Bipolar disorder first episode and suicidal behavior:
are there differences according to type of suicide attempt?

A polaridade do primeiro episódio no transtorno bipolar
é um preditor para tentativa de suicídio (violenta e
não violenta) futura?

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Abstract
Objective: The objective of this study was to test the hypothesis that the polarity of the first mood episode may be a marker for suicidal behavior, particularly the violent subtype. Method: One hundred and sixty-eight patients diagnosed with bipolar disorder (DSM-IV) were grouped according to type of first episode: depression or manic/hypomanic. Groups were compared for demographic and clinical variables. We performed logistic regression in order to test the association between first episode polarity and suicidal behavior. Results: We found that depressed patients have a lifetime history of more suicide attempts. However, univariate analysis of number of suicide attempts showed that the best model fits the bipolar II subtype (mean square = 15.022; p = 0.010) and lifetime history of psychotic episodes (mean square = 17.359; p = 0.021). Subgrouping the suicide attempts by subtype (violent or non-violent) revealed that manic/hypomanic patients had a greater tendency toward attempting violent suicide (21.2% vs. 14.7%, X² = 7.028, p = 0.03). Multiple logistic regression analysis confirmed this result. Conclusion: Depressed patients had more suicide attempts over time, which could be explained by the higher prevalence of bipolar II subtype in this group, whereas manic/hypomanic patients had a lifelong history of more frequent violent suicide attempts, not explained by any of the variables studied. Our results support the evidence that non-violent suicide attempters and violent suicide attempters tend to belong to different phenotypic groups.

Descriptors: Bipolar disorder; Suicide attempted; Psychotic disorders; Dangerous behavior; Diagnosis

Resumo
Objetivos: O estudo pretende avaliar se a polaridade do primeiro episódio de humor prediz o comportamento suicida no transtorno bipolar, especialmente a tentativa de suicídio violenta. Método: Foram avaliados 168 pacientes com diagnóstico de transtorno bipolar (DSM-IV) subdivididos em dois grupos de acordo com a polaridade do primeiro episódio de oscilação do humor: se primeiro episódio foi depressão (PD) ou se primeiro episódio foi de mania (PM). Comparamos as variáveis clínicas e demográficas dos dois grupos através do teste do qui quadrado e analisamos os resultados utilizando a regressão logística e análise univariada. Resultados: Os pacientes definidos como PD apresentaram maior número de tentativas de suicídio ao longo da vida. Entretanto, após analisar os resultados através do método estatístico univariado, verificou-se que as únicas variáveis associadas com histórico de múltiplas tentativas de suicídio foram o diagnóstico de transtorno bipolar do tipo II (mean square = 15,022; p = 0,010) e a história de sintomas psicóticos (mean square = 17,359; p = 0,021). Ao avaliar a questão sob a perspectiva do tipo de tentativa de suicídio (se violenta ou não violenta), encontramos que os pacientes PM apresentavam maior probabilidade de cometer tentativas de suicídio violentas ao longo da vida (21,2% vs. 14,7%, X² = 7,028, p = 0,03). A análise estatística por regressão logística múltipla confirmou os resultados encontrados. Conclusão: Apenas o diagnóstico de transtorno bipolar tipo II e a existência de sintomas psicóticos são fatores associados com histórico de múltiplas tentativas de suicídio. A polaridade do primeiro episódio não está associada com o número de tentativas de suicídio em geral, entretanto existe associação entre tentativa de suicídio violenta e primeiro episódio de polaridade maníaca. Os resultados reforçam a evidência de que a tentativa de suicídio violenta é diferente da tentativa de suicídio não violenta, do ponto de vista fenotípico.

Descritores: Transtorno bipolar; Tentativa de suicídio; Transtornos psicóticos; Comportamento perigoso; Diagnóstico

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Suicidal behavior is any deliberate action with potentially life-threatening consequences, such as taking a drug overdose or deliberately crashing a car. It is a complex phenomenon with biological, environmental, developmental and learning contributory factors. It is well established that suicidal behavior is under genetic control and that this familial transmission is independent of the transmission of psychiatric disorders itself and linked to a serotonergic dysfunction. Suicide method has been used in studies of suicide attempters to select patients who are more likely to have low indexes of serotonergic neurotransmission, which in turn tend to correlate with higher levels of aggression. Therefore, patients who have attempted suicide using violent methods, such as jumping from a height, shooting or hanging, should constitute a peculiar group with a stronger genetic determinism, what justifies the distinction between violent and non-violent attempters when studying suicidal behavior.

In recent years, there has been a growing interest in the polarity of bipolar disorder (BD) (polarity at onset, as well as predominance of polarity during the course of this disease), since some studies have suggested that polarity could be a critical marker of course and/or prognosis in BD. Recently, a study carried out by Chaudhury et al., replicating previous results, showed that patients presenting depression as the first episode were at higher risk of suicide attempts even when adjusting for years with disease and total number of lifetime major depressive episodes. These studies are important, since they can provide a better understanding of BD clinical heterogeneity and particularity of suicidal behavior in BD.

In fact, studies on the association between BD and suicidal behavior have gained interest in recent years. The disorder probably exhibits the highest risk of suicidal behavior amongst all psychiatric disorders. Suicide rates in BD patients average approximately 1% annually, about 60-fold the international population rate of 0.015%, while nearly one third of patients acknowledge at least one suicide attempt annually, about 60-fold the international population rate of 0.015%. Since we found non-normal distribution for some variables, groups were compared according to polarity of the first episode using Mann-Whitney test for quantitative variables. Categorical variables were analyzed using chi-square tests. For the variables presenting statistically significant differences between groups (gender, type of BD, and lifetime history of psychotic episodes) zero-inflated Poisson regression analyses were performed, considering the number of suicide attempts as a dependent variable. Finally, logistic regression analysis was used to test the relationship between the type of suicide attempt (violent vs. non-violent) and those variables that had shown statistically significant differences between groups (polarity of the first mood episode, lifetime history of psychotic symptoms, type of bipolar affective disorder, gender, and type of BD).

Results

Patients grouped according to polarity of the first episode into the FD or the FM group were statistically different in: higher proportion of females in the FD group ($X^2 = 8.579, p = 0.003$), higher proportion of bipolar type II patients in the FD group ($X^2 = 19.726, p = 0.0001$), and higher proportion of lifetime history of psychotic episodes in the FM group ($X^2 = 4.769, p = 0.037$). Other sociodemographic and clinical variables that did not reach statistical significance were: age, marital status, age at first mood episode, number of comorbidities, type of comorbidity, lifetime number of manic episodes and lifetime number of major depressive disorders (Table 1).

In terms of suicidal behavior, we found that the FD group had more frequent history of suicide attempts (51.4% vs. 37.9%, $X^2 = 7.028, p = 0.03$) compared to FD patients (Table 1). Nevertheless, FD patients had more suicide attempts over time ($1.48 \text{ vs. } 0.92, z = 2.03, p = 0.042$). Analysis of suicide attempts by subtype, violent or non-violent, revealed that FD patients had a higher tendency to attempt suicide violently (21.2% vs. 14.7%, $X^2 = 7.028, p = 0.03$) compared to FD patients (Table 1). Considering only subjects with history of hospitalization ($n = 134$; FM = 59; FD = 75), we found the same pattern of results, but the differences between polarity groups are statistically more significant.
Suicide and polarity in bipolar patients

We performed a zero-inflated Poisson regression analysis of the number of suicide attempts in order to examine its relationship with first episode polarity. Our primary model included the independent variables that had reached statistical significance in Table 1, namely, gender, bipolar type II diagnosis, polarity of the first episode and history of psychotic episodes. We found that the best model fitted with bipolar II subtype (B = 0.373; S.E. = 0.157; z = 2.37; p = 0.018; 95% CI = 0.065 to 0.681) and lifetime history of psychotic episodes (B = 0.552; S.E. = 0.243; z = 2.26; p = 0.023; 95% CI = 0.705 to 1.03). The other variables described above (gender and polarity of the first episode) did not reach statistical significance.

In addition, we performed multiple logistic regression analysis of patients with a history of violent suicide attempt in order to investigate its relationship with first episode polarity (manic) correcting for possible confounding factors (gender, bipolar II diagnosis and lifetime history of psychotic symptoms). This analysis confirmed that the FM subgroup had a higher association with history of violent suicide attempt (OR = 4.083, p = 0.015, 95% CI = 1.32 to 12.64).

Discussion

Our results are only partially in accordance with those reported by Chaudhury et al.10. These authors found a significant association between the FD group and a more frequent lifetime history of suicide attempt and number of suicide attempts. In our sample, the frequency of suicide attempts in the FD group was not statistically different from the frequency of suicide attempts in the FM group (51 vs. 37.9%, respectively, p = 0.08). Nevertheless, as found in the Chaudhury et al., 2007 study, suicide attempters belonging to the FD group made more suicide attempts than suicide attempters belonging to the FM group10.

In our sample, FD and FM were different in terms of the percentage of bipolar type II, which was higher in the FD group (38.2 vs. 15.2%, as well as proportion of female gender (77.5 vs. 56.1%), lifetime history of psychotic symptoms and finally, number of lifetime suicide attempts (1.48 vs. 0.92). After performing a zero-inflated Poisson regression analysis in order to verify the independence of these variables regarding suicidal behavior, we found that the only characteristics associated with number of suicide attempts were diagnosis of bipolar II and lifetime history of psychotic symptoms. In other words, with regard to the number of suicide attempts, the strongest association was with bipolar II diagnosis or history of psychotic symptoms and not first polarity depressive episode. This gives two distinct groups at higher risk of suicide: bipolar II patients and patients with lifetime history of psychotic symptoms. Several previous studies have shown that bipolar II patients have a higher risk of suicide attempt than both bipolar I patients22 or unipolar depressed patients23. This finding could possibly be explained by the higher propensity of bipolar II patients for comorbidity with personality disorders, substance abuse, and anxiety compared with other mood disorders11. Additionally, bipolar II patients spend longer in depression, have less inter-episode intervals and a higher number of episodes in general24. The association between number of depressive episodes and suicidal behavior is well known. Several studies and clinical observations from bipolar and unipolar samples have shown that depression is strongly correlated with suicide11. A study found that rates of suicide attempt varied markedly between different phases of BD, being more frequent during episodes accompanied with depressive symptoms (depression, mixed and depressive mixed) and being absent from the hypomanic/manic phase25.
previous suicide attempt, hopelessness, depressive phase at index episode and younger age at intake were independent risk factors for suicide attempts\textsuperscript{27}. In contrast to our findings, the authors did not find association with bipolar II. This lack of accordance maybe reflects the heterogeneity of bipolar II samples.

Our second positive association of lifetime history of psychotic symptoms and number of suicide attempts is harder to explain mainly because history of psychotic symptoms could be encompassed in a heterogenic group. Psychotic symptoms could be secondary to episodes, being a marker of severity of mood episodes, or mood episodes could act as a trigger for the manifestation of schizophrenic diathesis. Unfortunately, the methodology used in our study does not allow distinguishing these groups. Some studies using similar methodology to characterize psychosis have shown that psychotic symptoms in BD are associated with poor outcome\textsuperscript{28,29}, but the relationship between psychosis and suicide in mood disorders remains unclear. Previous studies have only shown risk of suicidality (suicide attempt and suicide ideation) to be associated with psychosis in pediatric patients\textsuperscript{30} and adolescents with BD\textsuperscript{31}, but not in adult patients\textsuperscript{32}. However, one larger follow-up study of 44 years found that psychotic symptoms in BD were associated with complete suicide in adults\textsuperscript{33}.

We performed an additional analysis, characterizing the type of suicide attempt as violent or non-violent, and showing that FM patients had a more frequent history of violent suicide attempt compared to FD patients. A multiple logistic regression analysis corrected for possible confounding factors confirmed this result and showed that the FM subgroup had a higher association with history of violent suicide attempt.

These results support the evidence that non-violent suicide attempters and violent suicide attempters tend to belong to different phenotypic groups. In fact, several studies with genetic and biological perspectives have shown that violent attempters represent a subgroup of suicide attempters with a more consistent phenotype\textsuperscript{34,35}. Furthermore, suicidal behavior is a complex phenomenon with biological, environmental, developmental and learning contributory factors. In view of this multi-determinism, we can speculate that some factors, for instance, polarity in BD, could play a major role in some categories of suicidal behavior (i.e. violent, non-violent, multiple suicide attempts etc.), but not in all.

Our study has several limitations. The most important one concerning the retrospective design of this study, for it is well known that many patients have difficulty recalling hypomanic episodes. Additionally, the use of retrospective analysis makes recall of severity and duration of manic and depressive episodes almost impossible, where these represent important variables with possible association with suicidal behavior. A prospective study would enable other issues to be explored, such as whether FM patients have a higher prevalence during episodes of higher scores on impulsivity, hostility or hopelessness. We also deem it necessary to consider the influence of treatment because many patients, before being diagnosed as bipolar II, could have been misdiagnosed as unipolar depression, thereby delaying appropriate treatment. Moreover, several studies have shown that lithium would be more efficacious than valproic acid or carbamazepine in the prevention of suicidal behavior\textsuperscript{36} and another study has shown that BD patients have low adherence (20-60\%) to the treatment\textsuperscript{37}. We believe that only prospective studies including periodical serum analyses of medication are able to definitively clarify the influence of this variable.

Our sample is overrepresented by more severe patients because these were drawn from secondary and tertiary services. Thus, it is difficult to extrapolate these results to the entire spectrum of BD patients. Should these data be confirmed by prospective studies, they could help predict an adverse course using relatively reliable data and the polarity of the first episode.

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Disclosures

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* Modest
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Note: UFRGS = Universidade Federal de Minas Gerais; FAPEMIG = Fundação de Amparo à Pesquisa do Estado de Minas Gerais; CNPq = Conselho Nacional de Desenvolvimento Científico e Tecnológico; IBN-NET = Rede Instituto Brasileiro de Neurociências.

For more information, see instructions for authors.
References


