Effect of age and anticonvulsants on seizure threshold during bilateral electroconvulsive therapy with brief-pulse stimulus: A chart-based analysis

Abhishek R. Nitturkar, Preeti Sinha¹, Virupakshappa I. Bagewadi¹, Jagadisha Thirthalli¹
Department of Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, Virginia 22908, USA,
¹Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India

ABSTRACT

Background: Efficacy and adverse effects of electroconvulsive therapy (ECT) depend on the extent to which the electrical stimulus exceeds patients’ seizure thresholds (STs). Titration method of estimating ST is recommended. Age and co-prescribed anticonvulsants (ACs) are known to affect ST. Literature on ST in bilateral ECT (BLECT) is sparse.

Objective: To explore the clinical and demographic determinants of ST in a clinically representative sample of patients prescribed with BLECT.

Materials and Methods: ECT records of 640 patients who received BLECT in 2011 in an academic psychiatric setting were studied. Demographic, clinical, pharmaceutical, and ECT details were analyzed. As per the standard practice, during the 1st ECT session, ST was determined by titration method, starting with 30 milli-Coulombs (mC) and increasing by 30 mC and thence in steps of 60 mC. Increase in ST over up to 6th session of ECT was noted. Receiver operating characteristic curve was used to find age cut-off with high specificity for ST ≥120 mC. The associations of ST and increase in ST with the age cut-off and other clinical factors were assessed using Chi-square test and logistic regression analysis.

Results: The mean age was 30.98 years (+11.23 years) and mean ST at 1st ECT session was 130.36 mC (+51.96 mC). There was significantly high positive correlation (r = 0.37, P < 0.001) between age and ST. Cut-off age of 45 years had high specificity: Only 4.6% of those older than 45 years had ST <120 mC. Higher proportion of patients on AC had ST ≥120 mC. These associations were seen even after controlling for potential confounds of each other using logistic regression analysis. The results were similar for increase in ST over the course of ECT. Sex, diagnosis, use of antipsychotics, antidepressants, lithium, and benzodiazepines (BZPs) had no effect on ST or its increase.

Conclusions: For BLECT using brief-pulse stimulus, ST depends on age and use of AC. For patients above the age of 45 years, ST estimation may be started at 120 mC with least risk of using unduly higher stimulus. Other medications including BZPs have little influence on ST.

Key words: Anticonvulsants, benzodiazepines, bilateral electroconvulsive therapy, brief-pulse electroconvulsive therapy, seizure threshold

INTRODUCTION

Electroconvulsive therapy (ECT) is considered as one of the most effective brain stimulation treatments for...
many psychiatric conditions, particularly depression and catatonia. The efficacy and cognitive adverse effects of ECT are influenced by the degree by which the electrical dose is greater than the seizure threshold (ST). ST is defined as the minimum charge required to induce unequivocal convulsions or cerebral seizures monitored using electroencephalography (EEG). While using bilateral ECT (BLECT), the recommended electrical dose is 1.5 times the ST. Higher electrical stimulus is associated with more neurocognitive adverse effects. ST, however, may vary substantially across and within individuals – sometimes by up to 56 folds. Various factors influence ST to variable extent; association of ST has been reported with age, gender, electrode placement, inion-nasion distance, and concurrent medications.

Titration method is recommended by a few authors and it is the most widely practiced method, including in India. This method typically involves the use of a number of subconvulsive stimulations. To avoid this, other methods have been proposed. The important ones are half-age and full-age methods, methods using other proportions of age, formula-based method, fixed dose method and the most recent, Benchmark method. Many of the studies assessing these methods have used RUL ECT, which is near exclusively used in Western centers. Contrary to it, BLECT is the most commonly used method in most Asian countries. Particularly in India, more than 90% of the institutions that use ECT use BLECT. An important reason for this is that patients with depression only form the 33–40% of the population receiving ECT in India in the absence of unequivocal evidence in favor of unilateral ECT (ULECT) for conditions other than depression, clinicians tend to use BLECT.

Studies exploring the formula-based-ST in bilateral ECT are sparse, and the accuracy in predicting ST is not satisfactory. Besides, most studies predicting ST did not include patients on anticonvulsants (AC) and benzodiazepines (BZPs). In the study by Gangadhar, Girish (20) patients were on BZP, but not on AC. AC and BZPs are commonly co-prescribed during ECT. There is no consensus regarding whether they should be continued, reduced, or stopped. most clinicians tend to continue their use at different dosages.

In this background, we examined the clinical and ECT-related variables associated with initial ST in a large series of consecutive patients who received ECT in 1 year in a tertiary care academic psychiatric setting. We did not exclude any patient’s data to ensure representativeness of our sample to clinical situations. Gradual rise has been noted in ST in 40–100% of the patients over the course of ECT. If the electrical stimulus is not raised accordingly in the later ECT sessions, it can lead to loss of efficacy of the treatment. There is little information available about factors associated with increase in ST over the treatment sessions. In this study, we also examined the factors associated with increase in ST over six ECT sessions.

**MATERIALS AND METHODS**

**Study population**

We reviewed the ECT records of 640 patients in the Department of Psychiatry at National Institute of Mental Health and Neurosciences, Bengaluru, India. These 640 patients had received BLECT between April 2010 and March 2011. The demographic, clinical, pharmacological treatment and ECT-related details over six sessions including ST of each patient were noted down for data analysis [Table 1]. The medicine details were mentioned at the beginning of the ECT in the pro forma, were noted down, and we held the assumption that the medicines would have remained the same till the six ECT sessions.

**Electroconvulsive therapy procedure**

The ECT multidisciplinary team consisted of psychiatrists, anesthetists, ECT nurses, dedicated staff, and a

| Table 1: Sociodemographic and clinical details |
|-------------------------------|-------------------|
| Variable                      | Distribution      |
| Mean age in years (SD)        | 30.98 (11.23)     |
| Males (n; %)                  | 370; 57.8         |
| Mean duration of IP care in days (SD) | 33.5 (27.08)     |
| Median duration of IP care in days | 26              |
| Mode duration of IP care in days | 17              |
| Mean duration of illness in years (SD) | 5.72 (6.33)     |
| Median duration of illness in years | 4               |
| Mode duration of illness in years | 4               |
| Mean duration of current episode in days (SD) | 35.62 (48.21) |
| Psychiatric diagnosis*        |                   |
| Depression (n; %)             | 234 (36.6)        |
| Mania (n; %)                  | 128 (20)          |
| Schizophrenia or other nonaffective psychosis (n; %) | 278 (43.4) |
| AC and BZP* (n; %)            |                   |
| AC only                       | 40 (6.3)          |
| Valproate                     | 39 (57.4)         |
| Carbamazepine                 | 17 (25.0)         |
| Both AC and BZP               | 28 (4.4)          |
| Other anticonvulsants**       | 12 (17.6)         |
| Lorazepam 144 (59.0)          |                   |
| BZP only                      | 216 (33.7)        |
| Clonazepam 87 (35.7)          |                   |
| Diazepam 13 (5.3)             | 356 (55.6)        |
| None of them                  |                   |
| Electrode placement (n; %)    |                   |
| Bitemporal ECT                | 456 (71.2)        |
| Bilateral ECT                 | 184 (28.8)        |
| Mean dose of thiopentone in mg (SD) | 169.9 (36.1) |
| Mean dose of Succinylcholine in mg (SD) | 29.1 (7.3) |

*Depression (unipolar/bipolar/schizoaffective - F31.3 to F31.5, F32, F33, F25.1); Mania (bipolar/schizoaffective - F30, F31.1, F31.2, F25.0); Schizophrenia or other nonaffective psychosis (F20, F21, F22, F23); AC – Anticonvulsants; BZP – Benzodiazepines, **Oxcarbazepine, lamotrigine, levetiracetam; ECT – Electroconvulsive therapy; SD – Standard deviation; AC – Anticonvulsants; IP – In-patient
state-of-the-art ECT suite. The same ECT procedure was followed for all patients whose ECT records are reviewed in this study. The patients were referred by the treating team after performing standard protocol-based pre-ECT evaluation. ST was determined during the 1st ECT session by the titration method.\cite{36} From the 2nd session, the electrical charge of 1.5 times the ST is administered. During the course of ECT, if seizures are not elicited at this dose, then the new threshold is determined by titration method again. Treatment was administered using a NIVIQURE machine (Technonivilak, Bangalore, India). Brief-pulse stimulus was 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 details of indications for ECT, electrical charge, and duration of seizures in each session, and ECT-related complications are documented in the ECT case records. The referring psychiatrist decides on the number of ECT sessions for each patient and according reason for stopping ECT was also recorded.

**Titration method**\cite{6}

For all patients, ECT stimulus was started at 30 milli-Coulombs (mC), if they did not get seizure stimulus at 60 mC; from this point, stimulus is increased in steps of 60 mC until a generalized tonic-clonic seizure lasting for a minimum of 20 s is induced. The minimum dose at which seizure was elicited was defined as ST. In all patients, cuff method was used to observe motor seizures. No patient had EEG monitoring during ECT.

**Statistical analysis**

The ST at 1st ECT session and whether the ST increased over the sessions of ECT were noted. As age was a consistent predictor of ST, initially, correlation between age and ST was examined using Pearson’s correlation coefficient. Receiver operating characteristic (ROC) curve was prepared with age as continuous variable and ST of ≥120 mC as positive state. Using ROC, the cut-off of age was calculated while giving importance to the high specificity, i.e., to have the higher ability to exclude the patients with ST < 120 mC in the group having age above the cut-off age. Chi-square test (with calculation of odds ratios) was performed to find the association of age cut-off, gender, psychiatric diagnosis, concurrent use of lithium, antipsychotics, and antidepressants with ST ≥120 mC as well as increase in ST over six ECT sessions. Backward stepwise logistic regression analysis was used to examine the predictors that were found significant in univariate analysis. Results with P < 0.05 were considered as statistically significant.

Depending on whether patients were on AC or BZP, they were categorized into four categories (on AC and BZP; on AC but not on BZP; on BZP, but not on AC, and on neither). Since the resultant Chi-square test would have degree of freedom >1, post hoc analysis was performed based on adjusted standardized residual analysis.\cite{37,38} The difference between the observed and expected frequency is called raw residual. It is then divided by expected frequency to have standardized normal distribution, which is further adjusted through estimated standard error. The higher the adjusted standardized residual, the larger the concerned category is different from other category. Negative or positive sign of this value indicates the direction of the difference. The cut-off for the statistical significance of its P value was the Bonferroni adjustment of 0.05, i.e., 0.006.\cite{37,38}

**RESULTS**

Mean ST at 1st ECT session was 130.36 mC (+51.96 mC). About 503 (78.6%) patients had ST ≥120 mC in the 1st ECT session. Age was significantly positively correlated with ST (r = 0.37, P < 0.001). Area under ROC curve [Figure 1] for age in years and ST ≥120 mC as a positive state was 0.76 (0.73–0.80); P < 0.001. The cut-off of 45 years yielded a sensitivity of 23% and specificity of 95.3% and was considered for categorization of age for further analysis. About 87 (13.6%) patients in our study were of age > 45 years.

Results of Chi-square analysis are shown in Table 2. Expectedly, older age (>45 years) was significantly associated with ST ≥120 mC, with an odds ratio of 6.57 (95% confidence interval [95% CI]: 2.36–18.26) for those who were above the 45 years of age to have ST ≥120 mC compared to those who were equal to or below 45 years of age. Being on AC/BZPs was another significant predictor of ST. Post hoc adjusted residuals for AC (with or without BZP) were negative and statistically significant (P < 0.006, the Bonferroni corrected P value), suggesting that significantly higher proportion of those on AC with or without BZPs had ST ≥120 mC compared to those who were on BZPs.
only and those who were not on either of them [Table 3]. This was further reflected in the odds ratio of 2.96 (95% CI: 1.29–8.54) for those on AC and 4.27 (95% CI: 1.59–12.35) for those on both AC and BZP compared to those on neither of these. There was no significant difference between those who had ST <120 mC and ST ≥120 mC in terms of sex, being on lithium, antipsychotics or antidepressants, and psychiatric diagnosis. Besides, all patients who were older than 45 years and on AC (n = 5) had ST ≥120 mC. This was true even when we included the patients older than 40 years and on AC (n = 9). Among those who were 40-year-old or younger than 40 years and on AC, 14.7% (5 out of 34) had ST <120 mC.

BZP use did not have any significant association with ST. The results of backward stepwise logistic regression analysis with ST category (<120 mC/≥120 mC) as dependent variable and age category, use of AC with or without BZPs are shown in Table 3. The model was significant with \( \chi^2 = 67.17; P < 0.001 \). Age was the strongest predictor of ST with an adjusted odds ratio of 6.12 (95% CI: 3.68–10.18).

In 178 (27.8%) patients, ST increased over six ECT sessions; in 61 (34.3%) of these 178 patients, ST increased at 3rd ECT session; in 50 (28.1%), it increased at the 4th session; in 43 (24.1%), it increased at the 5th session, and in 24 (13.5%), it increased at the 6th session. The same variables, which were significantly associated with the initial ST, were significantly associated with rise in ST through the course also. ST was 2.67 times (95% CI: 1.66–4.27) more likely to increase over the six sessions of ECT in those who were older than 45 years than in younger patients. Similarly, ST was 3.58 (95% CI: 1.84–6.97) times and 5.86 (95% CI: 2.59–13.11) more likely to increase in those on AC alone and on AC and BZPs than those who were on neither of these medications [Tables 3 and 5].

### Table 2: Variables significantly associated with seizure threshold in 1st electroconvulsive therapy session ≥120 mC

| Variable influencing 1st session ST | ST <120 mC n; % (n/N) | ST ≥120 mC n; % (n/N) | \( \chi^2; P \) | OR (95% CI) |
|-----------------------------------|------------------------|------------------------|----------------|--------------|
| Age (years)                       |                        |                        |                |              |
| >45 (n=83)                        | 133; 24.1              | 424; 75.9              | 16.94; <0.001  | 6.57 (2.36-18.26) |
| <45 (n=517)                       | 4; 4.6                 | 79; 95.4               |                |              |
| Gender                            |                        |                        |                |              |
| Males (n=370)                     | 68; 18.4               | 302; 81.6              | 1.71; 0.19     | 1.52 (1.04-2.22) |
| Females (n=270)                   | 69; 25.6               | 201; 77.4              |                |              |
| Psychiatric diagnosis             |                        |                        |                |              |
| Depression (n=234)                | 55; 23.5               | 179; 76.5              | 1.57; 0.46     | -            |
| Mania (n=128)                     | 29; 22.7               | 99; 77.3               |                |              |
| Schizophrenia/schizoaffective disorder (n=278) | 53; 19.1               | 225; 80.9              |                |              |
| Lithium                           |                        |                        |                |              |
| Yes (n=112)                       | 26; 23.2               | 86; 76.8               | 0.27; 0.61     | 0.88 (0.54-1.43) |
| No (n=528)                        | 111; 21.0              | 417; 79.0              |                |              |
| AP                                |                        |                        |                |              |
| Yes (n=552)                       | 121; 21.9              | 431; 78.1              | 0.62; 0.43     | 0.79 (0.44-1.41) |
| No (n=88)                         | 16; 18.2               | 72; 81.8               |                |              |
| AD                                |                        |                        |                |              |
| Yes (n=131)                       | 26; 19.8               | 105; 80.2              | 0.25; 0.62     | 1.13 (0.70-1.82) |
| No (n=509)                        | 111; 21.8              | 398; 78.2              |                |              |
| AC and BZP                        |                        |                        |                |              |
| AC only (n=40)                    | 4; 10.0                | 36; 90.0               | 16.77; 0.001   | -            |
| BZP only (n=216)                  | 43; 19.9               | 173; 80.1              |                |              |
| Both AC and BZP (n=28)            | 2; 7.1                 | 26; 92.9               |                |              |
| Neither AC nor BZP (n=356)        | 88; 24.7               | 268; 75.3              |                |              |

ST – Seizure threshold; AP – Antipsychotics; AD – Antidepressants; AC – Anticonvulsants (all medications other than benzodiazepines which are used for the treatment of seizures); BZP – Benzodiazepines; Total sample – 640 cases; OR – Odds ratio; CI – Confidence interval

### Table 3: Post hoc analysis* of Chi-square test between seizure threshold and categories of anticonvulsants and benzodiazepines

| Variable influencing ST increased over 6 sessions | 1st session ST ≥120 mC | ST increased over 6 sessions |
|--------------------------------------------------|------------------------|------------------------------|
|                                                  | Adjusted standardized residual | Z-score | P    | Adjusted standardized residual | Z-score | P    |
| AC only (n=40)                                   | -2.94                  | 8.64               | 0.003 | -3.14                  | 9.86               | 0.002 |
| BZP only (n=216)                                 | 0.77                   | 0.77               | 0.38  | -0.64                  | 0.41               | 0.52  |
| Both AC and BZP (n=28)                           | -4.39                  | 19.27              | <0.001| -4.86                  | 23.62              | <0.001|
| Neither AC nor BZP (n=356)                       | 2.40                   | 5.76               | 0.02  | 1.91                   | 3.65               | 0.06  |

*Based on adjusted residual analysis and Bonferroni adjustment for P value; here cut-off P value was 0.006. ST – Seizure threshold; AC – Anticonvulsants (all medications other than benzodiazepines which are used for the treatment of seizures); BZP – Benzodiazepines
Table 4: Logistic regression analysis for seizure threshold ≥120 mC in 1st electroconvulsive therapy session and increase in seizure threshold over 6 electroconvulsive therapy sessions

| Variable                        | Coefficient B | Adjusted OR (95% CI) | P      |
|---------------------------------|---------------|----------------------|--------|
| ST ≥120 mC in 1st ECT session   |               |                      |        |
| Age (as categorical variable, cut-off: 45 years) | 1.81          | 6.12 (3.68-10.18)    | <0.001 |
| Anticonvulsant*                 | 1.17          | 3.25 (1.66-6.3)      | 0.001  |
| Both anticonvulsant and benzodiazepine | 1.37          | 3.92 (1.76-8.78)     | 0.001  |
| Increase in ST over 6 ECT sessions |               |                      |        |
| Age (as categorical variable, cut-off: 45 years) | 1.07          | 2.91 (1.75-4.85)     | <0.001 |
| Anticonvulsant*                 | 1.20          | 3.31 (1.67-4.85)     | 0.001  |
| Both of anticonvulsant* and benzodiazepine | 1.87          | 6.51 (2.81-9.10)     | <0.001 |

*All medications other than benzodiazepines which are used for the treatment of seizures. ST – Seizure threshold; ECT – Electroconvulsive therapy; OR – Odds ratio; CI – Confidence interval

Table 5: Variables significantly associated with change in seizure threshold over six electroconvulsive therapy sessions

| Variable influencing 1st session ST | ST same n; % (n/N) | ST increased n; % (n/N) | χ²; P | OR (95% CI) |
|------------------------------------|--------------------|-------------------------|-------|-------------|
| Age (years)                        |                    |                         |       |             |
| >45 (n=83)                         | 44; 53.0           | 39; 47.0                | 17.37 | <0.001     | 2.67 (1.66-4.27) |
| <45 (n=557)                        | 418; 75.0          | 139; 25.0               |       |             |
| Gender                             |                    |                         |       |             |
| Males (n=370)                      | 272; 73.5          | 98; 26.5                | 0.70  | 0.40        | 0.86 (0.60-1.21) |
| Females (n=270)                    | 190; 70.5          | 80; 29.5                |       |             |
| Psychiatric diagnosis              |                    |                         |       |             |
| Depression (n=234)                 | 158; 67.5          | 76; 32.5                | 3.01  | 0.22        | -             |
| Mania (n=128)                      | 94; 73.4           | 34; 26.6                |       |             |
| Schizophrenia/Schizoaffective disorder (n=278) | 210; 75.5          | 68; 24.5                |       |             |
| Lithium                            |                    |                         |       |             |
| Yes (n=112)                        | 82; 73.2           | 30; 26.8                | 0.06  | 0.80        | 0.94 (0.59-1.49) |
| No (n=528)                         | 380; 72.0          | 148; 28                 |       |             |
| AP                                 |                    |                         |       |             |
| Yes (n=552)                        | 409; 74.1          | 143; 25.9               | 0.25  | 0.62        | 0.88 (0.53-1.45) |
| No (n=88)                          | 63; 71.6           | 25; 28.4                |       |             |
| AD                                 |                    |                         |       |             |
| Yes (n=131)                        | 89; 67.9           | 42; 32.1                | 1.51  | 0.22        | 1.29 (0.85-1.96) |
| No (n=509)                         | 373; 73.3          | 136; 26.7               |       |             |
| AC and BZP                         |                    |                         |       |             |
| AC only (n=40)                     | 19; 47.5           | 21; 52.5                | 29.623| <0.001     | -             |
| BZP only (n=216)                   | 161; 74.5          | 55; 25.5                |       |             |
| Both AC and BZP (n=28)             | 10; 35.7           | 18; 64.3                |       |             |
| Neither AC nor BZP (n=356)         | 272; 76.4          | 84; 23.6                |       |             |

ST – Seizure threshold; AP – Antipsychotics; AD – Antidepressants; AC – Anticonvulsants (all medications other than benzodiazepines which are used for the treatment of seizures); BZP – Benzodiazepines; Total sample – 640 cases; OR – Odds ratio; CI – Confidence interval

of logistic regression analysis were similar to that of initial ST [Table 4]. There was no significant association between initial ST ≥120 mC and increase in ST over ECTs sessions (χ² = 0.96; P = 0.383).

**DISCUSSION**

The Royal College of Psychiatrists recommends that stimulation titration method should be used for the estimation of ST, as it has the best balance between using unduly high electrical charge leading to cognitive adverse effects and using under-stimulation leading to inefficacy. However, the titration method commonly results in the administration of multiple sub-convulsive stimuli while establishing ST. Consistent with this, initial ST in our study varied from 30 to 500 mC.

This study aimed to examine the predictors of ST of BLECT in a real world situation. The major strength of this study is inclusion of a large sample of patients representative of those who routinely receive ECT in academic settings of Asia in general and India in particular. Patients were chosen irrespective of clinical diagnosis, received BLECT, and were on medications routinely co-prescribed in such settings, including those known to influence ST, such as AC and BZPs. Multivariate analysis was used to control the effects of potential confounders. Mean ST in this sample was much higher than most published studies. Several factors can explain this: (a) All patients received BLECT. In contrast, most studies from the West have used ULECT. ST is known to be higher with BLECT (b) Stepping up of electrical stimulus in multiples of 60 mC could have led to the overestimation of ST (c) EEG monitoring was not used – occasional patients could have experienced adequate cerebral seizures at lower stimulus doses in the absence of motor convulsions (d) Pulse-width of ECT stimulus was 1.5 ms. In most Western settings, lower pulse width is used.
The difference in pulse width could have contributed to relatively higher ST in our study.

Age of the patient emerged as a predictor of initial ST. ROC analysis suggested that a cut-off of 45 years had fairly high specificity of 95.3. In practical terms, if clinicians were to start dose titration for patients >45 years of age starting at 120 mC, then the chances of using a unduly higher stimulus dose is <5%. This would be particularly true if such patients are also concomitantly on AC: No patient above 45 years and on AC had ST <120 mC. In fact, even patients over 40 years of age had their ST ≥120 mC if they were on AC. Thus, if patients are older than 45 years or older than 40 years and on AC, then clinicians could straightaway start dose titration at 120 mC, with least risk of stimulating at unduly higher electrical stimulus.

Across all age groups, patients who were on AC were more than 2 times likely (OR = 2.5) to have ST ≥120 mC and about 3 times (OR = 3.11) likely to have ST ≥120 mC if they are on both AC and BZPs. Our results are consistent with the previous reports of AC being associated with higher ST.[39,40] However, substantial proportion (14.7%) of younger (<40 years) patients on AC had ST <120 mC. Hence, to avoid the use of unduly higher stimulus, the practice of estimating ST from the lowest stimulus may be continued in this group of patients. The ECT clinician should nevertheless expect the trials of subconvulsive stimuli in these patients.

We did not find any significant influence of BZPs on the initial ST. This is consistent with most of the earlier studies examining the influence of BZPs on ST.[19,20,29,41,42] The influence of BZPs on the effectiveness of ECT is also questionable, particularly in BLECT.[43] However, it may be noted that some authors have reported reduction in the predictability of age-based formula in those who were on BZPs.[28] We did not collect data on skipping of BZP dose the night before ECT, which some clinicians practice. However, given that BZPs used in these patients (lorazepam, clonazepam, and diazepam) have half-lives of more than 15–20 h,[44] this practice would have doubtfull effect on their serum levels. Finally, we did not have accurate data on the duration of use of BZPs. A hypothetical possibility of this factor influencing the results of this study cannot be ruled out. Notwithstanding this, one could infer that BZPs have little influence on ST during BLECT.

Initially, ST was not associated in our study with gender, psychiatric diagnosis, and concurrent use of lithium, antipsychotics, or antidepressants. This is in overall concurrence with the existing literature. While some studies found a significant increase in ST in males compared to that in females,[14,18,41,45] many others[12,19,24,29,42,46,47] did not. Evidence in the literature suggesting the influence of other concurrent medications such as lithium[12] and neuroleptics,[45] illness severity,[12] and inion-nasion distance[12,48] is limited, and variance of 4–9% had been explained by these factors.[12,49]

ECT-related parameters[11,45] such as electrode placement, pulse width, dynamic impedance, pulse frequency,[49,50] and anesthetic medications[41,51,52] are known to influence the initial ST. An important limitation of our study is that the results are generalizable only to BLECT with stimulus variables and anesthetic agents, similar to the ones used in our study. It may be noted, however, that vast majority of patients in Asian countries receive BLECT, and stimulus parameters are largely similar in most centers that use brief-pulse ECT.

Age and AC were similarly significantly associated with the increase in ST over the ECT sessions [Table 5]. In an important study assessing the factors influencing the rise in ST, age was the most important predicting factor.[29,31] Similar to our finding, these studies did not find the impact of initial ST significant. The effect of AC or BZP was not examined in the earlier study,[31] while the latter did not find them significant.[29] In an earlier reporting, patients with BPAD who were on ACs had higher ST in later sessions also.[46] Thus, the clinician needs to be cautious of possible rise in ST in further ECT sessions in those above 45 years of age irrespective of initial ST. The same might be needed as well in those on AC, but not for those on BZPs.

In our study, 27.8% patients had the rise in ST over the six ECT sessions. While the two earlier studies had similar proportion (21–22%),[29,53] another had the rise in ST by 6th session in 56% patients.[31] The increase in ST was almost equally distributed from 3rd to 6th ECT sessions. Hence, there is a need to be aware of the possibility of increase in ST over the sessions and to increase the electrical charge to 1.5 times the newer ST in the next session.

While this study reflects routine clinical practice from a naturalistic perspective, it suffers from the limitations of retrospective studies. The data were highly heterogeneous in terms of specific ACs, BZPs, antipsychotics and antidepressants, and their dosage. Moreover, while analyzing the rise of ST over the course of ECT, we did not record and analyze the change of medications and their dosage through the course. The changes in the dosing would have been particularly likely with BZPs, which are titrated more frequently than AC.

**CONCLUSIONS**

This chart-based analysis of bilateral brief-pulse ECT practice confirms the influence of age and concomitantly prescribed AC on both initial ST and its subsequent rise through the course of ECT. For patients above the age of 45 and for those above the age of 40 and receiving AC, clinicians...
might start the titration of stimulus from 120 mC. BZPs do not significantly influence ST and their use, if clinically useful, may be continued without adversely influencing ECT practice.

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Conflicts of interest

There are no conflicts of interest.

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