

Comparison of Bifrontal and Bitemporal Electroconvulsive Therapy in Patients with Major Depressive Disorder

Shahrokh Amiri, MD¹
 Mohamad Ali Ghorishizadeh, MD¹
 Salahadin Hekmatara, MD¹

1. Department of psychiatry,
 Tabriz University of Medical
 Sciences, Tabriz, Iran

Corresponding author:

Shahrokh Amiri, MD
 Assistant Professor, Department
 of psychiatry, Razi Hospital,
 Tabriz university of medical
 sciences, Elgoli Ave., Tabriz, Iran.
 Tel: +98-411-3804486-9
 Fax: +98-411-3803351
 E-mail: Amirish@tbzmed.ac.ir

Objective: The current study was conducted to compare the efficacy and side effects of bifrontal electrode placement with standard bitemporal electrode placement in the treatment of patients with major depression.

Method: Eighty nine patients with major depression were treated with a course of bifrontal or bitemporal ECT. All patients received 8 sessions of ECT treatment; and the Hamilton Rating scale for Depression and the standardized Mini-Mental state were administered 24 hours prior to the first session and 24 hours after the last session. This study was a Double Blind Randomized Clinical Trial.

Results: 68 of the 89 patients completed the study in the two groups of bifrontal (31 patients) and bitemporal (37 patients). The mean decrease in the Hamilton Rating scale for Depression score after ECT was the same in the both groups and was about 20 (SD± 3/2), showing a significant difference between the 2 groups. Nevertheless, the mean decrease in Mini-Mental state Examination score was different in the 2 groups and was 0/67 for the bifrontal ECT group (SD± 0/65) and 2/35 for the bitemporal ECT group (SD±0/94),, indicating a statistically significant difference (P<0/001).

Conclusion: The result of this study demonstrates that cognitive side effects of bifrontal ECT were significantly lower than bitemporal ECT ; however, the two methods are the same with regards to efficacy .

Keywords: *Electroconvulsive therapy, Major depressive disorder, Methods*

Iran J Psychiatry 2009; 4:13-16

Electroconvulsive therapy has evolved in many respects over the past 70 years since its introduction and remains our most effective treatment for major depression. In 1938, chemical induction methods were superseded by electrical induction. In the 1950s, the introduction of general anesthesia reduced morbidity from the treatment.

The move from sine wave electroconvulsive therapy (ECT) to brief pulse stimulation during the 1980s greatly reduced the severity of cognitive side effects of the treatment and provided the first clear demonstration that the type of electrical current applied to the scalp was a major determinant of side effects (1-4).

Recent research has extended that finding by demonstrating that electrode placement interacts with electrical dosage in determining efficacy as well as side effects (2).

ECT is the most effective treatment for severe depression (American Psychiatric Association, 2001)

Despite many evolutions in ECT methodology, the main limitation of ECT is cognitive side effects, particularly memory dysfunction. Memory impairment in ECT may be related to focal involvement of the dominant temporal lobe (5).

Variations in treatment technique, such as electrode placement and stimulus dose, have been investigated to maximize therapeutic efficacy while minimizing

cognitive side effects. Right unilateral ECT causes significantly fewer memory side effects than bitemporal ECT but is less clinically effective unless the stimulus is increased to relatively high doses. Bifrontal ECT has been studied less extensively, and conclusive clinical efficacy data have not been available, however, preliminary reports suggest that it has similar or better anti-depressant efficacy compared to bitemporal ECT (6).

Bitemporal ECT, bifrontal ECT, and right unilateral ECT all induce a "generalized" tonic-clonic seizure; however, these different methods of stimulation result in different focal clinical, EEG, and imaging manifestations.

Bitemporal ECT activates focal bilateral frontotemporal and parietal association cortex, sparing other regions; bifrontal ECT mainly activates prefrontal cortex; in right unilateral ECT the left frontotemporal region is relatively spared(7).

Thus, the pattern of neuronal involvement during ECT is not homogenous throughout the brain, and it differs depending on stimulus configuration. Bitemporal ECT, Bifrontal ECT, and right unilateral ECT all differ in their clinical effects and cognitive side effects. Right unilateral ECT causes significantly fewer memory side effects than bitemporal ECT, but is less clinically

effective unless the stimulus is increased to relatively high doses (7, 8).

Preliminary reports suggest that bifrontal ECT may have similar or better antidepressant efficacy and fewer cognitive side effects than bitemporal ECT (6).

Bifrontal ECT was found to cause increases in cerebral blood flow (CBF) in prefrontal and anterior cingulate regions.

Bifrontal ECT, however, caused CBF increases in the lateral frontal cortex and in the anterior temporal lobes. In bifrontal ECT, a greater increase in prefrontal activation may result in a better therapeutic response and fewer adverse effects on memory than bitemporal ECT while sparing the temporal lobes (5).

In a retrospective study, charts from 76 patients receiving ECT treatments at Harborview Medical center from 1994 to 2000 were reviewed to extract data on the characteristics of the course of ECT, clinical response, side effects, and treatment emergent need for assistance with daily activities. The bitemporal patients experienced more clinical improvement during their stay and were significantly less likely to be re-hospitalized within a 1-year time frame even after controlling for relevant covariates. Although the two patient groups had equal rates of headache and analgesic administration, the bitemporal placement caused a significantly greater cognitive impairment (9). In an 8-session, double-blinded parallel group study, 45 consecutive depressive patients who were referred for ECT to Noor Hospital were randomly assigned to bifrontal, moderate dose (50% above seizure threshold; n=15); bitemporal, low dose (just above seizure threshold; n=15); and right unilateral, high dose (400% above the seizure threshold; n=15) ECT applications. Primary outcome measures included assessment by mini-Mental state Examination and Hamilton Depression Rating Scale.

Thirty nine of the patients completed the course of treatment. The 3 groups did not show any difference in baseline characteristics. There was a significant difference between standardized mini-mental state scores of patients in bifrontal group compared with bitemporal and right unilateral patients ($p < 0.05$). Moderate-dose bifrontal ECT revealed fewer cognitive side effects in comparison with bitemporal and right unilateral ECT. The effectiveness of the 3 ECT methods, assessed by Hamilton Depression Rating Scale, did not show any significant difference (10).

The current study compares the clinical and cognitive effects of bifrontal electrode placement with standard bitemporal electrode placement in the treatment of patients with major depression.

Materials and Method

The present study is a double blind randomized clinical trial (RCT) of two different ECT procedures among 89 outpatients and inpatients referred for ECT in Razi hospital. (A mental health hospital in Tabriz -Iran)

Informed written consent was obtained from patients and their family after the local ethics committee of the university approved the study.

A psychiatric interview was performed for each patient to confirm the diagnosis of major depressive disorder (MDD) based on criteria of Diagnostic and statistical manual of mental Disorders, fourth Edition, Text Revision (DSM-IV-TR)

Patients also met the following inclusion/ exclusion criteria:

- 1) Between 18-65 years of age
- 2) Score higher than 17 on the 24-item version of the Hamilton Rating Scale for Depression (HRS-D)
- 3) Score higher than 24 on the standardized Mini – Mental State Examination (MMSE)
- 4) No history of any psychotic disorder (other than MDD), cognitive disorder and psychoactive substance abuse or dependence.
- 5) No history of any medical condition.

The patients received bifrontal or bitemporal ECT by random assignment. The psychiatrist who administered ECT, did none of the ratings and was the only investigator who knew the patients, electrode placements. (The raters and patients were kept blind to the type of ECT procedure) Anesthetic medications consisted of Thiopental sodium (2-3 mg/kg) and succinylcholine (/5 mg/kg), and atropine (/5 mg-stat) as pre-medication.

In bitemporal placement, each electrode was placed on the perpendicular line 3 cm above the midpoint of the line joining the external auditory meatus and the outer canthus of the eye. For bifrontal placement, each electrode was placed 5 cm above the outer angle of the orbit on a line parallel to the sagittal plane. ECT was done using the Thymatron™ DGx device (Somatics, ILC, Lake Bluff, IL, USA) with brief-pulse, square-wave (BPSW) stimulation.

All patients received 8 sessions of ECT treatment; and 24 hours prior to first session and 24 hours after the last session HRS-D and standard MMSE test were completed.

Electrical stimulating dose was determined with the use of titration in the first session; . bifrontal ECT with an electrical stimulating dose of 50 percent above the seizure threshold, and bitemporal ECT with the dose of just above the threshold were used.

At the end of trial, the data were analyzed by SPSS software using parametrically (t-test), and non-parametrically tests. For all analyses, $P < 0.05$ was defined as statistically significant.

Results

Eighty nine patients began treatment in the study. Sixty eight of the patients (31 patients in bifrontal, 37 in bitemporal) completed the course of treatment.

Twenty one of the patients dropped out of the study for reasons unrelated to ECT side effects. The reasons for drop outs included receiving fewer than 8 sessions of ECT treatment and withdrawal of consent for completion of HRS-D and standard MMSE test.

Patients receiving bifrontal and bitemporal ECT did not differ from each other in seizure durations. Age and level of education were also similar between both treatment groups.

The mean decrease in HRS-D score after ECT (Table1) was the same in the groups and was about 2.0 ± 3.2 , not indicating a significant differences between the 2 groups. However, the mean decrease in MMSE score was different between the 2 groups and was 0.67 ± 0.65 for bifrontal ECT group and 2.35 ± 0.94 for bitemporal ECT group, indicating a statistically significant difference ($P < 0.001$) (Table1).

Discussion

The results of our study showed bifrontal electrode placement to be as effective as bitemporal electrode placement and to have fewer cognitive effects. Another three – winged study with 45 patients suffering from major depression showed clinically equivalent efficacy but less cognitive decline after eight ECT treatments. (measured by MMSE (-2/3 points in bifrontal position (150%), -4/2 points in right unilateral position (400%) and -5/1 point in bitemporal position (just above 100%) (10).

These data indicate that bifrontal ECT is associated with fewer short term cognitive side effects although MMSE is a limited method of assessing the cognitive side effects of ECT.

A retrospective chart analysis of 76 patients who received bifrontal or bitemporal ECT showed bitemporal ECT to have a significantly superior antidepressive power, but also more cognitive side effects (9).

A study demonstrated a high efficacy of bifrontal and bitemporal ECT in 48 patients with a response rate of 96% after 12 sessions (6) the two groups did not differ in baseline MMSE scores, but after treatment, the group given bitemporal ECT showed a statistically significant worsening in their MMSE scores ($P=0/03$). (6).

Bifrontal ECT was found to cause increases in cerebral blood flow (CBF) in prefrontal and anterior cingulate regions. Bitemporal ECT, however, caused CBF increases in the lateral frontal cortex and in the anterior

temporal lobes. In bifrontal ECT, a greater increase in prefrontal activation may result in a better therapeutic response and fewer adverse effects on memory than bitemporal ECT while sparing the temporal lobes (5).

Another possible advantage of the bifrontal over the bitemporal placement is that the treatments might cause fewer dental injuries because the electrodes are farther away from the masseter muscles (6).

In a double-blind randomized controlled clinical study, 92 patients diagnosed with pharmaco-resistant major depression received either six right unilateral ECT treatments (250% stimulus intensity of titrated threshold) or six bifrontal ECT (150% of threshold) treatments over a 3-week period. Concomitant psychotropic medications were continued during ECT treatments. In both ECT groups, there was a reduction in the Hamilton Depression score from 27 to 17 points in both groups of the 46 patients, resulting in 12 responders (primary endpoint defined as a decrease > 50%) in each patient group (95% confidence interval for the odds ratio from 0/35 to 2/8). There was no reduction in the MMSE score. Both bifrontal and right unilateral electrode placements in ECT were safe and moderately efficacious in reducing symptoms of pharmaco – resistant major depression (11).

This study indicates that both bifrontal and right unilateral ECT are reasonably safe procedures, and not associated with major cognitive or medical adverse effects in the short term even when combined with co-administration of antidepressants, atypical antipsychotic or lithium. However, the clinical efficacy was quite low (11). Although right unilateral (RUL) electrode placement also yields fewer cognitive effects than bilateral placement, the treatment needs to be administered at 5 to 8 times threshold to achieve acceptable efficacy (1) Thus, dose titration is always required to ensure the likelihood of acceptable results and often requires doses in excess of those available with standard ECT devices. When such high energies are applied, the memory effects of right unilateral increase markedly (1). The limitation of our study is the inclusion of only one cognitive measure (mini-mental status exam, MMSE).

The evaluation of cognitive state by MMSE was

Table 1. Demographic and clinical characteristics of patients with major depression given bifrontal or bitemporal ECT

Characteristic	Bifrontal (N=31)		Bitemporal (N=37)		Pvalue
	N	%	N	%	
Sex					
Male	10	32/3	22	59/5	
female	21	67/7	15	40/5	
	Mean	SD	Mean	SD	
Age	34/7	11	36/7	10/8	0/472
Education	8/32	5/8	8/81	5/3	0/719
Duration of seizures (Seconds)	34	3	33	4	0/92
HRS-D* score	26/9	5/8	25/7	4/9	0/82
Baseline MMSE** score	28/2	2/2	27/9	2/1	0/87
Reduction in the HRS-D* score after 8 session ECT	20	3/2	19/9	3/2	0/946
Reduction in the MMSE** score after 8 session ECT	0/67	0/65	2/35	0/94	<0/001

* Hamilton Rating Scale for Depression

** Mini – Mental State Examination

probably not sufficiently sensitive to monitor the typical adverse effects on spatial orientation and delayed recall problems after several bilateral ECTs.

The result of our study suggests that the use of bifrontal ECT has the same efficacy compared with bitemporal ECT but fewer cognitive side effects.

Acknowledgments

The authors would like to thank all the patients, staff, residents and psychiatrists of Razi hospital for their help in conducting this research project.

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