Pharmacological Treatment of Bipolar Disorder: 2013 Update Summary

Rajiv Tandon, MD
Professor of Psychiatry
University of Florida College of Medicine

Introduction

The Florida Medicaid Drug Therapy Management Program guidelines for the treatment of bipolar disorder were first published in 2005 and have since been updated on a biennial basis. This fifth update, like the previous iterations, was based on a comprehensive review of the literature and its critical evaluation by a panel of academic and community clinicians. As in previous editions, three related but separate guidelines were developed for the pharmacological treatment of acute bipolar depression, acute bipolar mania/hypomania, and continuation/maintenance treatment of bipolar disorder, respectively. Beginning with recommendations for elements of a good diagnostic assessment, treatment options were categorized at different levels based on the strength of the evidence and clinical considerations of comparative efficacy and safety.

Comprehensive Assessment and Principles of Treatment

With the introduction of the DSM-5 in 2013, revisions in the diagnostic assessment became necessary in order to be consistent with changes made in the DSM-5 treatment of bipolar disorder. The category of major mood disorders was split into two chapters and bipolar disorder was explicitly separated from the depressive disorders. In the definition of mania/hypomania, increased emphasis was placed on the symptom of increased energy and activity, and both increased energy/activity along with heightened mood are necessary for a diagnosis of mania or hypomania. Particular care in the distinction of bipolar depression from unipolar depression is important for appropriate treatment planning and the use of the Mood Disorders Questionnaire (MDQ) was recommended for this purpose. The DSM-IV category of bipolar disorder-mixed was eliminated because of the rarity of its utilization in clinical practice and was replaced by the use of a "mixed features" specifier for both mania and depression if symptoms of depression were present in the context of mania or symptoms of mania/hypomania were present in the context of major depression, respectively. The presence of mixed features has important implications for proper treatment selection.

Since bipolar disorder is often co-morbid with addictive disorders, including smoking, these must be addressed at initial assessment and over the course of treatment. Increased mortality and morbidity due to medical illness must be addressed in this population, and therefore these need to be carefully assessed at initial presentation and on an ongoing basis. Since patients with bipolar disorder are at an increased risk for suicide and violent behavior, these need to be specifically monitored at initial presentation and during the course of treatment. Good pharmacological treatment needs to be combined with appropriate psychosocial care. Since treatment response varies across patients, careful assessment of symptomatology and side-effects is essential in the course of treatment. The use of appropriate rating scales is highly recommended.

Pharmacological Treatment of Acute Bipolar Depression

For acute bipolar depression, one important change was the addition of lurasidone as a therapeutic agent at Level 1. Lurasidone was found to be effective and safe in the treatment of bipolar depression in two large-scale clinical trials and was consequently approved by the Food and

Drug Administration (FDA) for the treatment of acute bipolar depression, both as monotherapy and as an adjunct to lithium or divalproex. It joins quetiapine as the Level 1a recommendation for bipolar I disorder, with quetiapine also recommended for bipolar II disorder. Despite its approval by the FDA for treatment of bipolar depression, the combination of [olanzapine + fluoxetine] remained as a Level 1b recommendation because of the metabolic safety concerns associated with the use of olanzapine. In the absence of an adequate response to level 1 treatment, it is recommended that a psychiatrist consultation be obtained. Level 2, level 3, and level 4 treatment recommendations were provided on the basis of declining evidence of efficacy and/or increasing risk of safety concerns or poor tolerability.

Pharmacological Treatment of Acute Bipolar Mania

For the pharmacotherapy of acute mania, updated treatment recommendations are provided, although the changes are relatively minor. Lithium is significantly underutilized in the treatment of acute mania in clinical practice and its prominent position as a level 1a recommendation, as monotherapy or in combination with certain antipsychotics, is re-emphasized. There are important distinctions between different antipsychotic agents with regards to their utility in the treatment of mania and this is explicitly reflected in the new treatment guidelines. For example, the use of olanzapine or haloperidol, in spite of their proven efficacy, is now relegated to a Level 1b recommendation because of metabolic and EPS safety concerns, respectively. Level 2, level 3, and level 4 treatment recommendations are provided on the basis of declining evidence of efficacy and/or increasing risk of safety concerns or poor tolerability.

Continuation and Maintenance Pharmacological Treatment of Bipolar Disorder

Several changes are apparent in the guidelines for maintenance treatment of bipolar disorder. Lithium remains a strong level 1a recommendation but divalproex is no longer recommended at this level since there are trials that have found it to be a less effective monotherapy maintenance treatment. Monotherapy with quetiapine, aripiprazole, long-acting injectable risperidone, and lamotrigine are recommended at level 1a, with distinctions made between the first three and lamotrigine with regards to utility in the prevention of manic episodes and depressive episodes, respectively. Despite its proven efficacy, olanzapine has been relegated to Level 1b because of metabolic safety concerns. Level 2 and level 3 treatment recommendations are provided on the basis of declining evidence of efficacy and/or increasing risk of safety concerns or poor tolerability.

References

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