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ECT in Bipolar Disorder: Incidence of Switch from Depression to Hypomania or Mania

Emily Bost-Baxter, Irving M Reti and Jennifer L Payne*

Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Broadway, Suite 305, Baltimore, MD 21205, USA

Abstract

Background: Electroconvulsive Therapy (ECT) is an effective treatment for bipolar depression. However, it remains unclear how often patients with bipolar disorder who are receiving ECT "switch" from a depressed to a hypomanic or manic state. Our objective was to determine the switch rate in a sample of inpatients with bipolar disorder who received ECT, and to determine which clinical variables were associated with a greater likelihood of switch.

Methods: We performed a retrospective chart review of 100 inpatients treated with ECT for a depressive episode who had a diagnosis of bipolar disorder type I or II. We determined the incidence of switch into hypomania or mania and the impact of clinical features and ECT treatment variables on switching.

Results: The incidence of switch in our sample was 24.8%. Diagnosis, concurrent antidepressant medications, lack of the use on an antimanic agent, and a history of rapid cycling were not associated with an increased risk of switch. In a subset of patients who were not taking anti-manic medications during ECT, switch was associated with receiving a higher number of ECT treatments (p=0.02).

Conclusions: A quarter of all patients with bipolar disorder switched from a depressive episode into hypomania or mania with administration of ECT. Psychiatrists should be alert to the substantial risk of mood switching when treating bipolar depression with ECT.

Keywords: ECT; Bipolar disorder; Switch rate

Introduction

Bipolar depression is a serious psychiatric condition with a high rate of completed suicide if not treated effectively [1]. Electroconvulsive Therapy (ECT) is a rapid and effective treatment for bipolar depression [2,3]. There has been limited research, however, examining the rate of "switching" from depression to hypomania or mania during ECT in patients with bipolar disorder (BP), or the clinical characteristics and ECT treatment parameters associated with switching. A switch from depression to hypomania/mania is an important phenomenon to understand as destabilization of a bipolar patient's mood may lead to more cycling in the future, as it has been shown in the Antidepressant (AD) induced switching literature [4]. Therefore, understanding more about the risk of ECT induced hypomania/mania in depressed bipolar patients is salient to clinicians.

The literature examining the incidence of a switch from depression to hypomania/mania in patients with BP in the setting of ECT is scarce. Beyond case reports, there are four studies examining the prevalence of a switch in patients with BP while receiving ECT. One retrospective study of 15 patients with BP showed only 6.7% became manic during ECT [5]. Another retrospective study of 40 patients, found 37.5% experienced a switch to hypomania/mania [6]. A prospective study showed 22 of 57 patients (38.6%), whose depression was successfully treated with ECT, developed at least mild hypomania [7]. Finally, Henry et al. [8] found that 36% of 11 patients receiving ECT switched into hypomania or mania and that this rate did not differ from the rate of switch with the use of antidepressant medications. There is one study which examined the rate of switch in a sample of 32 patients with Major Depression and found a 12.5% rate of switch into mania [9]. These studies are all limited by small sample size and were conducted at a time when fewer medications were available to treat BP. Additionally, BP II was not an accepted clinical diagnosis when these studies were performed.

The purpose of our study was to determine the switch rate from depression to hypomania/mania during a course of ECT in patients with either BP I or BP II disorder. An updated look at the switch rate is especially important because a number of psychiatric medications, including atypical antipsychotics, have been developed in the last 15 years, which could influence the incidence of switching. Further, previous research did not consider possible differences in the course of illness between BP I and BP II patients. It is not clear, if particular clinical features, such as whether the patient has a history of rapid cycling, mixed states or psychosis or whether the patient has a history of ECT or AD induced hypomania/mania, affect the incidence of switch. We examined these clinical features, as well as specific ECT parameters, to determine their role in switching. Finally, examining current clinical practices in response to switching is timely as there are presently no treatment guidelines for ECT induced switching in bipolar patients.

Patients and Methods

We conducted a retrospective review of charts of patients aged 18 to 85 with a diagnosis of BP I or II (based on DSM-IV criteria) who were hospitalized on the psychiatry service at The Johns Hopkins Hospital between 1998 and 2001 and received ECT for depression. In order to

***Corresponding author:** Jennifer L Payne, Department of Psychiatry and Behavioural sciences, Johns Hopkins School of Medicine, 550 N Broadway, Suite 305, Baltimore, MD 21205, USA, Fax: 410-502-3755; E-mail: jpayne5@jhmi.edu

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collect a homogenous sample, only patients who received inpatient ECT and methohexital for anesthesia were included which limited our sample to the years 1998-2001 when methohexital was the anesthetic of choice. Charts were pulled on the basis of an Axis I diagnosis for either BPI or BPII disorder in addition to billing for ECT. Additionally, we excluded patients who did not have a clear history of hypomania/mania documented in their chart in order to ensure that the sample was made up of patients with BP. Our goal was to assess the effect of ECT on 100 patients. In order to attain this sample size, we reviewed 141 charts, excluding 36 charts for the following reasons: 3 charts were excluded because the subject was under 18 years of age; 13 charts were excluded because the subjects were in a manic episode on admission; 15 charts were excluded because a clear history of mania or hypomania was not documented in the records despite having a diagnosis of BP; 1 chart was excluded because of medical complications, including a recent anoxic brain injury; 4 charts were excluded because they were not available for review. We ultimately reviewed 105 charts because 3 patients received ECT twice and one patient received ECT three times. We assigned patients with repeated hospitalizations that included ECT one ID number so their demographic data would only be analyzed once. However, we examined each ECT course separately to account for the possibility of a patient becoming hypomanic/manic during one course of ECT and not another.

During the chart review, we evaluated the incidence of a switch from depression to hypomania/mania during the course of ECT. The occurrence of a switch was determined by documentation in the attending physician's daily progress note. Specifically we determined that a switch had occurred if the physician noted "hypomania" or "mania" or if the current diagnosis was changed from "Bipolar, depressed" to either "Bipolar, hypomanic" or "Bipolar, manic. " Additionally, we defined a switch as occurring during the course of ECT and did not determine if the patient had switched later after the course of ECT was finished or after the hospitalization. The clinical features we examined included the chronicity of the illness, impact of the illness on functioning and whether the patient had a history of rapid cycling, mixed states or psychotic symptoms as documented in the past and current psychiatric history. Chronicity was defined as either a) Remitting meaning the patient had a history of discrete mood episodes with periods of euthymia or b) Chronic meaning the patient had chronic mood symptoms much of the time without distinct mood episodes and periods of euthymia. Impact of the illness on functioning was divided into four categories: a) Divorced or not working but not disabled, b) Disabled but living independently, or c) Disabled and not living independently (i.e. living in a group home) or d) none of the above. A history of prior ECT or AD induced hypomania/mania was also recorded and medications that were used during ECT were noted. We identified the presence of neuroleptics, mood stabilizers and/or benzodiazepines that were started before or at the beginning of ECT so that we could differentiate those from medications given to ameliorate hypomania/mania once it manifested. Other parameters of ECT, including length of seizure induced, number of treatments, and ECT charge dosage were also recorded.

Statistical analyses, including chi square and *t*-tests, were used to compare the clinical features and ECT treatment parameters in the group of patients who switched to hypomania/mania with those who did not switch and to compare patients with BP I and BP II to each other.

Results

In table 1 we present our sample population. Of the 100 patients reviewed, 65 were female and 35 were male. The average age was 47.3 ± 17.4 years. Fifty-four patients were diagnosed with BP I and 46 patients were diagnosed with BP II. Our sample was fairly ill as one third of the patients had a history of mixed states and rapid cycling, approximately half of the patients had a history of psychosis (either current or past) and the majority was found to have mood symptoms most of the time.

We first checked whether there were differences in the clinical features of BP I and BP II patients (Table 2) and observed BP I patients had a higher incidence of a history of psychosis (p=0.017) as expected because the definition of mania but not hypomania includes psychotic symptoms. There were no other significant differences in clinical characteristics between patients with BP I and BP II disorder.

Of the 105 charts reviewed, 26 (24.8%) patients became hypomanic/manic during the course of ECT. Next we examined the rates of a variety of clinical characteristics in both switchers and non-switchers and determined whether the rates of each clinical characteristic differed between the two groups (Table 3). The rates of BPI and BP II were similar in switchers. Of the patients that switched, 14 (53.8%) were diagnosed with BP I and 12 (46.2%) were diagnosed with BP II. Surprisingly, we did not find a prior history of rapid cycling, a history of AD or ECT induced hypomania/mania or concurrent use of an AD affected the chances of switching. Absence of an anti-manic drug, namely a mood stabilizer, benzodiazepine and/or a neuroleptic, also did not affect the rate of switching. We included benzodiazepines in this analysis even though they are not conventional anti-manic drug since their sedative properties have the potential to mask hypomanic symptoms. We also examined the BP I and BP II groups separately to determine if particular clinical characteristics influenced the rate of switching for either diagnosis (data not shown). There were no significant findings in either the BP I or BP II groups.

In table 4 we demonstrate that there was no significant difference in ECT parameters, including mean charge, mean seizure duration

Variable	Mean (S.D.) or %
Average age	47.3 (17.4)
Average age of onset of illness	28.4 (16.1)
Female Sex	65 %
Bipolar I	54 %
Bipolar II	46 %
History of Rapid Cycling	33 %
History of Mixed Episode	33 %
Chronic mood symptoms	53 %
Remitting mood symptoms	40 %
Loss of marital status or employment but not disabled	38 %
Disabled but lives independently	18 %
Disabled and not living independently	14 %

Table 1: Sample Clinical and Demographic Characteristics (N=100).

Variable	**BP I (N=54)**		**BP II (N=46)**		**Chi square (p value)**
	N	(%)	N	(%)	
History of rapid cycling	17	(31.4%)	16	(34.8%)	0.019 (0.891)
History of mixed states	22	(40.7%)	11	(23.9%)	2.466 (0.116)
History of AD induced mania	12	(22.2%)	11	(23.9%)	0.040 (0.841)
History of ECT induced mania	5	(9.3%)	10	(21.7%)	2.134 (0.144)
History of psychosis	34	(63.0%)	17	(37.0%)	5.722 (0.017)*

AD= antidepressant
*p value ≤ 0.05

Table 2: Sample Clinical Characteristics by Type of Bipolar Disorder (N=100).

Variable	Switch (N=26) N (%)	No Switch N=79) N (%)	Chi square (p value)
BP I	14 (53.8%)	42 (53.2%)	0.004 (0.952)
BP II	12 (46.2%)	37 (46.8%)	
History of rapid cycling	8 (30.7%)	28 (35.4%)	0.039 (0.844)
History of mixed state	6 (23.1%)	30 (38.0%)	1.322 (0.250)
History of AD induced mania/ hypomania	5 (19.2%)	17 (21.5%)	0.062 (0.803)
History of ECT induced mania/hypomania	5 (19.2%)	10 (12.7%)	0.258 (0.612)
AD use during ECT	5 (19.2%)	16 (20.3%)	0.013 (0.910)
Only AD use during ECT	0 (0%)	7 (8.9%)	1.250 (0.264)
AD and MS/Bz/N use during ECT	5 (19.2%)	9 (11.4%)	0.472 (0.492)
MS using during ECT	6 (23%)	13 (16.5%)	0.218 (0.641)
Bz use during ECT	0 (0%)	6 (7.6%)	0.922 (0.337)
N use during ECT	7 (26.9%)	22 (27.9%)	0.008 (0.927)
No MS/Bz/N use during ECT	6 (23.1%)	24 (30.3%)	0.216 (0.642)

AD=antidepressant MS=mood stabilizer Bz=benzodiazepine N=neuroleptic

Table 3: Sample Clinical Characteristics: Comparison of Patients Who Switched to Patients Who Did Not Switch to Hypomania/Mania (N=100).

Variable	Switch (N=26) Mean (S.D.) or N (%)	No Switch (N=79) Mean (S.D.) or N (%)	T test or Chi square (p value)
ECT charge (millicoulombs)	285.33 (123.64)	279.24 (130.62)	0.202 (0.840)
Length of seizure (seconds)	37.49 (10.82)	36.55 (7.37)	0.477 (0.635)
Number of ECT received	9.0 (4.41)	8.19 (4.72)	0.771 (0.442)
Only UL ECT received	12 (46.2%)	47 (59.5%)	0.924 (0.366)
Only BL ECT received	4 (15.4%)	9 (11.4%)	0.037 (0.847)

UL= unilateral, BL= bilateral

Table 4: ECT Parameters in Patients Who Switched and Who Did Not Switch to Hypomania/Mania (N=100).

Variable	Switch (N=15) Mean (S.D.) or N (%)	No Switch (N=47) Mean (S.D.) or N (%)	T test or Chi square (p value)
ECT charge (millicoulombs)	288.34 (125.93)	254.23 (113.99)	0.934 (0.354)
Length of seizure (seconds)	38.02 (12.11)	38.0 (7.37)	0.007 (0.994)
Number of ECT received	9.87 (4.42)	6.79 (4.37)	2.370 (0.021)*
Only UL ECT received	8 (53.3%)	31 (66.0%)	0.330 (0.5658)
Only BL ECT received	2 (13.3%)	5 (10.6%)	0.082 (0.774)

UL= unilateral, BL= bilateral
*p value ≤ 0.05

Table 5: ECT Parameters in the Subset of Patients Not Prescribed Neuroleptics, Mood Stabilizers or Benzodiazepines (N=62).

and number of ECT treatments performed, between the patients who switched to hypomania/mania and the patients who did not. Of the patients who switched to hypomania/mania, only 3 (11.5%) received an increase in charge dose in the two treatments prior to becoming manic/ hypomanic. Additionally, there was no significant difference in rates of either exclusive RUL placement or exclusive BL placement between switchers and non-switchers.

Next we excluded patients who were taking anti-manic agents during ECT and checked again whether ECT parameters differed between switchers and non-switchers (Table 5). In this subset, we found

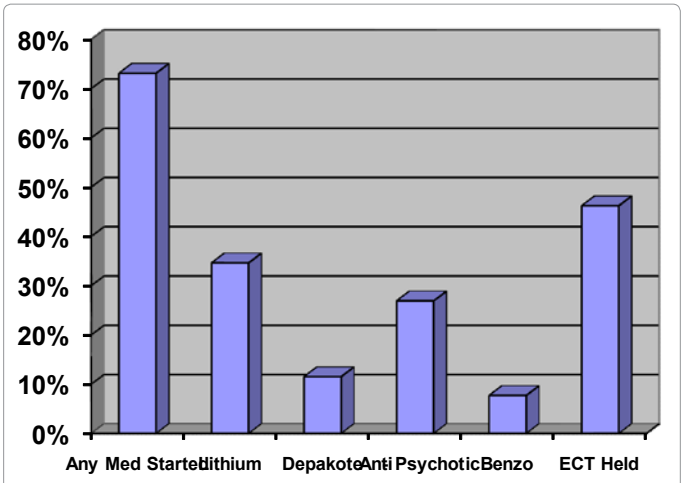

Figure 1: Interventions Performed in Response to Hypomania/Mania during ECT Treatment.

that patients who switched received an average of 9.9 ECT treatments, significantly more than the 6.8 treatments received by those who did not experience a switch (p=0.02). Only 2 (13.3%) patients received an increase in charge dose in the prior two treatments before becoming hypomanic/manic.

Finally, we examined the clinical treatment response to a switch to hypomania/mania which is shown in figure 1. The majority of patients (73.1%) who experienced a switch were started on a medication. Approximately one third were started on Lithium and a quarter received an antipsychotic. ECT was held in the setting of a switch in nearly half of patients.

Discussion

Our analysis shows the incidence of hypomania/mania in patients with BP during ECT is relatively common at 24.8%. The high frequency of switching is important for several reasons. Hypomania/mania can itself be associated with adverse outcomes, the appropriate treatment for switching is unknown and the long-term effects on future mood switching, rapid cycling and mood stability are also unknown. Accordingly, clinicians should be aware of the frequent occurrence of ECT triggered switching amongst BP patients and warn their patients about this potential adverse outcome. This is particularly important if ECT is being administered as an outpatient.

The incidence of hypomania/mania that we observed falls in the middle of prior reported rates. Our findings may differ from earlier reports because of a surge in the use and variety of pharmaceutical, including ADs and atypical antipsychotics, which could affect switching. It is also possible that due to shorter lengths of stays in hospitals in recent years, some episodes of hypomania/mania may have occurred after discharge and were therefore missed in our chart review.

We were not able to identify any clinical features of BP patients that predicted switching. The only significant predictor was the number of ECT treatments received in the subset of patients who were not taking anti-manic drugs during the course of ECT. This finding suggests that the longer one treats a bipolar depressed patient with ECT, the more likely that patient is to switch, if anti-manic agents are discontinued before ECT. Accordingly, the physician should be more cautious as the treatment course proceeds in patients who are not receiving an anti-manic treatment in conjunction with ECT. It remains unclear if this

finding suggests that patients with bipolar disorder who receive ECT should be maintained on an anti-manic agent during ECT in order to reduce the rate of switch.

AD medication triggered hypomania/mania may be dose-related [10]. We therefore examined the ECT charge dose to see if a similar phenomenon were true for ECT. Only 11.5% of all switchers and 13.3% of switchers free of anti-manic agents received an increased charge dose in the two treatments prior to a switch. Further, the overall average charge doses were the same in both switchers and non-switchers. These data suggest there is not a significant relationship between switching and the absolute charge dose.

We hypothesized that a patient with a history of rapid-cycling or of AD or ECT induced hypomania/mania would cycle more easily into hypomania/mania during ECT, but it was not observed. It is possible for ECT to be avoided in patients who have a history of easily becoming hypomanic/manic, though this is unlikely in our sample since 33% had a history of rapid cycling. It is also possible that these patients were watched more closely during ECT and treatments were stopped or the patient was medicated for preliminary signs of hypomania/mania. These interventions may not have been clearly documented in the chart. It might be expected that patients on a mood stabilizer during ECT would be less likely to become hypomanic/manic and patients on an AD might be more likely to become hypomanic/manic. Again, neither of these scenarios was supported by our study. Even when we separated patients who were only on an AD and not on any other anti-manic medications, we did not see a significant difference in switch rate. Thus, our data suggest these clinical features should not play a substantial role in deciding whether a patient should receive ECT.

There are no established treatment guidelines for ECT induced switching in patients with BP. Over 70% of patients in our study were started on a medication after the appearance of symptoms of hypomania/mania. The medication started varied amongst physicians but was usually a mood stabilizer or an antipsychotic. We do not know if a particular medication class resulted in a more desirable treatment outcome as we did not collect this information. ECT was discontinued in close to half the patients who switched despite evidence ECT is effective for mania [11]. However, it is unclear if ECT should be continued when a patient experiences a switch during treatment until a euthymic mood state is reached or if it should be stopped. A prospective study is needed to evaluate the efficacy of different treatment responses in the setting of a switch to establish guidelines for this clinical issue.

Additional limitations of our study include it being a retrospective chart review. We had to rely on chart documentation to obtain mood states and other clinical data. In addition more than 10 physicians treated the patients we studied and physicians vary in establishing diagnoses, clinical characteristics, and mood assessments. Ideally, a prospective study in which patients are examined daily using systematic mood rating scales should be undertaken.

Overall our study has demonstrated that the switch from depression to hypomania or mania is a common occurrence in patients with BP treated with ECT. BP type and clinical characteristics did not predict which patients will switch. However, the number of ECT treatments a patient receives, when not on anti-manic medications, impacted the likelihood of switching.

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