

Introduction

Long-Term Use of Mood Stabilizers in Bipolar Disorder

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© **M**any people in the United States are currently diagnosed with bipolar disorders. The effects of these disorders include significant health care costs for treatment (often including an array of medications and frequent hospital admissions), a loss of productivity causing broad economic repercussions, and a risk of suicide. Mood-stabilizing medications can be defined broadly as medications that decrease episode severity, duration, or frequency in one phase of bipolar disorder without causing negative effects on other phases. Included in this definition are such medications as lithium, carbamazepine, divalproex sodium, some atypical antipsychotic agents, and lamotrigine. With the possible exception of lithium, little research has been done into the long-term benefits and adverse side effects of mood stabilizers. Nevertheless, mood stabilizers are often employed in the long-term treatment of bipolar disorder.

Given the prominent role played by mood stabilizers in the treatment of bipolar disorder, it is crucial that a long-term perspective of the benefits and adverse effects be gained. Such a perspective can only be achieved through research into the efficacy and adverse side effects of mood stabilizers. Pursuant to these goals, 5 experts gathered to review previously collected data and present new research on the nature of bipolar disorder and the effects of the long-term use of mood stabilizers in treating the disease.

Frederick K. Goodwin, M.D., addressed the importance of long-term treatment of bipolar disorder. The value of long-term treatment is evident given the great morbidity and mortality, increased health care costs, and loss of productivity associated with bipolar disorder. Of the available pharmacotherapies, lithium is the only U.S. Food and Drug Administration–approved medication for maintenance treatment, and its efficacy is more well supported than most other medications. Research shows that patients with bipolar disorder respond favorably to lithium prophylaxis. Despite recent declines in lithium prescription rates, lithium remains at the front line of bipolar treatments because of its demonstrated therapeutic effectiveness.

Paul E. Keck, Jr., M.D., and Susan L. McElroy, M.D., reviewed the data available from randomized clinical trials of carbamazepine and valproate to determine their efficacy and tolerability in the maintenance phase of bipolar management. Despite limited data, preliminary evidence suggests that each agent appears to prevent relapse when used as monotherapy in patients with bipolar disorder.

Joseph R. Calabrese, M.D., and colleagues presented data on the long-term treatment of bipolar disorder with lamotrigine. Data suggest that lamotrigine plays a role in delaying relapse and recurrence of depressive episodes. However, until a single agent demonstrates efficacy in treating both manic and depressive phases, combination therapy, such as lithium and divalproex sodium, remains a common treatment strategy.

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Vivek Kusumakar, M.D., F.R.C.P.C., reexamined the results of various studies on the long-term safety and efficacy of antidepressants and antipsychotics in treating bipolar disorder. These agents are frequently used as mood stabilizers, but unfortunately often have deleterious side effects. Some antidepressants have been found to induce mania, hypomania, and rapid cycling. Conventional antipsychotics have been associated with tardive dyskinesia, while some novel antipsychotics have been linked to difficult-to-manage adverse side effects such as weight gain and agranulocytosis. The lack of research into the long-term effects of the use of these agents in treating bipolar disorder underscores the need for further investigation.

Trisha Suppes, M.D., Ph.D., and Ellen B. Dennehy, Ph.D., reviewed the limited and sometimes contradictory data on bipolar II disorder and found that more research into prophylactic and maintenance treatment tailored specifically to bipolar II disorder is warranted. Although many expect the treatments of bipolar I and II disorders to be similar, data suggest that patients with bipolar II disorder respond differently to pharmacologic treatments than do patients with bipolar I disorder, thus underscoring the importance of further research.

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