RESPONSE TO FIRST ECT IN DEPRESSION : A PREDICTOR OF OUTCOME ?

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ABSTRACT

Response to first ECT in depression and its value as a predictor of response to ECT is a poorly researched subject. Twenty-two antidepressant-free patients of severe depression (ICD - 10) were administered a course of 6 ECTs using bilateral sine-wave electrical stimulation with serial assessments on Hamilton Depression Rating Scale (HDRS). Using ' a priori' definition for 'good response' ($\geq$ 60% reduction is baseline HDRS scores) patients were grouped and analysed. The reduction in HDRS scores after first ECT was significantly greater for Good Responders (GR) in comparison to 'Poor responders'. It appeared that $\geq$ 9% reduction in baseline HDRS scores after the first ECT was associated with 'Good Response'. Thus, it can be concluded that response to first ECT could be taken as a viable predictor of response in depression.

Key Words : Electroconvulsive therapy, depression, predictor, response

Electroconvulsive therapy (ECT) is a useful treatment for psychiatric disorders, especially depression. In comparison to antidepressant drugs, ECT is associated with better and faster response (Coryell, 1978; Gangadhar et al., 1982; Andrade, 1990). While it is generally agreed that the average number of ECT required for optimal response is 6-8 (Taylor, 1982), certain patients require just 2-3 while others may need as many as 10-12 (Kendell, 1981). Some authors describe subgroups of good responders and poor or nonresponders to ECT. In a poor responder, administering ECT would mean exposing the patient to unnecessary cognitive side-effects, more expensive treatment and prolonged hospital stay. Therefore, delineation of factors that predict good response to ECT assumes importance.

Numerous sociodemographic, clinical and ECT-related parameters have been studied in search for 'predictors of response'. Some patients respond from the very first ECT (Keisling 1984; Rich 1984). Therefore, response to first ECT could be a predictor of good response. Andrade et al. (1989) studied 29 drug-naive, non-psychotic endogenous depressives diagnosed according to RDC of Spitzer et al. (1978). Modified bilateral ECT (either sinewave or brief-pulse waveform) thrice a week was administered. A variable number of ECTs were administered till the patients recovered or had plateauing of response. Satisfactory response was prospectively defined as $\geq$ 75% reduction in baseline HDRS scores. This study found response to first ECT as a predictor of outcome. However bias in sample selection, control for the setting of treatment as well as the number of ECTs given were not taken care of. There is a paucity of similar research and this study was carried out to determine whether the response of an endogenously depressed patients to the first ECT predicted the ultimate

response to ECT.

MATERIAL AND METHOD

Sample : The study sample comprised a single group of 22 subjects admitted to the inpatient unit with the ICD-10 (World Health Organisation - WHO, 1992) diagnosis of current "severe depressive episode with or without psychotic features". For patients on antidepressant therapy before the start of inpatient treatment, a 5 day washout period was given (Extein et al., 1984). Patients with organic/physical illness, ECT in the previous 6 months and those who had any contraindication for the administration of ECT were excluded from the study.

Design of the study : The study had a prospective design with serial assessments of the severity of depression before and during the course of ECT.

ECT-description and schedule : The ECT device was an electronic sinewave model manufactured by Associated Electronic Engineers, Bangalore, India. There was, however no facility for EEG monitoring in the ECT machine. Patients were administered modified ECT three times a week i.e. on Mondays, Wednesdays and Saturdays at relatively fixed times between 9 am and 10 am. Anaesthesia was given by thiopentone sodium (150-300mg) and succinylcholine (30-50mg) was used as a muscle relaxant. All were premedicated with atropine and ventilated with 100 percent oxygen during induction and recovery after ECT. ECT was administered by one of the authors (NG) using standard bilateral fronto- temporal electrode placement. The initial stimulus was 110 V for 0.6 seconds. During each ECT, voltage and duration parameters were noted. Seizure duration was measured by the cuff-method using two trained observers (Addersley and Hamiltion, 1953). Occurrence of seizure duration i.e. presence of convulsion in the cuffed arm for at least 20 seconds was required for an adequate seizure (Andrade, 1993). If there was inadequate seizure response, then restimulation was done at a higher voltage (raised by 10V) and/or with greater time duration (increased by 0.1 sec-

onds). This was required in only one patient on a regular basis.

No concurrent medicines, apart from benzodiazepines, were used during the inpatient stay. Benzodiazepines were administered whenever necessary (e.g. for night time sedation), and a careful record was kept. Of the total subjects, three did not require these, whereas others needed them for night-time sedation. An average dose of 14.08 mg of Diazepam equivalents were required for each patient during the course of ECT.

Operational criteria : A maximum of 6 ECTs were planned for each patient. The course of ECT was limited to 6 as an endogenously depressed patient generally requires an average of 6-8 ECT (Taylor, 1982). However, any patients who had a scores of less than 8 on HDRS, as given by Bech et al. (1975), was deemed to have recovered and ECT was stopped.

Therefore, two sets of 'a priori' definitions were kept for determining 'Good response' to ECT. In terms of percentage reduction, 'Good Response' was defined as sixty percent or greater reduction in baseline HDRS score (Sackeim et al., 1987) while in terms of absolute final HDRS scores, it was defined as HDRS < 8 by the end of the course of ECT.

Assessment : After obtaining informed consent from the patients and/or their relatives, severity of depression was assessed on the 21 item HDRS (Hamilton, 1967) by the principal investigator. All the ratings on HDRS were done by the same rater. HDRS was administered one day prior to the commencement of the course of ECT and again about 30 hours after each ECT. This was done so as to avoid the effect of diurnal variation of mood and influence of ECT related immediate side effects on the assessments.

Statistical analysis : Sociodemographic variables in the group were subjected to either Chi-square test or Fisher's Exact Probability Test. Parametric values were analysed by Student's t-test.

RESULTS

This study was carried out over a period

of 15 months. Of 35 patients screened, 10 did not fulfil the proposed diagnostic criteria while 3 patients did not give consent. The remaining 22 patients were included. Fourteen were antidepressant naive and eight were given the minimum required washout period. After completion of the prescribed course of ECT, the patients were evaluated for the degree of response. Using the first 'a priori' definition for Good Response i.e. based on percentage reduction, the sample was subdivided into 'Good Responders' (GR) (N=11) and 'Poor Responders' (PR) (N=11). These two groups did not differ on any sociodemographic variables (sex, marital status, education, family type, locality etc).

The two groups of subjects did not differ from each other on baseline HDRS scores (H_0) as well as the scores obtained after the first ECT (H_1). However, there was statistically significant difference in the scores obtained between the baseline and post-first ECT assessments H_0-H_1) (Table 1). Converting the reduction in HDRS scores from pre-ECT to post-first ECT into percentage values, it was seen that there was mean reduction of 23.40% and 7.21% in 'Good responders' and 'Poor Responders' respectively. To individualize the concept of degree of response, percentage reduction scores after the first ECT were calculated and plotted. On visual scan, it was seen that a 9% attenuation of the baseline HDRS scores after the first ECT could differentiate fairly distinct groups of 'Good Responders' and 'Poor Responders' to ECT (Figure 1). Nine patients had a ≥ 9% reduction in HDRS scores in GR group while nine patients had < 9% reduction in HDRS scores in PR group. To test whether there was any significant difference in the two groups, chi-square test (with Yates correction) was applied. It was seen that both groups differed significantly as regards the number of patients showing ≥9% HDRS reduction (X^2=6.55; d.f.=1; p<0.01). Additionally, misclassification of two subjects each in both these groups yielded a sensitivity value of 81.8% and a specificity value of 81.8%. The overall positive and negative predictive values obtained were 81.8% each.

Quantification of response to the first ECT showed that ≥ 7 HDRS points reduction indicated a GR while < 2 HDRS points reduction indicated a PR (Table 1). On visual scan, however, it was seen that only four GR had ≥ 7 HDRS points reduction whereas eight PR had < 2 HDRS points reduction after the first ECT (Figure 2). In terms of percentage reduction in baseline HDRS score, ≥ 9% reduction would indicate again a GR. Having evaluated the sample on basis of percentage reduction in HDRS score, the same was reclassified on the basis of the second 'a priori' definition for good response; based on the absolute final HDRS score. Using this definition, there were 10 GR and 12 PR. Both these groups were comparable on sociodemographic variables. The baseline and post-first ECT HDRS scores, for both groups, were comparable (Table 2). The difference in the baseline and post-first ECT HDRS scores was also comparable (Table 2).

TABLE 1
HDRS SCORES IN THE 'GOOD RESPONDERS' AND 'POOR RESPONDERS' GROUPS DERIVED ON BASIS OF PERCENTAGE REDUCTION IN HDRS SCORES

Parameters	Good responders (N=11)	Poor responders (N=11)
Baseline HDRS (H_0)	28.73 (5.27)	26.91 (4.72)
	t=0.852; d.f. = 20, NS	
Post-first ECT HDRS (H_1)	21.91 (7.50)	24.91 (5.24)
	t=1.087; d.f.= 20, NS	
(H_0-H_1)	6.82 (6.71)	2.00 (3.29)
	t=2.120; d.f. =20, NS	

FIGURE 1
PERCENTAGE REDUCTION IN HDRS SCORES IN GOOD RESPONDERS AND POOR RESPONDERS


PERCENTAGE VALUES
· Poor Responders   - Good Responders
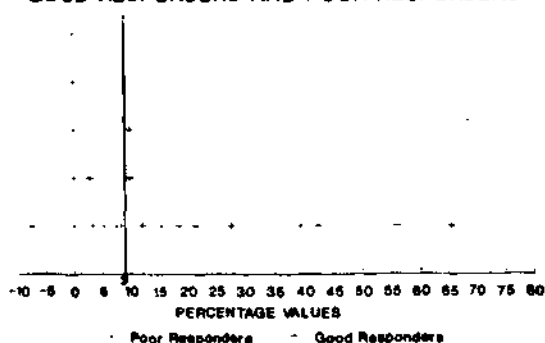
TABLE 2
HDRS SCORES IN THE 'GOOD RESPONDERS' AND
'POOR RESPONDERS' GROUPS DERIVED ON BASIS
OF ABSOLUTE FINAL HDRS SCORES

Parameters	Good responders (N=11)	Poor responders (N=11)
Baseline HDRS (H_0)	28.00 (4.94)	27.67 (5.21)
	t=0.153; d.f. = 20, NS	
Post-first ECT HDRS (H_1)	21.50 (7.78)	25.00 (5.01)
	t=1.276; d.f.= 20, NS	
(H_0-H_1)	6.50 (6.98)	2.67 (3.89)
	t= 1.620; d.f. =20, NS	

FIGURE 2
ABSOLUTE REDUCTION IN HDRS SCORES IN
GOOD RESPONDERS AND POOR RESPONDERS

· Poor Responders   ⁻ Good Responders
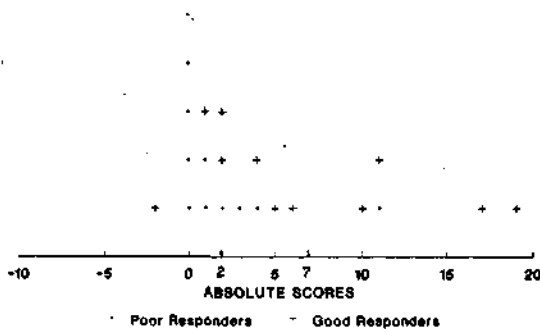
DISCUSSION

In the search for predictors of response to ECT only a few studies have investigated the 'response to first ECT' either directly or indirectly. The first experimental evidence was provided by Price et al. (1978) on a sample of 14 patients who received ECT along with antidepressant drugs. These workers demonstrated that response to the first two ECT correlated highly with the overall change in affective state after completion of the course of ECT, regardless of the number of ECT administered. Later, Rich and Black (1985) reported that first ECT was associated with the maximum antidepressant effect. However, these two studies did not ascertain the correlation of 'response to first ECT' with the overall response and also did not attempt to quantify it.

We show that the response to first ECT differentiated between the good responders and poor responders to ECT. However, this was not helpful in predicting as to which patient would recover before or by the end of course of six ECTs. Each good responder but one recovered before or by the end of course of six ECTs. Therefore, it appears that shift of one patient led onto different results in the groups derived from the two sets of 'a priori' definitions, which could be a reflection of the small size.

Our study supports the observations of Andrade et al. (1989), who demonstrated that ECT responders show a greater response to the first ECT. Our finding that a 9% reduction in the baseline HDRS scores could help classify patients into good responders and poor responders is somewhat different from the 15% reduction proposed by Andrade et al. (1989). There are differences between these two studies on the use of diagnostic criteria (RDC instead of ICD-10), 'a priori' criteria of good response ($\geq$ 75% instead of $\geq$ 60%), and quality of depressives (only non-psychotic versus both psychotic and non-psychotic). In fact, the use of RDC criteria by Andrade et al. (1989) compromised the sensitivity obtained due to inclusion of patients with additional diagnosis of 'minor depressive disorder', which has been circumvented in this study.

Although there was the additional finding that $\geq$ 7 points reduction in absolute HDRS score was associated with a good response (Table 1), yet the visual scan did not appear to support this result (Figure 2). Therefore, it can be concluded that probably percentage reduction in HDRS score appears to be a more viable yardstick, for predicting type of response to the ECT, than absolute reduction in HDRS scores.

Caution should, however, be exercised in relation to the generalisability of the findings. The results so obtained do not necessarily apply to right unilateral electrode placement or brief pulse ECT methods of treatment and even to all diagnostic or clinical (unselected vs. treatment-resistant) categories of depression. Also, it could be possible that about 20% of the good responders may have been missed.

This study was carried out on antidepressant free patients with a rigorous methodology. However, there were certain limitations viz small

sample size, course of ECTs restricted upto a maximum of six and the possibility of poor responders at the end of 6 ECTs turning out to be good responders with further course of ECTs.

To conclude, response to first ECT may itself act as a predictor of outcome. Further research is required to confirm these findings. This would help in giving more rational treatment with lesser cognitive side-effects and treatment costs. But such a practice may be unacceptable to some on account of using ECT as a therapeutic trial.

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