A clinical study comparing manic and mixed episodes in patients with bipolar disorder

Estudo clínico comparativo entre episódios de mania e mistos em pacientes com transtorno bipolar

Ángela Maria Schwartzmann,1 José Antonio Amaral,1 Cilly Issler,1
Sheila C Caetano,1,2 Renata S Tamada,1 Karla Mathias de Almeida,1
Marcia Brito de Macedo Soares,1 Rodrigo da Silva Dias,1,3
Cristiana C Rocca,1 Beny Lafer1,4

Abstract

Objective: Mixed episodes have been described as more severe than manic episodes, especially due to their longer duration and their association with higher rates of suicide attempts, hospitalization and psychotic symptoms. The purpose of this study was to compare the severity between mixed and pure manic episodes according to DSM-IV criteria, through the evaluation of sociodemographic data and clinical characteristics. Method: Twenty-nine bipolar I patients presenting acute mixed episodes were compared to 20 bipolar I patients with acute manic episodes according to DSM-IV criteria. We analyzed (cross-sectionally) episode length, presence of psychotic symptoms, frequency of suicide attempts and hospitalization, Young Mania Rating Scale scores, Hamilton Depression Rating Scale scores and the Clinical Global Assessment Scale scores. Results: Young Mania Rating Scale scores were higher in manic episodes than in mixed episodes. There were no differences in gender frequency, CGI scores and rates of hospitalization, suicide attempts and psychotic symptoms, when mixed and manic episodes where compared. Patients with mixed episodes were younger. Conclusion: In our sample, mixed states occurred at an earlier age than manic episodes. Contrary to previous reports, we did not find significant differences between manic and mixed episodes regarding severity of symptomatology, except for manic symptoms ratings, which were higher in acute manic patients. In part, this may be explained by the different criteria adopted on previous studies.

Descriptors: Comparative study; Psychotic disorders; Bipolar disorder; Suicide, attempt; Hospitalization

Rev Bras Psiquiatr. 2007;29(2):130-3

Original Article

Angela Maria Schwartzmann
Projeto de Assistência e Pesquisa em Transtorno Bipolar (PROMAN) do Instituto de Psiquiatria do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo
Rua Ovidio Pires de Campos, 785
05003-010, São Paulo, SP, Brazil
E-mail: schwangela@terra.com.br

Correspondence

Angela Maria Schwartzmann
Projeto de Assistência e Pesquisa em Transtorno Bipolar (PROMAN) do Instituto de Psiquiatria do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo
Rua Ovidio Pires de Campos, 785
05003-010, São Paulo, SP, Brazil
E-mail: schwangela@terra.com.br

Conflict of interest: None
Submitted: April 10, 2006
Accepted: October 6, 2006

Rev Bras Psiquiatr. 2007;29(2):130-3

Descritores: Estudo comparativo; Transtornos psicóticos; Transtorno bipolar; Tentativa de suicídio; Hospitalização

1 Bipolar Disorder Research Program (PROMAN), Institute of Psychiatry, Department of Psychiatry, Universidade de São Paulo Medical School, São Paulo (SP), Brazil
2 Department of Psychiatry, University of Texas, Health Science Center, San Antonio (TX), USA
3 Massachusetts General Hospital, Harvard Medical School, Boston (MA), USA
4 Department of Psychiatry, Universidade de São Paulo Medical School, São Paulo (SP), Brazil
Introduction

In bipolar patients, mixed states have been reported to be more severe than manic episodes. Mixed states have been reported to be associated with longer episode length, frequency of hospitalization and psychotic symptoms when compared to pure manic episodes. More specifically, the occurrence of suicide attempts have been found to be higher among patients during mixed episodes in most studies that compared them to patients during manic states.

The few comparative studies regarding manic and mixed states have used different diagnostic criteria. DSM-III-R mixed episode criteria are as strict as DSM-IV criteria regarding the number of depressive symptoms necessary for defining a mixed episode (at least five depressive symptoms). However, DSM-III-R and DSM-IV are more restrict than Cincinnati criteria, which accept at least two depressive symptoms. When mixed episodes are defined by broad criteria, differences between the two types of episodes tend to diminish.

Using broad criteria for mixed states, Akiskal et al. reported that suicidal ideation and depressive mood are more frequent in mixed episodes when compared to manic episodes. Irritability has been found to be more frequent than depressive mood in mixed episodes. Dell’Osso et al. observed lower latency for hospitalization, more incongruent psychotic symptoms, and tendency to longer episodes in patients with history of mixed episodes compared to the ones without these episodes, they found no differences in CGI scores between the two groups.

Regarding manic symptoms, data are not uniform and different scales have been used: Swann et al. showed higher global rates of mania in non-treated inpatient adults with mixed episodes compared with patients with pure mania. However, they applied a scale rarely used by other authors (Affective Disorders Scale [ADRS], Murphy et al.). Baker et al. described higher Young Mania Rating Scale (YMRS) scores in a large sample of patients with mixed episodes. On the other hand, McElroy et al. found similar YMRS scores in manic and mixed episodes, using the Cincinnati or the DSM-III-R definition in patients who aged above 12 years.

Mixed episodes are more frequent in adolescents than in adults. Nonetheless, patients in mixed episodes were not found to be younger than patients in mania. We hypothesized that patients with mixed episodes defined by DSM-IV criteria would have episodes with greater severity than patients with manic episodes. Younger age at index episodes, higher occurrence of psychotic symptoms, suicide attempts and hospitalizations were considered indicators of greater severity.

Method

We studied outpatients who have been followed up in average for five years at the Bipolar Research Program at the Institute of Psychiatry, Universidade de São Paulo Medical School. The study was approved by the ethical review committee of the University Hospital. Written consent was obtained from all patients when in euthymia. Patients were diagnosed with bipolar disorder subtype I using the SCID-I/P (Structured Clinical Interview for DSM-IV) and were assessed using the Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale-31 items (HAM-D), and the Clinical Global Assessment Scale (CGI).

We selected bipolar patients that met DSM-IV criteria for acute mania, presented YMRS scores equal or higher than twelve during follow-up, and did not present mixed episodes in their past clinical history. The DSM-IV criteria for mixed episode were used. For each patient, the first mixed or manic episode during follow-up that met these criteria was considered the index episode. Only one episode was analyzed per patient. We also collected sociodemographic and clinical data such as age at index episodes, gender, and presence of psychotic symptoms, suicide attempts and hospitalization, the last three used in the literature as severity parameters. This was a transversal study, based on data stored at each patient visit.

1. Statistic analysis

We applied the Kolmogorov-Smirnov test to ascertain if the distribution of the collected data was normal. Mean scores were compared using Student’s t-test or the Mann-Whitney U test. We used the Chi-square or the Fisher’s Exact test for categorical variables.

2. Clinical data

Clinical data are displayed in Table 2. Manic patients had significantly higher YMRS scores than patients in mixed episode (p < 0.001). Manic and mixed episodes had no statistically significant differences regarding episode length, presence of psychotic symptoms, suicide attempts and hospitalizations. The following manic symptoms were significantly more frequent in manic episodes in comparison to mixed episodes: distractibility and racing thoughts, decreased need of sleep, lack of care with appearance, and lack of insight. There was no difference in the presence of irritability between mixed and manic episodes.

As expected, HAM-D scores were higher in patients in mixed episode compared to the ones in mania (Mean = 20.0, **Manic group**).
Depressive mood and insomnia were the two most common depressive symptoms in mixed episodes, differently from the report from Akiskal et al., who observed a higher occurrence of depressive mood and suicide ideation. Irritability was equally present in both groups, differing from some authors’ findings who reported irritability to be more frequent in mixed episodes.

In this study, there were no significant differences between manic and mixed episodes regarding severity of the episodes, except for manic symptoms severity scores. A possible explanation is that manic patients present less suffering than patients with depressive symptoms, and probably look for treatment later on than patients in mixed episode. This delay would imply in higher manic scores in the patients with pure mania. Despite the relatively smaller YMRS scores in mixed episodes, we found that patients with mixed episodes and psychotic symptoms had higher manic symptoms scores compared to patients with mixed episodes and no psychotic symptoms (M = 19.56, SD = 5.46, versus M = 14.02, SD = 2.3, p = 0.003, Mann-Whitney). We found large confidence intervals, which signalizes a possible type I error.

To reduce this effect we would have had to significantly increase our sample, and this was not possible because we began the study with a defined number of patients. Our criteria were stricter than the ones used in other studies (Cincinnati criteria which require less depressive symptoms, or Perugi’s criteria which require less symptoms and a shorter period of presentation). We observed a low frequency of suicide attempts and hospitalizations, probably because the majority of patients were under treatment. These low frequencies can lead to a higher probability of a type II error than previously estimated.

The results of this study do not support our initial hypothesis that mixed episodes are more severe than manic. This can be due to: the small sample size (which in part can be attributed to the methodology used); and to the use of medications that diminished the severity of the episodes. An analysis of the efficacy of therapeutic regimes was not included among our objectives due to our dependence on the patients’ ability to recall previous treatments and their difficulty to distinguish antidepressants from other specific medications.

To our knowledge, this is the first controlled study analyzing Brazilian bipolar patients during mixed states. Despite the caveats described above, our results do not indicate that mixed episodes are more severe than manic ones. Future studies should evaluate whether the DSM-IV criteria for mixed states are the most appropriate one when comparisons with pure mania are conducted.

**Reference**


