

CLINICAL PREDICTORS OF SEIZURE THRESHOLD IN BILATERAL ECT

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ABSTRACT

Research on determinants of ECT seizure threshold is inadequate. In view of differences in ECT populations and confounding factors, there is a need for examining this in our population. Consecutive consenting inpatients (N=100), referred for bilateral (BL) ECT by treating psychiatrists at National Institute of Mental Health and Neuro Sciences Hospital, Bangalore, formed the sample for the study. Thiopentone, succinylcholine and atropine were used for modification. Seizure threshold (dependent variable) was determined by titration method at the first ECT. The independent variables were age, gender, diagnosis, illness severity (Clinical Global Impression; CGI), concurrent drugs, head circumference (HC) and inion-nasion distance (IND). Age, IND and CGI severity predicted seizure threshold in forward, stepwise, linear regression model.

Key Words : ECT, seizure threshold, predictors

Seizure threshold is the minimum electrical stimulus which yields an adequate seizure (25 seconds on EEG) (American Psychiatric Association, 1990). Recent literature provides ample evidence that stimulus relative to the seizure threshold is more important than the absolute stimulus in determining the therapeutic and adverse effects of ECT (Sackeim et al., 1987).

Threshold can vary several folds both within an individual over sessions and across individuals. Various factors influence seizure threshold. Age increases the threshold (Sackeim et al., 1987). Males have higher threshold than females (Sackeim et al., 1987) but not consistently replicated (Beale et al., 1994). Manics have lower threshold than the depressive (Mukherjee et al., 1994). Threshold increases with increasing ECT schedule (Janakiraniah et al., 1992). Threshold may increase with antiepileptic drugs and decrease

with proconvulsants (caffeine, theophylline, clozapine and perhaps even lithium). More recently, McCall et al. (1993) observed an effect of head size; larger inion-nasion distance (IND) was associated with higher threshold. This observation needs application and if confirmed, may explain the sex differences too.

MATERIAL AND METHOD

Consecutive consenting inpatients who were prescribed bilateral ECT (BLECT) by treating psychiatrists at the National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore, were screened. Patients with history of ECT in the past six months, epilepsy and medication known to influence seizure threshold (Carbamazepine, n=1; clozapine, n=2; xanthine alkaloids, n=2) were excluded. The final sample was 100 (male = 59, female=41). All patients were diagnosed

according to the ICD-10, (WHO, 1992). Severity of illness was assessed using the Clinical Global Impressions (CGI, Guy, 1978) by the same clinician (KG). IND and head circumference (HC) were measured using a nonstretch tape. Patient's age, sex and treatment with concurrent drugs were recorded. Detailed physical examination was done to rule out the contraindications for ECT.

General anaesthesia was given using thiopentone (3mg/Kg), succinylcholine (0.75mg/Kg) and atropine (0.65mg) intravenously. Positive pressure ventilation with 100% oxygen was given throughout the procedure using a face mask. The partial pressure of oxygen in the arterial blood (PaO₂) was maintained between 95% and 100%. The Cardiocap II pulse oximeter continuously monitored the heart rate, blood pressure, electrocardiogram (EKG), and PaO₂ till spontaneous and regular respiration.

Stimulus was administered using the computerized ECT system developed by NIMHANS in collaboration with the National Institute of Quality and Reliability (NIQR). This delivers constant current (800mA), bipolar brief pulse (1.5 msec wide and 125 pps) stimulus of varying train length. In the 'Auto' mode of this computerized machine, stimulus increments (upto a maximum of 540 mC) in nineteen steps can be chosen by increasing duration of stimulus train. However in the 'manual' mode other parameters too can be varied. For this study the 'Auto' mode was used. Stimulus electrode placement was bifrontotemporal. The stimulus dose was titrated with an initial setting dose of 30mC. If the seizure was not adequate, the first two increments were in steps of 15mC. Subsequent increments, if required, were in steps of 30mC. Patients were restimulated with higher setting after one minute in case of subconvulsion (EEG seizure <25 seconds) and after 20 seconds in case of no EEG seizure. EEG was recorded on two channels from F₃ and F₄ leads referenced to ipsilateral mastoids according to international 10-20 system. The EEG seizure duration was measured in seconds by

displaying the EEG on a computer monitor (Gangadhar *et al.*, 1995) and adequate EEG seizure (≥ 25 seconds) was ensured in all patients. The mean \pm SD of EEG seizure duration was 79.2 \pm 51.2 seconds (range 25-250 seconds). The motor seizure was monitored using the cuff method on the right side. Ten patients did not have adequate motor seizure. In the remaining ninety patients the mean \pm SD of motor seizure was 52.2 \pm 38.3 seconds (range 15-80 seconds). The mean \pm SD threshold was 96.4 \pm 42.7mC (range 45-240 mC). Prolonged seizures (≥ 120 seconds, n=15) were terminated by 10mg intravenous diazepam.

Statistical methods : Pearson's correlation coefficients were computed to examine the relationship between seizure threshold and each of the continuous clinical variables (age, head measurements and illness severity). Sex and diagnosis (affective/nonaffective) as well as presence or absence of each of the concurrent drugs (Phenothiazines, tricyclic antidepressants, lithium, benzodiazepines and other neuroleptics) were dichotomous variables. Independent sample t-test was used to test the differences in threshold within each variable. The relationship between the dependent (seizure threshold) and the independent variables was examined using forward, multiple, stepwise, linear regression analysis. The significance (*) was fixed at 5% or less.

RESULTS

Threshold correlated positively and significantly with age and IND (Table-1). Threshold was also higher in those with more severe illness though this was not significant. Threshold was significantly lower in females (Table 2). Diagnosis or drug status did not affect the threshold (Table 2). In stepwise linear regression, age ($\beta=0.51$, $p=0.000$), IND ($\beta=0.23$, $p=0.007$), and CGI severity ($\beta=0.17$, $p=0.0486$) accounted for 23%, 5% and 4% of variance in threshold respectively.

TABLE 1
RELATIONSHIP OF SEIZURE THRESHOLD TO CONTINUOUS VARIABLES

Variable	Mean	SD	Range	Pearson's r	p
Age (yrs)	29.5	10.5	13-65	0.5	0
IND (mm)	329.6	18.1	285-381	0.23	0.05
HC (mm)	542.2	19.7	485-610	0.04	0.6
CGI severity	5.3	0.7	3-7	0.17	0.1

TABLE 2
DISTRIBUTION OF SEIZURE THRESHOLD (mC) ACROSS DIFFERENT VARIABLES

Variables	Mean	SD	t	p
Sex				
Male (N=59)	104.5	46.2		
Female (N=41)	84.7	34.3	2.33	0.02
Diagnosis				
Affective disorder (N=48)	94.1	43.4		
Non affective disorder (N=52)	98.6	42.1	0.5	0.6
Benzodiazepines				
no (N=61)	92.9	40.4		
yes (N=39)	101.9	46.0	0.4	0.3
Phenothiazines				
no (N=31)	104.7	49.2		
yes (N=69)	92.7	39.2	1.3	0.2
Tricyclics				
no (N=74)	97.4	44.7		
yes (N=26)	93.7	36.9	0.38	0.7
Lithium				
no (N=83)	98.4	43.0		
yes (N=17)	86.5	40.8	1.05	0.3
Other neuroleptics				
no (N=81)	95.6	41.6		
yes (N=19)	100.0	48.2	0.41	0.7

DISCUSSION

Seizure threshold is known to be influenced by various parameters. Hence, the need to optimise the stimulus for an adequate seizure. Repetitive subshocks may add to cardiovascular risk. On the other hand, over stimulation has risk of prolonged seizure and cognitive adverse effects. Studying clinical

factors influencing seizure threshold, therefore, is important for individualising stimulus dose.

The present finding that increasing age, male sex and higher IND were associated with higher threshold (Table 1 and 2) confirm some earlier reports (Sackeim et al., 1987; McCall et al., 1993). However, in view of the possible type 1 error due to multiple univariate tests, multivariate analysis was used. The results indicated that age, IND but not sex emerged as significant factors. It is likely that gender differences in threshold may be due to the differences in head size; larger size was associated with higher threshold. In this sample too men had significantly ($p < 0.05$) larger head size than women (men, IND 333.8 ± 20 mm, HC 547.3 ± 20.0 mm; women IND 323.7 ± 13.1 mm, HC 535 ± 16.6 mm). The role of illness severity (explaining 4% of variance) merits replication before venturing any speculation.

Drug-free status was not attempted as most ECT patients in our country are on concurrent psychotropic medication (benzodiazepines, neuroleptics, antidepressants and lithium). Interestingly, neither benzodiazepines nor other drugs had any relation to seizure threshold. It would be of interest to examine the variables predicting seizure threshold in unilateral ECT.

The relationship of the clinical variables to the threshold can be used to develop a regression equation (Gangadhar et al., in press). Recently Fink (1997) recommended use of a formula method to individualize the stimulus dose. Prospective validation of such an approach is suggested.

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REFERENCES

American Psychiatric Association (1990) The practice of ECT : Recommendations for treatment, training and privileging - background.

Convulsive Therapy, 6 (2), 84-85.

Beale, M.D., Kellner, C.H., Pritchett, J.T., Bernstein, H.J., Burns, C.M. & Knapp, R. (1994) Stimulus dose-titration in ECT : A two year clinical experience. *Convulsive Therapy*, 10 (2), 171-176.

Fink, M. (1997) Stimulus dosing in ECT : the debate. Energy dosing in ECT ; threshold stimulation or formula ? *Convulsive Therapy*, 13 (1), 1-4.

Gangadhar, B.N., Candade, V.S., Laxmanna, G., Janakiramiah, N. & Mahapatra, P.K. (1995) Computers in ECT and paperless EEG monitoring. *Indian Journal of Psychiatry*, 37 (2), 98.

Gangadhar, B.N., Girish, K., Janakiramiah, N., Subbakrishna, D.K., Parameshwara, G. & Prasad, K.M.R. (1998) Formula method for stimulus setting in bilateral electroconvulsive therapy : relevance of age. *The Journal of ECT*, (In press).

Guy, W. (1978) ECDEU assessment manual for psychopharmacology. US Department of Health, Education and Welfare, Rockville, M.D.

Janakiramiah, N., Jyoti Rao, K.M., Praveen, J., Sujatha, B.L., Gangadhar, B.N. & Subbakrishna, D.K. (1992) Seizure duration over ECT sessions : influence of spacing ECTs. *Indian Journal of Psychiatry*, 34, 124-127.

McCall, W.V., Shelp, F.E., Weiner, R.D., Austin, S. & Norris, J. (1993) Convulsive threshold differences in right unilateral and bilateral ECT. *Biological Psychiatry*, 34, 606-611.

Mukherjee, S., Sackeim, H.A. & Schnur, D.B. (1994) ECT in acute manic episodes : A review of fifty years of experience. *American Journal of Psychiatry*, 151, 169-176.

Sackeim, H.A., Decina, P., Parohovnik, I. & Malitz, S. (1987) Seizure threshold in ECT. *Archives of General Psychiatry*, 44, 355-360.

World Health Organisation (1992) The International Classification of Diseases. Edn. 10, Geneva : WHO.

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