CARDIOVASCULAR RESPONSE TO ECT IS UNAFFECTED BY EXTENT OF MOTOR SEIZURE MODIFICATION

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ABSTRACT

Effect of the extent of motor seizure modification on cardiovascular responses in ECT was studied at the second ECT session in 50 (ULECT=25) consenting patients. Twenty five patients each received either 0.5 mg/kg or 1 mg/kg of succinylcholine in a random design. Blood pressure and heart rate were recorded on five occasions during the ECT session. Extent of motor seizure was assessed on a five point scale by two raters blind to succinylcholine dose. Two raters had good interrater agreement on the scale. Significantly more patients had poor modification with 0.5 mg/kg (68%) than with 1 mg/kg (12%) of succinylcholine. Rate-pressure-product (RPP=systolic BP x Heart rate) significantly changed over the five occasions, maximal being in ictal occasion, but the two succinylcholine dose groups did not differ. Ictal RPP positively correlated with post-anaesthesia RPP, ECT stimulus dose, seizure threshold and both seizure durations (Motor and EEG). Likewise, postictal RPP correlated with seizure threshold and actual ECT stimulus dose. Neither correlated with the motor seizure modification scores. In multiple, stepwise, linear regression models neither ictal nor post-ictal RPP variance was significantly explained by the extent of motor seizure modification scores. Hence, RPP changes during ECT may be reflecting cerebral mechanisms of ECT.

Key words : Rate pressure product, ECT, motor seizure modification, succinylcholine dose.
the ECT stimulus (Jones & Knight, 1981). Use of atropine as premedication during ECT increase RPP response (Mayur et al., 1998b). Postical RPP was significantly higher after threshold BLECT than threshold ULECT (Mayur et al., 1998a). However, unilateral threshold ECT produced significantly lower RPP than unilateral suprathreshold and bilateral suprathreshold ECT conditions within the same group of patients (Gangadhar et al., 1999).

Succinylcholine is a muscle relaxant, commonly used in ECT. By its depolarising properties it increases serum potassium levels and variably modifies peripheral motor convulsions. These factors can affect cardiovascular responses both directly and indirectly. It is likely that a more pronounced convulsive response contributes to higher RPP, which was examined in this study.

**MATERIAL AND METHOD**

**Patients:**
Consenting consecutive patients referred for ECT (n=50; 31 males; Unilateral=25, Bilateral=25) formed the sample. Their mean ± SD age was 27.92±9.9 years and mean ± SD body weight 49.25±10.65 kilograms. Their diagnoses were schizophrenia (n=27), mania (n=4) and depression (n=19). After obtaining additional consent for this trial, they were part of the study at the second ECT session. All patients were right handed and continued to receive one or more psychotropic drugs, not lithium. None had cardiovascular clinical abnormalities or liver dysfunction (supported by biochemical liver function tests).

**Anesthesia:**
Patients were anesthetised with thiopentone (4 mg/kg) and atropine (0.65 mg). During the second ECT session, they were equally randomized to receive either 0.5 mg/kg or 1.0 mg/kg body weight of succinylcholine. Intermittent positive pressure ventilation with 100% oxygen was provided till resumption of spontaneous and regular breathing.

**ECT administration:**
ECT was administered using a computerized constant current (800mA) bidirectional brief pulse (1.25 msec width) device (NIVIQUE) with EFG monitoring (F3 & F4 referenced to linked mastoids). The ECT machine provides pulses at a rate of 125 pps. The total stimulus dose (mC) is adjusted by setting the stimulus train length (0.2-3.6s). The stimulus laterality was as prescribed by the referring psychiatrist. Standard bifrontotemporal and nondominant (right) D’Elia stimulus electrode positions were used for bilateral (BLECT) and right unilateral (ULECT) ECT patients respectively. ULECT patients received 2.5 times threshold stimulus and BLECT patients received 60 mC above the threshold. Motor seizure was monitored with the cuff above the right ankle. Last clonic movement on any part of the body was considered the end of motor seizure and unequivocal absence of epileptiform transients for more than five seconds on both channels was considered as the end of the EEG seizure (Gangadhar et al., 1995).

**Cardiovascular monitoring:**
Online cardiovascular and pulse oximetric parameters were monitored using Cardiocap-II. Blood pressure and heart rate were recorded before and after induction of anesthesia, 20 seconds post stimulus (ictal), postical and after spontaneous resumption of respiration.

**Assessments:**
One independent investigator (MN) was responsible for recruiting and randomising patients to two different doses of succinylcholine. The anesthetist (Rater - A; SKS) and one other psychiatrist (Rater - B; SESM) who were unaware of the dose of succinylcholine, independently rated the extent of motor seizure modification using a standardized scale (Appendix). A score of less than three and 3 or more on the scale were operationally defined as 'poor' and 'good' modifications respectively. Rater-B noted the motor and EEG seizure durations using the digital counter in the ECT machine. Two milliliters
of blood was drawn from the patients before the administration of anesthetic agents and immediately after ECT for the estimation of the serum potassium levels. Serum potassium assays on coded samples were performed without knowledge of patient data (RC).

Statistics:
Independent sample t-test and chi-square test were used to compare variables of patients with 'low dose' (0.5 mg/kg) and 'high dose' (1 mg/kg). Change in serum potassium levels from pre- to post- ECT occasions was examined using paired t-test. Interrater reliability on the modification score between raters (Rater-A and Rater-B) was assessed using Kappa correlation. For further analyses, scores by the psychiatrist (Rater-B) were used. Two way repeated measure analysis of variance (RMANOVA) was used to examine the change of RPP across five occasions (within-subject factor) with 'poor'/'good' modification as between-subject factor. RMANOVA was repeated with succinylcholine dose and with laterality as between-subject factors separately. Pearson's correlation was applied to determine factors influencing RPP in each of the five occasions. Multiple, step-wise, linear regression was used to determine the factors influencing ictal and postictal RPP for entire patient sample. The probability (alpha) was fixed at <0.05.

Results:
Socio-demographic and ECT variables were comparable between patients who received 'low' and 'high' dose succinylcholine (Table 1). The two raters showed good agreement for the scores of extent of modification (Kappa Coefficient=0.88) as well as for recorded scores of 'good' and poor modification (Kappa Coefficient=0.91) respectively. The modification score was higher in the 1 mg/kg group. Also only 3 (12%) patients in this group had 'poor' modification as against 17 (68%) of the 0.5 mg/kg group. Serum potassium levels (mean±SD meq/L) significantly rose from pre- (4.34±0.2) to post- (4.58±0.3) ictal occasion in the patients with succinylcholine of 1 mg/kg (t=4, df=23, p=0.001). No such changes were noted in the ECT session with 0.5 mg/kg (pre=4.53±0.3; post=4.57±0.3 : t=0.57, df=23, p=0.57).

RPP changed significantly over the five occasions, being highest in ictal recording (Table 2). Neither, succinylcholine dose, nor stimulus laterality, nor extent of modification (as between-subject factors) affected RPP differentially (Table 2). Ictal RPP positively correlated with post-anaesthesia RPP, ECT stimulus dose, and seizure threshold, seizure durations (both motor and EEG) but did not correlate with motor seizure modification scores. Likewise, postictal RPP correlated with threshold and actual ECT stimulus dose but not with motor seizure modification scores (Table 3).

In view of multiple correlations, ictal and postictal RPP as dependent variables, were examined in two separate multiple, stepwise, linear regression models. Age, threshold, actual

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### Table 1

| Variable                          | Low dose (0.5mg/kg) (n=25) | High dose (1mg/kg) (n=25) | T/χ², df, p |
|-----------------------------------|-----------------------------|---------------------------|-------------|
| Age (years)                       | 27.2±9.6                    | 29.2±10.2                 | 0.68, 48, 0.50 |
| Gender M: F                       | 15:10                       | 16.9                      | 0.08, 1, 0.77 |
| BLECTULECT*                       | 12.13                       | 13.12                     | 0.08, 1, 0.77 |
| ECT stimulus dose (mC)            | 139.2±58.6                  | 151.2±49.4                | 0.78, 48, 0.44 |
| EEG seizure duration in (s)       | 66.52±26.3                  | 63.1±25.7                 | 0.48, 48, 0.64 |
| Motor seizure duration in (s)     | 58.1±22.2                   | 50.8±22.7                 | 1.14, 48, 0.26 |
| Extent of motor seizure           | 2.4±0.7                     | 3.3±0.65                  | 4.15, 48, 0.001 |
| Modification on five point scale  | 14.11                       | 3.22                      | 10.7, 1, 0.001 |
CARDIOVASCULAR RESPONSE TO ECT & MOTOR SEIZURE MODIFICATION

TABLE 2
COMPARISON OF MEAN±SD RPP VALUES ACROSS DIFFERENT GROUPS

| Occasion       | Group → | Pre-anaesthesia | Post-anaesthesia | Ictal | Post-ictal | Post-RR recovery | Two-way RMANOVA |
|----------------|---------|-----------------|------------------|-------|------------|------------------|----------------|
|                |         |                 |                  |       |            |                  | F, df, p        |
|                | Succinylcholine  |                 |                  |       |            |                  |                |
| 0.5mg/kg (n=25)|         | 12253 ±3584     | 13814 ±2468      | 17700 ±4064 | 13649 ±3156 | 14248 ±4012      | F, =0.18; 46; 1.0.64 |
| 1mg/kg (n=25)  |         |                 |                  |       |            |                  | F, =0.12; 4; 0.19 |
| Laterality ULECT (n=25) |         | 11338 ±2272     | 13504 ±2370      | 18971 ±4735 | 15069 ±2977 | 14620 ±2651      | F, =0.78; 48; 1; 0.38 |
|                | BLECT (n=25) | 11939 ±3046     | 13242 ±2170      | 16971 ±5062 | 15069 ±3397 | 13419 ±3495      | F, =0.19; 4; 0.03 |
| Modification 'poor' (n=20) |         | 11552 ±3020     | 14075 ±2586      | 16839 ±3259 | 13878 ±2824 | 14611 ±3429      | F, =0.68; 4; 0.001 |
| 'Good' (n=30)  |         | 12203 ±1877     | 13666 ±1962      | 18020 ±4455 | 14140 ±2816 | 14791 ±2197      | F, =0.13; 48; 1; 0.71 |
|                |         | ±3401 ±1877     | ±13646 ±1962     | ±17452 ±1962 | ±15151 ±1962 | ±14275 ±1962     | F, =0.66; 4; 0.001 |

F, = Group effect; F, Interaction effect; F, Occasion effect; RR-Respiratory recovery

TABLE 3
PEARSON'S CORRELATION MATRIX, (VALUES REFER TO 'r' VALUES; TWO TAILED SIGNIFICANCE **p<0.01, *p<0.05)

| RPP post anaesthesia | RPP Ictal | RPP Postictal | Seizure threshold | ECT actual stimulus dose duration | Motor seizure duration | EEG seizure duration | Motor seizure modification score | RPP post anaesthesia | RPP Ictal | RPP Postictal | Seizure threshold | ECT actual stimulus dose duration | Motor seizure duration | EEG seizure duration | Motor seizure modification score |
|----------------------|-----------|---------------|-------------------|-------------------------------|-----------------------|---------------------|-------------------------------|----------------------|-----------|---------------|-------------------|-------------------------------|-----------------------|---------------------|-------------------------------|
| RPP post anaesthesia |           |               |                   |                               |                       |                     |                               | 0.49**               |           |               |                   |                               |                       |                     |                               |
| RPP Ictal            | -0.34**   | -0.06         |                   |                               |                       |                     |                               |                      |           |               |                   |                               |                       |                     |                               |
| RPP Postictal        |           |               |                   |                               |                       |                     |                               |                      |           |               |                   |                               |                       |                     |                               |
| Seizure threshold    | -0.12     | 0.37**        | 0.34**            |                               |                       |                     |                               |                      |           |               |                   |                               |                       |                     |                               |
| ECT actual stimulus dose | -0.16      | 0.34**        | 0.36**            | 0.80**                       |                       |                     |                               |                      |           |               |                   |                               |                       |                     |                               |
| Motor seizure duration | 0.05     | 0.52*         | 0.25              | -0.33**                      | -0.35**               |                     |                               |                      |           |               |                   |                               |                       |                     |                               |
| EEG seizure duration  | 0.07      | 0.32*         | 0.23              | -0.34**                      | -0.30*                | 0.89**              |                               |                      |           |               |                   |                               |                       |                     |                               |
| Motor seizure modification score | -0.09 | 0.03         | -0.19             | 0.13                         | 0.09                  | -0.23                | -0.09                         |                      |           |               |                   |                               |                       |                     |                               |
| age                  | -0.25     | -0.14         | -0.11             | 0.56**                       | 0.51**                | -0.40                | -0.39**                       | 0.18                 |           |               |                   |                               |                       |                     |                               |

239
stimulus dose, stimulus laterality, postanaesthesia RPP, extent of modification scores, EEG and motor seizure durations were the independent variables. Postanaesthesia RPP ($\beta=0.54, t=4.9, p=0.001$), stimulus laterality ($\beta=-0.37, t=3.4, p=0.01$) and motor seizure duration ($\beta=0.31, t=2.9, p=0.006$) explained respectively 24%, 13% and 10% of variance in ictal RPP. Unilateral ECT and longer motor seizure duration were associated with higher ictal RPP. Actual stimulus dose used ($\beta=0.36, t=2.7, p=0.009$) explained 13% of variance in postictal RPP; higher stimulus was associated with higher postictal RPP. Motor seizure modification scores (continuous or dichotomous) were not significant in both regressions.

**DISCUSSION**

In this study most of the patients with 1 mg/kg succinylcholine had deeper muscle relaxation and good motor seizure modification. Succinylcholine being a depolarising muscle relaxant, mobilizes intracellular potassium to extracellular compartment. Significant increase in serum potassium levels from pre- to post-ECT occasion was seen only in patients with 'high' dose succinylcholine, which validates the dose effect. However none had clinical complications, such as cardiac arrhythmia or prolonged apnea. Succinylcholine dose used in this study did not produce differential cardiovascular responses (Table 2).

Twenty patients had `poor' motor seizure modification. However, modification status did not affect RPP measures (Table 2). This observation is contrary to the belief that the violent seizures may increase myocardial stress. Subjects of this study had no cardiovascular problems, and were relatively young. Thus findings of this study may not apply to elderly or cardiac compromised patients.

There was no differences in RPP between BLECT and ULECT patients receiving suprathreshold stimulus. However, Mayur et al. (1988a) reported differences between ULECT and BLECT patients both receiving threshold stimulus. Similar observations have been reported recently (Gangadhar et al., 1999) in an intraindividual crossover design. However in the multiple regression model, unilateral ECT was associated with higher ictal RPP.

As the dose of succinylcholine and extent of motor seizure modification did not influence RPP (ictal or postictal), it can be argued that the observed effects on RPP were mediated by stimulus dose and seizure duration. Thus RPP response may be window to cerebral mechanisms during ECT. RPP response may hence, be a tool to understand the therapeutic or adverse effects of ECT. Some trends suggest that higher RPP during ECT may be associated with better therapeutic potency (Webb et al., 1990). RPP holds promise as a noninvasive, but indirect measure of CNS effects during ECT to understand neurophysiological mechanisms of ECT.

**APPENDIX**

Scale to score extent of motor seizure modification.
(A score of 2 or less indicates poor modification)

| Score | Location & intensity of convulsions |
|-------|-----------------------------------|
| 1     | Violent convulsions as in unmodified ECT |
| 2     | Bilateral motor convulsions and they are equal in intensity in both cuffed and uncuffed limbs. |
| 3     | Bilateral motor convulsions and the intensity is more in cuffed limb when compared to corresponding uncuffed limb. |
| 4     | Motor convulsions in cuffed limb and face. |
| 5     | Motor convulsions only in cuffed limb. |

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CARDIOVASCULAR RESPONSE TO ECT & MOTOR SEIZURE MODIFICATION

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