Antidepressants in Bipolar Disorder: Caveats in Interpreting and Applying the Findings of Altshuler et al

To the Editor: I am writing with concerns about the interpretation and application of the important findings of the recent study reported by Altshuler et al. In my work at a university-affiliated teaching hospital and in other settings over the past 5 years, I have seen near-universal (well in excess of 80%) prescribing of antidepressants to patients with bipolar disorder. In many cases, these patients have not had a trial or trials of traditional mood stabilizers (lithium, divalproex, or carbamazepine) in the absence of antidepressants. A recent study showed antidepressants to be the first-choice agent for bipolar patients twice as often as mood stabilizers.

Case vignette. An obviously disabled 53-year-old man was recently seen for initial evaluation at a public mental health center. No old records were available, but his concerned and supportive sister, a good historian, accompanied him. He gave, and his sister confirmed, an unequivocal history of bipolar I disorder, with a first admission 20 years earlier for mania and a total of 6 psychiatric admissions, with 5 of the 6 being at nearby university-affiliated teaching hospitals, with lengthy periods of outpatient follow-up with the hospital psychiatrist. The sixth hospitalization was at a state hospital. His diagnosis was bipolar disorder throughout, and he had been treated with numerous antidepressants and antipsychotics over the years. On specific questioning, both he and his sister denied his ever having been treated with lithium, divalproex sodium, or carbamazepine, but after discussion of the options, they readily consented to a trial of lithium.

Altshuler et al are very careful to point out limitations related to the current study involving “a very specific subpopulation of patients with bipolar disorder: namely, those who, despite adequate mood stabilizer treatment, have a depression and are treated adjunctively with antidepressants.” On the basis of prior experience, however, I am concerned that the current findings may be uncritically misapplied to justify the unproven strategy of widespread antidepressant prescribing to all or almost all bipolar patients, regardless of bipolar type or recent or historical polarity. I would therefore offer the following caveats:

1. The percentage size of the “very specific subpopulation of patients with bipolar disorder” is not mentioned in the current study, but in a prior study by the same group, it was 15.3% (84 of 549 patients). A positive result in a subset of 15% of bipolar disorder patients would not seem to provide an adequate basis for a practice applied in over 80% of patients in clinical practice in many geographic areas.
2. “Acute partial responders” in the current study were less likely to respond to continued coadministration of antidepressants added to mood stabilizers and are treated adjunctively with antidepressants. On the basis of prior experience, however, I am concerned that the current findings may be uncritically misapplied to justify the unproven strategy of widespread antidepressant prescribing to all or almost all bipolar patients, regardless of bipolar type or recent or historical polarity. I would therefore offer the following caveats:
3. The patients in this study had already failed to respond satisfactorily to carefully monitored adequate blood level–proven trials of lithium, divalproex, or carbamazepine, prescribed in the absence of antidepressants.
4. The patients were maintained on therapeutic (albeit somewhat modest in the case of divalproex and carbamazepine) blood levels of the above agents while being treated concurrently with antidepressants.
5. The conditions described in points 3 and 4 above are often not seen in clinical practice. There would appear to be far more reliance in clinical practice on the atypical antipsychotics in place of traditional mood stabilizers, and this strategy is not addressed by the current study.

References

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