The incidence of prolonged post-electroconvulsive therapy delirium: A retrospective study

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ABSTRACT

Objective: The objective of the study was to assess the incidence and determinants of electroconvulsive therapy (ECT)-induced delirium.

Materials and Methods: Using a retrospective study design, data of 488 patients undergoing modified ECT were evaluated for the development of new-onset prolonged delirium. Demographic and clinical parameters of patients who developed delirium and those who did not develop delirium were compared.

Results: 5.7% of the patients developed prolonged post-ECT delirium. The use of quetiapine in higher doses and the lack of use of antidepressants while receiving ECT were associated with the development of prolonged post-ECT delirium. None of the other clinical and ECT-related parameters emerged as a significant factor associated with the development of prolonged post-ECT delirium.

Conclusions: A small proportion of patients undergoing ECT develop post-ECT prolonged delirium.

Key words: Electroconvulsive therapy, delirium, India

INTRODUCTION

Electroconvulsive therapy (ECT) is one of the important treatment strategies in the hand of mental health professionals to manage various psychiatric conditions, which usually do not respond to medications. Various treatment guidelines recommend the use of ECT in different clinical situations. However, the use of ECT is associated with both short-term and long-term side effects. One of the important short-term or immediate side effects of the use of ECT includes post-ECT delirium. Post-ECT delirium is known to be associated with multiple complications, including the discontinuation of ECT. A recent review evaluated the factors associated with development of post-ECT delirium. This review included 43 studies. Most of these available studies have evaluated the efficacy/effectiveness of ECT in patients with major depressive disorder or affective disorders and have reported post-ECT delirium as one of the secondary outcomes of the ECT procedure. However, some of the studies have specifically focused on the side effects of ECT and these have reported factors associated with the development of post-ECT delirium. The incidence rate of post-ECT delirium has been reported to range from 3.23% to 18%.

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These studies have not reported any consistent factors associated with the development of post-ECT delirium. The various risk factors reported in one or the other study include the presence of catatonic features, impaired cholinergic functions (i.e., dementia, Parkinson’s disease), patients with cerebrovascular accident involving caudate nucleus, those with abnormalities of basal ganglia, those with moderate-to-severe deep white matter hyperintensities, those with moderate-to-severe periventricular hyperintensities, bitemporal electrode placements, concomitant use of lithium, brief pulse (compared to ultrabrief pulse), high-dose right unilateral ECT (compared to low-dose right unilateral ECT), longer ECT-related seizure, use of two stimuli in a session (compared to 1 stimulus), no clozapine use (compared to clozapine use), use of atropine (compared to use of glycopyrrolate), the use of ketamine as a premedication or an inducing agent. However, it is important to note that some of the studies have also refuted these associations.

Some of the data available also suggest that the use of haloperidol, dexmedetomidine, diazepam, and midazolam before the ECT are associated with a lower incidence of post-ECT delirium.

However, one of the problems with the available literature is that many authors have used the term post-ECT delirium for confusion occurring after the procedure of ECT, whereas others have used the same term for delirium, lasting for a long duration after the procedure of ECT, which is characterized by the full-blown picture of delirium, as defined by the nosological system. This often makes it difficult to understand, what are the factors associated with the development of post-ECT delirium. Data of prolonged post-ECT delirium are mostly limited to the case reports, which have provided the details of the course of long-lasting delirium, and some of these case reports have implicated factors such as the use of clozapine, lithium, comorbid Parkinson’s disease, or a combination of various medications.

In this background, this study, a retrospective chart review, aimed to evaluate the incidence of prolonged post-ECT delirium and to identify the possible contributing factors for the development of prolonged post-ECT delirium.

MATERIALS AND METHODS

This retrospective study was conducted at a multispecialty tertiary care teaching hospital in North India, which provides health-care services to a major part of North India. The study was approved by the ethics committee of the institute.

In this institute, bilateral modified brief-pulse ECT is administered using an indigenous machine (Medicaid India Ltd., Chandigarh, India), thrice a week (Monday, Wednesday, and Saturday). Premedications for ECT include the use of atropine or glycopyrrolate. Usually, thiopental sodium is used for induction, and succinylcholine is used for muscle relaxation during the ECT procedure. Seizure duration is monitored by the cuff method. Electrical dose is varied by changing the duration of current, with frequency and pulse width being kept constant. During the ECT course, usually, the ongoing medications are not discontinued except for the reduction of doses of benzodiazepines and antiepileptic medications.

For this retrospective study, the ECT register of the department was used to identify the patients who received ECT during the period of 2014–2016. Treatment records of patients who received ECT were screened for the development of prolonged post-ECT related delirium. ECT-related delirium for this study was defined as acute-onset confusional state, which started within 24 h of administration of ECT session and lasted for more than 24 h and was characterized by the presence of a combination of symptoms characterized by altered level of consciousness, disturbance in the attention, disorientation, disturbance in other cognitive functions, altered sleep–wake cycle, new-onset psychotic symptoms in the form of hallucination or delusions which lasted for the period of confusion only, new-onset agitation, and fluctuating course of symptoms. Patients with short-lasting post-ECT confusion were not categorized as having post-ECT delirium.

Data in terms of sociodemographic variables, clinical variables, and treatment data were extracted from the records of all the patients who received ECT, and these data were compared between those with and without delirium.

Data were analyzed using Statistical Package for the Social Science Version 14 (SPSS for Windows, Version 14.0. Chicago, SPSS Inc.). Continuous variables were evaluated as mean and standard deviation, whereas discontinuous variables were evaluated in the form of frequency and percentages. Comparisons were done using t-test, Mann–Whitney U-test, Chi-square test, and Fischer’s exact test.

RESULTS

During the study period, 488 patients received ECT, of whom 28 (5.7%) patients developed prolonged post-ECT-induced delirium. The demographic and the clinical profile of the patients who developed delirium and those who did not develop delirium is shown in Table 1. When those with and without post-ECT delirium were compared, no significant difference was observed in any of the demographic and clinical parameters, except for the fact that those with delirium were significantly more educated. In terms of various psychotropics used, there was no significant difference in the type of antidepressant, mood stabilizer,
| Table 1: Comparison of sociodemographic and clinical profile of those with and without postelectroconvulsive therapy delirium |
|---------------------------------------------------------------|
| **Without delirium** (n=460) | **With delirium** (n=28) | **χ²/t-test (P)** |
| **Age** | 42.1 (16.23) | 46.17 (14.95) | 1.29 (0.196) |
| **Age groups (years)** | | | |
| <65 | 409 (88.9) | 25 (89.3) | 0.004 (0.951) |
| ≥65 | 51 (11.1) | 3 (10.7) | |
| **Gender** | | | |
| Male | 259 (56.3) | 12 (42.9) | 1.93 (0.164) |
| Female | 201 (43.7) | 16 (57.1) | |
| **Socioeconomic status** | | | |
| Low | 58 (12.6) | 3 (10.7) | 0.51 (0.77) |
| Middle | 372 (80.9) | 24 (85.7) | |
| High | 30 (6.5) | 1 (3.6) | |
| **Education (years)** | 10.36 (4.7) | 14.76 (13.89) | 3.9 (<0.001)*** |
| **Source** | | | |
| Inpatient | 217 (47.2) | 13 (46.4) | 0.006 (0.94) |
| Outpatient | 243 (52.8) | 15 (53.6) | |
| **Diagnosis** | | | |
| Schizophrenia | 114 (24.8) | 9 (32.1) | 0.758 (0.38) |
| Bipolar disorder | 90 (19.6) | 7 (25) | 0.489 (0.484) |
| Depression | 119 (25.9) | 6 (21.4) | 0.273 (0.60) |
| Recurrent depressive disorder | 117 (25.4) | 6 (21.4) | 0.225 (0.635) |
| Acute and transient psychosis | 2 (0.4) | 0 (0.0) | |
| Psychosis NOS | 5 (1.1) | 0 (0.0) | |
| OCD with depression | 3 (0.7) | 0 (0.0) | |
| Schizoaffective | 3 (0.7) | 0 (0.0) | |
| First episode mania | 1 (0.2) | 0 (0.0) | |
| Organic psychosis | 6 (1.3) | 0 (0.0) | |
| **Presence of catatonic symptoms** | 131 | 10 | 0.673 (0.412) |
| **Medical comorbidities** | | | |
| None | 336 (73.04) | 18 (64.3) | 1.016 (0.31) |
| Hypertension | 41 (8.91) | 0 | 1.68 (0.193)† |
| Diabetes mellitus | 11 (2.39) | 0 | 0.03 (0.863)‡ |
| Hypothyroidism | 11 (2.39) | 1 (3.6) | 0.15 (0.695)§ |
| Others | 33 (7.17) | 5 (17.9) | 2.83 (0.09)∗ |
| More than one | 28 (6.08) | 4 (14.3) | 1.71 (0.19)∗ |
| **Medical comorbidities** | | | |
| None | 336 (73.04) | 18 (64.3) | 1.016 (0.31) |
| Present | 124 (26.94) | 10 (35.7) | |
| **Antidepressants** | | | |
| Venlafaxine | 108 (23.5) | 2 (7.1) | 3.152 (0.075)§ |
| Mirtazapine | 24 (5.2) | - | 0.62 (0.42)† |
| Fluoxetine | 22 (4.8) | - | 0.511 (0.47)‡ |
| Bupropion | 14 (3.0) | 2 (7.1) | 0.40 (0.52)§ |
| Escitalopram | 58 (12.6) | 3 (10.7) | 0.087 (0.76)‡ |
| Imipramine | 8 (1.7) | - | 0.495 (0.481)§ |
| Sertraline | 31 (6.7) | 2 (7.1) | 0.007 (0.934)§ |
| Amitriptyline | 5 (1.1) | 1 (3.6) | FE=0.299 |
| None | 189 (41.1) | 18 (64.3) | 5.81 (0.01)** |
| **Mood stabilizers** | | | |
| Lithium | 32 (7) | 1 (3.6) | 0.093 (0.76)† |
| Valproate | 14 (3) | - | 0.125 (0.72)‡ |
| Lamotrigine | 1 (0.2) | - | FE=1.0 |
| None | 413 (89.8) | 27 (96.4) | 0.672 (0.412) |
| **Antipsychotics** | | | |
| Risperidone | 36 (7.8) | 2 (7.1) | 0.026 (0.87)† |
| Olanzapine | 171 (37.2) | 6 (21.4) | 2.831 (0.092) |
| Quetiapine | 51 (11.1) | 8 (28.6) | 7.59 (0.005)** |
| Clozapine | 44 (9.6) | 4 (14.3) | 0.238 (0.62)‡ |
| Aripiprazole | 14 (3.0) | 2 (7.1) | 0.233 (0.63)‡ |
| Haloperidol | 4 (0.9) | 1 (3.6) | FE=0.256 |
| Trifluoperazine | 7 (1.5) | 0 (0.0) | 0.432 (0.51)† |

Contd...
Table 1: Contd...

| Without delirium (n=460) | With delirium (n=28) | $\chi^2$/$t$-test (P) |
|-------------------------|----------------------|---------------------|
| More than one           | 5 (1.1)              | 0 (0.0)             | 0.307 (0.58)$^a$ |
| None                    | 128 (27.8)           | 5 (17.9)            | 0.868 (0.35)$^a$ |

**Benztodiazepines**

| Lorazepam               | 46 (10.0)            | 3 (10.7)            | 0.015 (0.90)$^a$ |
| Clonazepam              | 107 (23.26)          | 2 (7.1)             | 3.07 (0.079)$^a$ |
| Nitrazepam              | 7 (1.52)             | 0                   | 0.432 (0.510)$^a$ |
| Zolpidem                | 6 (1.30)             | 0                   | 0.370 (0.543)$^a$ |

**Anticholinergics**

| Trihexyphenidyl         | 23 (5.0)             | 1 (3.6)             | 0.115 (0.743)$^a$ |
| Promethazine            | 19 (4.13)            | 0                   | 0.353 (0.552)$^a$ |

**Mean number of medications**

| 2.00 (0.93)             | 1.50 (0.92)          | 2.78 (0.006)$^{**}$ |

$^aP<0.01$. $^{**}P<0.001$. $^*\chi^2$ with Yates correction. SD – Standard deviation; NOS – Not otherwise specified; OCD – Obsessive compulsive disorder; FE – Fischer’s exact value

benzodiazepine, and antipsychotic received during the course of ECT, except for the fact that significantly higher proportions of those with prolonged post-ECT delirium were receiving quetiapine. Although no significant difference was seen for individual antidepressants, overall those who developed post-ECT delirium were less often receiving an antidepressant [Table 1]. Further, overall those who developed post-ECT delirium received a significantly lower mean number of medications. No significant difference was noted between those who developed post-ECT delirium and those who did not develop post-ECT delirium in terms doses of any medications [Table 2].

However, a trend was seen for the association of the development of post-ECT delirium with the use of higher doses of quetiapine ($P = 0.07$), use of other medications ($P = 0.09$), lack of use of venlafaxine ($P = 0.075$), and the lack of use of olanzapine (0.092) [Tables 1 and 2]. ECT parameters were not associated with the development of post-ECT delirium.

**DISCUSSION**

The present study aimed to evaluate the incidence and risk factors associated with the development of prolonged post-ECT delirium. In the present study, the incidence of prolonged post-ECT delirium was 5.7%. When one attempts to compare the findings of the present study with the existing literature, our findings are in the reported range.$^{[10,11,39]}$ Accordingly, it can be said that the clinicians using ECT should monitor their patients carefully for the emergence of post-ECT delirium, which is often associated with discontinuation of the ECT course. In terms of risk factors for the development of prolonged post-ECT delirium, the present study suggests that the use of quetiapine was associated with the development of prolonged post-ECT delirium. These associations can be understood from the perspective that quetiapine was used in higher doses in patients who developed post-ECT delirium.

In the present study, there was no association of age, gender, presence or absence of catatonia, ECT parameters, and the use of various psychotropics with high anticholinergic properties with the development of prolonged post-ECT delirium. Available literature has inconsistently linked the incidence of post-ECT delirium with these variables.$^{[17,9,27,40]}$ In view of this, it can be said that the issue of reliable risk factors...
for the development of prolonged post-ECT delirium is not yet settled. Accordingly, there is a need to have prospective studies focusing on prolonged post-ECT delirium as the primary outcome to understand the various risk factors.

The present study has certain limitations. These include retrospective study design, lack of data on neuroimaging findings, serum electrolytes, and other physical parameters which could also influence the development of prolonged post-ECT delirium. In view of multiple comparisons, the possibility of a type-1 error (false positive) cannot be ruled out. There could be other confounding variables, which were not evaluated and could have influenced the incidence of post-ECT delirium.

CONCLUSIONS

The present study suggests that 5.7% of the patients receiving ECT go on to develop prolonged post-ECT delirium. There is a lack of consistent risk factors for the development of prolonged post-ECT delirium. However, the use of quetiapine in higher doses and lack of use of antidepressants while receiving ECT were associated with the development of prolonged post-ECT delirium.

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Conflicts of interest
There are no conflicts of interest.

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