two groups were comparable. The clinical diagnosis had high interrater reliability (Kappa=0.75). The mean baseline BFCRS scores were similar between the two groups (Fig-1). The intraclass correlation coefficient was 0.76.

Both groups demonstrated an improvement in BFCRS by the end of third week. The improvement was greater in ECT group compared to risperidone group at any treatment week and was statistically significant (p=0.035, Fig-2). In ECT group, ECT was required to be continued beyond the three-week study period in four patients. In three patients of the risperidone group, ECT was advised after the study period.

PANSS scores improved both in the ECT group and the risperidone group by the end of third week. The improvement in positive psychopathology scores was significantly greater in ECT group compared to risperidone group (p=0.04).

There were no major untoward side effects either with ECT or risperidone.

TABLE 1: Sociodemographic and clinical variables between ECT group and risperidone group (mean±SD)

Variables	ECT Group (n=8)	Risperidone Group (n=6)
Age (years)	24.7±4.7	22.5±3.4
Sex (male:female)*	1:7	2:4
Diagnosis (schizophrenia:psychosis NOS)*	5:3	4:2
Duration of illness (months)	33.0±41.9	50.3±40.6
Range (months)	0.25-120	6-108
Duration of catatonic signs (weeks)	14.9±20.7	69.8±113.79
Range (weeks)	1-48	2-288
Baseline BFCRS scores	13.6±3.3	13.0±2.0
Range	8-17	10-15

*frequency.

The two groups were comparable in all the variables measured.

There was higher incidence of headache (n=6) and transient memory impairment (n=4) in ECT group. There was no major on-the-table complication with ECT except one having prolonged seizures at two ECT sessions (aborted using 5mg intravenous diazepam). Two patients in risperidone group had tremors and mild rigidity and received trihexyphenidyl (2-4mg/day) along with risperidone. One had akathisia but no additional intervention was needed clinically.

None had dystonia or neuroleptic malignant syndrome.

DISCUSSION

The results of this study demonstrated that ECT was more efficacious than risperidone in the treatment of non-affective catatonia non-responsive to lorazepam. BFCRS and PANSS scores improved more

with ECT than risperidone and were statistically significant. To our knowledge this is the only double blind randomised study that has compared two different treatments in catatonia. Hence no comparison is possible. The study consisted of a homogenous group of non-affective catatonic patients from a representative inpatient sample. There was high interrater reliability in clinical diagnosis and baseline BFCRS scores.

Most of the catatonic patients (73.5%) improved with lorazepam and within 48-72 hours. This response was in comparison to earlier studies (Greenfield et al, 1987; Ungavari et al, 1994; Bush et al, 1996; Payee et al, 1999). On comparison with the non-responders (n=18), the earlier group had relatively short duration of catatonia (12.5 weeks v/s 38.4 weeks) and were largely males (38 v/s 3).

Unlike lorazepam, which is useful in ameliorating the catatonic signs, ECT also produced marked improvement in underlying psychiatric illness. The PANSS scores improved better with ECT compared to risperidone. Positive symptoms improved more than negative symptoms.

Univariate analysis was attempted to examine predictors of response in catatonia. Patients treated with ECT and shorter duration of catatonia had lower BFCRS scores at the end of three-week. There was no association between the number of catatonic signs and outcome. These findings support earlier observations (Rosebush et al, 1992; Bush et al, 1996).

Response to ECT was dramatic in catatonia in previous studies (Rosebush et al, 1992; Bush et al, 1996). The average number of ECT ranged from 2-4 and clinical improvement was marked. In our study though patients improved with ECT, the average number of ECT was 8.87 (range 6-13) in ECT group. We deliberately selected non-affective catatonia. Nearly 65% of the patients in previous studies had affective illness (Bush et al, 1996). Secondly the duration of catatonia prior to entry in their study was less than a week while it was 38.4 weeks in our study.

Catatonia scores reduced significantly in the ECT group. However four out of eight patients continued to receive ECT beyond a three-week period (10-13 ECT) though

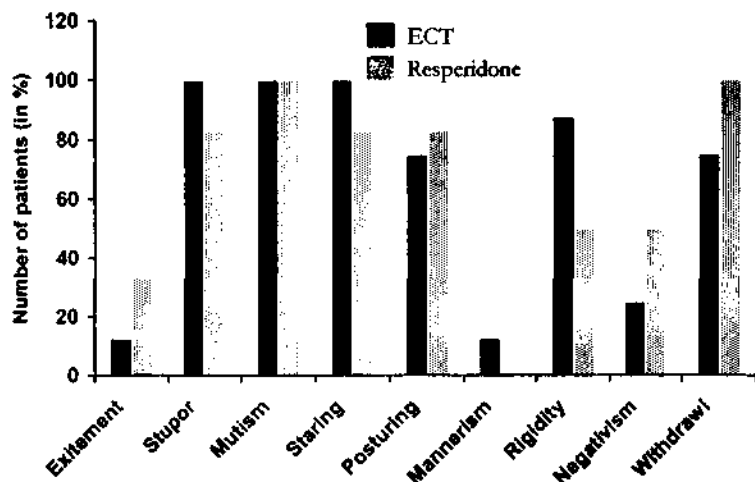


Fig-1. Baseline 14-item BFCRS scores for ECT group and risperidone group. Y-axis indicates the percentage of patients having the catatonic sign. The scores were comparable between the two groups.

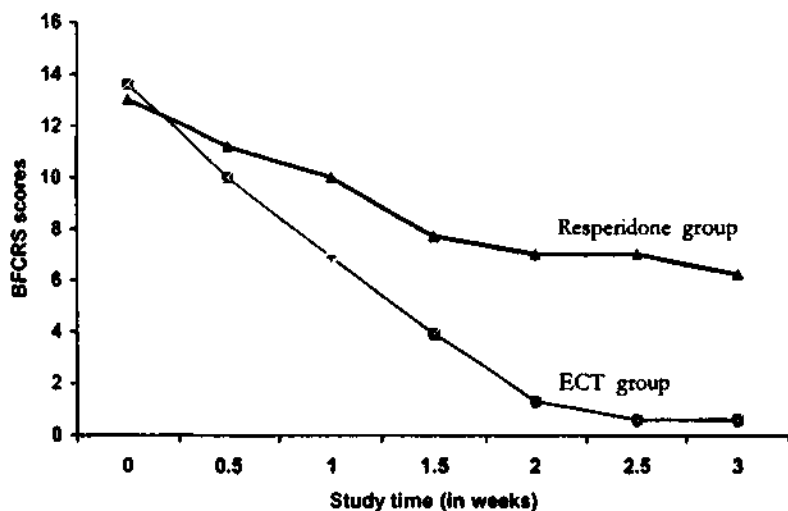


Fig-2. Two-way RMANOVA comparing BFCRS scores over three-weeks between the ECT group and risperidone group.

the catatonic signs had improved. ECT was continued in these patients for their psychotic symptoms. Three patients from risperidone group received ECT along with risperidone (6mg/day) after the study period as the catatonic signs persisted. Two of them completely remitted while the third persisted to have near mutism and negativism. These observations suggest that ECT treatment may be initiated early in catatonic patients, when indicated, to produce maximum benefits. Some advocate the use of ECT to augment antipsychotic response in catatonic schizophrenia (American Psychiatric Association, 1997). However it needs to be explored whether ECT plus antipsychotic drug in catatonia has an advantage over ECT alone.

In this study, four patients were excluded as they had depressive catatonia. It is likely that when patient is brought in catatonic state, the primary diagnosis is difficult to establish. However, once underlying organicity is ruled out and patient is non-responsive to lorazepam treatment, ECT can be administered safely instead of giving a prolonged trial of psychotropic drugs (such as risperidone). In our study too except one who had prolonged seizure, none of the ECT patients had complications. However, EEG and ECG monitoring during ECT may be preferred in catatonics.

Some have argued that addition of neuroleptics in catatonic patients may precipitate catatonic signs (Gelenberg, 1977; Taylor, 1990). There is also risk of NMS (Mann et al, 1986; Philbrick and Rummans, 1994) which is life threatening. However, none in our sample had any such serious effects. However, one has to be cautious and watch for such symptoms and gradually increase neuroleptics if preferred over ECT.

Although ECT is better than neuroleptic drugs in the treatment of catatonia as suggested by our study too, one needs to be cautious in use. Fifty percent of the patients in both the ECT group and risperidone group needed ECT beyond the three-week study period. ECT patients did not obtain total recovery. This may indicate that the extent of improvement with ECT in catatonia may not be as dramatic as generally believed.

There are technical difficulties in con-

ducting trials of this kind. Although ECT is better in catatonic patients the inherent difficulties include: a) most of the patients with catatonia improve with benzodiazepines, b) it is difficult to classify catatonic patients into affective and non-affective illness on presentation, c) if non-affective catatonia, whether risperidone is the choice in treatment or continuing benzodiazepine improves the clinical condition? Under these considerations the results of this study is to be weighed with caution. Further, the limitations of the study. These include relatively small sample size and the study restricted to three-week period. Antipsychotic effects are maximum after three to four weeks of treatment. Also the dose of risperidone was gradually increased over first few days. This might have resulted in lower response in both the catatonic signs and psychopathology scores in the risperidone group.

Summarising the literature existing, benzodiazepam should be chosen as the treatment of choice in catatonia. In those not responding, one should not wait for the prolonged drug trials continuing clinical deterioration. Many have supported the usage of ECT in lorazepam non-responsive catatonia. Fricchione (1989) recommend, "given the significant morbidity and mortality associated with catatonia, ECT should be considered if an expeditious 48-72 hours benzodiazepine trial is unsuccessful". This double blind design favours the usage and safety of ECT over risperidone.

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