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Treatment of Electroconvulsive Therapy–Emergent Hypomania and Mania:
A Systematic Review of the Literature

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ABSTRACT

Objective: Electroconvulsive therapy (ECT)–emergent hypomania/mania is a clinically significant problem that has lacked evidence-based guidelines for effective management. The aim of this systematic literature review is to compile the current published literature on treating ECT-emergent hypomania/mania to help guide treatment course in patients with unipolar and bipolar depression.

Data Sources: MEDLINE/PubMed was searched for studies published from 1980 through August 2020 that evaluated the treatment of ECT-emergent hypomania/mania. Search terms included Boolean combinations of the following: *mania*, *hypomania*, *ECT*, *ECT induced mania*, and *ECT induced hypomania*.

Study Selection: There were 1,662 articles reviewed, and all published studies detailing the treatment of ECT-emergent hypomania/mania written in English that met inclusion criteria were included. Due to the limited number of articles, there were no restrictions.

Data Extraction: Two reviewers extracted relevant articles and assessed each study based on inclusion criteria.

Results: The literature review identified 12 articles that described the treatment course of ECT-emergent hypomania/mania in 17 patients. There were 9 patients who had no known history of manic or hypomanic episodes and were diagnosed with unipolar depression and 8 patients diagnosed with bipolar disorder. There were 4 primary treatment courses identified: continuing ECT alone, continuing ECT in conjunction with lithium, discontinuing ECT with no medication treatment, or discontinuing ECT and starting a medication.

Conclusions: The available data are insufficient to support definitive conclusions; however, potential treatment guidelines are suggested within the review to providers based on the limited data available.

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Electroconvulsive therapy (ECT) is considered a safe and effective treatment for bipolar depression and is particularly effective in cases of treatment-resistant depression (TRD).[1] However, a known adverse reaction of ECT in patients with bipolar affective disorder (BPAD) is emergent hypomania/mania, in which a patient switches into a potentially dangerous phase of their illness. The patient may present with inflated self-esteem or grandiosity, flight of ideas, euphoria, decreased need for sleep, increased distractibility, talkativeness, and increased goal-directed activity. The reported incidence of this phenomenon varies widely, with study rates ranging from as low as 2% to as high as 38.6%.[2–10] The most recent retrospective chart review, performed by Bost-Baxter and colleagues in 2012[8] and involving the largest sample of patients of all studies examining ECT-emergent switching, retrospectively studied 105 patients with a history of BPAD I or II who received ECT and reported a 24.8% incidence of switch to hypomania or mania. Their study analyzed for predictors that would increase a risk of switching, but they were unable to find any significant clinical features of BPAD patients that predicted switching.[8] There was also no significant difference in rates of either exclusive right unilateral electrode placement or exclusive bilateral electrode placement in patients who experienced a switch compared to those who did not.[8] The only significant predictor identified was the number of ECT treatments received in the subset of patients not receiving antimanic agents.[8] Additionally, ECT-emergent hypomania/mania has been suggested to occur less frequently than switching associated with antidepressant medications.[9] This finding is particularly interesting because there have been no studies to evaluate if ECT causes the switch to hypomania/mania or if it is the natural course of BPAD cycling.

Regardless of whether hypomania/mania during ECT represents a recurrent mood episode in an individual with BPAD or if it is an adverse effect of ECT, there are no established guidelines on how to treat the emergent hypomania/mania. The second edition of the American Psychiatric Association (APA) Task Force Report on electroconvulsive therapy[11] notes that there is "no established strategy" to treat ECT-emergent mania and lists several options, including continuing ECT, holding ECT and observing for spontaneous remission, or aborting ECT and starting a mood stabilizer.

There is also limited literature on patients treated with ECT for unipolar depression who develop their first episode

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Clinical Points

- Electroconvulsive therapy (ECT)–emergent hypomania/mania is a clinically significant problem that has lacked evidence-based guidelines for effective management.
- The literature review revealed a difference in treatment approaches to ECT-emergent hypomania and mania in patients with unipolar depression compared to patients with bipolar affective disorder.
- These provisional guidelines provided in the literature review are based on limited data and are meant only to serve as a template to consider for the treatment of this very complex and potentially serious complication of ECT treatment. Further systematic collection of clinical outcome data is needed to help guide clinical management of ECT-emergent mania and hypomania.

of emergent hypomania/mania during an ECT treatment course. Of the 5 studies that examined incidence of ECT-emergent hypomania/mania,[2–5,8] only 2 studies evaluated patients with diagnoses other than bipolar depression. Lewis and Nasrallah[2] performed a retrospective chart review of all patients who received ECT while hospitalized over a 3-year period and identified that 6.4% (n = 6) of 94 patients developed ECT-emergent symptoms of mania; of those 6 patients, 4 were diagnosed with primary unipolar depression. Similarly, Angst and colleagues[3] performed a retrospective chart review that found 8.6% of 139 patients diagnosed with unipolar depression who were treated with ECT developed emergent symptoms of hypomania/mania.

The treatment of ECT-emergent hypomania/mania in patients with no known history of episodes of mania or hypomania becomes particularly challenging because of the unclear etiology and cause of the symptoms. Recent changes in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (*DSM-5*), now classify ECT-emergent mania as meeting criteria for a manic episode and thus categorize the patient as having a bipolar I disorder.[12] Ultimately, the lack of literature examining treatment of ECT-emergent hypomania/mania leaves providers questioning if patients with no known history of manic or hypomanic episodes should be treated the same as patients with a known history of mania. This is especially true when patients develop ECT-emergent symptoms of organic euphoria. *Organic euphoria* is defined as a transient state of euphoria occurring over a few hours to days that is associated with some cognitive impairment, but does not meet full criteria for a hypomanic or manic episode within *DSM-5*, especially in terms of duration of symptoms.[13] This transience may lead providers wondering if the emergent symptoms are not representative of a true switch and may instead represent a euphoria related to relief from the depression. This distinction is significant because without established treatment guidelines to support providers when this known phenomenon occurs, providers may prematurely discontinue ECT treatment courses, and relapse in depression may occur.

Therefore, the aim of this systematic literature review is to compile the current published literature on treating ECT-emergent hypomania/mania to help guide treatment course in patients with unipolar and bipolar depression.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines were followed for the current systematic review[14]; however, the protocol for this systematic review was not registered prior to conducting the review. MEDLINE/ PubMed was searched for reviews, meta-analyses, and primary studies published in print from 1980 through August 2020 that evaluated the treatment of ECT-emergent mania/hypomania. Search terms included Boolean combinations of the following: *mania*, *hypomania*, *ECT*, *ECT induced mania*, and *ECT induced hypomania*. Two rounds of screening were conducted by two reviewers independently (authors A.A.C. and A.C.). During stage 1 of the search, all records were screened for relevance based on title, and then on title and abstract. Articles not written in English and that did not evaluate ECT-emergent hypomania/mania were removed prior to the next round of screening. In the subsequent stage of screening, full texts of articles were thoroughly reviewed for inclusion. All published adult human studies from 1980 through August 2020, written in English, assessing and detailing the treatment course of ECT-emergent hypomania/mania were included. Articles and events that did not meet criteria for a mania or hypomania event and did not detail post-hypomania/mania treatment courses and outcomes were not included in the literature review results. Due to the limited number of articles, there were no restrictions regarding type of article, quality of study, randomization, or use of a control group. One study[15] was an abstract published online, but was not included in this review because it did not clearly describe the treatment of the ECT-emergent hypomania/mania and because the full study was not published. Finally, studies that did not provide descriptions of the treatment of ECT-emergent hypomania/mania were excluded.

RESULTS

Search Results and Study Selection

A MEDLINE/PubMed search yielded 1,662 articles including duplicates, which were screened by title to obtain 149 associated articles. Duplicates were removed, and 111 articles were further screened by title and abstract, which resulted in 52 articles. The 52 full-text articles were thoroughly reviewed for inclusion, and 12 articles met full criteria and were included in this review. A PRISMA flow diagram is provided in Figure 1.

An instance of a study in which inclusion criteria were not met but that warranted acknowledgment was a reported initial episode of ECT-induced mania in a 78-year-old woman.[16] The initial episode was observed and treated not by the author, but rather in a separate community hospital and was only vaguely described by the patient's sister to the author 2 months later.[16] The author suggested it may

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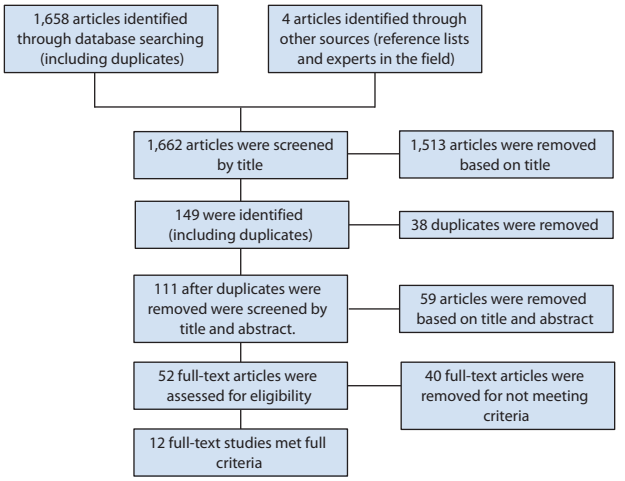
Figure 1. PRISMA Flowchart



have represented a delayed onset of ECT-induced mania 2 months later; however, the treatment course of the emergent symptoms, time course of onset and duration, and relation to ECT were unclear. The episode did not meet inclusion criteria and was not incorporated in to the results.[16] Serby[16] detailed the occurrence of ECT-emergent mania in a subsequent hospitalization, and its treatment course, therefore meeting inclusion criteria and allowing for inclusion in the results.

Literature Review Results

The treatment of ECT-emergent hypomania/mania was described in 12 articles, all of which were case reports or case series. The literature review included 17 total patients whose treatment courses were documented, 9 patients who had no known history of manic or hypomanic episodes and were diagnosed with unipolar depression and 8 patients diagnosed with bipolar disorder. There were 4 primary treatment courses identified: discontinuing ECT with no medication treatment, discontinuing ECT and starting a medication, continuing ECT alone, and continuing ECT in conjunction with lithium. The results of each article are detailed in Table 1.

1. ECT discontinuation and spontaneous remission. Andrade and colleagues[6] described 4 patients diagnosed with "depressive illness" or "depressive disorder" with no documented history of prior episodes of mania or hypomania who developed mania in response to ECT. All 4 patients were treated with discontinuation of ECT, and their ECT-emergent symptoms of mania spontaneously resolved within 2–5 days. Andrade and colleagues[17] also described a teenage patient with a first episode of depression with psychotic features and no prior history of episodes of mania or hypomania who developed recurrent mania after separate ECT treatments. The symptoms of mania resolved within 2 days of discontinuing ECT except for the last episode, in which lithium was added to achieve resolution.[17] Of the 3 cases described by Devanand and colleagues,[13] 1 patient, a 43-year-old woman diagnosed with "unipolar psychotic depression," developed symptoms of mania after the fifth ECT treatment, which worsened after the sixth treatment. Thus, ECT was discontinued and the symptoms resolved after 5 days.[13]

There was only 1 patient with a history of BPAD treated with discontinuation of ECT, and that discontinuation was followed by spontaneous resolution of manic symptoms. DeQuardo and Tandon[18] described a patient diagnosed with bipolar disorder, depressed melancholic type, based on *DSM-III* criteria who was initiated on ECT and within 24 hours of the first session developed symptoms of mania. ECT was discontinued, and the mania resolved within 36 hours. Upon resolution of the symptoms of mania, the patient developed another depressive episode that was treated concurrently with lithium and ECT for 4 additional ECT treatments with resolution of depression and no subsequent development of mania.[18]

2. ECT discontinuation and medication initiation. There were reports 6 of patients, 3 with no known history of manic or hypomanic episodes and 3 with diagnoses of bipolar disorder, who developed ECT-emergent hypomania/mania and were treated with discontinuation of ECT plus initiation of a mood stabilizer.

The 3 patients with no known history of manic or hypomanic episodes were treated in a variety of ways. Lee and colleagues[19] described a patient with a diagnosis of MDD whose treatment course consisted of discontinuing ECT after symptoms of mania progressively worsened over "several days." The patient was started on quetiapine, which resulted in the resolution of mania symptoms over an unclear duration of time.[19] The patient later developed depressive symptoms, and sertraline was started with resolution of depression over the next week. Serby[16] described treatment of ECT-emergent hypomania/mania in the only older adult patient described in the literature, a 78-year-old woman with a diagnosis of "major depression and anxiety attacks." She developed emergent symptoms of mania after 7 ECT treatments; discontinuation of ECT and initiation of valproic acid were followed by resolution of the manic symptoms.[16] The authors did not report the amount of time the manic symptoms took to resolve in this patient.[16]

Saatcioglu and Guduk[20] described the more complex medication treatment course of a 33-year-old patient with MDD with psychotic features who was immediately initiated on treatment with lithium and chlorpromazine during the first episode, haloperidol and switch to lithium and chlorpromazine during the second episode, and haloperidol, biperiden, and diazepam during the third episode. This patient had Young Mania Rating Scale (YMRS) scores of 28 during her first episode of ECT-emergent mania, indicating moderate mania, and 24 during the second and third episodes, indicating mild mania, all of which were immediately treated with medications; duration of episodes was not described.

The 3 patients with BPAD diagnoses whose ECT was discontinued were all started on lithium either as the sole antimanic agent or in combination with other

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Table 1. Results of the Systematic Review of Treatment of ECT-Emergent Hypomania/Mania

Study	Study Type	Age (y)/Sex/ Diagnosis	Medications Immediately Preceding ECT	Type of ECT Utilized	Onset of Mania or Hypomania	Treatment Course
Andrade et al 1988[6]	Case series	40/F/"depressive disorder"	Not listed	Alternate-day bilateral sinusoidal wave treatment ECT	Within 12 hours of sixth ECT	• ECT was discontinued, and mania spontaneously resolved within 2 days • Depressive symptoms returned, so ECT was reinitiated. After third ECT, mania returned. ECT was discontinued, and mania spontaneously resolved within 2 days
		25/F/"depressed"	Not listed	Alternate-day bilateral brief-pulse ECT	Within 24 hours of ninth ECT	• ECT was discontinued, and mania spontaneously resolved within 5 days
		45/F/"depressive illness"	Not listed	Alternate-day bilateral sinusoidal wave treatment ECT	Within 24 hours of first ECT	• ECT was discontinued, and mania spontaneously resolved within 2 days • Depressive symptoms returned, so ECT was reinitiated. There was no resurgence of mania during 6 ECT treatments
		55/M/"depressed"	Not listed	Alternate-day bilateral brief-pulse ECT	After second ECT	• ECT was discontinued, and mania spontaneously resolved within 3 days
DeQuardo and Tandon 1988[18]	Case report	42/F/"*DSM-III* diagnosis of bipolar disorder, depressed, melancholic type"	"Combination of tricyclic antidepressants, lithium, carbamazepine, neuroleptics, and L-thyroxine"	Unilateral, nondominant, brief-pulse ECT	Within 24 hours of first ECT	• ECT was discontinued, and mania spontaneously resolved within 36 hours • Patient became depressed again. She was started on lithium (serum level, 0.89 mEq/L), and ECT was resumed. She was euthymic after 4 ECT treatments. There was no resurgence of mania during 7 ECT treatments
Devanand et al 1988[13]	Case series	22/M/bipolar disorder, current episode "severe depression"	Imipramine 200 mg/d, lithium 600 mg/d; medications discontinued 2 weeks before ECT except lorazepam 1 mg twice daily as needed	Right, unilateral, brief-pulse, constant current stimulation ECT	After fifth ECT, patient became hypomanic. Manic symptoms developed after sixth ECT	• ECT was discontinued, and mania spontaneously resolved in 5 days • During the next week, patient became depressed and ECT was resumed. After third ECT, hypomania returned. He continued ECT for 5 sessions but remained hypomanic. Symptoms improved after initiation of lithium 1,800 mg/d (serum level, 0.96 mEq/L) and nortriptyline 125 mg/d
		57/F/*DSM-III* diagnosis of bipolar disorder, depressed, with psychotic features	Lorazepam 1 mg twice daily PRN and haloperidol 5 mg once 2 days prior to ECT for agitation	Bilateral ECT	After second ECT, patient became hypomanic. Manic symptoms developed after fourth ECT	• ECT was discontinued, and patient was hypomanic for next 5 days • Lithium was started, and patient was discharged 2 weeks later on lithium 1,800 mg/d
		43/F/"unipolar psychotic depression"	Imipramine 200 mg/d, haloperidol 6 mg/d; medications discontinued 1 week before ECT except lorazepam 1 mg twice daily as needed.	Bilateral ECT	After fourth ECT, patient was noted to be "laughing uncontrollably about minor things"	• ECT was continued. After fifth ECT, noted to be disoriented. MMSE score had decreased from 20/30 to 14/30 after sixth ECT and to 11/30 after tenth ECT. ECT was discontinued after 20 treatments due to partial response • Later responded to fluphenazine decanoate 37.5 mg every 2 weeks, desipramine 75 mg at bedtime, and benztropine 1 mg twice daily
Andrade et al 1990[17]	Case report	16/F/first-episode *DSM-III* diagnosis of MDD with psychotic features	Not listed	Alternate-day brief-pulse bifrontotemporal sinusoidal wave ECT 120–130 V × 0.6s	"Immediately after recovery" from fourth ECT	• ECT was discontinued, and mania spontaneously resolved within 2 days • 10 days later, psychotic depression returned. ECT initiated with imipramine 150 mg at bedtime. After sixth ECT, mania returned. ECT was discontinued, and mania spontaneously resolved within 2 days • 10 days later, psychotic depression returned. ECT was initiated with imipramine 150 mg at bedtime and trifluouperazine 15 mg at bedtime. After third ECT, mania returned. ECT was discontinued, and mania spontaneously resolved within 2 days • Lithium 1,500 mg/d was started, and patient remained euthymic

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Table 1. (continued)

Study	Study Type	Age (y)/Sex/ Diagnosis	Medications Immediately Preceding ECT	Type of ECT Utilized	Onset of Mania or Hypomania	Treatment Course
Sanders and Deshpande 1990[23]	Case report	65/F/"bipolar illness" current episode "manic and psychotic"	Chlorpromazine and verapamil	Non-dominant unilateral ECT	Received 5 ECT treatments with dramatic improvement. Discharged from inpatient but developed mania within 2 days of first maintenance ECT treatment	• ECT was continued and mania spontaneously resolved after first of 4 additional treatments
Serby 2001[16]	Case report	78/F/"major depression and 'anxiety attacks'"	Not listed	Bilateral square wave ECT treatments		• Patient was hospitalized for depression and received 7 bilateral "square-wave" ECT treatments and was subsequently discharged. Within 1 week of the seventh ECT treatment, she developed mania and was treated with discontinuation of ECT, readmitted to psychiatric unit, and treated with valproic acid until mania resolved
Saatcioglu and Guduk 2009[20]	Case report	33/F/*DSM-IV* diagnosis of major depressive disorder with psychotic features	Haloperidol 20 mg/d, biperiden 4 mg/d	First 3 ECT used bilateral "unmodified ECT with no anesthesia." Initial ECT dose of 126 mC. Subsequent ECT dose range between 118 mC and 120 mC. The last ECT session used "modified ECT with anesthesia and muscle relaxants"	After seventh ECT session, patient developed psychomotor agitation, euphoria, and grandiosity with YMRS score of 28	• ECT was discontinued. Patient was discharged on lithium 900 mg/d and chlorpromazine 300 mg/d • Two years later, patient stopped medications due to pregnancy but developed postpartum depression. ECT was initiated. After third ECT, patient developed mania with YMRS score of 24. ECT was discontinued; symptoms improved with lithium 1,200 mg/d and chlorpromazine 300 mg/d • 21 months later, patient developed depression. She received 5 sessions of ECT. She was discharged AMA with slight improvement of depression • 6 months later, the patient was hospitalized with a "similar presentation." She was started on haloperidol 30 mg/d and biperiden 4 mg/d. After 5 sessions of ECT, she developed mania with YMRS score of 24. ECT was stopped. She had full remission of symptoms with haloperidol 20 mg/d, biperiden 4 mg/d, and carbamazepine 400 mg/d
Zavorotnyy et al 2009[24]	Case report	66/F/bipolar disorder, current episode depression	"All other drugs tapered off" except quetiapine 200 mg/d, which was continued throughout ECT course	Right unilateral ECT 3 times per week	After 12 ECT sessions, during week 5, patient developed depressive and manic symptoms cycling in 24- to 48-hour intervals	• ECT was discontinued. Ultrarapid cycling continued, and depression worsened • 1 week later, ECT and lithium were restarted. After 7 days, symptoms improved. At 2 weeks, the symptoms had resolved
Lee et al 2014[19]	Case report	55/M/major depressive disorder	Citalopram 20 mg/d, mirtazapine 30 mg at bedtime	Not listed	After third ECT session, patient developed manic symptoms including sexual disinhibition, which worsened over several days	• ECT and all medications were discontinued • The patient was started on quetiapine and symptoms of mania and sexual disinhibition subsided; however, depression resumed. Sertraline was started. His symptoms gradually improved over the next week

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Table 1. (continued)

Study	Study Type	Age (y)/Sex/ Diagnosis	Medications Immediately Preceding ECT	Type of ECT Utilized	Onset of Mania or Hypomania	Treatment Course
Huber and Burke 2015[25]	Case report	67/F/bipolar disorder type I, current episode depressed	Venlafaxine 300 mg/d, olanzapine 5 mg/d, lithium 250 mg/d; venlafaxine and lithium were discontinued before initiation of ECT, but olanzapine was continued during ECT	Right unilateral ECT 3 times per week for first 8 treatments. Bilateral stimulation was used starting at treatment 9	After eleventh ECT session, patient began experiencing improvement of symptoms. After twelfth ECT session, she developed mania that cycled in 12- to 72-hour intervals	• ECT discontinued and olanzapine increased to 10 mg/d • Ultrarapid cycling worsened, so ECT was recommenced after 3 missed sessions in combination with lithium, which was restarted • Symptoms slowly improved. After 23 ECT treatments, patient was euthymic
Li et al 2015[21]	Case report	40/F/bipolar I, current episode depressed, without psychotic features	Lamotrigine 100 mg/d, ziprasidone 80 mg/d, bupropion 300 mg/d; medications were discontinued before initiation of ECT	Not listed	After second ECT session, patient developed "euphoria and grandiosity." After third ECT session, she had "full-blown manic episode" with YMRS score of 23	• ECT was continued, but mania worsened • After the fifth session, ECT was discontinued and patient was started on lithium 800 mg/d, thioridazine 100 mg/d, and clonazepam 6 mg/d • Patient had full remission of the mood episode 3 weeks later
Thomas et al 2018[22]	Case report	50/M/major depressive disorder for past 3 years; "however, his wife reported 2 episodes of mania in the past 10 years both lasting over 2 months"	Valproic acid 1,000 mg twice daily and venlafaxine 375 mg daily; medications were discontinued before initiation of ECT	Bifrontal ECT, pulse width = 1 ms, pulse frequency = 20 Hz, train duration = 6 s, current = 800 mA	"Within hours" of third ECT treatment presented with YMRS score of 17	• ECT was continued and hypomania spontaneously resolved after his fourth ECT treatment with YMRS score of 5 • Then started on lithium 1,200 mg/d monotherapy and remained euthymic at 6-month follow-up

Abbreviations: AMA = against medical advice, ECT = electroconvulsive therapy, MMSE = Mini-Mental State Examination, YMRS = Young Mania Rating Scale.

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medications.[13,21] Devanand and colleagues[13] described 2 patients with history of BPAD. One patient's symptoms were treated with discontinuation of ECT plus lithium 1,800 mg/d with resolution of manic symptoms over the course of 2 weeks prior to being discharged. The other patient was treated with discontinuation of ECT plus lithium 1,800 mg/d in combination with nortriptyline 125 mg/d. It took 2 months for mood symptoms to resolve prior to discharge.[13] Li and colleagues[21] discontinued ECT and treated the patient with a diagnosis of BPAD type 1 with lithium 800 mg/d, thioridazine 100 mg/d, and clonazepam 6 mg/d. The patient had a full remission of the acute mood episode 3 weeks later.[21]

3. ECT continued as the sole antimanic agent. Two case reports detailed treatment of patients with known history of manic and hypomanic episodes who were continued on ECT treatment alone.[22,23] Sanders and Deshpande[23] reported treatment of a patient with "bipolar illness" who developed symptoms of ECT-emergent hypomania/mania after the first ECT treatment that resolved after the subsequent ECT treatment. The patient tolerated a total of 5 ECT treatments without recurrence of ECT-emergent hypomania/mania.[23] Thomas and colleagues[22] reported a second episode of ECT-emergent hypomania/mania in a patient who had no documented prior diagnosis of bipolar disorder, but whose wife reported his having "2 episodes of mania in past 10 years both lasting over 2 months," who was successfully treated with a ECT as the sole antimanic agent.[22]

4. ECT continued in combination with lithium. Two case reports[24,25] described treating ECT-emergent hypomania/mania with continuation of ECT in combination with lithium in patients with BPAD. Zavorotnyy and colleagues[24] reported the case of a 66-year-old woman with BPAD who, after approximately 12 sessions of ECT, developed "rapid changes of mood with depressive and manic symptoms," which initially were managed with discontinuation of ECT; however, despite ECT discontinuation, the symptoms persisted. The patient's ECT was resumed, and lithium was started, resulting in resolution of symptoms within 2 weeks.[24] Similarly Huber and Burke[25] described a 62-year-old woman with BPAD type I whose lithium was discontinued prior to initiation of ECT, who then developed "rapid mood changes" after 12 treatments of ECT. The patient's symptoms were initially treated with discontinuation of ECT and an increase of olanzapine from 5 mg to 10 mg.[25] However, symptoms persisted, and her treatment team decided to resume ECT and restart lithium.[25] The patient displayed approximately 4 more possible discrete mood episodes of rapid cycling that occurred after restarting ECT and lithium, but after 10 days symptoms progressively resolved and she reached complete remission after a total of 23 ECT treatments.[25]

DISCUSSION

Overall, case reports and case series in the literature suggest that there are 4 primary methods of treatment, and contrary to the popular approach of discontinuing ECT on development of ECT-emergent hypomania/mania, there is evidence to support the continuation or resumption of ECT to effectively treat patients in these circumstances.

Within the literature reviewed, 9 of the 17 patients had a history of unipolar depression prior to ECT and subsequently developed ECT-emergent symptoms of hypomania/mania. The patients with unipolar depression were all treated with discontinuation of ECT, and either symptoms of hypomania/mania resolved spontaneously in 2–5 days or medications were started including quetiapine, valproic acid, or lithium in combination with other medications.[6,13,16,17,19,20] These reports described manic syndromes in patients who did not have a previous diagnosis of bipolar disorder. A total of 4 cases of unipolar depression spontaneously resolved in less than 4 days and may not represent true switches into mania, but rather temporary mood elevations from ECT, as the *DSM-5* duration criteria of a manic or hypomanic episode were not reached prior to resolution of symptoms. Only 1 patient was documented to have a manic episode that lasted at least 1 week, consistent with the *DSM* criteria for mania,[16] while 2 other patients experienced symptoms of mania of approximately 4 days' duration, representing a *DSM* diagnosis of hypomania.[6,13] These results suggest that if emergent hypomania/mania occurs during treatment with ECT in a patient with no history of bipolar disorder, it is reasonable to hold ECT treatment temporarily and monitor, as most reviewed cases resolved spontaneously.[6,17] However, if the symptoms continue, medication management with an antimanic agent is recommended. These results are based on limited research, and further studies are needed to elucidate the underlying etiology, cause, and treatment of ECT-emergent hypomania/mania that occurs in patients with no known history of manic or hypomanic episodes.

Seven of the remaining 8 patients with a prior diagnosis of BPAD were each treated more aggressively with medications and/or continuation of ECT. Three patients were treated with discontinuation of ECT and initiation of medications, 2 were treated with continuation of ECT as the sole antimanic agent, and 2 were treated with ECT continuation concurrently with lithium.[13,21–25] There was only 1 patient with a history of bipolar disorder, depressed melancholic type, based on *DSM-III* criteria who was treated with discontinuation of ECT, and the symptoms of mania resolved within 36 hours.[18] The 3 patients whose ECT was discontinued were all started on lithium either as the sole antimanic agent or in combination with other medications as described in the Results section.[13,21] This suggests patients with a history of BPAD or more complex unipolar depression such as MDD with psychotic features may require adjunctive mood stabilizer pharmacotherapy as opposed to unipolar depression patients, whose symptoms of ECT-emergent mania may resolve spontaneously on discontinuation of ECT. If the manic switch occurs in a patient with established BPAD, it may be reasonable based on the literature reviewed to hold ECT temporarily and resume any mood stabilizers that were being held during ECT treatment. There has been extensive literature documenting the treatment of

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hypomania and mania with mood stabilizers. The algorithm of Mohammad and Osser[26] suggests treating acute mania with lithium, followed by quetiapine or another second-generation antipsychotic based on effectiveness. Therefore, it would also be reasonable to start additional antimanic agents to treat the symptoms of ECT-emergent mania as needed, and hospitalization should be considered in patients with history of severe manic episodes.

The dilemma, however, of discontinuing ECT on emergence of hypomania/mania is that patients may again develop TRD, particularly those with more complex pathology. ECT is one of the most effective treatments for MDD and the gold standard for treatment of TRD.[11] Therefore, based on the results of this literature review, it may be suggested that continuation or resumption of ECT when symptoms of mania do not resolve may be considered. Continuing ECT alone was reported as the sole antimanic agent in 2 cases. This approach is supported by studies that have demonstrated upwards of 85% efficacy of ECT alone in reduction and clinical improvement of acute mania.[27]

The other treatment course described in the literature is the continuation of ECT in combination with lithium. There were 2 cases[24,25] for which successful treatment of ECT-emergent hypomania/mania with a combined treatment course of continued ECT with initiation of lithium was reported. However, the literature on the combination of lithium and ECT is controversial.[28] Some case reports and literature reviews suggest concurrent use of lithium and ECT to be safe and effective.[29,30] However, a more recent retrospective cohort study of a national sample of 64,728 adult psychiatric inpatients[31] found 11.7-fold higher odds of developing delirium for those treated with the combination of ECT and lithium compared to those treated with ECT alone. Patel and colleagues[31] also found an elevated risk of cognitive impairment in patients treated with lithium and ECT in combination.[31] The APA Task Force[32] recommends withholding lithium for 24 hours before starting ECT. Caution should be taken when treating patients with lithium and ECT in combination, suggesting this combination should not be first line for the treatment of ECT-emergent hypomania/mania if the acute ECT is going to be continued as well. Continuation or maintenance ECT with concurrent lithium may be better tolerated because of the decreased frequency of ECT treatment, although lithium should still be held the day before treatment.

There are no cases described in the literature of treating ECT-emergent hypomania/mania with ECT continuation in combination with any other mood-stabilizing or antipsychotic medications besides lithium. However, the current literature on the treatment of acute mania with ECT provides more insight into the efficacy of combining other mood stabilizers and medications with ECT. Rakesh and colleagues[33] performed a randomized controlled trial (RCT) examining outcomes of bitemporal ECT combined with anticonvulsants, specifically valproic acid and carbamazepine in half or full doses, versus ECT alone. Their data indicated a significant reduction in YMRS score when ECT was given in combination with full doses of anticonvulsants compared to the halved doses.[33] There were no significant differences observed in seizure threshold or cognition in the anticonvulsant-and-ECT group versus the ECT-alone group within their study.[33] Similarly Jahangard and colleagues[34] performed an RCT of ECT with valproic acid versus ECT alone and also showed significant improvement in YMRS scores without report of any significant adverse effects. Penland and Ostroff[35] presented a case series suggesting that lamotrigine combined with ECT is safe and has no impact on ECT stimulus dosing. Despite the evidence suggesting efficacy of combining ECT with mood stabilizers for the treatment of acute mania, no definitive conclusions can be reached given the dearth of studies examining the effects of anticonvulsants in combination with ECT for the treatment of ECT-emergent hypomania/mania.

The benefit of antipsychotic use in the context of ECT is the overwhelming evidence that it is well tolerated when concurrently utilized and thus can be continued during ECT treatment.[28,36,37] The literature also suggests that the combination may be beneficial and have an additive effect.[38] Antipsychotics are commonly used in the acute treatment of mania; however, there is limited research evaluating the combined effect of ECT and antipsychotic medication in the treatment of mania. Case reports[39–42] describing the combination of ECT with clozapine or chlorpromazine in the treatment of mania suggest it may be safe and effective. A recent RCT[43] examined the treatment of 50 patients whose mania was unresponsive to conventional psychotropic medications who were randomized to bilateral, brief-pulse ECT treatment at stimulus doses either just above or at 2.5 times above their individually titrated dose. The patients were continued on risperidone or olanzapine and as-needed intramuscular lorazepam or haloperidol.[43,44] The results indicated that 88% of patients achieved remission with no adverse effects reported, although the study failed to include a control group.[43] While there is limited literature on the combination of antipsychotics with ECT for the treatment of acute mania, this appears to be a promising combination that may be considered in the treatment of ECT-emergent hypomania/mania.

This literature review is limited by the lack of published articles documenting the treatment of ECT-emergent hypomania/mania. There is a need for more research including randomized controlled trials and prospective studies with larger sample sizes to fully elucidate the etiology and cause of ECT-emergent hypomania/mania and the most effective method of treating ECT-emergent hypomania/mania in different patient populations such as patients who develop ECT-emergent mixed-mood hypomania/mania states. Of note, there were no articles detailing the treatment of ECT-emergent mixed-mood episodes that may occur during ECT treatment courses. This phenomenon may require a more tailored ECT treatment course and should be further studied. Additionally, there are currently no studies evaluating the incidence rate of ECT-emergent hypomania/mania in older adult or child and adolescent populations, nor

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are there any recommendations on how to treat the symptoms when they occur in this subset of patients, who often require nuanced approaches to treatment.

Finally, while Bost-Baxter and colleagues[8] found no significant difference in rates of either exclusive right unilateral electrode placement or exclusive bilateral electrode placement in patients who experienced a switch compared to those who did not, there are currently no studies evaluating the role of ECT electrode placement in treating ECT-emergent hypomania/mania. For example, there is more extensive literature documenting the benefit of bilateral or bifrontal electrode placement in the treatment of acute mania, which thus may suggest that patients receiving unilateral electrode placement of ECT could benefit from a switch to bilateral or bifrontal electrode placement when symptoms of ECT-emergent mania occur.[45] However, the role of electrode placement, stimulus dose, and delivery frequency in the treatment of ECT-emergent hypomania/mania needs more rigorous study and evaluation to make more precise clinical recommendations.

CONCLUSION

In conclusion, ECT-emergent hypomania/mania is a common event during the course of ECT with an estimated incidence of 24.8%.[8] There are no existing clinical guidelines recommending how to treat ECT-emergent hypomania/mania. The available data are insufficient to support definitive conclusions; however, the following guidelines are suggested based on the limited data that are available and described in the preceding sections:

1. If ECT-emergent mania occurs in a patient with no history of BPAD, it is reasonable to hold the ECT temporarily and monitor, as most cases reviewed resolve spontaneously. If the symptoms of mania continue, medication treatment with an antimanic agent is reasonable.
2. For patients with a history of BPAD, the patient and family should receive informed consent about the risk of possible switch and how to monitor for early signs of potential switch. If the manic switch occurs in a patient with established BPAD, any held mood stabilizers should be resumed and additional antimanic agents added as needed. If the patient has a history of severe manic episodes, hospitalization should be considered.
3. If in either aforementioned case the symptoms do not resolve, resuming ECT is reasonable, preferably in the hospital setting. Attempts should be made to dose antimanic agents and mood stabilizers in a manner such that they do not need to be completely held the day prior to treatment (eg, morning or split dosing). Antipsychotics have the additional benefit of not needing to be held for ECT and are reasonable to consider in combination with ECT for treatment of emergent symptoms of mania.
4. Following resolution of the manic symptoms, it is reasonable to resume continuation or maintenance ECT to prevent further cycling into depression. In these cases, mood stabilizers and/or antimanic agents should be continued to help prevent future switches and to aid in promoting remission in the overall course of the illness.

This review demonstrates the heterogeneity in treatment of different patient populations experiencing a manic switch during the course of ECT. These provisional guidelines are based on limited data and are meant only to serve as a template to consider for the treatment of this very complex and potentially serious complication of ECT treatment. Further systematic collection of clinical outcome data is needed to help guide clinical management of ECT-emergent mania/hypomania.

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