

## Psychopharmacology for the Clinician Psychopharmacologie pratique

To submit questions for this regular feature, please send them to Journal of Psychiatry and Neuroscience/Revue de psychiatrie et de neuroscience, Royal Ottawa Hospital, LG 2044, 1145 ave. Carling Ave., Ottawa ON K1Z 7K4, Canada; fax 613 722-5871. Please include details of any relevant case and your name, address, telephone and fax numbers as well as your email address.

### What is the best approach to management of acute depression in bipolar disorder?

The depressed phase of bipolar disorder is common, accounts for substantial dysfunction in social and work settings, and is associated with a suicide rate comparable to that in unipolar major depression. Despite the fact that acute bipolar depression remains a substantial and common therapeutic challenge, there are few empirical data to support differing viewpoints on the best approach to treatment. There are essentially 2 differing approaches to management. In the first, 1 or more mood-stabilizing drugs are used, either *de novo* or added to existing mood stabilizers when depressive episodes occur. The literature and clinical experience suggest that this is a safe but only moderately effective approach to treatment.

The second approach involves the addition of an antidepressant to a mood stabilizer. While the efficacy of antidepressants in acute bipolar depression is undisputed, there are major concerns about the risk of switch to mania or cycle acceleration. Although some antidepressants (selective serotonin reuptake inhibitors and bupropion) are claimed to be less likely to cause a switch to mania or cycle


acceleration, these findings remain uncertain owing to limitations in the data on which the conclusions have been reached. It is remarkable that the research data are too limited to determine whether one of these approaches is indeed superior and whether the clinical dogma that single or combined mood stabilizers are preferable is accurate. In fact, as far as we are aware, a preliminary study we have completed is the first to compare directly the addition of an antidepressant, paroxetine, to an additional mood stabilizer, either lithium or divalproex sodium, in patients with bipolar disorder experiencing a breakthrough episode of depression. In this 6-week study, we observed that the treatments were comparably effective, although discontinuation from the study was significantly more common in the group receiving combined mood stabilizers. Furthermore, limited follow-up data suggest that there was no difference in switch rates between the groups. Our data require replication in larger samples with longer periods of treatment and follow-up, but these findings challenge the notion that antidepressants are less preferable than combined mood stabilizers in the treatment of acute depression. In fact, the opposite may be true, and the judicious use of anti-

depressants in combination with mood stabilizers may offer some advantage in selected patients with bipolar disorder.

The dilemma of the use of antidepressants in bipolar depression has not been fully resolved. Switch to mania and cycle acceleration remain therapeutic challenges that complicate treatment of the disorder and cause substantial suffering and dysfunction in patients. The issue of whether antidepressants are an important etiological factor in switch to mania and cycle acceleration needs to be clarified. Moreover, other factors, such as the antidepressant class and the dose, as well as the natural course of the patient's illness as risk factors for switch and cycle acceleration, require further rigorous observation and study. Data on these issues are urgently needed to establish guidelines for the treatment of acute bipolar depression that are evidence-based rather than only expert opinion and anecdotal clinical observation.

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**The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.**

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