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.[1] 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.[2]

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."[1(p456)] 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"[1(p456)] is not mentioned in the current study, but in a prior study by the same group,[3] it was 15.3% (84 of 549 patients).[4] 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 were more likely to switch into mania, and in clinical practice response is often only partial.
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

1. Altshuler LL, Post RM, Hellemann G, et al. Impact of antidepressant continuation after acute positive or partial treatment response for bipolar depression: a blinded, randomized study. *J Clin Psychiatry.* 2009;70(4):450–457.
2. Baldessarini RJ, Leahy L, Arcona S, et al. Patterns of psychotropic drug prescription for US patients with diagnoses of bipolar disorders. *Psychiatr Serv.* 2007;58(1):85–91.
3. Altshuler LL, Suppes T, Black D, et al. Impact of antidepressant discontinuation after acute bipolar depression remission on rates of depressive relapse at 1-year follow-up. *Am J Psychiatry.* 2003;160(7):1252–1262.
4. Post RM. Towards rational complex combination treatment in bipolar illness, including findings of the Stanley Foundation Bipolar Network. CME seminar sponsored by Ohio State University Medical Center; April 17, 2004; Columbus, Ohio.

Roger Sparhawk, MD
sparhawkr@summa-health.org

Author affiliations: Department of Psychiatry, St Thomas Hospital, Akron, Ohio, and Northeast Ohio Universities College of Medicine, Rootstown.

Potential conflicts of interest: Dr Sparhawk has received speaker and/or consultant honoraria from AstraZeneca, Bristol-Myers Squibb, Cephalon, Forest, GlaxoSmithKline, Janssen, Eli Lilly, Otsuka, Pfizer, and Wyeth and research support (principal investigator, Bijan Bastani, MD) from AstraZeneca, Bristol-Myers Squibb, Cephalon, GlaxoSmithKline, Janssen, Eli Lilly, Neurocrine, Sepracor, and Wyeth. ***Funding/support:*** None reported.
doi:10.4088/JCP.09lr05463gre