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Original article

Are comorbid anxiety disorders a risk factor for suicide attempts in patients with mood disorders? A two-year prospective study

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ABSTRACT

Background: Comorbid anxiety disorders have been considered a risk factor for suicidal behavior in patients with mood disorders, although results are controversial. The aim of this two-year prospective study was to determine if lifetime and current comorbid anxiety disorders at baseline were risk factors for suicide attempts during the two-year follow-up.

Methods: We evaluated 667 patients with mood disorders (504 with major depression and 167 with bipolar disorder) divided in two groups: those with lifetime comorbid anxiety disorders (n = 229) and those without (n = 438). Assessments were performed at baseline and at 3, 12, and 24 months. Kaplan-Meier survival analysis and log-rank test were used to evaluate the relationship between anxiety disorders and suicide attempts. Cox proportional hazard regression was performed to investigate clinical and demographic variables that were associated with suicide attempts during follow-up.

Results: Of the initial sample of 667 patients, 480 had all three follow-up interviews. During the followup, 63 patients (13.1%) attempted suicide at least once. There was no significant difference in survival curves for patients with and without comorbid anxiety disorders (log-rank test = 0.269; P = 0.604). Female gender (HR = 3.66, P = 0.001), previous suicide attempts (HR = 3.27, P = 0.001) and higher scores in the Buss-Durkee Hostility Inventory (HR = 1.05, P < 0.001) were associated with future suicide

Conclusions: Our results suggest that comorbid anxiety disorders were not risk factors for suicide attempts. Further studies were needed to determine the role of anxiety disorders as risk factors for suicide attempts.

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1. Introduction

Suicidal behavior is highly prevalent among patients with mood disorders [1]. The rate of suicide in such patients can be as high as 15-20% [2]. Suicide attempts are also prevalent in this population, with studies showing that up to 50% of patients with bipolar disorder (BD) and 30-40% of patients with major depressive disorder (MDD) have lifetime history of suicide attempts [3-5]. Bipolar disorder and MDD share certain risk factors for suicide attempts, such as previous suicide attempts, greater severity of depression, comorbidity with alcohol or substance use, and comorbidity with anxiety disorders [6-8].

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Anxiety disorders have been linked to suicidal behavior in the general population and in individuals with other psychiatric disorders. In a recent meta-analysis [9], patients with anxiety disorders were more likely to report suicidal ideation (OR: 2.89, 95% CI: 2.09-4.00), to have attempted suicide (OR: 2.47, 95% CI: 1.96-3.10), and to have died by suicide (OR: 3.34, 95% CI: 2.13–5.25) in comparison with patients without anxiety disorders, even after adjusting for comorbid depression.

There are few prospective studies investigating the role of lifetime comorbid anxiety disorders in future suicide attempts. These studies have produced conflicting results. A prospective study with a 3-year follow-up period, showed that the risk of suicide attempt was four times greater among patients with anxiety disorders and comorbid mood disorders than among those with anxiety disorders only (OR: 4.15, 95% CI: 1.34-12.9) and among those with mood disorders only (OR: 2.44, 95%

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CI: 0.709-7.55) [10]. Other prospective studies have also shown that suicide attempts and suicide ideation during follow-up are more common among BD and MDD patients with comorbid anxiety disorders than among those without [11,12]. In a three-year follow-up study of patients with MDD, anxiety disorders were associated with suicide attempts (OR: 2.31, CI: 1.19-4.47, P < 0.005) [11]. In another three-year follow-up study with patients with bipolar disorders, there was an association between comorbid anxiety lifetime and suicide ideation (OR: 1.66, CI: 1.07-2.57, P = 0.02). Interestingly in this study future attempts were not associated with comorbid anxiety (OR: 1.56, CI: 0.74-3.30, P = 0.2) [12].

In another prospective study with a two-year follow-up involving MDD and BD patients, comorbidity with anxiety disorders was not a risk factor for suicide ideation and attempts [13], a finding that was replicated by other prospective studies with mood disorders patients [14,15]. Thus, the role of comorbidity with anxiety disorders and its relationship to suicide attempts in individuals with mood disorders remains unclear.

Anxiety symptoms are common in patients with mood disorders, even in those without a diagnosis of an anxiety disorder [16,17]. Recent studies have shown that anxiety symptoms (nervousness, uneasiness and anxiety) and self-reported anxiety can predict suicidal ideation and suicide attempts [18]. However, some studies have shown that anxiety symptoms have a protective effect against suicidal behavior in patients with mood disorders or MDD [19,20]. Therefore, the nature of the relationship between anxiety symptoms and suicide attempts is not conclusive.

To date, there have been few studies involving well-characterized, large samples of patients with mood disorders that investigated comorbidity with anxiety disorders as a risk factor for suicide attempts. This topic has fundamental clinical implications, as anxiety disorders are highly comorbid with mood disorders and mood disorders confers the highest risk for suicide attempts among psychiatric disorders [1]. The primary aim of this prospective study was to evaluate the risk for suicide attempts among patients with mood disorders, with and without comorbid anxiety disorders at baseline. We hypothesized that the patients with comorbid anxiety disorders would make more suicide attempts during follow-up than would those without such comorbidity. A secondary and exploratory aim was to determine whether baseline anxiety symptoms were associated with suicide attempts during follow-up.

2. Material and methods

2.1. Patients and procedures

We evaluated 667 patients who volunteered for studies of mood disorders and suicide behavior between January-1990 and July-2013, from two sites: New York, NY (New York State Psychiatric Institute, Columbia University) and Pittsburgh, PA (Western Psychiatric Institute and Clinic). The inclusion criteria were: age between 18 and 70 years; diagnosis of Bipolar Disorder (any type) or Major Depressive Disorder according to Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised, and Fourth Edition Axis I disorders, patient edition (SCID-I) and signed a written informed consent. Exclusion criteria were current substance or alcohol abuse or dependence according to SCID-I, pregnancy and presence of neurological or unstable medical diseases (e.g. a patient with well controlled hypertension or diabetes was included). The study was approved by the Institutional Review Board of the New York State Psychiatric Institute at Columbia University and Western Psychiatric Institute and Clinic.

Trained research assessors with at least master's degree in psychology or psychiatric nurses performed all the interviews, and all diagnoses were confirmed including all available data, by consensus, by senior research psychologists and psychiatrists.

At baseline, all patients were diagnosed with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised, and Fourth Edition Axis I disorders, patient edition (SCID-I). Of those, 161 (24.4%) were diagnosed with BD-I, BD-II, or BD not otherwise specified (BD-NOS) and 506 (75.6%) with MDD. In patients with BD, 122 were current depressed at baseline, 2 were in manic episode and one was in a mixed episode. In the MDD subgroup, 434 patients were currently depressed. Manic symptoms at baseline were measured using the Young Mania Rating Scale (YMRS) and the mean score \pm SD was 4.08 (\pm 5.78).

Depressive symptoms were rated using the Beck Depression Inventory (self-report scale with 21 items with scores between 0 to 63, with Cronbach's alpha of 0.86) [21] and the 24-item Hamilton Depression Rating Scale (HAM-D-24; with scores between 0 and 70 and a Cronbach's alpha of 0.92) [22]. Anxiety symptoms were evaluating by using the following HAM-D-24 item scores: agitation, psychic anxiety, somatic anxiety, and hypochondriasis. Hopelessness was rated with the Beck Hopelessness Scale (selfreport instrument with 20 questions and scores between 0-20, Cronbach's alpha of 0.88) [23]. Lifetime aggression and hostility were rated with the Brown-Goodwin Aggression Scale (11 items, with scores between 22 and 44, Cronbach's alpha 0.88) [24] and the Buss-Durkee Hostility Inventory (self-report scale for with 75 items with "true or false" answers and Cronbach's alpha of 0.74) [25]. Impulsivity was rated with the Barratt Impulsivity Scale (30 questions with scores between 30–120 and Cronbach's alpha of 0.83) [26].

A suicide attempt was defined as a self-destructive act carried out with at least some intent to end one's life. The Scale for Suicide Ideation (scale with 19 items to evaluate the severity of suicidal ideation with scores between 0–38 and Cronbach's alpha of 0.83) [27] assessed suicide ideation at baseline. All this scales are widely used, validated and reliable measures.

In the follow-up assessments, presence of suicide attempts was evaluated at 3, 12 and 24 months by using the Columbia Suicide History Form (semi-structured interview that evaluates the presence, date, methods and lethality of each attempt. In this study, we used only the presence or absence of attempts) [28].

2.2. Statistical analysis

Patients were divided in two groups according to the presence or absence of lifetime comorbid anxiety disorders. In patients with and without lifetime comorbid anxiety disorders at baseline, categorical and continuous variables were compared using Chi-square tests and t-tests as appropriate.

Given that anxiety disorders tend to cluster together and are highly comorbid with each other, we initially examined the effect that anxiety disorders as a group had on the risk for future suicide attempts. In sensitivity analyses, we further examined the effect of each anxiety disorder separately.

The main outcome measure was suicide attempt during followup. Survival curves for the first suicide attempt after study entry were estimated using the Kaplan-Meier method, and the log-rank test was used in order to compare the groups. The Kaplan-Meier curve is defined as the probability of surviving in a given length of time and the log-rank test was used to compare the survival distribution of the sample.

An exploratory analysis of the relationships between each of the HAM-D-24 anxiety symptoms and suicide attempts during follow-up were analyzed using Cox proportional hazard regression. Also,

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