Introduction

The Role of Atypical Antipsychotics in the Treatment of Bipolar Disorder

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Bipolar disorder is a pernicious psychiatric illness with long-lasting effects on all aspects of an affected individual's life: social, family, and work. The most severe form of bipolar disorder, bipolar I, has a lifetime prevalence of 1%. The inclusion of less severe forms of the illness, such as bipolar II and cyclothymia, increases the prevalence of bipolar disorder to between 2% and 7%.[1] Bipolar disorder is sixth among all causes of years lived with disability worldwide and third among psychiatric disorders, after major depressive disorder and alcohol abuse.[2]

The number of options for acute treatment of bipolar disorder is increasing rapidly. For many years, the therapeutic options for acute mania were limited to lithium and the conventional neuroleptics. In the mid-1990s, valproate was shown to be efficacious in the treatment of mania. The past several years have seen burgeoning evidence for the utility of atypical antipsychotics in the treatment of acute mania. More recently, options have emerged for acute treatment of bipolar depression as well.

This supplement provides an overview of our current knowledge of the treatment of acute mania as well as maintenance therapy for bipolar disorder. A group of world-leading experts on bipolar disorder summarizes useful information in both areas.

The first article, by Paul E. Keck, Jr., provides an overview of the use of second-generation antipsychotics in the treatment of acute mania, including traditional first-line treatments such as lithium, valproate, and carbamazepine. The article summarizes data on olanzapine, perhaps the best-studied medication in the treatment of bipolar disorder, focusing on acute monotherapy studies. There are also data from monotherapy studies of risperidone and discussions of data from studies of ziprasidone and aripiprazole in the treatment of mania. While second-generation antipsychotics show comparable efficacy results, special attention should be paid to the safety and tolerability profiles of each when choosing treatment options for individual patients.

Increasingly, clinicians are turning from monotherapy to combination treatments in managing acute mania as well as for maintenance treatment. The reasons for this include attempts at more rapid stabilization and improved rates of remission. Data addressing the issue of antipsychotic augmentation of mood stabilizer therapy are presented by Charles L. Bowden, who concludes that augmentation produces better clinical results than monotherapy.

David L. Dunner discusses the use of antipsychotics among bipolar disorder subpopulations, including patients with mixed mania or psychotic episodes, children and adolescents, and the elderly. Although substantially less research has been conducted on the use of atypical antipsychotics in these subgroups, some data allow us to form judgments on the treatment of outpatients in these groups. Notably, many patients fall into the "subgroup"

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category, and information is particularly important in trying to manage patients with bipolar disorder in these groups.

A number of differences exist in the safety and tolerability profiles of the atypical antipsychotics. They are described and summarized in the fourth article, by Roger S. McIntyre and Jakub Z. Konarski. The authors classify adverse events into 6 categories: metabolic, neurologic, cardiovascular, hyperprolactinemia, reproductive health and safety, and affective symptom induction. Available data for each of the atypical antipsychotics are presented in each category. This review is particularly timely in light of increasing concerns that obesity, type 2 diabetes, and metabolic syndrome are associated with some atypical antipsychotics.

In the final article in this supplement, Roy H. Perlis examines the existing guidelines and algorithms for the treatment of bipolar disorder. These include the 2002 revision of the American Psychiatric Association guidelines, the British Association for Psychopharmacology guidelines, the Expert Consensus Guideline Series, and the Texas Medication Algorithm Project. Dr. Perlis identifies commonalities and differences among the guidelines and tries to summarize them in a way that is helpful to the individual clinician. One of the biggest differences among the guidelines is the recommendation on the use of atypical antipsychotics in combination with a mood stabilizer. The American Psychiatric Association guidelines recommend first-line combination therapy of an antipsychotic with a mood stabilizer, whereas the British Association for Psychopharmacology guidelines support the use of an atypical antipsychotic or divalproex but do not specifically recommend lithium. However, there are more similarities than differences in the guidelines' approaches to the treatment of mania. Dr. Perlis's article is, therefore, an important resource for choosing an appropriate approach to the manic patient.

In summary, atypical antipsychotics represent an important advance in the treatment of bipolar disorder. This advance is derived from the demonstrated efficacy of atypical antipsychotics as monotherapy and augmentation therapy with mood stabilizers, as well as a better tolerability profile than conventional antipsychotics. The U.S. Food and Drug Administration's approval of 5 atypical antipsychotics—risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole—for the treatment of bipolar mania is indicative of the increasing acceptance of this class of drugs.

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