Mood Stabilizers and Atypical Antipsychotics: Bimodal Treatments for Bipolar Disorder

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ABSTRACT - Treatment options for bipolar disorder have rapidly expanded over the last decade, but providing optimal management remains an elusive goal. The authors reviewed the literature on the efficacy of agents with the best clinical evidence supporting their use in bipolar disorder, including the mood stabilizers lithium, valproate, lamotrigine, and carbamazepine, as well as the atypical antipsychotics olanzapine, risperidone, quetiapine, ziprasidone, and aripiprazole. Most medications appear to be more effective for symptoms of mood elevation than for symptoms of depression. The efficacy, tolerability, and safety profiles of agents must be considered when making clinical decisions. Several agents, including lithium, valproate, olanzapine, quetiapine, and risperidone, can cause problematic weight gain. In addition, the use of atypical antipsychotics has been associated with an increased risk of metabolic abnormalities such as dyslipidemia, hyperglycemia, and diabetes mellitus. In most patients, monotherapy offers inadequate efficacy. Further investigation of combinations of agents such as mood stabilizers and atypical antipsychotics may yield valuable insights into the potential of combination therapies to enhance clinical outcomes in patients with bipolar disorder. Psychopharmacology Bulletin. 2006;39(1):120-146.

INTRODUCTION

Bipolar disorder, formerly known as manic depressive illness, is a disease characterized by dramatic mood swings, between abnormal euphoria, expansiveness, or irritability (during manic or hypomanic episodes), and pervasive sadness and anhedonia (in depressive episodes), often with interspersed periods of subsyndromal symptoms as well as times with normal mood.1

Current estimates of the lifetime prevalence of bipolar spectrum disorders range from 3% to 6.5% of the population.2,3 Although bipolar illness can develop at different ages, the peak period of onset appears to be during late adolescence or early

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adulthood. Common presentations include major depressive episodes, and in children and adolescents, atypical affective disorders with more continuous and mixed symptoms as well as disruptive behavior disorders such as attention-deficit/hyperactivity disorder. Patients commonly have concurrent difficulties with other psychiatric conditions such as alcohol and substance abuse, anxiety disorders, eating disorders, and Cluster B personality traits/disorders. Thus, early diagnosis presents a substantial challenge, and a decade commonly passes between first symptoms and appropriate diagnosis and treatment.

As described in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR), primary bipolar disorders are divided into four categories: bipolar I disorder, bipolar II disorder, cyclothymic disorder, and bipolar disorder not otherwise specified (NOS). Bipolar I disorder is characterized by a history of one or more manic or mixed episodes, usually accompanied by one or more major depressive episodes. Bipolar II disorder is characterized by a history of recurrent major depressive episodes, with one or more hypomanic episodes, and the absence of manic and mixed episodes. Cyclothymic disorder is characterized by a chronic pattern of numerous periods of mood elevation and depressive symptoms that do not meet the criteria for mania, hypomania, or major depressive episodes. Bipolar NOS includes disorder with bipolar features that do not meet the criteria for any specific bipolar disorder.

This complex and devastating illness is associated with a significant social and economic burden. There is a high risk of suicide attempts, and studies in bipolar patients indicate that 25% to 50% have attempted suicide at least once. In addition, it is suggested that up to 19% of patients with bipolar disorder die from suicide. The disease can also cause significant psychosocial morbidity that may affect multiple aspects of patients’ lives, including relationships with family members, caregivers, and employment. Each year in the United States alone, about 100,000 people will have an initial acute episode of bipolar disorder. Thus, bipolar disorder results in significant human and economic burdens. Based on incidence data and the projected course of illness, the total lifetime cost of people with onset of bipolar disorder in 1998 was estimated at $24 billion (US).