

## Effectiveness of Bifrontal ECT in Practice: A Comparison with Bitemporal ECT

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### ABSTRACT

**Background:** Bifrontal (BF) placement of electrodes in electroconvulsive therapy (ECT) has emerged as an alternative option to the conventional bitemporal (BT) and right unilateral electrode placement in view of fewer cognitive adverse effects. However, the results have been contradictory in terms of clinical efficacy. **Materials and Methods:** We studied the records of all patients referred for ECT between the months of August 2008 and July 2010 ( $n=1575$ ). One hundred and five of these patients had received BF-ECT. These records were compared with the records of 105 patients who received BT-ECT. For each patient who received BF-ECT, the very next person posted for BT-ECT was taken as the control. All patients received bilateral ECTs at 1.5-times the threshold stimulus dose. The number of ECTs administered, duration of hospital stay after ECT initiation, seizure threshold and failure to achieve adequate seizures were compared. Two raters who achieved good inter-rater reliability assessed the initial severity using the clinical global impression scale and clinical improvement using a Likert scale. **Results:** The speed of response, as assessed by the number of ECTs received and the duration of hospital stay after ECT initiation was similar in the two groups. In addition, both groups were comparable in terms of clinical improvement scores on the Likert scale. BF-ECT patients also had a significantly higher seizure threshold, which remained significant in spite of controlling for age. This study is chart based, with its inherent limitations. Standard outcome measures were not used. Cognitive adverse effects were not studied. **Conclusions:** BF-ECT performed similar to BT-ECT with regard to therapeutic efficacy. Given the consistent results of the former, with fewer cognitive side-effects, the findings of the present study support BF-ECT as the first line for electrode application.

**Key words:** Bifrontal, bitemporal, effectiveness, electroconvulsive therapy

### INTRODUCTION

Electroconvulsive therapy (ECT) is an efficacious treatment modality in several psychiatric disorders, like major depression (unipolar and bipolar), mania and schizophrenia.<sup>[1]</sup> Research has focused on the

development of methods to optimize efficacy while reducing cognitive adverse effects.<sup>[2]</sup> Shifting electrode placement has been a commonly used strategy in this regard.<sup>[3]</sup> Bifrontal (BF) placement of electrodes has emerged as an alternative option to the conventional bitemporal (BT) and right unilateral (RUL) electrode placement in view of fewer cognitive adverse effects.<sup>[4]</sup>

BF-ECT and BT-ECT/RUL-ECT have been compared in at least five prospective, randomized clinical trials in depressive disorder. BF-ECT was found to be superior in efficacy in one study,<sup>[5]</sup> while two studies showed equivalent efficacy between the groups.<sup>[6,7]</sup> Another study that compared the threshold BF-ECT with suprathreshold RUL-ECT found the former to be of

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inferior efficacy.<sup>[8]</sup> A recent multicenter, randomized, double-blind, controlled trial found that BT-ECT led to more rapid symptom reduction than BF-ECT.<sup>[9]</sup> There have been two studies in mania. One found BF-ECT to have a faster onset of response and comparable final clinical outcome.<sup>[10]</sup> The other one found BF-ECT to be as efficacious as BT-ECT.<sup>[11]</sup> The only study in schizophrenia<sup>[12]</sup> has shown that BF-ECT effected faster response than BT-ECT, although the final outcome was comparable; this study also showed that BF-ECT had a significant cognitive advantage. A retrospective study in a community hospital setting found that BT-ECT had a higher clinical improvement than the BF-ECT group.<sup>[13]</sup> Overall, it appears that BF-ECT is equally efficacious if not better than BT-ECT. Despite this, it has been suggested that "...there is no justification for the use of BF-ECT."<sup>[14]</sup> On the other hand, findings regarding the superiority of BF-ECT with respect to cognitive adverse effects have been very consistent. To date, there is no single study that has convincingly shown that BF-ECT is inferior to BT-ECT in terms of cognitive adverse effects. With this background, the suggestion against the use of BF-ECT can potentially deter clinicians from using BF-ECT due to concerns regarding efficacy and, therefore, use BT-ECT, which is cognitively inferior.

As BF-ECT has been found to be consistently better cognitively, the practice in our institute has changed, and BF-ECT is prescribed more frequently than before. The main purpose of the study was to elucidate whether this change of practice has led to any perceptible change in treatment effectiveness. In this study, we compared the treatment effectiveness by studying the speed of response of BF-ECT versus BT-ECT in unselected patients referred for ECT.

## MATERIALS AND METHODS

### Setting

The National Institute of Mental Health and Neurosciences, Bangalore, is a tertiary care psychiatric institute in south India, with bed strength of 550. Annually, about 500 patients are prescribed ECTs, of which most are inpatients. All patients are evaluated by a multidisciplinary mental health team under the supervision of academic faculty. ICD-10 criteria are used to diagnose the psychiatric disorders.<sup>[15]</sup> Consistent with the practice in the rest of the developing countries, the need to reduce the number of days of hospital stay with the hope of rapid response forms an important indication for starting ECTs.<sup>[16,17]</sup>

The ECT team consists of psychiatrists, anesthesiologists, ECT nurses, dedicated staff and a state-of-the-art ECT suite. Each patient undergoes a pre-ECT evaluation consisting of detailed psychiatric and medical history, clinical examination with particular emphasis

on neuropsychiatric aspects, pertinent laboratory investigations and, where necessary, ECG as well as brain imaging. Seizure threshold is determined during the first ECT session by the titration method.<sup>[18]</sup> During the course of ECT, if seizures are not elicited at the electrical stimulus that was used during an earlier session, then the new threshold is determined by a titration method again, starting from the previously used electrical dose. Treatment is administered using a NIVIQUE machine (Technonivilak, Bangalore, India). Brief-pulse stimulus is delivered with constant current at 800 mA, with a frequency of 125 pulses per second (62.5 Hz) and pulse width of 1.5 ms; the duration of train is altered to adjust the dose. All ECTs are administered under anesthetic modification (thiopentone 3–4 mg/kg and succinylcholine 0.5–1 mg/kg). The cuff-method is used to record the duration of motor seizures. The details of indications for ECT, seizure threshold, duration of seizures and ECT-related complications are documented in the case records. Changes in the clinical picture of the patients are recorded by the nurses, psychiatry postgraduate resident doctors, senior registrars and consultant psychiatrists. The referring psychiatrists decide on the number of ECTs for each patient – the reasons for stopping ECT (clinical improvement/complication/withdrawal of consent, etc.) are noted in the file.

### Sample

We studied the records of all patients referred for ECT between the months of August 2008 and July 2010 ( $n=1575$ ). One hundred and five of these patients had received BF-ECT. These records were compared with the records of 105 patients who received BT-ECT. For each patient who received BF-ECT, the very next person posted for BT-ECT was taken as the control. A sample of 105 patients in each group had an 85% power to detect a mean difference of 1 ECT (an outcome measure) with an estimated SD of 2.4. All patients received bilateral ECTs at 1.5-times the threshold stimulus dose. Data regarding one patient who received an extraordinarily greater number of BF-ECTs (34 ECTs) as part of his maintenance regimen was excluded from the analysis.

### Outcome measures

Two raters (BV and JCN) studied the records. It was noted that reason for stopping ECT was achievement of clinically significant improvement in all patients of both groups. Hence, the number of ECT sessions received by the patients was used as a measure of speed of response. An important reason for which ECT is prescribed in this setting is to shorten the hospital stay.<sup>[17]</sup> With this background, the number of days of hospital stay following initiation of ECT was also considered as an outcome measure.

The initial severity of illness was measured using the clinical global Impression (CGI) scale. The overall improvement was rated using a five-point Likert scale (1=20% improvement or less, 2=20–40% improvement, 3=40–60% improvement, 4=60–80% improvement, 5=80–100% improvement). The inter-rater reliability between the two raters was good (on 20 randomly selected records, kappa=0.67,  $P<0.01$ ).

**Statistical analysis**

Statistical analysis was conducted using the statistical package for social sciences (SPSS) version 13.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were analyzed using the independent sample *t* test and categorical variables were analyzed using the Chi-square test. To control for the potential confounding effects of age and diagnostic category on the outcome variable, multiple linear regression analysis was used. The improvement level from the Likert scale was analyzed using the Mann–Whitney-U test.

**RESULTS**

Table 1 shows the socio-demographic and clinical details of the study samples. Patients who received BF-ECT were older than those who received BT-ECT, at a trend level ( $P=0.07$ ). There were significantly higher numbers of schizophrenia patients in the BF-ECT group ( $P=0.05$ ). The samples were comparable in other details.

Table 2 shows the differences in the two groups in outcome variables. There was no significant difference between the groups on clinical improvement scores on the Likert scale and the duration of hospital stay after initiation of ECTs. The BT-ECT group received a significantly lower number of ECTs than the BF-ECT group on univariate analysis ( $P=0.05$ ). Schizophrenia patients received significantly higher number of ECTs (mean=7.2; SD=2.5) than the mood disorders' patients (mean=6.5; SD=2.4;  $P=0.05$ ). As the two groups differed with respect to diagnosis and age, multiple linear regression analysis was conducted with number of ECTs as the dependent variable and group (BF-ECT vs. BT-ECT), age and diagnostic category (mood disorder vs. schizophrenia) as independent variables. After controlling for the effects of diagnosis and age, the difference between the BF-ECT and BT-ECT groups was not significant ( $t=1.52$ ;  $P=0.13$ ).

Seizure threshold at the first session was significantly higher in the BF-ECT patients than in the BT-ECT patients. In addition, there was a positive correlation between age and seizure threshold ( $r=0.44$ ,  $P<0.001$ ). When multiple linear regression analysis was conducted with seizure threshold as the dependent variable and

**Table 1: Socio-demographic and clinical details**

Test	BF-ECT	BT-ECT	t/Chi-square	P
Mean age in years (SD)	32.5 (12.9)	29.6 (9.8)	1.84	0.07
Females [n (%)]	55 (52.9)	45 (46.7)	2.10	0.15
Mean duration of illness in months (SD)	76.7 (90.3)	62.6 (63.6)	1.30	0.20
Diagnoses [n (%)]				
Depression	35 (33.6)	40 (38.1)		
Mania	21 (20.2)	33 (31.4)	6.20	0.05*
Schizophrenia	48 (46.2)	32 (30.5)		
Presence of comorbidity [n (%)]	24 (23.1)	20 (19.1)	0.51	0.48
Good response to past ECTs [n (%)]	31 (29.8)	32 (30.5)	0.01	0.92
Mean duration of treatment before ECT in days (SD)	8.6 (10.6)	7.6 (8.8)	0.76	0.45
Weight in kilograms (SD)	54.6 (13.4)	55.6 (13.8)	-0.54	0.59
Indications for ECT [n (%)]				
As a first-line therapy	87 (83.7)	89 (84.8)		
To augment pharmacotherapy/ medication resistant	18 (16.3)	16 (15.2)	0.05	0.83
Clinical global impression – severity at the start of ECT sessions (SD)	5.3 (0.6)	5.2 (0.5)	1.32	0.19
Thiopentone – mg/kg (SD)	3.0 (0.3)	3.0 (0.4)	-1.15	0.25
Succinylcholine – mg (SD)	27.6 (7.3)	28.9 (6.7)	-1.37	0.17
Concurrent use of anti-epileptics [n (%)]	10 (9.5)	12 (11.4)	0.20	0.65

\*Statistically significant, BF – Bifrontal; BT – Bitempora; ECT – Electroconvulsive therapy

**Table 2: ECT related and outcome variables**

Mean values (SD)	BF-ECT	BT-ECT	t/ Chi-square/z	P
Clinical variables				
Number of ECTs	7.1 (2.7)	6.4 (2.2)	2.01	0.05*
Duration of inpatient stay after ECT initiation in days	23.4 (19.9)	21.5 (25.1)	0.62	0.54
Improvement as per Likert scale	3.8 (1.0)	4.0 (0.9)	-1.25	0.21
Seizure-related variables				
Threshold at first ECT in milli-coulombs	101.0 (69.8)	80.2 (44.6)	2.56	0.01*
Average duration of motor seizure in seconds	49.6 (13.4)	47.4 (13.0)	1.22	0.22

\*Statistically significant, BF – Bifrontal; BT – Bitempora; ECT – Electroconvulsive therapy

group (BF-ECT vs. BT-ECT) and age as independent variables, the difference was still significant at  $P=0.05$ . There was no difference in terms of the other seizure parameters.

**DISCUSSION**

The main purpose of the study was to elucidate whether a change in the practice of prescribing more BF-ECTs has led to any perceptible change in treatment efficacy.

We compared patients receiving BF-ECT and BT-ECT for clinically important variables: Number of ECTs received, duration of inpatient stay after ECTs were initiated and clinical improvement scores. The two groups did not differ with respect to the number of ECTs received, duration of inpatient stay after ECT initiation and clinical improvement scores on the Likert scale. It was noted that BF-ECT patients had a significantly higher seizure threshold than the BT-ECT group.

Our findings are consistent with previous studies that have found clinical improvement scores to be comparable between BF-ECT and BT-ECT.<sup>[6,7,10,11]</sup> The speed of response to ECTs, as assessed by the number of ECTs received and the duration of hospital stay after ECT initiation, was similar in BF-ECT and BT-ECT. An earlier study with a similar design<sup>[13]</sup> had also reported the number of ECTs received to be similar between the two groups. This is in contrast to randomized, double-blind, controlled trials that have used similar outcome measures, and found that BF-ECT had a faster action than BT-ECT.<sup>[10,12]</sup> Only one randomized, double-blind, controlled trial found BT-ECT to be faster than BF-ECT.<sup>[9]</sup>

The finding that seizure threshold is higher in BF-ECT is consistent with the past literature,<sup>[13]</sup> and validates the findings of our study. A positive correlation between age and seizure threshold might explain this finding because the BF-ECT group was older. However, even after controlling for age, the difference in seizure threshold was significant. BF-ECT is associated with non-convulsive seizures.<sup>[19]</sup> Because the patients in this study did not have EEG monitoring during ECT, there is a possibility that calculation of threshold at a higher level could have been due to non-convulsive seizures. Routine use of EEG monitoring has been suggested as a standard of practice. This practice is all the more important with BF-ECT. It may be interesting that in spite of greater seizure threshold, the past studies have found fewer cognitive adverse effects.

Could the lack of a statistically significant difference between the two electrode placements be due to small sample size and the consequent type-II error? This is unlikely. Our sample had an 85% power to detect a clinically meaningful difference of 1 ECT between the two groups. Further, the effect size of the difference between the numbers of ECTs received in the two groups was 0.28, which further suggests that the observed difference was inconsequential in clinical terms.

This being a chart-based study, the findings could have been biased by confounding factors. The nature of illness of patients receiving BF-ECT might have been different from that of patients receiving

BT-ECT. As previously noted, the BF-ECT sample had a higher number of schizophrenia patients. Multiple linear regression analysis was carried out to control for confounding factors of age and diagnostic category.

The absence of standardized methods of assessing the severity of illness and adverse effects limits the interpretation of our study. However, the number of ECTs administered to achieve clinically significant improvement and the number of hospital days form meaningful outcome measures – previous studies have also used similar measures.<sup>[10,12]</sup> Further, the fact that two raters who were blind to each others' scores achieved a high reliability in their CGI and Likert scale scores partially validated this as a measure of meaningful clinical outcome. Cognitive adverse effects did not form an outcome in this study. However, there is substantial consistency in previous reports about the cognitive superiority of BF-ECT over BT-ECT.

In summary, BF-ECT performs similar to BT-ECT with regard to therapeutic efficacy. Given the consistent results of the former with fewer cognitive side-effects, the findings of the present study support BF-ECT as the first line for electrode application.

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