

Antidepressant Use and Risk for Suicide Attempts in Bipolar Disorder

To the Editor: The use of antidepressants in bipolar disorder remains controversial with respect to whether, and when, they may destabilize mood and worsen clinical course. Despite previously identified links between suicide attempts and the proportion of time spent with depression in bipolar disorder,¹ few longitudinal studies have examined the relationship between antidepressant use and suicidal behavior specifically in bipolar disorder. Retrospective studies have reported a *greater* risk for suicide attempts among bipolar patients taking antidepressants alone than among those taking concomitant mood stabilizers^{2,3} or mood stabilizers alone,³ while prospective studies have found either *no* link between suicidal acts and antidepressant use⁴ or *fewer* suicide attempts when antidepressants are combined with mood stabilizers than during mood stabilizer therapy alone.⁵ Interpretations about suicidal behavior in most naturalistic outcome studies also may be hampered by temporal confounding when antidepressants are started because of, rather than before, the emergence of suicidal behavior.

Leon and colleagues⁶ present findings from a useful and important 27-year observational study of suicide attempts and antidepressant therapy in a large mood disorder cohort. Using a propensity-adjusted mixed-effect survival model, they demonstrate a 20% reduction in overall risk for suicide attempts among all subjects taking versus not taking an antidepressant. However, their model did not stratify for unipolar versus bipolar diagnosis as a correlate of suicide attempt risk during antidepressant use. While the majority of their subjects (nearly 80%) had index diagnoses of (unipolar) major depression, their available subgroup of 119 subjects with index bipolar mania should nevertheless provide adequate power for the inclusion of unipolar versus bipolar diagnosis as a covariate of suicidal behavior. Given the potential for differences between bipolar and unipolar patients in antidepressant response, as well as the potential for antidepressants to exacerbate concomitant manic symptoms during bipolar depressive syndromes,⁷ such an analysis in this unique cohort would be of great value for determining whether antidepressants may differentially affect suicide risk in bipolar versus unipolar patients.

REFERENCES

1. Tondo L, Baldessarini RJ, Hennen J, et al. Lithium treatment and risk of suicidal behavior in bipolar disorder patients. *J Clin Psychiatry*. 1998;59(8):405-414.
2. Pacchiarotti I, Valenti M, Colom F, et al. Differential outcome of bipolar patients receiving antidepressant monotherapy versus combination with an antimanic drug. *J Affect Disord*. 2011;129(1-3):321-326.
3. Yerevanian BI, Koek RJ, Mintz J, et al. Bipolar pharmacotherapy and suicidal behavior, pt 2: the impact of antidepressants. *J Affect Disord*. 2007;103(1-3):13-21.
4. Gilbert AM, Garno JL, Braga RJ, et al. Clinical and cognitive correlates of suicide attempts in bipolar disorder: is suicide predictable? *J Clin Psychiatry*. 2011;72(8):1027-1033.
5. Angst F, Stassen HH, Clayton PJ, et al. Mortality of patients with mood disorders: follow-up over 34-38 years. *J Affect Disord*. 2002;68(2-3):167-181.
6. Leon AC, Solomon DA, Li C, et al. Antidepressants and risks of suicide and suicide attempts: a 27-year observational study. *J Clin Psychiatry*. 2011;72(5):580-586.
7. Goldberg JF, Perlis RH, Ghaemi SN, et al. Adjunctive antidepressant use and symptomatic recovery among bipolar depressed patients with concomitant manic symptoms: findings from the STEP-BD. *Am J Psychiatry*. 2007;164(9):1348-1355.

Joseph F. Goldberg, MD
joseph.goldberg@mssm.edu

Author affiliations: Department of Psychiatry, Mount Sinai School of Medicine, New York, New York, and Affective Disorders Research Program, Silver Hill Hospital, New Canaan, Connecticut. **Potential conflicts of interest:** Dr Goldberg has been a consultant to Dey, Grünenthal Group, and Eli Lilly; has received honoraria from AstraZeneca and Eli Lilly; and has been on the speakers/advisory boards of AstraZeneca, Eli Lilly, Dey, Merck, and Sunovion. **Funding/support:** None reported.
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