Seizural Variables and Clinical Response to ECT : A Follow up Study

Azza A. El-Bakry, T. M.S.A. Gawad, Soaad Mossa, Maha W. Mobasher. and A. A. Khoweiled

This study was carried on a total sample of 105 patients with acute onset of their illness at Abassia Mental Hospital. All patients were receiving bilateral ECT and were further randomly subdivided into 2 groups receiving their ECT treatment, either with a minimal or a moderate suprathreshold stimulus intensity. All patients were subjected to physical and clinical assessment, as well as psychometric assessment. Evaluation of patients was done 1-3 day after admission, once weekly, at discharge and at follow-up 6 weeks after discharge.

(Egypt.J.Psychiat., 2001, 24 : 55 - 73).

INTRODUCTION

Recent years have witnessed an upsurge of research aiming at safer and more effective forms of Elector-convulsive therapy. This led to the renewed interest in understanding how basic electrical stimulus parameters have an impact on the delivery of optimal treatment. It became clear (particularly during the past two decades) that many of the basic assumptions about how ECT should be administered have been challenged by findings from scientific investigations. For example outcome studies using titrated , low dose unilateral ECT have contradicted the long-held view that the elicitation of an adequate generalized seizure is the sine quo non of therapeutic efficacy of ECT (Nobler & Sackeim, 1993) .

For many years, research in ECT has largely ignored the concept of dose response effects in determining optimal stimulus dosing. There appears to be a therapeutic window for the dose of stimulus . It is not the absolute dose which determines clinical response, but the degree by which the stimulus exceeds seizure threshold (Nobler & Sackeim, 1993 & Freeman, 1995).

Regardless of electrode placement, the best results, in terms of the therapeutic effects and minimizing the side effects, are obtained with moderately supra-threshold dose between 50% and 200% (above seizure threshold) (Freeman, 1995; Weiner, 1997 & Fink, 1997). Other seizural variables believed to be correlated with clinical response to ECT are seizure threshold and seizure duration. The term seizure threshold refers to the minimum electrical intensity necessary to produce a generalized seizure of at least a 20 to 25 second duration (Nobler & Sackeim, 1993) . Recent studies indicate that the magnitude of increase in seizure threshold over the ECT course is a positive sign with respect to efficacy and it may result in slowing of clinical response if a fixed dosage is used. This is because the extent to which electrical dosage exceeds seizure threshold diminishes over the course (Sackeim, 1999).

Azza A. El-Bakry, T. M.S.A. Gawad, Soaad Mossa, Maha W. Mobasher, Assistant Professors, and A. A. Khoweiled Lecturer, Department of Psychiatry, Faculty of Medicine, Cairo University.

As regards seizure duration, it has been a long held belief that longer seizures (or at least those that exceeded arbitrary cutoffs of 25 - 30 secs) are more likely to be efficacious (Fink, 1979 ; Abrams, 1988 & APA, 1990). Moreover, other researchers argued that patients are unlikely to respond if the cumulative duration is less than 210 seconds and that beyond 1000, few patients will manifest clinical response if they have not already done (Maletzky, 1978). However other researchers as Sackeim et al. (1991; 1993; 1999) and Nobler et al., (1993) stated that seizure duration is largely independent of efficacy.

The aim of this work was to study the different seizural factors (stimulus dose, seizure threshold and seizure duration) associated with and possibly influencing clinical response to ECT in acutely ill psychiatric patients. Our hope is that research into the ECT stimulus will promote clearer guidelines for the practitioner as to safer and more effective ways to use ECT .

SUBJECTS AND METHODS:

The study was conducted on 105 acute inpatients in Abbasia Mental Hospital after approval of Surveillance Board for Psychiatric Practice . They were subdivided randomly according to a randomization table (Mendenhall, 1968) into 2 groups. A group of 52 patients who received high dose stimulus energy, the second group consisted of 53 patients who received a minimal suprathreshold stimulus energy for seizure induction. All patients were on psychotropic medication the dose and type of which were adjusted by the attending psychiatrist, but no patient was taking benzodiazepines, lithium or anticonvulsant medications, and patients were kept only on one type of medication during the study period, whether antipsychotic or tricyclic antidepressants.

Inclusion criteria:

Consent from the patient & or family for inclusion in the study and receiving ECT.

Acute onset: of their presenting illness or episode.

Age : 16 60 years.

No ECT for the previous 6 months.

No symptoms suggestive of organic cerebral disease .

No serious physical illness.

Exclusion criteria :

An admission period of less than 2 weeks.

Discontinuation of ECTs before the 3rd one.

Side effects from treatment procedure.

Chronic and sub-chronic cases.

METHOD :

A full psychiatric sheet and full physical examination including detailed neurological examination were carried out for each patient. Patients were diagnosed by 2 psychiatrists using DSM IV axes.

Assessment Procedures :

Patients were assessed 1-3 days after admission (i.e. baseline assessment) then on weekly basis for six weeks, then six weeks following discharge (follow up assessment) by the following instruments :

Brief Psychiatric Rating Scale: (Bigelow ad Murphy, 1979) .

Nurses Observation Rating Scale (NORS) (Shaalan & El Gueneidy, 1982)

The Global Assessment scale (Endicott et al., 1976).

Clinical Global Impressions Scales (Guy,1976):

A) of Severity of Illness. B) global Improvement.

The Family Opinion rating scale.

Montgomery and Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979).

ECT Administration :

ECT was administered three times a week. The total number of treatments was determined by the attending psychiatrist according to each patients clinical response. The number of ECT treatments ranged from 3 to 10. Anesthesia was induced with sodium thiopental preceded by atropine sulfate. Stimulus electrodes were in the standard bitemporal position for all patients .

Stimulus Dosing and Delivery :

Convulsions were induced using a constant current, pulsatile, square waveform instrument (MECTA model JRI).

For identification of the seizure threshold of each patient, the stimulus dose of the 1st treatment was specified according to a titration method (Coffey et al, 1995). For the second treatment, patients were randomized either to continue on the same schedule of titration or to receive a moderately supra-threshold stimulus (150% of the initial dose) (Sackeim and Weiner, 1995).

Monitoring of the seizure:

The peripheral motor seizure duration was timed with a stop-watch from the end of the warning tone of the electric stimulus to the cessation of all observable clonic activity. Convulsions were observed for their characteristics, however, all were bilaterally distributed and consisting of tonic and clonic convulsions and including muscles of the face, body and extremities.

Data Management and Statistical Analysis:

The data was coded and entered on IBM Compatible Computer using the statistical package SPSS veer 8.0. The mean, standard deviation and percent were used to summarize the data. The t test and ANOVA were used to assess differences between groups. For internal consistency and statistical reliability we used the Alpha reliability test. Kappa test was used to assess inter-rater agreement.

Correlation for degree of association and stepwise regression analysis were also used.

RESULTS

The majority of patients were literate, single and residing in an urban area . The most frequent diagnosis was that of schizophreniform disorder (45.8%), followed by bipolar disorder (31.4%). As regards axis II the most common trait disorder was the schizoid (32,4%).

Table (2) shows comparison between the mean scores of patients who received high dose (n = 52) and low dose (n = 53) stimulus energy.

As the table shows, there is a significant difference between the mean (total, positive and negative) scores of the BPRS only on ratings after the ECT course ($P < 0.05$), with lower mean scores for the group who received the high dose stimulus energy. No significant difference is shown at discharge or at follow-up mean scores.

As tables 3 and 4 show, patients receiving high dose energy stimulus showed significant improvement from week to week over the first four weeks, while, for those receiving low dose, the significant difference reflecting improvement continued up till the sixth week. As reflection of improvement, patients receiving high dose were dis-

charged more rapidly than the patients receiving low dose.

Table (5) shows no significant correlation between the total number of ECT treatments during the administered ECT course and the Clinical response ($p > 0.05$).

Table (6) Shows a significant negative correlation between the peripheral motor seizure duration of the 1st ECT treatment and scores of BPRS and NORS after the ECT course ($p< 0.01$, $p< 0.05$ respectively). Also a significant negative correlation is shown at discharge for the scores of BPRS, NORS, MADRS, and CGI of severity of illness. This means that the longer the seizure duration the lower the scores obtained and the better the response.

Table (7) shows no significant correlation between the total peripheral motor seizure duration and the scores of the different scales after the ECT course and on discharge except of MADRS at discharge.

Table (8) shows a continuous increase of mean seizure threshold through ECT course .

Table (9) shows no significant difference between patients with and without history of ECT treatment as regards their mean seizure threshold ($p=0.08$).

Table (10) shows a highly significant negative correlation between patients seizure threshold and seizure duration of the 1st ECT treatment ($p = 0.000$), this means that the higher the patients seizure threshold the shorter the seizure duration.

Table (11) shows a difference between the means of seizure threshold of males ($n = 62$) and females ($n=43$). However this is not statistically significant ($P=0.59$).

Tables (12, 13) show no significant correlation between the dose of 1st week of either antipsychotic or antidepressant medications and patients seizure threshold ($P > 0.05$).

Table (14) shows no significant difference between patients with different diagnoses and their mean seizure threshold ($p = 0.132$).

Table (15) shows a positive significant correlation between the patients seizure threshold and their age ($p = 0.001$). This means a higher seizure threshold for older patients.

Table (16) represents correlation between different factors and clinical response of patients receiving ECT group by a stepwise regression analysis.

As shown from the table ratings after the ECT course show a positive correlation between the BPRS baseline scores and the total BPRS and NORS scores ($sig = 0.00$), which means that the higher the symptoms scored at base line the higher the scored symptoms after the ECT course.

Also a negative significant correlation is shown between the degree of previous improvement to ECT treatment and the Total NORS scores, and between the dose of stimulus energy and the MADRS scores. This means that the more the degree of previous improvement to ECT treatment the more the improvement after the ECT course on the NORS, and the higher the dose of stimulus energy the lower the scores of depression.

For the discharge ratings, the table shows that the presence of diagnosis of schizophrenia is the 1st variable influencing the total BPRS scores, followed by the patients age and lastly the presence of personality disorder. This means that these 3 variables are associated with higher scores and worse outcome on BPRS scores at discharge.

Table 1
Demographic and Clinical Characteristics of Subjects

Mean age (years)		Diagnosis
Sex :		**Axis I**
Male 62 (59%)	female 43 (41%)	Schizophrenia Paranoid type with
Occupation :		Episodic course 14 (12.4%)
Student	17 (16.2%)	Schizophreniform disorder with
Housewife	25 (23.8%)	Good prognostic features 25 (24.8%)
Not workin	21 (20%)	Schizophreniform disorder without
Working	42 (40%)	Good prognostic features 22 (21%0
Education		Major depressive disorder 11 (10.5%)
Illiterate	15 (14.3%)	Bipolar I Manic without psychotic
Reads & write	8 (7.6%)	Features 14 (13.3%)
Primary	15 (14.3%)	Bipolar I manic without psychotic
Preparatory	30 (28.6%)	Features 19 (181%)
Secondary	27 (25.7%)	**Axis II**
Higher education	10 (9.5%)	No diagnosis 61 (58%)
Marital status		Paranoid traits
Single	65 (61.9%)	Schizoid traits 34 (32.5%)
Married	30 (28.6%)	Antisocial traits 5 (4.8%)
Divorced	7 (6.7%)	Borderline traits 1 (0.9%)
Widowed	3 (2.9%)	Dependent traits 1 (0.9%)
Residence		
Rural	25 (23.8%)	
Urban	80 (76.2%)	

Table 2
Comparison Between Mean Scores of Both Groups
Receiving High and Low Dose Energy Stimulus

Scale	High Dose Energy		Low Dose Energy		t	p
	Mean ± S.D.	N	Mean ± S.D.	N		
After ECT course						
BPRS (Total)	9.23 ± 8.65	52	12.79 + 8.40	53	- 2.14	0.035*
BPRS (+ve)	3.21 ± 5.35	52	6.13+,5.24	53	- 2.82	0.006**
BPRS (-ve)	3.11 ± 2.57	52	4.98 + 3.77	53	- 2.97	0.004**
NORS (Total)	38.90 ± 9.07	52	37.84 + 8.87	53	0.60	0.548
MADRS	7.66 ± 7.28	18	9.30 + 6.44	20	- 0.73	0.468
At Discharge						
BPRS (Total)	7.53 ± 9.57	52	7.37 + 6.80	52	0.10	0.921
BPRS (+ve)	2.55 ± 4.57	52	3.37 + 3.97	52	- 0.98	0.329
BPRS (-ve)	2.69 ± 2.88	52	3.35 + 3.27	53	- 1.10	0.272
NORS (Total)	36.57 ± 9.15	52	34.20 +8.78	53	1.35	0.179
MADRS	2.00 ± 4.07	18	1.60+4.93	20	0.27	0.788
CGI (Severity of illness)	1.65 ± 1.06	52	1.71+1.00	53	- 0.3	0.755
At Follow-up 6 weeks						
BPRS (Total)	10.28± 15.84	42	5.82+8.10	42	1.50	0.139
BPRS (+ve)	5.97 ± 9.06	42	4.15+6.24	42	1.08	0.282
BPRS (-ve)	4.33 ± 4.83	42	3.75+4.19	42	0.60	0.552
CGI (Severity of illness)	1.71 ± 1.71	42	1.45+1.41	42	0.77	0.446
Family Opinion	1.65 ± 0.92	50	1.45+0.77	50	1.11	0.268

Table 3
Mean Total Scores of BPRS of Patients Receiving High and low Dose Energy Stimulus: Comparison from Week to Week Assessment

BPRS Total	High Dose Energy				Low Dose Energy			
	Mean ± S.D	Percentage Decrease of Means	P	N	Mean ± S.D	Percentage Decrease of Means	P	N
Base Line Week I	44.86 ± 17.81 2.1.55 ± 16.95	50.0	0.000 * *	52	48.69 ± 1620 29.66 ± 14.54	39.0	0.000 * *	53
Week I Week II	21.55 ± 16.95 12.55 ± 11.77	41.8	0.000 * *	52	29.66 ± 14.45 18.18 ± 9.87	38.0	0.000 * * *	53
Week II Week III	13.02 ± 11.59 9.55 ± 10.47	36.3	0.034*	45	18.50 ± 14.45 18.18 ± 9.87	38.0	0.000 * * *	51
Week III Week IV	9.53 ± 7.51 6.96 ± 5.95	27.0	0.005*	28	13.00 ± 8.59 9.41 ± 7.78	27.0	0.000 * * *	46
Week IV Week V	7.25 ± 6.65 6.68 ± 5.66	7.9	0.756	16	12.30 ± 7.84 9.60 ± 7.41	22.0	0.000 *	23
Week V Week VI	8.30 ± 6.16 5.90 ± 5.56	29.0	0.208	10	11.64 ± 6.83 9.07 ±7.04	22.0	0.007 * *	14

Table 4
Comparison of Mean Total Scores of NORS of Both Groups of High and Low Dose Energy Stimulus Week to Week Assessment

NORS Total	High Dose Energy			Low Dose Energy		
	Mean ± S.D	P	N	Mean ± S.D	P	N
Week I Week II	68.28 ± 13.61 44.42 ± 12.99	0.000 * *	52	70.25 ± 12.34 51.58 ± 15.53	0.000 * * *	53
Week II Week III	45.82 ± 13.00 40.46 ± 9.69	0.001 * *	45	51.82 ± 13.55 40.32 ± 11.18	0.000 * *	52
Week III Week IV	40.78 ± 9.55 36.85 ± 9.60	0.002 * *	28	41.28 ± 11.18 36.02 ± 9.85	0.000 * *	45
Week IV Week V	37.12 ± 9.46 34.68 ± 7.13	0.105	16	39.36 ± 10.83 36.45 ± 9.55	0.003 * *	22
Week V Week VI	33.45 ± 6.77 31.81 ± 4.93	0.167	11	38.64 ± 9.47 37.92 ± 9.90	0.027* *	14

Table 5
Correlation Between the Total Number of ECT Treatments and the Clinical Response of Patients

Total No. of ECTs (3 - 10)	After ECT Scores		Discharge Scores		F - Up scores	
	r	p	r	p	r	p
BPRS (Total)	0.0179	.068	0.004	0.966	0.043	0.802
BPRS (+ve)	0.210	0.091	0.096	0.329	0.087	0.228
BPRS (-ve)	0.157	0.100	0.106	0.280	0.182	0.232
NORS (Total)	0.031	0.852	-0.184	0.261	0.088	0.229
MADRS	0.023	0.814	0.030	0.759	0.092	.0310
CGI (Severity of Illness)			0.091	0.358		

Table 6
Correlation Between the Seizure Duration of First ECT Treatment and Patient's Clinical Response

Seizure Duration of 1st ECT Treatment (31.66 + 6.66) sec	After ECT Scores		Dischrage Score	
	r	p	r	p
BPRS (Total)	-0.275**	0.005	-0.257**	0.008
BPRS (+ve)	-0.310**	0.001	-0.301**	0.002
BPRS (-ve)	-0.278**	0.004	-0.352**	0.000
NORS (Total)	-214*	0.029	-0.250*	0.010
MADRS	-0.093	0.580	-0.323*	0.045
CGI (Severity of Illness)			-0.338**	0.000

Table 7
Correlation Between Total Seizure Duration and Patient's Clinical Response

Total Seizure Duration (187.05 + 62.76) sec	After ECT Scores		Dischrage Score	
	r	p	r	p
BPRS (Total)	-0.017	0.865	0.009	0.025
BPRS (+ve)	0.047	0.635	0.051	0.604
BPRS (-ve)	-0.024	0.808	0.020	0.838
MADRS	-0.013	0.937	-0.350*	0.029
NORS (Total)	0.160	0.103	0.174	0.075
CGI (Severity of Illness)			0.111	0.258

Table 8
Mean Seizure Threshold Variation Through the ECT Course (53 patients)*

	Seizure threshold (J) Minimum	Seizure threshold (J) Minimum	Seizure threshold	N
1st ECT	11.60	31.00	19.74 ± 5.14	53
2nd ECT	13.60	31.20	20.97 ± 4.91	53
3rd ECT	13.80	33.20	21.92 ± 5.37	53
4th ECT	14.30	43.60	22.20 ± 6.11	47
5th ECT	14.30	43.60	22.20 ± 6.11	35
6th ECT	17.60	29.60	22.64 ± 4.12	10
7th ECT	20.00	29.10	23.25 ± 4.28	4
8th ECT	20.00	29.90	24.95 ± 7.00	2

*Those who continued on titration schedule

Table 9
Comparison of Mean Seizure Threshold of Patients with and without Previous History of ECT Treatment

	Past His. of ECT	N	Mean±S.D.	T	p
Seizure Threshold	No	61	18.36 ± 5.18		
	Yes	40	20.85 ± 8.95	-1.77	0.0980

Table 10
Comparison Between Seizure Threshold and Seizure Duration of 1st ECT Treatment

Seizure Threshold	r	p
Seizure duration	-0.369**	0.000

Table 11
Comparison of Mean Seizure Threshold of Patients With Gender Difference

	Sex	Mean ± S.D.	N	T	p
Seizure Threshold	Male	20.53 ±7.43	62	1.862	0.59
	Female	17.93 ±6.40	43		

Table 12
Correlation Between the Dose of Antipsychotic (Equivalent Dose of Chlorpromozine) Drugs of First Week and Seizure Threshold

Seizure Threshold	r	p
Dose of Antipsychotics of 1st Week	0.113	0.228

Table 13
Correlation Between the Dose of Tricyclic Antidepressant Drugs of First Week and Seizure Threshold

Seizure Threshold	r	p
Dose of Antidepressant Drugs of 1st Week	0.113	0.228

Table 14
Correlation Between Mean Seizure Threshold of Patients With Different Diagnoses

Diagnosis	N	Seizure Threshold (J) Mean± S.D.	F	P
Schizophrenia	14	20.07 ± 5.97		
Schizophreniform	47	17.70 ± 5.59	1.914	0.132
Depression	11	21.81 ± 4.97		
Mania	33	20.93 ± 9.40		

Table 15
Correlation Between Seizure Threshold and Patients Age

Seizure Threshold	r	p
Age	0.314**	0.001

Table 16
Correlation Between Different Variables and Clinical Response (Stepwise Regression Analysis)

Dependent Variables	Independent Variables	B	Beta	T	Sig
After. ECT. Scores					
BPRS (Total)	BPRS Baseline Scores	0.984	0.856	5.301	**0.000
NORS (Total)	BPRS Baseline Scores	0.567	0.546	4.743	**0.000
	Previous Imp*. On ECT	4.253	0.483-	4.192-	**0.000
NADRS	Dose of Stimulus Energy	0.403-	0.580-	2.254-	*0.047
Discharge Scores	Diagnosis of Schizophrenia	20.08	1.129	4.555	**0.001
BPRS (Total)	Age of Patients	0.409-	0.534-	3.422-	**0.002
	Personality trait Disorder	8.983	0.506	2.201	*0.037
NORS (Total)	BPRS Baseline Scores	0.575	0.568	4.446	**0.000
	Previous Imp. to ECT	3.411-	0.397-	3.108-	**0.004
MADRS	Presence of chronic stressors	15.77	0.669	3.897	**0.004
CGI (Severity of Illness)	Diagnosis of Schizophrenia	2.008	0.722	6.517	**0.000
	Gender of patients	0.918-	0.405-	3.7984-	**0.000
	Presence of acute stressors	0.700-	0.306-	2.859-	**0.008
	F.H. of psychiatric disorders	0.279	0.230	2.087	*0.047
Follow-up Scores	Diagnosis of schizophrenia	24.780	0.845	7.604	**0.000
BPRS (Total)	Diagnosis of schizophrenia	3.366	0.865	8.462	**0.000
CGI (Severity of Illness)	Diagnosis of schizophrenia	1.456	0.832	7.821	**0.000
Family Opinion					

Imp = Improvement

For the total scores of NORS, BPRS baseline scores are positively correlated followed by the degree of previous improvement to ECT treatment which is negatively correlated , which means that the better the previous improvement to ECT treatment, the lower the scores of NORS at discharge.

For the MADRS scores, the higher the seizure threshold and the presence of chronic stressors are associated with less improvement of depressive symptomatology.

For the CGI scale (Severity of Illness), diagnosis of schizophrenia is associated with worse outcome, as well as male gender and presence of F.H. of psychiatric disorders. The presence of acute stressors before the onset of the illness is associated with better outcome on CGI scale at discharge .

For the follow up ratings 6 weeks after discharge, the presence of schizphrenia diagnosis is shown as the only variable associated with the higher scores of all scales.

DISCUSSION

Stimulus Dosing and Therapeutic Response:

Results of this study show a significant difference between the rates of the clinical response of both groups, with a quicker response for the higher dose stimulus group. This significant difference is revealed via the mean total, positive and negative BPRS scores rated after the ECT course but disappears at discharge and follow-up. This is also ev-

ident from the rate of discharge of patients in both groups, with earlier discharge of patients in the high-dose stimulus group (number of patients of the high-dose group in week IV was 28 compared to 46 for the low-dose group). Besides, comparison of the week to week mean scores of the BPRS, NORS and CGI (Clinical Global Improvement) of both groups showed the same relation.

The findings of accelerated response with higher-dose stimuli are consistent with those of Robin & Tissera (1982), Sackeim, et al. (1991), Pettinati et al. (1994), and McCall et al. (1995).

Practically, these findings make us aware that increasing the stimulus dose accelerates the clinical response, and this may minimize the number of ECTs required to achieve a therapeutic response as well as the duration of hospitalization influencing the total costs of therapy. This may be of particular interest in patients who are at heightened risk for anaesthesia and ECT treatment. Likewise , if patients manifest serious threatening symptoms e.g. suicidal thoughts, or show a steady but slow clinical response, it might be possible to accelerate their response by increasing the stimulus dose. However, there were no significant difference between the groups receiving high and low dose stimulus energy regarding their response to ECT at discharge and at follow-up 6 weeks after discharge. This indicates that both stimuli with high and low dose energy are grossly equivalent in efficacy, and that the final clinical response is independent of the electrical energy used as long as it results in an adequate seizure. It is to be noted that the American Psychiatric Association (APA) 1990 reported that stimuli marginally above seizure threshold may be less therapeutic than those delivered at higher intensity. On the other hand, grossly supra threshold stimuli may be associated wit greater cognitive side effects. Because of these issues, a moderately supra threshold dosing strategy is recommended.

Number of ECT Treatments :

In this study, there was not a fixed number of ECT treatments prescribed for each patient. This was determined by their treating psychiatrist and according to their clinical response. So patients received a varying number of ECTs during their treatment course which ranged between three to ten ECTs. The number of received ECTs did not correlate with the patients response immediately after the ECT course, at discharge, nor at follow-up 6 weeks after discharge.

This means that patients who responded to a lower number of ECTs did not get worse at discharge or at follow-up, and this is against the suggestions of those who viewed that stoppage of a course of ECT once the patient demonstrates a satisfactory clinical response is associated with a higher relapse rate (Fink, 1994). However, Barton et al. (1973) in their controlled follow up study could not confirm this common rationale of giving additional ECTs to prevent relapse. This is also confirmed by Abrams (1997) who advised to withhold further ECT when a patient shows marked improvement early in a course of ECT, and to follow-up the patient cautiously pending return of symptoms.

Variation of the Seizure Threshold:

Estimated seizure threshold of patients in this study ranged from (6.7 J and 32.3 J) . Which means a (4-5) fold variation . Contributing to the variability of seizure thresholds across different patients are factors like age, sex, diagnosis.

and medication . In this study, a positive significant correlation ; is shown between patients age and seizure threshold. Older patients were requiring higher stimulus energy to elicit a seizure. This has been one of the most consistent research findings in the field of ECT (Sackeim et al., 1987, 1993; McCall et al., 1993 ; Coffey et al., 1995; Shapira, et al., 1996; Colenda and McCall , 1996; Fink, 1997; Mansour, 1997; Scott and Dykes , 1999).

In relation to gender difference, this study did not show a significant difference between the mean seizure threshold of male and female patients. This is contrary to the findings of Sackeim et al. (1987, 1990), which considered gender as one of the most important factors affecting seizure threshold. This may be attributed to the simpler (more clinically oriented) method of titration used in this study .

The present study revealed that there is a significant increase in seizure threshold over the ECT course, and showed no significant difference between the mean seizure threshold of patients with and without past history of ECT treatment. This means that there was a dynamic increase in seizure threshold across the ECT course, and that this increase is not a life time one and most probably subsides after a certain period of time. This is consistent with the findings by Sackeim et al., (1991) ; Nobler et al.,(1994) ; Krystal et al. (1998) ; and Sackeim (1999) . These findings are in favour of the suggestion of an anticonvulsant role of ECT which is linked in some studies to its therapeutic effect (Sackeim, 1999).

Finally, this study showed no significant correlation between either the dose of antipsychotics or antidepressants and seizure threshold. This is consistent with studies suggesting a minimal effects of antidepressants and neuroleptics on seizure threshold (Hashem and Frey, 1988 ; Nobler et al, 1994).

From the previous findings, one can notice that in the present study, age was the only factor which significantly influenced patients seizure threshold. Taking this in consideration, together with the narrow range of seizure variation reported in this study, the recommendation of the use of titration method for each patient receiving ECT to ensure a supra-threshold dose is questionable. Age-based dosing formula provide a simpler and effective method for delivering a supra-threshold stimulus in routine clinical work at the risk of causing increased cognitive side effects in some patients. This method provides a stimulus dose averaging approximately 2.5 times threshold (Weiner, 1980 ; Beale et al. 1994; Enns and Karvelas, 1995).

Seizure duration and Clinical Response :

For the assessment of the relationship between the seizure duration and the clinical response to ECT in this study, seizure duration of the 1st ECT treatment is the one tested for correlation with the outcome . This is because all patients were receiving their 1st treatment with stimulus intensity corresponding to their estimated seizure threshold. A significant correlation was shown between the duration of the 1st seizure and the outcome. The longer the duration the better the outcome. These findings are consistent with the findings of two other Egyptian researchers (Ghazy & Mawsouf, 1996; Mansour, 1997) and with those of Fink (1979). The American Psychiatric Association (1990) reported that, with few exceptions , those seizures that are briefer than 20 seconds and seizure that do not bilaterally generalize are believed to have reduced therapeutic properties. The Royal College of

Psychiatrists (1995) recommended timing of the length of bilateral generalized convulsions, with a minimum of 15 seconds of peripheral motor convulsions at the 1st treatment as one of the criteria of an adequate seizure. The physiological basis of the importance of seizure duration for the efficacy of treatment came from the observation that seizures of shorter duration do not release thyrotropin which was thought to be related to the mode of action of ECT (Dykes et al., 1987 ; Scott et al., 1979 , 1989), and therefore presumably lack the expected physiological impact. On the other hand, many studies failed to show a reliable correspondence between seizure duration and therapeutic effects of ECT, concluding that short seizures are not necessarily less effective than longer ones (Miller et al., 1985 ; Weiner et al., 1986; Swartz, 1993 ; Nobler et al., 1993 ; Abrams, 1997; Sackeim, 1999). Also, others noticed that generalized seizures that meet conservative standards for the adequacy of duration can be reliably produced but may lack therapeutic properties (Sackeim et al., 1987, 1991, 1993, Sackeim 1999). This clinical observation was also noted during this study, patients were showing a good response even with short seizures. The positive correlation found in this study may be inflated by a statistical artifact, where both very long and very short seizures were not disqualified before analysis, which may influence the validity of the linear correlation coefficient (Pearsons). Other possible causes might be the interacting factors influencing the seizure duration or the clinical response.

Another point concerning seizure duration was emphasized by Maletzky (1978) and Warren & Groome (1984), suggesting a therapeutic window for cumulative seizure time, with patients unlikely to respond if cumulative duration is less than 210 seconds or beyond 1000 seconds . In this study, findings do not show any significant correlation between the cumulative seizure time and patients response, This is corresponding with many other negative results (Miller et al., 1985; Weiner et al., 1986; Sackeim et al., 1987; Sackeim 1999) . Also we have to notice that the study of Maletzky (1978), was an uncontrolled study, including patients receiving multiple monitored ECT (MMECT).

To conclude, it seems difficult to take both the seizure duration and the cumulative seizure time as the most important requirements to ensure adequate seizures and to improve the therapeutic efficacy of ECT. Seizure duration may be a necessary condition for efficacy , but it seems insufficient as a measure of seizure activity, it does not express much about its intensity or the uniformity of its distribution through the brain apart form the cerebral cortex, and especially the motor cortex, during peripheral monitoring. Unlike the therapeutic serum level of antidepressants, a therapeutic window for ECT seems unhelpful to be used as an index to decide whether to continue or terminate ECT treatment for patients, long stand clinical observation and assessment is the most important indicator of whether the patient will benefit or not from further ECT treatment. This was one of the recommendations of the Royal Collage of Psychiatrists (1995).

Factors Affecting Seizure Duration:

Studying different factors which may affect the seizure length, results of this study showed a negative significant correlation between seizure threshold and seizure duration , patients with higher seizure thresholds exhibited shorter durations. This is consistent with the findings of other studies (Sackeim et al.,

1991 ; Coffey et al., 1995 ; Shapira et al., 1996).

To study the relationship between stimulus intensity and seizure duration, the second ECT treatment was the one chosen for analysis, because half of the patients were receiving a just above threshold stimulus dose and the other half received a moderately supra-threshold stimulus. No significant correlation was shown between stimulus intensity and the seizure length. This findings is not in agreement with many other studies (Robin et al., 1985 ; Sackeim et al., 1991 ; Zis et al., 1996) suggesting a longer seizure duration with doses close to the the seizure threshold. This was explained by the suggestion that higher doses result in more profound potentiation of endogenous inhibitory process leading to earlier seizure termination (Sackeim , 1999).

A possible explanation for the negative findings in this study concerning the relation between stimulus intensity and seizure duration is that during , the course of ECT and when electrical dosage is unaltered (as in patients who received their course of ECT with a just above threshold stimulus dose), patients who manifest a larger threshold increase will receive dosages closer to the threshold compared with patients with smaller threshold increase. The fact that threshold is dynamic and that electric dose relative to threshold alters seizure duration complicates the attempt to determine covariation between changes in this domain. Also, another possible contributing factor is the sensitivity of the titration method used for determination of seizure threshold , as it is believed that there is a very narrow dosage window around the threshold where a dose increment will lengthen seizure duration.

Also, findings of the present study showed a significant difference between male and female patients regarding their mean seizure duration , Male patients have a shorter seizure duration than females. This may be related to the findings that male patients in this study had a higher seizure threshold. This was also reported by (Alexander et al., 1987; Weiner et al., 1991; and Mansour, 1997) . while some other studies found that seizure duration did not vary with gender difference of patients (Finner , 1954; Sackeim 1991). Also a significant correlation was shown between seizure duration and age of patients, which was reported by others (Weiner et al., 1991; Sackeim et al., 1991; Sackeim 1999).

Stepwise Multiple Regression Analysis of Predictive Factors of ECT Response :

We used stepwise multiple-regression analysis to study the confounding effects of different demographic, clinical and seizural factors influencing response to ECT.

It seems logical that predictive factors emerging immediately after the ECT course are probably more specifically related to ECT, while those that did emerge at discharge might be related to both ECT and the general response of the illness, and finally those emerging at follow-up are more related to the general course of illness.

Following the ECT course, none of the demographic data, and only the degree of the previous response to ECT and the severity of illness at baseline are the clinical factors which entered the final equation. Better scores are obtained by patients with less severe illness at baseline and good history of improvement with previous ECT. This final finding Is consistent with the clinical experience and expectation, where demographic data are not usually inflencing the decision to give ECT, while

good previous response to ECT was recommended as an indication for ECT treatment by the APA (1990). Also, inline with these findings is the study of Lam et al., (1999) where they found no significant clinical predictors of ECT outcome on a stepwise multiple regression analysis. This may be explained by the fact that favorable and unfavorable features do not exist independently of ill patients but tend to group together naturally into syndromes, often with substantial overlap. For seizural factors, the intensity of the stimulus was the only factor which entered the final equation when correlated with only the measures of depressive symptoms.

This means that increasing the stimulus dose above threshold is an important factor for the efficacy of ECT in depressive symptoms.

The diagnosis of schizophrenia entered the final equation at discharge and was the only factor at follow-up measures. From this, we can conclude that diagnosis of schizophrenia is most probably influencing the general response of patients rather than the immediate response to ECT, and that other diagnoses with acute onset like depression, mania and schizophreniform disorders have no great influence on response to ECT.

Age and sex of the patients entered the final equation at discharge, with better scores obtained by female and older patients. Also the presence of personality trait disorder, chronic psychosocial stressors, and positive family history of psychiatric disorders, all appeared in the analysis as associated with a worse response, while acute stressors are associated with better response. However these factors seem more related to the general course of illness rather than degree of response to ECT.

Conclusions

Combined ECT with pharmacotherapy has a superior advantage with regard the speed of clinical response in acutely ill patients. This seems of important value especially in patients at high risk e.g. suicidal and seriously psychotic patients. Global outcome of acutely ill patients at follow-up 6 weeks after discharge is superior with combined ECT and pharmacotherapy. This may be consistent with hypothesis suggesting delayed mode of action of ECT due to alteration in neurological substrates.

The study seems in line with a large body of consistent clinical observations and research studies which reported high rate of relapse following respon se to ECT. Similar rate of relapse is also shown for the control group at follow-up.

Clinical and demographic characteristics reported to exhibit an association with ECT do not predict clinical response. We can not rely on these items in referring patients for ECT. Although some of these variables showed significant correlation with clinical response such as : age, gender difference, personality trait disorder, acute onset of illness, patients diagnosis, however none of them showed same correlation in the final stepwise regression analysis. We can conclude that ECT response is not influenced by delineated individual factors, but, it is the result of the interaction of many different variables.

The extent to which electrical dosage exceeds the initial seizure threshold influence the determination of the speed of clinical improvement to ECT. Moderately suprathreshold stimuli results in a more rapid clinical response compared to lower-doses stimuli. This is of clinical importance especially for patients at high-risk of anaesthesia where proper doses of stimulus intensity will acceler-

ate the response and may minimize the number of ECT treatments. This also applicable for patients with serious symptoms, and when response to ECT is slow or delayed.

The only variable found to correlate with seizure threshold was age. We can conclude that dosing strategies depending on age-base formula are effective and useful for most of the patients in clinical practice. Dose-titration is not a must for all patients, except for very elderly, in whom higher energies might be needed than suggested by age estimation.

Duration of the seizures does not appear to be a function of stimulus energy. Increase in stimulus intensity does not lead to a significant variation in seizure duration. In this study, the absence of a significant correlation between cumulative seizure duration and clinical response, together with the disappearance of such correlation between seizure duration and clinical response in the final stepwise regression analysis, lead us to conclude that seizure duration could not be used as a sole or primary therapeutic variable of ECT.

Clinical response of patients is not correlated with the number of ECT treatments. There is no rationale for giving a fixed number of treatments in an ECT course, or additional treatments after maximal therapeutic response.

RECOMMENDATIONS

ECT practitioners must be aware of the importance of administering a stimulus does which moderately exceeds patients seizure theshold. Thus, the practice of administering the same absolute electrical dose to all patients in no longer tenable.

Stimulus dosage should be adjusted to meet the needs of the individual patient. This could be done either by dose-titration methods or age-based formula.

Therapists should be aware with the increasing patient6s seizure threshold during the ECT course. Stimulus intensity should be raised to ensure a moderately suprathreshold dose.

For seriously-ill patients and for those showing slow or delayed response, it is advisable to increase the stimulus dose for faster improvement.

Prefixed course of ECT should not be routinely prescribed. It is advised to assess patients between treatments for the decision of continuation or termination of the ECT.

It is recommended to combine ECT with pharmacotherapy in acutely-ill patients with different diagnoses for faster improvement.

The field of research on ECT is suitable for further scientific exploration, the present findings both positive and negative, should be confirmed by replication of the study using a group of patients homogeneous in their diagnosis, with controlled doses of treatments, and EEG monitoring for the seizural activity.

Research on ECT should be directed towards identification or risky factors for early relapse Alternative schedules for ECT withdrawal, and maintenance should be tested, aiming to decrease high rates of relapse following ECT.

Using a more sophisticated method for stimulus dose estimation, researchers could examine the relation between seizure threshold increase during ECT course and effectiyeness.

Acknowledgment

We are deeply indebted to Professor. Momtaz Ahmed and Prof. Zeinab Sarhan for their generous support and encouragement.

REFERENCES

Abrams, R. (1988) interview with Lothar Kalinowsky. Convuls ther, 4:24-39.

Abrams, R. (1997) Electro convulsive Therapy. New York: Oxford University Press.

Alexander, L. Miller M, Raymond A, Faber M. (1987) Factors affecting amnesia, seizure duration, and efficacy in ECT. Am J. Psychiatry , 142 : 692 -696.

American Psychiatric Association. Task Force on ECT. (1990) The practice of ECT: Recommendations for treatment, training and privileging. Washington DC: American psychiatric press, Inc.

Barton. J. Mehta, S. Snaith, R. (973) The prophylactic value of extra ECT in depressive illness. Acta Psychiatr Scand, 49 : 386 -92.

Beale. M, Kellner C, Prichett J, Bernstein H, Burns C, Knapp R. (1994) Stimulus dose-titration in ECT: a 2 year clinical experience. Convuls Ther, 10: 171-76.

Bigelow, M. Murphy J.(1979) The Brief Psychiatric Rating Scale. In Hamdy E. et al., 1984. Egyptian J. Psychiatry, (7) : 56 -71.

Coffey, C. Lucke J, Weiner R, et al. (1995) Seizure threshold in Electro convulsive therapy. Initial seizure threshold. Biol. Psychiatry, 37 : 713-20.

Colenda, C. McCall W.(1996) A statistical model prediciting the seizure threshold for right unilateral ECT in 106 patients. Convuls. Ther. 12: 3-12.

Dykes, S. Scott, A, Gow, S, Whalley L. (1987) Effects of seizure duration on serum TSH concentration after ECT. Psychoneuroendocrinology, 12: 477 -82

Endicott, J., Spitzer R, Fleiss J., et al. (1976) The Global Assessment Scule : A procedure for measuring overall severity of psychiatric disturbance. Arch. Gen. Psychiatry, 33: 766 -771

Enns, M. Karvelas, L. (1995) Electrical dose titration for Electro convulsive therapy: a comparison with dose prediction methods . Convulsive Ther, 11: 86-93.

Fink, M. (1979) Convulsive therapy : theory and practice. New York, Raven Press.

Fink, M. (1994) Optimizing ECT. L Encephale, 20 (3) : 297 -302.

Fink, M. (1997) Energy dosing in ECT: Threshold stimulation or formula? Convuls Ther, 13 (1) : 4-6.

Finner, R. (1(54) Duration of convulsion in electric shock therapy. J. Nerv Ment Dis, 119 : 530

Freeman, C. (1995) Prescribing ECT. In : C. Freeman, ed. The ECT handbook. London: Royal College of Psychiatrists. 58-59 .

Ghazy, M. Mawsouf N. (1996) The duration of Induced ECT seizure and therapeutic outcome. Current Psychiatry.3(1):51 – 56.

Guy, W. (1976) ECD EU. Assessment manual for psychopharmacology. US dept. of health & human Services publication (ADM) 76 -338. Rockville, Md., pp 534 - 535.

Hashem, A. Frey, H. (1988) The effect of neuroleptics and neuroleptic/analgesic combinations on the sensitivity to seizures in mice. Anaesthesist, 37: 631-635.

Krystal, A. D. Coffey, CE, Weiner RD, Holsinger T. (1998) Changes in sezure threshold over the course of ECT affect therapeutic response and are detected by Ictal EEG ratings. J. Neuro-psychiatry Clin. neurosci, 10 (3) : 178-186.

Lam, R.W. Barthey, S, Yathan L, Zis A. (1999) Clinical predictors of short term outcome in Electro convulsive therapy . Can JH. Psychiatry , 44 (2) : 158-63.

Maletzky, B. M . (1978) Seizure duration and clinical effect in electro-convulsive therapy. Compr Psychiatry , 19 : 541-50.

Mansour, H. A. (1997) A study of some technical considerations in modified Electro

convulsive therapy. Unpublished thesis.

McCall, W. Cohen, R. Lawton, P. (1999) Pretreatmen differences in specific symptoms and quality of life among depressed patients who do and do not receive ECT: A hypothesis regarding why the elderly are more likely to receive ECT. J. ECT, 15 (3) : 193-201.

Miller, A. Faber, R. Hatch, J. Alexander, H. (1985) Factors affecting amnesia, seizure duration , and efficacy in ECT. Am J. Psychiatry, 142 : 692-6.

Montgomery, S., and Asberg, M. (1979) A new depression scale designed to be sensitive to the change. Br. J. Psychiatry , 134 : 382

Nobler, M. S. and Sackeim , H. A. (1993) ECT stimulus dosing; Relations to efficacy and adverse effects. In The Clinical Science of Electro convulsive Therapy. Ed CE Coffey. Washington DC : American Psychiatric Press. Pp. 29

Nobler, M.S. Sackeim, H. A. Solomou, M. et al. (1994) EEG manifestations during ECT: effects of electrode placement and stimulus intensity . Biol. Psychiatry , 34 : 321-30.

Pettinati, H. M. Tamburello, B. Ruetsch, R. Kaplan, F. N. (1994) Patient attitudes toward electroconvulsive therapy. Psychopharmacol Bull, 30 : 471-75.

Riddle, W. J. Scott, A. I. Benie, J. Carroll S, Fink G. (1993) Current intensity and oxytocin release after electro-convulsive therapy. Biol. Psychiatry, 33 : 830 -841.

Robin. A, Binnie CD, Copas JB. (1985) Electrophysiological and hormonal responses to three types of electroconvulsive therapy. Br. J. Psychiatry, 147 : 707-12.

Royal College of Psychiatrists. (1995) The ECT handbook: The second report of the Royal College of Psychiatrists Special Committee on ECT. London : Royal College of Pschiatrists.

Rudorfer, M. V. & Goodwin, F. K. (1993) Introduction. In The Clinical Science of Electro-convulsive Therapy. Ed C E Coffey. Washington DC: American Psychiatric Press. P. xvii.

Sackeim, H. A. Decina, P. Kanzler, M. Kerr, B. Malitz, S. (1987) Effects of electrode placement on the efficacy of titrated, low dosage ECT. Am J. Psychiatry, 144: 1449-55.

Sackeim, H. A. Devanand, D. P. Prudic, J. (1991) Stimulus intensity, seizure threshold , and Seizure duration : Impact on the efficacy and safety of Electro-convulsive therapy. Psychiatr Clin North Am, 14 : 803 843.

Sackeim, H. A. Prohovnik, I. Moeller, J. R. (1990) Regional cerebral blood flow in mood disorders: I. Comparison of major depressives and normal controls. Arch Gen Psychiatry , 47 : 60- 70 .

Sackeim, H. A. Prudic, J. Devanand, D. P. Kiersky, J. E. Fitzimons, L. Moody, B. J. McElhiney, M. C. Coleman, E. Z. Settembrino, J. M. (1993) Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. N Engl J. Med, 328 : 839 -46.

Sackeim, H. A. (1999) The anticonvulsant hypotheis of the mechanism of action of ECT: Current status. J. ECT, 15 (1) : 5 - 26.

Scott, A. I. Dykes, S. (1999) Initial seizure threshold in the clinical practice of bilateral Electro-convulsive therapy in Edinburgh, Scotland . J. ECT, 15 (2) : 118 -24.

Scott, A. I. F. Milner J. B. Shering, P. A. (1989) Diminished TSH release after a course of ECT : altered monoamine function or seizure activity ? Psychoneuroendocrinology , 14 : 425 -31.

Salan, M. El Guneidy. (1982) Personal communication.

Shapira, B. Lidsky, D. Gorfine, M. Lerer, B. (1996) Electro-convulsive therapy and rsistant depression : clinical implications of seizure threshold. J. Clin Psychiatry, 57 : 32- 8.

Small, I. F. Milstein, V. Miller, M. J. et al. (1986) Electro-convulsive treatment indications, benefits, and limitations. Am J., Psychother, 40 : 343-356.

Swartz, C. M. (1993) Clinical and laboratory predictors of ECT response. In: CE Coffey, ed. The Clinical Science of Electroconvulsive Therapy Washington DC : Am psychiatric Press. Pp, 53 -72.

Weiner, R. D. Rogers, H. J. Davidson, J. R. T. Squire, L. R.(1986) Effects of stimulus parameters on cognitive side effects. Ann NY Acad Sci, 462: 315-25.

Weiner, R. D. (1980) ECT and seizure threshold effects of stimulus waveform and electrode placement : Biol Psychiatry , 15:225-241.

Weiner, R. D. (1997) Stimulus dosing with ECT: To titrate or not to titrate-That is the question. Convuls Ther, (13) 1: 7-9.

Zis, A. P. Yatham L, Lam R, Clork C, McGarvey K. (1986) Effect of stimulus intensity on prolaction and cortisol release induced by unilateral electroconvulsive therapy. Neuropsychopharmacology, (15) : 26-70

العلاقة بين خصائص النوبة التشنجية والاستجابة الإكلينيكية للعلاج بالصدمات الكهربية

أجرى هذا البحث بهدف مراجعة العوامل المختلفة التى قد تؤثر على الاستجابة الإكلينيكية للعلاج بالصدمات الكهربية التشنجية، مما قد يدقق ويحسن من الاستخدامات الطبية لهذا العلاج. وتتلخص تلك العوامل فى ما يلى: ١) عوامل خاصة بالنوبات التشنجية: مثل عدد الجلسات المستخدمة لكل مريض، مدة هذه التشنجات والزمن التراكمى لها، العتبة التشنجية. وكذلك مدى تأثر هذه العوامل بعوامل أخرى كالسن والجنس والعلاج الدوائى والتشخيص، والتاريخ السابق للعلاج بالصدمات الكهربية، وكذلك توالى وتتابع الصدمات. ٢) الجرعة الكهربية: المستخدمة لإحداث النوبة التشنجية العلاجية، سواء كانت تفوق العتبة التشنجية بنسبة متوسطة أو بسيطة. وقد اشتمل هذا البحث على ١٠٥ مريضا نفسيا داخل مستشفى العباسية للأمراض العقلية ، وقد روعي فى اختيارهم أن يكون ظهور أعراض مرضهم حادة البداية. وقد تم إعطاء الصدمات الكهربائية على فصى المخ بمعدل ثلاث جلسات اسبوعياً وقد تم تقسيم هذه المجموعة تقسيم عشوائى إلى مجموعتين ، وتعرضت كل مجموعة لجرعات كهربائية مختلفة لإحداث النوبات التشنجية. وقد أجريت لجميع المرضى مقابلات اكلينيكية نفسية كاملة، مع الفحص البدنى، وقياسات نفسية عند الدخول وعند الخروج والمتابعة ٦ أسابيع بعد الخروج، ومرة اسبوعياً اثناء العلاج لتقييم مدى استجابتهم الاكلينيكية. وقد تم تحليل نتائج البحث إحصائياً مع مناقشتها بالمقارنة بالأبحاث الأخرى.