Cartas aos editores

Comment on “Antidepressant treatment-emergent switch in bipolar disorder: a prospective case-control study of outcome”

Comentário sobre “Ciclagem afetiva associada a tratamento com antidepressivo no transtorno bipolar: estudo caso-controle prospectivo”

Dear Editor,

Treatment of bipolar depression is understudied and is a major unmet clinical need. Although antidepressants are effective in relieving depressive symptoms in some patients,

almost all antidepressants have been reported to induce a manic/hypomanic switch although there are some differences in propensity for switch between different antidepressants.[1] Therefore, a clinician is often faced with the dilemma of treating depression with antidepressants and risking a manic/hypomanic switch vs not using antidepressants and potentially prolonging patient suffering with syndromal or sub-syndromal depressive symptoms if other treatments are ineffective. Thus, studies that can provide predictors of who switches into mania vs who does not and what happens to those who switch vs those who have spontaneous mania have high clinical utility as they provide important insights into the optimal management of bipolar disorder.

In this regard, the article by Tamada et al. entitled "Antidepressant treatment-emergent switch in bipolar disorder: a prospective case-control study of outcome", which compares spontaneous mania and antidepressant-induced mania in a 12-month follow-up is very timely.[2] Most of the previous studies to date have focused on the switch rates during the treatment of depressed bipolar patients, comparing those who switched with those who did not.[1,3] The paper in this issue differs form others in that it includes a comparison with spontaneous mania, and thus providing important insights into the course of the disorder after an antidepressant induced manic switch. The findings indicate that almost twice as much patients with antidepressant induced mania had a relapse (11 vs 6) within the 12 -month follow-up period compared to those who had spontaneous mania (Differences were not statistically significant probably due to a small sample size). Furthermore, depressive relapse occurred more commonly in the antidepressant-induced mania group compared to the spontaneous mania group.

The study has several strengths: first, it was a prospective study. Second, it includes consecutive consenting patients. Third, inclusion criteria included not only a diagnosis based on DSM-IV but it also included severity criteria on a Young Mania Rating Scale. Fourth, response, relapse and remission were prospectively defined using a cut-off score on a rating scale.

Thus, the study was methodologically well conducted. The main limitation of the study is the small sample size. Further, it would have been helpful to the reader if they had provided information on what treatment patients in each group were receiving after remission of manic episodes and if there were any numerical or statistical differences in terms of proportion of patients on mood stabilizers, atypical antipsychotics or lamotrigine between the two groups.[4] Lastly, the study findings would have been much stronger if they had compared patients with a spontaneous first manic episode with those that had their first manic episode induced by antidepressants.

Not withstanding these minor limitations, the findings of this study suggest that patients with antidepressant-induced mania have a worse course compared to those who have spontaneous mania. Further, the fact that those who have antidepressant-induced mania are more likely to relapse into depression indicates that the management of these patients is more complex. Discontinuation of an antidepressant may prevent further manic switch but this strategy certainly seems to increase the risk of depressive relapse. Thus, these patients clearly need to be aggressively treated with other treatments to prevent recurrence of a depressive episode. The options may include lamotrigine or quetiapine in addition to a mood stabilizer or a combination of two mood stabilizers psychosocial strategy such as CBT. If the above fail, continuing an antidepressant that has a low propensity to switch such as bupropion or an SSRI with an atypical antipsychotic or an atypical antipsychotic and a mood stabilizer might be appropriate.

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