

Psychopharmacology of Bipolar Disorders in Children and Adolescents



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KEYWORDS

• Bipolar disorder • Pharmacotherapy • Children • Adolescents • Pediatric

KEY POINTS

- Bipolar disorder is a chronic condition that oftentimes requires pharmacologic intervention.
- There are limited medication data available.
- Most studies targeted short-term treatment.

INTRODUCTION

Bipolar disorder is a chronic and debilitating illness that often begins early in life, with the first episode frequently occurring in adolescence.^{1,2} Compared with adults, youth diagnosed with bipolar disorder experience more severe symptoms and have poorer prognosis.³ Bipolar disorder is estimated to be the fourth leading source of disability in individuals of 10 to 24 years of age.⁴

The recommended treatment for bipolar disorder includes a combination of psychopharmacological and psychosocial interventions.⁵ Until recently, very limited data pertaining to pharmacologic management of pediatric bipolar disorder were available, and children were essentially treated as “small adults,” with clinicians adapting

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information from clinical trials on adults. However, the efficacy and safety profiles of pharmacologic interventions appear to be different in youth and adults.⁶

Pharmacotherapy of youth with bipolar disorder can be challenging. The choice of medication mostly depends on the phase of illness (manic, depressive, or maintenance treatment). In this review, we examine the current evidence for pharmacologic management of bipolar disorder in youth based on the phase of illness. In addition, we discuss medications currently approved by the Food and Drug Administration (FDA) for the treatment of bipolar disorder (Table 1), and summarize studies directly comparing monotherapy options (Table 2) and combinations of different classes of medications (Table 3). Although the focus of this review is pharmacotherapy of pediatric bipolar disorder, psychosocial interventions are important and should not be discounted.

ACUTE MONOTHERAPY OF MANIC AND MIXED STATES

Lithium and Anticonvulsants

Lithium has been the gold standard for treatment of bipolar disorder in adults. It is also the first medication approved by the FDA for pharmacotherapy of bipolar disorder in children 12 years and older. At the time of its approval, all recommendations regarding dosing, safety, and efficacy were adapted from adult data. In efforts to bridge this gap, the Collaborative Lithium Trials (CoLT) examined dosing strategies, pharmacokinetics, safety, and short-term and long-term efficacy of lithium in youth aged 7 to 17.⁷ In an open-label trial, lithium was found to be reasonably effective in reducing symptoms of a manic or mixed episode. Interestingly, only initial responders to lithium during the first 8 weeks maintained mood stabilization over the next 16 weeks.⁸ The efficacy of lithium as a treatment for bipolar disorder has been further documented in a double-blind placebo-controlled trial⁹ (Table 4). Lithium was superior to placebo in reducing symptoms during manic or mixed episode as well as increasing Clinical Global Impression-Improvement scores.

The Treatment of Early Age Mania Study (TEAM) describes a direct comparison of lithium, divalproex, and risperidone. In this randomized clinical trial, more youngsters with bipolar disorder responded to risperidone than to lithium or divalproex.^{10,11} However, the risperidone group had higher rates of metabolic side effects.

Based on a randomized placebo-controlled trial and open-label studies discussed previously, lithium has been shown to be effective for acute treatment of manic and mixed states of pediatric bipolar disorder. However, acutely, it is less effective when compared with antipsychotics. In addition, lithium requires careful monitoring due to a narrow therapeutic window, which limits its use in some patients.

Table 1 Medications approved by the Food and Drug Administration for the treatment of pediatric bipolar disorder			
Medication	Phase of Bipolar Disorder	Age, y	Daily Dose Range, mg/d
Lithium	Mixed/manic	12–17	300–2400
Risperidone	Mixed/manic	10–17	0.25–2.5
Olanzapine	Mixed/manic	13–17	2.5–20
Aripiprazole	Mixed/manic	10–17	2–30
Quetiapine	Mixed/manic	10–17	50–600
Olanzapine/fluoxetine combination	Depressive episode	10–17	3/25–12/50

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