Reply to Dr. Kauer-Sant'Anna and Dr. Yatham's letter "Comment on 'Antidepressant treatment-emergent affective switch in bipolar disorder: a prospective case-control study of outcome'"

Resposta à carta dos Drs. Kauer-Sant'Anna e Yatham "Comentário sobre 'Ciclagem afetiva associada a tratamento com antidepressivo no transtorno bipolar: estudo caso-controle prospectivo'"

Dear Editor,

We appreciate the thoughtful letter from Drs. Kauer-Sant´Anna and Yatham who made a very careful analysis of our article entitled "Antidepressant treatment-emergent affective switch in bipolar disorder: a prospective case-control study of outcome".[1]

Bipolar depression may be very complex and difficult to treat because acute treatment may be harmful to the long-term outcome of the disorder. In our prospective study, we included consecutive consenting patients with inclusion criteria that included only patients who met both the DSM-IV and the severity criteria on a Young Mania Rating Scale. We found that antidepressant-associated mania was less severe than spontaneous mania,[2] but the long-term outcome was poorer in the former group: they had more relapses in a 12-month follow-up period, and the relapses were all depressive episodes.[1]

We agree that the small sample size – 12 patients in each group – was the main limitation of our study, but on the other hand one of its strengths is that we were able to follow-up all the 24 patients until any relapse occurred and they completed the 12-month follow-up. We think that studies with larger sample sizes using the same study design might be better powered to find statistical significance in relapse and cycle acceleration rates between groups.

In our study, we tried to control most factors that could have influenced our results. Regarding the medications used after manic episode remission, in the antidepressant-associated mania group all patients were using mood stabilizers (11 in monotherapy and one in association), six patients were using atypical antipsychotics, six were receiving benzodiazepines and six were on T4. One patient was using lamotrigine and another one was using sertraline - both presented relapses. In the spontaneous mania group, all patients were using mood stabilizers (six in monotherapy and six in association), six were also receiving antipsychotics (three typical and three atypical), two were using benzodiazepines and three were on T4. We were not able to find any statistical difference between the groups regarding medications used after remission. Considering this analysis, our data suggest that the differences found on relapse rates in our study were not related to the medications that the patients were receiving prospectively.

Undoubtedly, comparing patients presenting first episodes of spontaneous mania with those presenting induced mania would be ideal to make the group more homogeneous, but in practice this would be difficult since we see patients in a tertiary care university-based, bipolar outpatient clinic with many of them coming for treatment after multiple episodes.

The risk of switching and predictor factors are very important to be studied in order to help the clinician in the difficult task of treating bipolar depression. Furthermore, the fact that those who had antidepressant-associated mania were more likely to relapse into depression indicates that the management of these patients is even more complex. The therapeutical options suggested by Drs. Kauer-Sant'Anna and Yatham to aggressively treat these patients in order to prevent depressive relapses are mostly based on well-conducted monotherapy short-term controlled trials.[3] Long-term, controlled trials comparing different combination therapies might help us establish the most appropriate therapeutical options for these very difficult-to-treat patients.

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Financing: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) # 99/02079-4
Conflict of interests: None

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