Clinical outcome of maintenance electroconvulsive therapy in comorbid Posttraumatic Stress Disorder and major depressive disorder

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ABSTRACT

Background: Post-traumatic stress disorder (PTSD) and major depressive disorder (MDD) are prevalent and frequently comorbid. Approximately 42–48% of patients with PTSD also meet diagnostic criteria for MDD. Maintenance electroconvulsive therapy (mECT) has been found to be efficacious for the prevention of recurrence of MDD. This study investigated the efficacy of mECT in the treatment of MDD with and without comorbid syndromal PTSD.
Methods: This retrospective study includes 36 patients, 26 with MDD and 10 with comorbid MDD & PTSD receiving monthly mECT for a mean of 1.5 years. The mean age was 52 ± 14 years and 25% were female. The change in PTSD and MDD symptoms in response to mECT was assessed using Clinical Global Impression - Severity Scale (CGI-S). Heart rate variability (HRV), 12-month hospitalization rate, suicide rate and all-cause mortality in response to mECT were assessed and compared between groups using repeated generalized linear regression (GLM) analysis.
Results: At mECT baseline, there were no statistically significant differences in CGI-S scores, HRV between patients with MDD alone and those with comorbid PTSD ($P > 0.05$). After 12-months of mECT, a significant increase in HRV (mean difference: 10.9 95%CI 4.8–20.3, $p = 0.001$) and decrease in CGI-S overall (mean difference: 3.5, 95% CI 3.3–3.6, $p = 0.001$)], PTSD (mean difference: 3.4, 95% CI 3.2–3.6, $p = 0.001$)], and MDD (mean difference: 3.8, 95% CI 3.5–3.9, $p = 0.001$)] symptoms in both groups were noted ($p < 0.05$). No psychiatric hospitalization or suicide occurred in any of the patients.
Conclusions: Maintenance ECT is associated with improved HRV, reduction of both major depression and PTSD symptoms, and a favorable clinical outcome.

1. Introduction

The prevalence of combat posttraumatic Stress Disorder (PTSD) in United States is 5–20% and is even greater in military personnel serving in Iraq and Afghanistan. Syndromal PTSD and major depressive disorder (MDD) are frequently comorbid, as our previous report in which 42–48% of patients with PTSD meet DSM criteria for MDD (Ahmadi et al., 2016).

Prior studies showed that electroconvulsive therapy (ECT) (Yrondi et al., 2018) is more effective than antidepressants in reducing depression and suicidal intent among patients with severe depression (Group, 2003). We recently reported the efficacy of an acute course of ECT in patients with comorbid PTSD and MDD (Ahmadi et al., 2016). An acute course of ECT produced a significant reduction in symptoms of

PTSD compared to antidepressant therapy alone (Ahmadi et al., 2016). Furthermore, ECT treatment were independently associated with a reduced risk of mortality in PTSD patients, most robust in reduction of cardiovascular mortality (Ahmadi et al., 2016).

Previous studies showed that decreased heart rate variability (HRV), an early reversible stage of alterations in autonomic nervous system activity between sympathetic and parasympathetic input, is associated with the severity of PTSD and MDD symptoms. Furthermore, improved HRV in response to the acute course of ECT was associated with favorable clinical outcomes (Ebert et al., 2010; Kemp et al., 2012).

The American Psychiatric Association (APA) task force on ECT states that maintenance ECT (mECT), carried out more than 6 months after an index course should be available to patients who have responded well to ECT treatment and when the treatment is preferred by

the patient (APA Task Force, 2001). Recurrence of MDD symptoms occur in more than 50% of MDD patients, who responded to an index course of ECT treatment over the ensuing 6–12 months in spite of receiving appropriate psychotropic medications (Bourgon and Kellner, 2000). Numerous studies suggest that maintenance ECT (mECT) prevents recurrence of MDD after acute ECT, improve patients' response to psychotropic medications, and reduce health care costs (Martinez-Amoros et al., 2012). Although PTSD is frequently comorbid with other psychiatric disorders and a predicator of poor outcome of the comorbid disorders (Boscarino, 2006; Dedert et al., 2010), the effect of mECT on patients with comorbid PTSD and MDD has not been extensively studied.

The Veteran Health Administration (VHA) is the largest health care system in the nation and provides integrated comprehensive assessment of psychiatric and other medical disorders among all veterans in the primary care setting (Baker et al., 2008). We hypothesized that mECT would improve core PTSD and MDD symptoms as well as heart rate variability and is associated with favorable clinical outcome. This study investigated the efficacy of mECT in MDD patients with and without PTSD using VHA electronic medical records.

2. Methods

This retrospective cohort study is inclusive of 36 consecutive mECT patients [10 with both MDD and PTSD, and 26 with MDD alone] in the Captain James Lovell Federal Health Care Center (FHCC) in North Chicago, IL. mECT was recommended to all patients who responded to an acute course of ECT (90% of patients received ECT), associated with high patients' acceptance rate (65%), as well as high retention rate (92%) to receive and continue mECT > 12-month, respectively.

All consecutive patients with MDD, with and without comorbid PTSD, who were free of other major psychiatric disorders without known CAD and vasoactive drugs who underwent bifrontal mECT at FHCC during 2012–2014 after completion of their acute course of ECT were included.

Demographic characteristics, clinical data, and outcome of studied patients were obtained using VHA administrative, research and clinical electronic medical records. Based on APA guidelines (APA Task Force, 2001), mECT was recommended as one of the first-line treatment options for MDD at FHCC, and upon obtaining informed consent, eligible patients received mECT. All patients were evaluated for a mean follow up period of 18 months [interval 12–36 mo].

2.1. Definition of MDD and PTSD

PTSD and MDD were diagnosed using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

2.2. ECT procedure

All studied patients received monthly mECT using a Thymatron IV ECT device (Somatics LLC, Lake Bluff, Illinois, USA). All patients received bifrontal (BF) mECT, with stimulus dose administration at least 200% above the seizure threshold based on the age-based method, with an average of 14 ± 1 ECT sessions. Procedures for anesthesia and determination of seizure adequacy (electroencephalogram (EEG) ≥ 25sec) followed standardized clinical protocols compatible with current standards of care. Anesthesia management consisted of pre-treatment with glycopyrrolate, followed by induction with an anesthetic agent (methohexital, 0.75 mg/kg or propofol 1 mg/kg in 5 cases), followed by succinylcholine (0.75 mg/kg) for muscle relaxation. Patients received oxygen with 100% O_2 with positive pressure throughout the procedure, using a disposable bag and mask. Blood pressure, heart rate, and pulse oximetry were monitored before, during, and after mECT. Electroencephalogram (EEG) was recorded from a two-channel device using right and left frontomastoid placements and

quantitative EEG indices of mECT were measured. Motor duration of seizures was recorded using a two-lead EMG from the right foot.

2.3. Clinical Global Impression – severity of illness scale (CGI-S)

The CGI-S is rated on a 7-point scale measuring the severity of symptoms at baseline and 12-month of mECT. The range of responses are from 0 = Not assessed, 1 = Normal, 2 = Borderline ill, 3 = Mildly ill, 4 = Moderately ill, 5 = Markedly ill, 6 = Severely ill, to 7 = Among the most extremely ill patients. The CGI-S of overall symptoms, PTSD symptoms, and MDD symptoms in patients at baseline, after the acute course of ECT and after mECT were measured.

2.4. Heart rate variability (HRV)

The time-domain method was used to measure HRV. The standard deviation of the average NN interval (SDANN) of the 5-min mean RR intervals was calculated at baseline and 12-month mECT. CGI-S and HRV were captured from electronic medical records by trained physicians with inter-rater reliability of 98%.

2.5. Clinical outcomes

The end primary points were psychiatric hospitalization, all-cause mortality, and suicide verified by the Social Security Death Index obtained from electronic medical records including VA Beneficiary Identification and Records Locator system (BIRLS), VA Centers for Medicare & Medicaid Services (CMS) vital status, Social Security Administration death index (SSA), and National Death Index Data. Suicide and all-cause mortality was ascertained in all patients.

3. Statistical analysis

Characteristics of the studied patients summarized as Mean $\pm$ SD and proportions. Continuous variables were compared by analysis of variance (ANOVA) and categorical variables were compared by Cochran–Mantel–Haenszel statistics. Generalized linear model regression analyses were used to assess the change in CGI-S and HRV in PTSD and MDD symptoms in response to mECT. Multivariable mixed regression analyses were employed to assess the relation on improved HRV (above median of 85 ms) with change in CGI-S. All statistical analyses were performed with SPSS version 24 (SPSS Inc., Chicago, IL, www.spss.com) and STATA version 14.0 (www.stata.com, StataCorp, College Station, TX). The level of significance was set at P < 0.05 (2-tailed). This study was approved and overseen by the Institutional Review Board Committee of the Hines VA Health Care System, Chicago, IL.

4. Results

There was no recurrence of PTSD and MDD symptoms between the end of the acute course of ECT and the start of mECT (p > 0.05). Baseline mECT CGI-S PTSD and MDD symptoms were significantly lower compared to corresponding values before acute course of ECT (p < 0.001).

At mECT baseline, there were no significant differences in age, sex, body mass index, prevalence of diabetes mellitus, coronary artery disease, family history of psychiatric disorder, history of psychiatry hospitalization, duration of MDD as well as antidepressant therapy in the MDD patients with and without PTSD (p > 0.05). The mECT baseline CGI-S of overall symptoms and HRV, prior to mECT, were not significantly different between the MDD group with and without PTSD (Table 1) (p > 0.05). At 12-month mECT, no recurrent episode of MDD, PTSD, psychiatry hospitalization or suicide occurred in either of the treatment groups. There was no statistically significant difference in mortality rate in patients with MDD alone (n = 0), compared to