Bipolar disorder in adults: Indications for and efficacy of electroconvulsive therapy

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INTRODUCTION

Patients treated with electroconvulsive therapy (ECT) receive general anesthesia and muscle relaxation, followed by a small electric current administered to the scalp to produce a generalized cerebral seizure. ECT is a standard treatment for unipolar major depression; it is also used for bipolar major depression and less commonly for mania and bipolar mood episodes with mixed features. Indications for ECT include failure to respond to multiple antidepressant medication trials, or acute illness (eg, severe suicidality) that requires a rapid and definitive response. A course of ECT typically consists of 6 to 12 treatments given two or three times per week.

This topic reviews the indications and efficacy of ECT for bipolar disorder. Separate topics provide an overview of ECT (including pre-ECT evaluation, use of concurrent medications, treatment course, and adverse effects), and discuss the indications for and efficacy of ECT in unipolar major depression, the medical consultation for ECT, and the technique for performing ECT.

- (See "Overview of electroconvulsive therapy (ECT) for adults".)
- (See "Unipolar major depression in adults: Indications for and efficacy of electroconvulsive therapy (ECT)".)
- (See "Medical evaluation for electroconvulsive therapy".)
- (See "Technique for performing electroconvulsive therapy (ECT) in adults".)

DEFINITION OF BIPOLAR DISORDER

Bipolar disorder is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3) [1]. The subtypes of bipolar disorder include bipolar I and bipolar II. Patients with bipolar I disorder experience manic episodes and nearly always experience major depressive and hypomanic episodes. Bipolar II disorder is marked by at least one hypomanic episode, at least one major depressive episode, and the absence of manic episodes. Additional information about the clinical features and diagnosis of bipolar disorder is discussed separately. (See "Bipolar disorder in adults: Clinical features" and "Bipolar disorder in adults: Assessment and diagnosis".)

OVERVIEW OF ECT

A separate topic review provides an overview of ECT, including the pre-ECT evaluation, treatment of patients with comorbid general medical illnesses, use of concurrent medications, informed consent, treatment course, adverse effects, and maintenance ECT. (See "Overview of electroconvulsive therapy (ECT) for adults".)

INDICATIONS

In bipolar disorder, as in unipolar major depression, severe symptoms in the current mood episode compel the use of electroconvulsive therapy (ECT). Treating bipolar patients with ECT is consistent with numerous practice guidelines [2,3].

ECT as first-line treatment — Studies of ECT (primarily in patients with unipolar major depression) indicate that ECT provides a rapid clinical response and may thus be indicated as first-line treatment in urgent clinical situations, including [4-8]:

- Severe suicidality (eg, explicit intent to carry out a well thought out suicide plan) (see "Suicidal ideation and behavior in adults")
- Severe psychosis (eg, nearly continuous auditory hallucinations commanding patients to kill themselves) (see "Psychosis in adults: Epidemiology, clinical manifestations, and diagnostic evaluation")
- Malignant catatonia – Prominent psychomotor disturbances (eg, immobility, mutism, or waxy flexibility) accompanied by fever, autonomic instability (labile or elevated blood

pressure, tachycardia, tachypnea, and diaphoresis), delirium, and rigidity (see "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis")

- Depression with fluid and food refusal that worsens general medical status due to dehydration, weight loss, and malnutrition

Administration of ECT as first-line treatment for bipolar disorder usually occurs in patients with major depression. ECT is rarely used as first-line treatment in mania because almost all of these patients receive pharmacotherapy as initial treatment. Nevertheless, manic delirium, which is rare but life threatening, is a primary indication for ECT [4,9-11].

Bilateral ECT is generally recommended in clinically urgent situations because of its greater efficacy and speed of response, compared with unilateral ECT. (See "Technique for performing electroconvulsive therapy (ECT) in adults", section on 'Electrode placement'.)

Medication-resistant patients — ECT is often indicated for bipolar mood episodes that are resistant to several (eg, three to five) courses of pharmacotherapy [7,12]:

- **Bipolar major depression** – The most common indication for ECT in bipolar patients is severe major depression [7]. The risk of precipitating hypomania or mania with ECT is very low; by contrast, antidepressant medications may be problematic because of switching. (See "Bipolar major depression in adults: Efficacy and adverse effects of antidepressants", section on 'Risk of switching to mania'.)

  For patients with bipolar depression who switch to hypomania or mania during treatment with ECT, we generally continue ECT because it is effective for mania. Alternatively, it is reasonable to continue ECT and add lithium or a second-generation antipsychotic (eg, olanzapine or risperidone), or to discontinue ECT and start pharmacotherapy.

- **Mania** – Although mania typically responds to ECT [4,13], it is used less frequently for this indication than major depression because acutely manic patients typically respond to pharmacotherapy. However, ECT may be life saving for manic delirium [9,14,15].

- **Bipolar mood episodes with mixed features**

- **Rapid cycling** (see "Rapid cycling bipolar disorder in adults: Treatment of major depression", section on 'Refractory patients')

However, reserving ECT for patients who are highly resistant to pharmacotherapy may entail months or years of suffering with futile treatment [7].

CONTRAINDICATIONS TO ECT

There are no absolute medical contraindications to electroconvulsive therapy (ECT) [4]. Rather, there is a relative risk benefit ratio for patients and their specific clinical situation. This is determined by assessing the seriousness and urgency of the psychiatric illness and the severity of any comorbid general medical conditions. Patients with severe general medical illnesses can usually be treated with ECT safely, when appropriate precautions are taken. (See "Overview of electroconvulsive therapy (ECT) for adults", section on 'Patients with comorbid general medical illness' and "Medical evaluation for electroconvulsive therapy".)

EFFICACY

Electroconvulsive therapy (ECT) is effective for bipolar mood episodes, including those resistant to pharmacotherapy [2,12,16]. As an example, a prospective observational study included 500 patients with bipolar disorder who failed pharmacotherapy for acute mood episodes and were then treated with ECT plus pharmacotherapy (eg, antidepressants, antipsychotics, and/or lithium) as indicated; response (much or very much improvement) occurred in 69 percent [17]. In addition, a prospective observational study followed 70 patients with bipolar disorder (36 with major depression, 34 with a mixed episode) for a mean of 57 weeks after a successful course of acute ECT and found that approximately 60 percent had a favorable course of illness without onset of new major mood episodes [18].

Bipolar major depression — Open label randomized trials suggest that for patients with bipolar major depression, ECT is superior to pharmacotherapy [2,16]:

- A six-week randomized trial compared ECT with prespecified algorithm-based medications in patients who had failed two lifetime trials of pharmacotherapy (n = 66) [19,20]. ECT was administered three times per week with right unilateral electrode placement and brief pulse stimulation. The analysis per protocol found that response (reduction of baseline symptoms ≥50 percent) occurred in more patients who received ECT than medications (74 versus 35 percent). However, remission in the two groups was comparable (35 and 30 percent). It is worth noting that improvement with ECT may have been greater had bilateral electrode placement been used rather than right unilateral, but cognitive impairment may have also been greater with bilateral ECT [21-24].

- An eight-week trial assigned patients (n = 76) to one of five treatments; marked improvement with each treatment was as follows [25]:

- ECT – 78 percent of patients
- Imipramine – 59 percent
- Phenelzine – 45 percent
- Isocarboxazid – 7 percent
- Pill placebo – 37 percent

ECT was superior to isocarboxazid and placebo.

In addition, a review found that in patients with bipolar major depression (most of whom had failed pharmacotherapy), response to ECT occurred in approximately 50 to 75 percent [2]. A prospective observational study included 295 patients with bipolar major depression who failed pharmacotherapy and were then treated with ECT plus pharmacotherapy (eg, antidepressants, antipsychotics, and/or lithium) as indicated; response (much or very much improvement) occurred in approximately 70 percent [17]. A review conducted by the US Food and Drug Administration concluded that the evidence for treating bipolar major depression with ECT is strong [26,27].

Numerous randomized trials have demonstrated the efficacy of ECT for unipolar major depression [26,27], and observational studies suggest that symptom resolution of bipolar major depression with ECT is comparable to that of unipolar depression [28,29]:

- A pooled analysis of six observational studies compared the efficacy of ECT in bipolar major depression (n = 316) with the efficacy in unipolar major depression (n = 790 patients); each study included bipolar and unipolar patients, and five studies were prospective [30]. Remission rates were similar for bipolar and unipolar patients (53 and 51 percent).

- A subsequent study found that the rate of response (much or very much improved) with ECT was comparable for patients with bipolar major depression (n = 113) and patients with unipolar major depression (n = 559) (78 and 81 percent) [31].

The predictors of response to ECT in bipolar major depression are generally similar to those in unipolar depression and include the presence of psychosis, psychomotor retardation, and catatonia [4]. However, the absence of these predictors does not imply the likelihood of poor response as response to ECT in bipolar depression is excellent.

Some studies suggest that response to ECT occurs more rapidly in bipolar major depression than unipolar major depression [32-35]. However, the difference is small, and other studies have found that time to response is comparable [28,36].

Additional information about the efficacy of ECT for unipolar major depression is discussed separately. (See "Unipolar major depression in adults: Indications for and efficacy of electroconvulsive therapy (ECT)", section on 'Efficacy'.)

Mania — Evidence for the efficacy of ECT for mania includes the following studies, which indicate that response occurs in approximately 80 percent of patients [2,4,7,16,17,37]:

- A randomized trial compared ECT (eight bilateral treatments) plus chlorpromazine (600 mg per day) with simulated (sham) ECT plus chlorpromazine in 30 manic patients [38]. Improvement was greater with ECT, and the rate of recovery with ECT compared with simulated ECT was 80 percent (12 out 15 patients) versus 7 percent (1 out 15).

- A review of observational (mostly retrospective) studies examined the effectiveness of ECT in a total of 589 manic patients, most of whom were resistant to pharmacotherapy [39]. Marked improvement or remission occurred in 80 percent. A subsequent retrospective study, in patients treated with ECT and concurrent antipsychotic medication (n = 33), also found that response occurred in approximately 80 percent [40].

In addition, ECT may be superior to pharmacotherapy for mania [2]:

- Data drawn from two randomized trials compared ECT (n = 22 patients) with lithium plus haloperidol (n = 5) in manic patients who initially did not respond to lithium or a first-generation antipsychotic [39,41]. The rate of remission with ECT compared with lithium plus haloperidol was 59 percent (13 out of 22) versus 0 percent (0 out of 5).

- A randomized trial compared ECT with lithium (serum concentration 0.6 to 1.5 mEq/L [0.6 to 1.5 mmol/L]) in 34 patients with mania [42]. During the first eight weeks of the study, improvement was greater with ECT; however, subsequent outcomes were comparable.

- A retrospective study that compared ECT (n = 37) with lithium (n = 203; minimum serum concentration 0.9 mEq/L [0.9 mmol/L]) found that marked improvement occurred in more patients who received ECT (78 versus 62 percent) [43].

For patients with mania or bipolar major depression, response to ECT may be comparable. In a retrospective study, the effectiveness of ECT was similar for the following groups [44]:

- Mania (n = 37 patients) – Marked improvement occurred in 78 percent
- Bipolar major depression (n = 55) – 69 percent
- Unipolar major depression (n = 368) – 70 percent

For patients with mania, there are no well-established predictors of response to ECT. Response may be decreased in treatment-resistant patients who have not responded to multiple medication trials, compared with patients who receive ECT as first-line treatment [4,39].

Mixed features — ECT may be effective for medication-resistant bipolar mood episodes with mixed features [2,16,45]. In three prospective observational studies in patients with bipolar mixed states, response occurred in approximately 70 percent [17,46,47].

Rapidly cycling — Evidence for the efficacy of ECT in treating rapid cycling bipolar patients with major depression is discussed separately. (See "Rapid cycling bipolar disorder in adults: Treatment of major depression", section on 'Refractory patients'.)

Peripartum patients — ECT may be efficacious for pregnant and postpartum bipolar patients and appears to be safe for perinatal patients.

- (See "Bipolar disorder in pregnant women: Screening, diagnosis, and choosing treatment for mania and hypomania".)
- (See "Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy", section on 'Electroconvulsive therapy'.)
- (See "Technique for performing electroconvulsive therapy (ECT) in adults", section on 'Pregnancy'.)
- (See "Bipolar disorder in postpartum women: Treatment".)

Maintenance treatment — Maintenance ECT may be useful for patients unresponsive to maintenance pharmacotherapy. (See "Bipolar disorder in adults: Choosing maintenance treatment", section on 'Electroconvulsive therapy'.)

ADVERSE EFFECTS

An overview of the adverse effects of electroconvulsive therapy (ECT) is discussed separately. (See "Overview of electroconvulsive therapy (ECT) for adults", section on 'Adverse effects'.)

Cognitive effects — Bipolar patients treated with ECT generally do not suffer adverse neurocognitive effects:

- A six-week randomized trial compared right unilateral ECT (high dose and brief pulse) with pharmacotherapy in patients hospitalized for bipolar major depression [48]. Seven domains of neurocognitive function were assessed, including processing speed, attention, working memory, verbal learning (anterograde memory), visual learning, reasoning, and

autobiographical (retrograde) memory. Neurocognitive performance in nearly all domains improved and was comparable for the two groups. However, retrograde memory worsened in both groups, and was more impaired in the group that received ECT than medications.

- A review of eight prospective studies (seven were observational) examined cognitive functioning in patients with bipolar disorder who were treated with ECT (total n = 143) [29]. The primary findings were as follows:
  - In studies that compared patients who received ECT with patients who received pharmacotherapy, cognitive functioning was generally comparable. Although one study found that performance on two cognitive tests was worse with ECT than pharmacotherapy, patients were not randomly assigned to treatment, and it is likely that ECT was administered to patients who were more severely ill (including patients with greater cognitive impairment).
  - Among patients with mania who received ECT, neuropsychological functioning after the course of treatment was generally improved from baseline.
  - Among patients with bipolar major depression, cognitive functioning before and after the course of ECT was comparable.

Additional information about the cognitive effects of ECT is discussed separately. (See "Overview of electroconvulsive therapy (ECT) for adults", section on 'Adverse cognitive effects'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Bipolar disorder".)

SUMMARY

- Bipolar disorder is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3) [1]. The subtypes of bipolar disorder include bipolar I and bipolar II. (See 'Definition of bipolar disorder' above and "Bipolar disorder in adults: Clinical features" and "Bipolar disorder in adults: Assessment and diagnosis".)
- Clinicians prescribing electroconvulsive therapy (ECT) should be familiar with the pre-ECT evaluation, treatment of patients with comorbid general medical illnesses, use of

concurrent medications, informed consent, treatment course, adverse effects of ECT, and use of maintenance ECT. (See "Overview of electroconvulsive therapy (ECT) for adults".)

- ECT provides a rapid clinical response and may thus be indicated as first-line treatment in urgent clinical situations, including (see 'ECT as first-line treatment' above):
  - Severe suicidality
  - Severe psychosis
  - Malignant catatonia
  - Depression with fluid and food refusal
  - Manic delirium
- ECT is often indicated for medication-resistant bipolar major depression, mania, and mood episodes with mixed features, based upon the apparent effectiveness of ECT for bipolar patients who do not respond to several courses of pharmacotherapy. (See 'Medication-resistant patients' above and 'Efficacy' above.)
- There are no absolute medical contraindications to ECT; rather, there is a relative risk benefit ratio for patients and their specific clinical situation. (See 'Contraindications to ECT' above.)
- Patients with bipolar disorder can be safely treated with ECT. (See 'Cognitive effects' above and "Overview of electroconvulsive therapy (ECT) for adults", section on 'Adverse effects'.)

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