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Original Article

Dose-Response Relationship of Clinical Efficacy and Side Effects of Electroconvulsive Therapy

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Abstract

Background: The electrical dose selected for electroconvulsive therapy (ECT) must have an acceptable efficacy and no or minimal cognitive side-effects. We evaluated the clinical efficacy and cognitive side-effects of ECT in relation to the stimulus dose administered.

Method: This study assessed 71 depressed patients who were treated with bilateral ECT. For evaluation of depressive and cognitive states the mini-mental state examination (MMSE) and Hamilton scale for depression (HAM-D) were used before starting ECT and after the fourth and last sessions.

Results: The baseline mean MMSE was significantly (p=0.005) different with that evaluated after the fourth (p=0.005) and the final (p=0.002) sessions among the four groups receiving various doses of ECT. The mean Hamilton score did not change significantly over the study. No decrease in cognition was observed with employing higher doses (224–345.6 mc) of ECT compared to lower doses. The rate of improvement did not change significantly among the studied groups.

Conclusion: Cognitive function does not decreased with higher doses of ECT (224–345.6 mc) as compared to the other groups. The rate of improvement does not differ with the stimulus dose administered.

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Keywords ● Electroconvulsive therapy (ECT) ● major depression ● Psychiatry

Introduction

Electroconvulsive therapy (ECT) remains an important effective and safe treatment for a variety of psychiatric disorders. One of its adverse effects is induction of some cognitive dysfunctions.[1] The effects of the magnitude of the electrical charges used for ECT were assessed in previous studies. It was shown that there were no significant correlations between the electrical dose administered and memory changes,[2,3] or disorientation.[4,5] However, post-ECT reorientation was found to be correlated to the magnitude of the electrical doses given.[6] When a fix dose is used, many patients receive stimulations grossly above the seizure threshold, hence the incidence of cognitive side effects is probably increased.[7] However, memory impairment is one of the side effects of ECT.[8]

An ECT-induced generalized seizure of adequate duration is necessary for antidepressant effects become apparent. The

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intensity of the electrical stimulus contributes to decreased cognitive function—the principal side effect—but not to therapeutic efficacy.[9] Furthermore, the antidepressant efficacy of the right unilateral ECT depends on the magnitude of the stimulus dose relative to the seizure threshold.[6] Therefore, the assessment of the relationship between stimulus dose and clinical efficacy and cognitive side effects seems to be important for the detection of therapeutic windows with the least cognitive side effect. The objective of the present study was to examine such a relationship in a series of depressed patients.

Patients and Methods

This study included 71 (44 female and 27 male) depressed patients admitted to the Psychiatry Wards of the teaching hospitals of Shiraz University of Medical Sciences from 2002–04. ECT was prescribed for treatment of all of them. The protocol of the study was explained to the patients and/or their guardians, and written informed consents were obtained.

The patients had not received ECT during the previous five years. Patients who had history of physical disorders, or use of alcohol or other drugs were excluded from the study. Those who were on medications such as anticonvulsants, lithium, clozapine, bupropion, theophylline and reserpine, which could interfere with the seizure threshold, were also excluded from the study. The only exception was use of benzodiazepines; the maximum acceptable mean daily dose of clonazepam, as benzodiazepine equivalent, was 0.89 mg.

All patients were assessed at the time of admission to the Psychiatry Ward for the diagnosis of depression using the criteria of Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) for depression. They were also assessed for cognitive and depressive states using Hamilton scale for depression (HAM-D) and mini-mental state examination (MMSE), respectively on the day prior to and the day after the fourth and last sessions of ECT. Moreover, some parameters including electrical dose administered, seizure time as well as the doses of the anesthetic (sodium thiopental), muscle relaxant (succinyl choline) and atropine were registered at each session for each patient.

Electroconvulsive therapy

ECT was administered three times a week with a square wave, brief-pulse, constant current devise (MECTA J R-1) using intravenous sodium thiopental (2-3 mg/kg) succinyl choline (0.4-0.5 mg/kg) and 0.5 mg atropine. The stimulus dose was set by the preselection method, which involves administering an intensity that will produce seizure in a great proportion of patients at the first treatment. If this intensity was successful at the first treatment session, it was also used in subsequent sessions. If the cognitive side effects displayed by the patient were unusually severe or the stimulus setting used failed to elicit an adequate seizure, appropriate adjustments were made in subsequent sessions. The dosage values used on MECTA SR/JR devices (Instructions Manual SR and JR Models, MECTA Corporation, USA) were arbitrary. All patients were encouraged to continue ECT until they experienced complete or almost complete resolution of their depressive symptoms or to continue for at least 8–12 sessions without showing improvement during the last 2–3 bilateral ECT treatments. The seizure time in seconds was assessed by monitoring tonic-clonic movements of convulsions.

The electrical doses were calculated in millicoulombs using the following formula;

$$C = \frac{PW}{1000} \times 2 \cdot F \times D \times I$$

Where C is the charge to be administered in milicoulombs, I represents current in in mA, PW is the pulse width in ms, F is the frequency in Hz, and D represents stimulus duration in seconds.The patients were categorized into four groups according to the stimulus dose administered; the dose schedule included those who received 65.1–119.9 mc (group 1), 120–149.9 mc (group 2), 150–223.9 mc (group 3) and 224–345.6 mc (group 4).

After completion of ECT therapy, patients with HAM-D scores of ≤ 10 were classified as responders.

Statistical Analysis

Quantitative data were presented as Mean±SD. We evaluated change of MMSE and Hamilton score compared to baseline values at two points—after the fourth and final sessions.

Comparison of means among the four study groups was done by one-way analysis of variance (ANOVA). If necessary, least significant difference test (LSD) was used as a post hoc test. A p value <0.05 was considered statistically significant.

Results

The mean±SD age of patients was 35±10.3 (range: 17–60) years. Number of ECT sessions administered ranged from five to 14.

The baseline mean MMSE was significantly (p=0.005) different with that evaluated after the

fourth (p=0.005) and the final (p=0.002) sessions among the four groups receiving various doses of ECT (table 1 and fig 1). The change in MMSE is more pronounced in the group with high stimulus dose than other groups. The mean Hamilton score did not change significantly over the study (table 1 and fig 2). No decrease in cognition was observed with employing higher doses (224–345.6 mc) of ECT compared to lower doses. The rate of improvement did not change significantly among the studied groups. For small sample in subgroups, assessment of the effects of age, gender, dose and type of medications, and number of treatment sessions could not be possible.

Table 1: MMSE and Hamilton score during the study among the four studied groups.

	Stimulus dose(mc)	N	Means±SD	min	max
Diff MMSE (0-4)	224-345.6	26	2.88±3.26	-0.3	11
	150-223.9	13	-0.69±4.37	-11	5
	120-149.9	13	0.08±3.77	-6	6
	65.1-119.9	19	-0.89±4.17	-12	6
	Total	71	0.70±4.11	-12	11
Diff MMSE (0-f)	224-345.6	26	3.08±3.94	-3	13
	150-223.9	13	-2.23±5.85	-16	6
	120-149.9	13	-0.15±3.51	-5	5
	65.1-119.9	19	-1.31±4.93	-13	8
	Total	71	0.34±4.96	-16	13
Diff Hamilton (0-4)	224-345.6	26	18.19±9.86	0.00	38
	150-223.9	13	23.31±9.48	9	37
	120-149.9	13	20.23±8.96	7	40
	65.1-119.9	19	25.63±9.91	11	43
	Total	71	21.49±9.40	0.00	43
Diff Hamilton (0-f)	224-345.6	26	28.15±10.08	13	47
	150-223.9	13	31.54±12.95	12	55
	120-149.9	13	34.15±11.78	7	54
	65.1-119.9	19	36.05±7.75	24	49
	Total	71	31.98±10.73	7	55

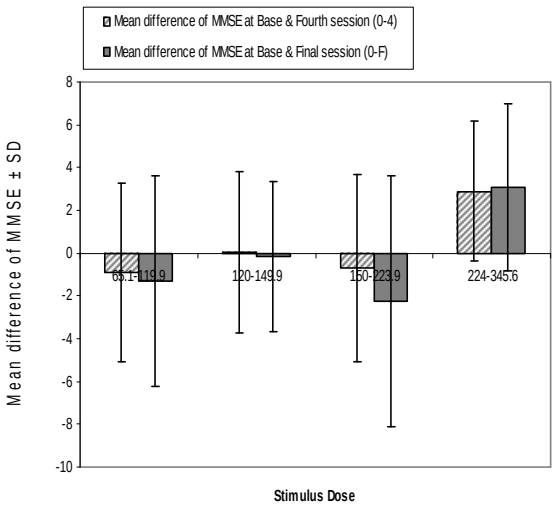

Fig1: Comparison of mean difference of MMSE at Base & Fourth session (0-4) and mean difference of MMSE at Base & Final session (0-F)

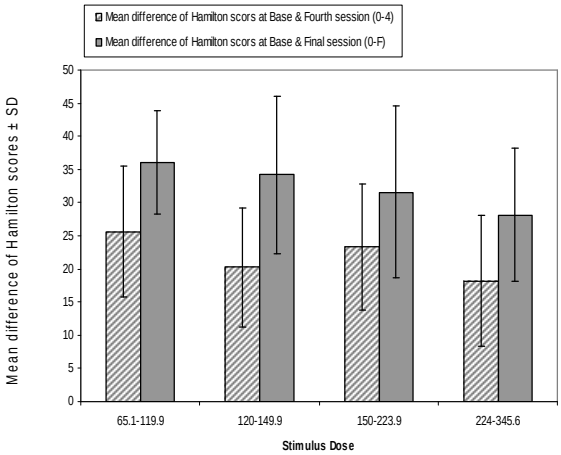

Fig2: Comparison of mean difference of Hamilton score at Base & Fourth session (0-4) and mean difference of MMSE at Base & Final session (0-F)

Discussion

As it was shown, with increasing stimulus dose, there is some improvements in the cognitive functions. Some studies performed on patients aged ≥60 years, showed improvement in cognitive functions by the end of ECT.[5,10] These results has reviewed by Prudic, Peyser and Sackiem who reported that this cognitive improvement was due to the "affective state."[11] Furthermore, the effect of medication (e.g., atropine), gender, age and number of treatment sessions should be considered. However, Brodaty concluded that ECT, an effective treatment for depression, dose not cause significant side effects on neuropsychological impairment, which are more likely to be a depressive phenomena. ECT appears to be safe for old and very old patients.[12] Similar results was also reported by Frey.[13]

We found that with increasing the stimulus dose, the rate of improvement during and at the end of treatment course did not change significantly, although the highest improvement rate was seen in the group with the higher doses administered (224–345.6 mc). In a study by Chanpattana on bilateral ECT in schizophrenic patients, higher doses of ECT caused more rapid improvement. This preliminary study indicated that treatment with high-dosage bilateral ECT speeds up clinical response in patients with schizophrenia. This may be a therapeutic window of stimulus intensity in impacting on the efficacy of bilateral ECT, which needs further study.[14] In Frey's study, the rate of improvement was higher among those who received higher doses of stimulus—82% in those received 312 mc *vs* 36% in those received 92 mc.[13]

Finally, we found that decrease in cognitive function was not observed in those who re-

ceived higher doses of ECT (224–345.6 mc) as compared to the other groups. Furthermore, rate of improvement did not show any significant difference among the groups studied.

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