Introduction

Managing Bipolar Depression

Charles L. Bowden, M.D.

Bipolar disorder can be found in 1.2% to 3.4% of the general population.[1] Patients with bipolar disorder attempt suicide at a higher rate than patients with other psychiatric disorders, exhibit substantially more depressive symptoms than manic or hypomanic symptoms,[2,3] are at risk for relapse into subsequent bipolar episodes, suffer from subsyndromal symptoms that interfere with functioning and quality of life, and frequently do not respond adequately to standard treatment. Lithium, valproate, and carbamazepine remain the standard of care for the treatment of bipolar disorder, and the U.S. Food and Drug Administration has approved the use of lithium for the treatment of both acute episodes of mania and maintenance therapy in bipolar disorder and the use of the anticonvulsant lamotrigine and the atypical antipsychotic olanzapine for maintenance therapy. However, more treatment options for all phases of bipolar disorder are needed, especially for the depression phase. Although lithium may not be of substantial benefit in treating bipolar depression, antidepressants used without mood stabilizers often destabilize mood in bipolar patients[4,5] and must be used with caution. In addition, some atypical antipsychotics and anticonvulsants are under investigation for their efficacy in bipolar depression.

Four articles in this supplement by leading authorities in bipolar disorder provide up-to-date strategies for managing specific aspects of bipolar depression: suicidal behavior, breakthrough depression, relapse, and subsyndromal symptoms. The fifth article reviews the current status of investigations into the efficacy of the new anticonvulsants in treating bipolar disorder.

Suicidal behavior is a major concern in bipolar disorder. Patients with bipolar disorder, regardless of diagnostic type, are at greater risk for suicide than patients with any other psychiatric disorder. Although there is some disagreement about predictors for suicide, David L. Dunner, M.D., reviews several strong possibilities, such as previous or current depression, substance and alcohol abuse, suicidal ideation, increased feelings of hopelessness, and few reasons for living. A genetic variant of the serotonin transporter gene is also under investigation for its role in suicidal behavior. Whether risk factors for suicide are proven or unproven, lithium appears to have a protective effect against suicidal behavior in patients with bipolar disorder and should be initiated as a prevention strategy.

Recurrence of bipolar disorder is characterized by cycles of mania and depression following a period of euthymia. Patients are frequently able to identify prodromal symptoms (such as mood change, psychomotor symptoms, increased anxiety, and appetite changes) in advance of a recurrence of bipolar depression. If recognized early, treatment can be initiated to thwart an emerging depressive episode. Paul E. Keck, Jr., M.D., describes prodromal symptoms and the role of mood stabilizers and antidepressants in managing breakthrough depressive episodes.

From the Department of Psychiatry, University of Texas Health Sciences Center at San Antonio.

This article is derived from the teleconference "Managing Bipolar Depression," which was held June 18, 2003, and supported by an unrestricted educational grant from GlaxoSmithKline.

Corresponding author and reprints: Charles L. Bowden, M.D., University of Texas Health Sciences Center at San Antonio, Department of Psychiatry, MC7792, 7703 Floyd Curl Dr., San Antonio, TX 78229-3900 (e-mail: bowdenc@uthscsa.edu).

Historically, lithium has been the treatment of choice for bipolar episodes and maintenance therapy. Other agents, such as valproate, olanzapine, risperidone, lamotrigine, and antidepressants, have also been studied as primary and adjunctive treatments in managing bipolar disorder. Although some anticonvulsants and atypical antipsychotics have been effective in preventing relapse in mania, they have been understudied in relation to preventing relapse of depression. Further, the lack of controlled trials, inconsistent study designs, and inadequate sample sizes have complicated the interpretation of data regarding strategies for treating the different phases of bipolar disorder. S. Nassir Ghaemi, M.D., and colleagues emphasize the need for placebo-controlled trials, comprising both the experimental drug and an active control, to determine the best method for preventing relapse of depression in bipolar disorder. In addition to pharmacotherapy, the authors describe the importance of psychotherapy and patient insight in achieving better medication compliance and outcome, which may help to prevent a relapse or recurrence of manic or depressive episodes.

Depressive or manic symptoms that fail to reach clinical significance for the diagnosis of an episode but nonetheless impair functioning are common in patients with bipolar disorder. Subsyndromal symptoms in bipolar disorder, especially depressive symptoms, impair functioning, reduce quality of life, and increase the risk of relapse of bipolar disorder. Lauren B. Marangell, M.D., stresses the importance of recognizing and aggressively treating these symptoms before relapse occurs.

Although the mood-stabilizing effects of lithium, valproate, and carbamazepine have led to their use as standard treatments for bipolar disorder (particularly acute mania), many patients do not respond adequately to these therapies. Lakshmi N. Yatham, M.D., describes findings from placebo- and comparator-controlled trials of newer anticonvulsants in bipolar disorder. Lamotrigine, the most widely studied of the newer anticonvulsants, has been approved as maintenance treatment for bipolar disorder, and strong evidence supports its use in bipolar depression. Other anticonvulsants have shown efficacy in treating core bipolar disorder or symptoms, while others have not. More treatment options for all phases of bipolar disorder are needed.

REFERENCES

1. Goodwin FK, Jamison KR. Manic-Depressive Illness. New York, NY: Oxford University Press; 1990
2. Judd LL, Akiskal HS, Schettler PJ, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. Arch Gen Psychiatry 2003;60:261–269
3. Judd LL, Akiskal HS, Schettler PJ, et al. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry 2002;59:530–537
4. Ghaemi SN, Lenox MS, Baldessarini RJ. Effectiveness and safety of long-term antidepressant treatment in bipolar disorder. J Clin Psychiatry 2001;62:565–569
5. Nemeroff CB, Evans DL, Gyulai L, et al. Double-blind, placebo-controlled comparison of imipramine and paroxetine in the treatment of bipolar depression. Am J Psychiatry 2001;158:906–912