SPECIAL ARTICLE

Suicidal ideation and suicide attempts in bipolar disorder type I: an update for the clinician

Ideação suicida e tentativas de suicídio no transtorno afetivo bipolar tipo I: uma atualização para o clínico

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Abstract

Objective: *This article reviews the evidence for the major risk factors associated with suicidal behavior in bipolar disorder.* ***Method:*** *Review of the literature studies on bipolar disorder, suicidal behavior and suicidal ideation.* ***Results:*** *Bipolar disorder is strongly associated with suicide ideation and suicide attempts. In clinical samples between 14-59% of the patients have suicide ideation and 25-56% present at least one suicide attempt during lifetime. Approximately 15% to 19% of patients with bipolar disorder die from suicide. The causes of suicidal behavior are multiple and complex. Some strong predictors of suicidal behavior have emerged in the literature such as current mood state, severity of depression, anxiety, aggressiveness, hostility, hopelessness, comorbidity with others Axis I and Axis II disorders, lifetime history of mixed states, and history of physical or sexual abuse.* ***Conclusion:*** *Bipolar disorder is the psychiatric condition associated with highest lifetime risk for suicide attempts and suicide completion. Thus it is important to clinicians to understand the major risk factors for suicidal behavior in order to choose better strategies to deal with this complex behavior.*

Descriptors: *Bipolar disorder; Suicide; Behavior; Risk factors; Review*

Resumo

Objetivo: *O artigo revisa as evidências relacionadas aos principais fatores de risco associados ao comportamento suicida no transtorno bipolar.* ***Método:*** *Revisão de artigos da literatura em transtorno bipolar, tentativa de suicídio e ideação suicida.* ***Resultados:*** *O transtorno bipolar está fortemente associado à presença de ideação suicida e a tentativas de suicídio. Em amostras clínicas, entre 14% e 59% dos pacientes apresentam ideação suicida e entre 25% e 56% têm pelo menos uma tentativa de suicídio ao longo da vida. Aproximadamente 15% a 19% dos pacientes com transtorno afetivo bipolar morrem por suicídio. As causas do comportamento suicida são múltiplas e complexas. Alguns preditores de comportamento suicida vêm sendo demonstrados consistentemente na literatura, tais como estado de humor atual, gravidade da depressão, ansiedade, agressividade, hostilidade, presença de comorbidades com outros transtornos do eixo I e eixo II, presença de estados mistos ao longo do curso da doença e história de abuso físico ou sexual.* ***Conclusão:*** *O transtorno bipolar é o transtorno psiquiátrico com maior risco ao longo da vida para tentativas de suicídio e suicídio completo. Sendo assim é importante para o clínico identificar os principais fatores de risco para comportamento suicida visando a escolha das melhores estratégias para lidar com esse comportamento complexo.*

Descritores: *Transtorno bipolar; Suicídio; Comportamento; Fatores de risco; Revisão*

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Introduction

Bipolar disorder (BD) is strongly associated with suicidal ideation, suicide attempts, and suicide completion. In the Epidemiological Catchment Area study (ECA), 29% of bipolar patients in the general population made at least one suicide attempt during their lives.[1] In clinical samples, 25% to 56% of the patients with BD report at least one suicide attempt during their lives and 10% to 19% die by suicide.[2,3]

The causes of suicidal behavior are multiple and complex. Although bipolar disorder is an important trigger, BD alone is not sufficient to explain suicidal behavior without the interaction of other factors such as severity of disease, hopelessness, impulsivity, hostility and aggressiveness among others. Clinical predictors of suicidal behavior are generally not robust, which means they are not reproducible for every sample of patients or for a given patient individually, in part because suicide and suicidal behavior are the result of a combination of individual risk factors, precipitating stressors and the disease's features at that time. Although there are inconsistent results in the literature regarding suicidal behavior in bipolar disorder type I and bipolar disorder type II, a review based on six independent studies,[4-9] reported that the lifetime prevalence of suicide attempts was 17% (range: 10-18%) for bipolar disorder type I and 24% (range: 18-56%) for bipolar type II, although in three of these studies, bipolar type I was associated with more frequent suicide attempts than bipolar type II. This discrepancy may be in part mediated by a liability for comorbidity with personality disorder, substance use disorders, anxiety disorders,[10] and longer duration of the depressive episodes for bipolar type II compared to bipolar type I patients.

Nonetheless, our aim was to provide an update for clinicians focused on clinical risk factors for suicidal ideation and suicide attempts in BD type I. This may ultimately help clinicians prevent suicidal behavior in patients with bipolar I disorder.

Definitions of suicidal ideation and suicide attempts

One major problem in identifying suicidal ideation and suicide attempts is the variability in definitions for these terms, which vary across sites. In this review, we adopted the following definitions:[11]

- Suicidal ideation: refers to the thoughts about the desire, intent and method for committing suicide.[12] Suicidal ideation may be of varying intensity, ranging from occasional fleeting thoughts to rumination about one's own death and a current plan to committing suicide. - Suicide attempt: a self-injurious act committed with at least some intention to die (intent need not be 100%). If there is any intention to die associated with the act, then it can be considered an actual suicide attempt. Sometimes, even if an individual denies the intent, we can infer it clinically from the circumstances or the behavior.

- Interrupted attempt: occurs when the attempter is interrupted and prevented by outside circumstances from beginning the self-injurious behavior. Of note, interrupted attempters are reported to be three times more likely to eventually commit suicide than are uninterrupted attempters.[13]

- Aborted attempt: occurs when the individual begins the suicidal act but stops himself or herself before any destructive behavior has been completed. A critical aspect of defining an aborted attempt is that the person not only had suicidal ideation with a detailed plan and availability of the contemplated method, but also the person must report taking actual steps toward initiating a suicidal act, thus being in imminent danger of acting before deciding against it.

- Ambiguous attempt: suicidal act that appears to have been carried out with intent to die, but the individual denies intent and the clinician cannot infer it.

Another important definition of suicide behavior is that adopted by the Center for Studies of Suicide Prevention at the National Institute of Mental Health, which has been refined by O'Carrol et al.[14] Adjusting the definitions of suicide attempts or completion to a more general term, suicide-related behavior, two sub-categories are described.

- Instrumental behavior: it can have one of three outcomes: no injury, injury or death. It is the lack of intent to die that differentiates instrumental behavior from suicide acts (here there is no intent to die).

- Suicide acts: self-injurious acts committed by an individual with either explicit or implicit intent to die. If the outcome of a suicidal act is death, it is called a completed suicide. Otherwise, if the individual survives the suicidal act either with or without injuries, it is a suicide attempt.

Stress-diathesis model

In the stress-diathesis model (Figure 1),[15] a suicidal behavior is the result of the interaction between an individual's threshold for suicidal acts and the stressors that can lead to such a behavior. This threshold is a trait, hence the term diathesis, and is influenced by risk factors such as aggressiveness, impulsivity, substance abuse, and family history of suicide. Stressors appear to be state-dependent and include acute psychiatric conditions and interpersonal problems such as, parental loss, interpersonal problems, unemployment and other life stressors.

This model can be effective in order to identify patients at risk of suicidal behavior, as it focuses on clinical aspects, stressors and

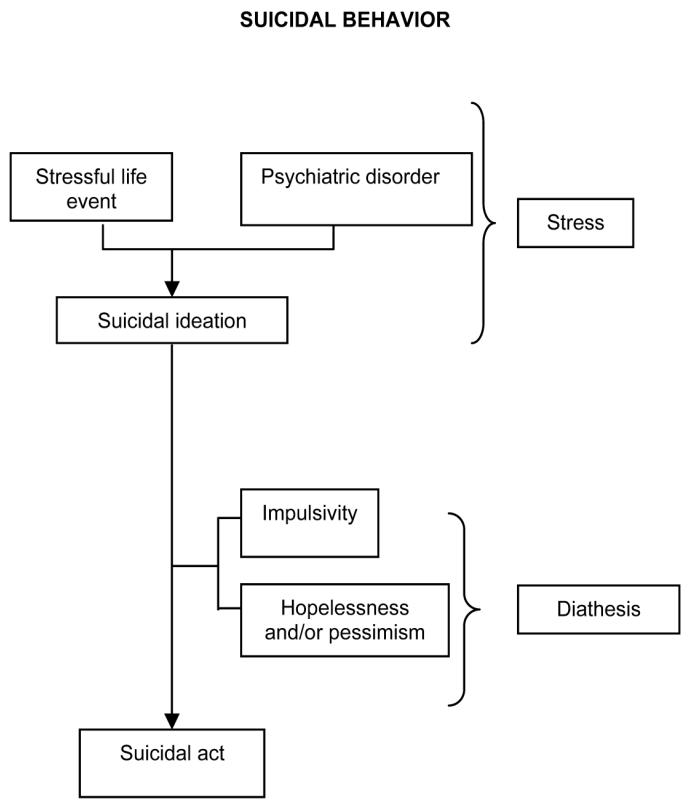

Figure 1 - Stress-Diathesis model (adapted from Mann et al., 2005)

the diathesis. This model also helps clinicians understand why some patients may attempt or commit suicide, but the majority do not.[16,17]

Suicidal ideation and bipolar disorder

Suicidal ideation is common in BD and it remains unclear if it is a predictor of future suicidal acts.[18,19] Reports of the prevalence of suicidal ideation vary from 14% to 59% in bipolar samples[20-25] and only a few cross-sectional studies have examined variables that influence suicidal ideation in BD and its relationship with suicide attempts. Some risk factors associated with the presence of suicidal ideation are positive family history for affective disorder, severe depression,[12] psychotic symptoms,[26] past suicide attempt,[23,26] comorbidity with alcohol abuse or dependence,[23] panic spectrum symptoms,[27] and earlier age of onset.[28]

Valtonen et al., in a cross-sectional study with a sample of 191 patients with bipolar disorder, showed that 61% (n = 116) reported suicidal ideation during the index-episode and 20% (n = 39) had attempted suicide in the same episode.[29] Of the patients who reported suicidal ideation, 42% (n = 81) reported it lasted the entire episode and 55% (n = 105) reported it at some point during the episode. In this study, none of the patients who attempted suicide did so without suicidal ideation, which suggests a strong association between suicidal ideation and suicide attempts in bipolar disorder. In comparison with non-suicidal patients, they had significantly higher levels of depression, hopelessness, anxiety, fewer symptoms of mania, longer duration of the last episode and greater prevalence of current comorbidity with anxiety disorders. Oquendo et al. observed that attempters had more suicidal ideation prior to hospitalization even when the most recent suicide attempt preceded the index hospitalization by more than six months.[30] Fagiolini et al. showed that previous suicide attempters were significantly more likely to endorse severe suicidal ideation during the acute phase of treatment when compared to non-attempters.[31]

Four prospective studies have evaluated suicidal ideation in BD. Johnson et al. showed that depression, mixed episodes and hopelessness were predictors of suicidal ideation and suicide attempts, and all these factors contributed to an increased suicide risk in BD.[32] Valtonen et al. also showed that suicidal ideation was a predictor of suicide attempts in univariate analyses of a bipolar sample, but in a multivariate analysis, suicidal ideation was no longer a predictor of suicide attempts.[33] Galfavy et al. demonstrated a strong correlation between higher levels of suicidal ideation and future attempts in bipolar samples.[34] Marangell et al., in a sample of 1,556 individuals with bipolar I and bipolar II, also showed that previous attempters reported more suicidal ideation at baseline and an increased risk for suicide attempts during follow-up.[35]

Studies have also suggested that suicidal ideation is mostly associated with depressive and mixed episodes,[20,22] indicating that suicidal ideation can vary across different mood states. In a second analysis of the same sample during different episodes, Valtonen et al. found marked differences regarding the level of.

Suicidal ideation during different episodes, being the highest level of suicidal ideation during mixed states, followed by depressive states.[36] In this sample, suicidal behavior occurred only during mixed and depressive episodes. This confirms findings from a psychological autopsy study by Isometsa et al. in which 79% of the suicides studied occurred during depressed or mixed states.[37]

In studies with mixed samples (patients with bipolar disorder and major depression), three prospective studies found that suicidal ideation predicted completed suicide,[38-40] but others found that suicidal ideation was not a predictor, despite being more prominent in patients with previous attempts,[41] Oquendo et al. suggests that measures of suicidal ideation can be more useful to identify patients at higher risk of suicide behavior when integrated into a "pessimism factor" which encompasses measures of subjective depression, reasons for living and hopelessness rather than a single predictor of suicidal behavior.[18]

In conclusion, although suicide ideation has been understudied until recently, it can be an important risk factor for suicide attempts. Suicide ideation can be a trigger in two different ways: as a state-dependent symptom (i.e., it can appear or worsen during depressive and mixed episodes) and as a trait (i.e. it can be related to the pessimism factor, such as hopelessness and subjective severity of depression). Therefore, it is important to evaluate the presence of suicide ideation, its intensity and frequency, how it varies in each patient (i.e., if it varies across different episodes or in different lifetime situations) and if there are any current specific precipitants for suicidal ideation.

Suicide attempts and bipolar disorder

There is an extensive literature documenting the strong association between a history of suicide attempt and subsequent suicidal behavior. Oquendo et al. showed that a history of suicide attempts can increase the risk for future suicide attempts fourfold.[42] Nordstrom el al. reported completed suicide rates of 15% for recent suicide attempters and 5% for non-attempters in patients with mood disorders.[43] Studies of completed suicides have shown that more than 50% of suicide completers had a previous attempt.[37,44] Tsai et al. conducted a chart review in a sample of 125 bipolar patients who died from suicide and found that 51.2% of them had previous attempts, especially in the first seven years of disease (at least 1 suicide attempt in the previous seven years before the completion).[44]

Other clinical risk factors associated with suicide attempts include: early onset of bipolar disorder, psychiatric hospitalization due to depression, rapid cycling, comorbidity with anxiety disorder, and alcohol and drug abuse.[45]

The most important risk factors for suicide attempts in BD have been reported to be the following:

1) Past suicide attempts

Past suicide attempt is one of the strongest predictors of future suicide attempts and suicide completion in the literature.[2] Harris and Barraclough,[3] in a meta-analysis of psychiatric disorders and suicide attempts and completion, found that a suicide attempt created a 37-fold risk for completed suicide. Oquendo et al. demonstrated that for each suicide attempt in a patient's history, the risk of another attempt during a two-year follow-up period increases by 30%.[46] In a prospective study with a sample of 308 patients with major depressive episode (21% bipolar), Oquendo et al. found that the three strongest predictors for suicidal acts were history of suicide attempt, subjective ratings of depression and cigarette smoking.[42]

Marangell et al., in a large prospective study with 1,556 patients with bipolar disorder, after controlling for other variables found that the only significant predictive variable for future suicidal behavior (including suicide completion) was previous history of suicide attempt (Odds Ratio = 3.87, p = 0.0029).[35] Galfalvy et al. also found in two prospective studies that baseline previous suicide attempts were independent risk factors for suicide attempts in the follow-up period.[34] Valtonen et al. found that previous suicide attempt was an independent risk factor for future suicide attempts.[33]

2) Sex

In the general population, women have higher rates of suicide attempts and men have higher rates of completed suicide.[47] In BD,

the pattern of suicidal behavior shows similarities and differences from that seen in the general population.

In the same way that in the general population, bipolar women attempt suicide more often than bipolar men, although there are studies showing no difference regarding suicide attempts in men and women.[48,49] Tondo et al. found that rates of suicide attempts among bipolar females were nearly twofold that for men.[50] Oquendo et al., in a prospective study comparing gender differences, showed that women with previous attempt at baseline had a six-fold risk for future suicide attempts in comparison to three-fold greater risk for men.[51]

In contrast with the general population (four times as many men killed themselves than women), there is no clear preponderance of males among bipolar patients who committed suicide. In a review, Tondo et al. demonstrated that the average SMR (standard mortality rate), which is a measure of the relative risk of death for a particular disorder compared to the expected death rate in the general population was 14.9 for males versus 21.1 for females, with no significative differences between gender.[50] The SMR can be also calculated for a specific cause of death such as suicide, in a particular population such as bipolar disorder patients. Based on estimates of projected lifetime risk of suicide as a proportion of causes of death among bipolar patients, Clark and Goebel-Fabbri estimated that the male:female risk was less than two-fold, with a relative risk of 1.85.[52]

Gender itself not only affects rates of suicidal behavior, it can be associated with different risk factors. In a cross-sectional study in Campinas, Brazil, 210 suicide attempters were evaluated in an emergency room. Of these patients, 68.1% were women and they reported more sexual and physical abuse in the past. Men reported more psychoactive substances intake, including at the moment of suicide attempt.[53]

Oquendo et al. compared risk factors between men and women.[1] They found that substance abuse, family history of suicide, cigarette smoking, borderline personality disorder and early parental loss each more than tripled the risk of future suicidal acts in men. Regarding women, past suicide attempts increased the risk for future acts six-fold. Suicidal ideation, hostility, lethality of attempts, fewer reasons for living, subjective depression symptoms, comorbidity with personality disorders and cigarette smoking also increased the risk for future suicidal acts in women.

3) Age of onset

Many studies have found a positive association between the early age of onset of the BD and suicidal behavior in these patients. Perlis et al. observed that patients with very early onset (before 13 years old) had 2.85 greater risk of making at least one suicide attempt when compared to those with age of onset above 18 years.[54] In the same study, they observed that early age of onset (between 13 and 18 years) was associated with a greater likelihood of suicide attempts and comorbidity with anxiety and alcohol abuse and dependence, which also increases the risk for suicidal behavior. In a systematic review, Hawton et al. found that early age of onset was correlated with suicide attempts.[45] Galfavy et al., in a prospective study, reported that younger age was related to suicide attempts,[34] and Lopez et al. found that 23% of patients with an age of onset earlier than 25 years attempted suicide versus 10% of those patients who had ages of onset higher than 25.[49] Grunebaum et al. showed that suicide attempters had a nearly 9-year earlier age of onset for a first mood episode when compared to patients without attempts.[55] Tondo et al. found an estimated age of onset 6 years lower in individuals with suicide attempts.[56] Leverich et al. evaluated 648 bipolar patients in a naturalistic follow-up study and found that attempters had an earlier age of onset of bipolar disorder when compared to non attempters (17.2 *versus* 20.6 years).[48]

There have been conflicting results regarding association between age of onset and suicidal behavior. Oquendo et al. found no differences between attempters and non attempters regarding age of onset of first depressive episode and age of onset of first manic episode.[30] Marangell et al. also found no differences in age of onset (attempters: 16.16 ± 8.8 *versus* non attempters 17.56 ± 8.82).[35]

What remains unclear is whether age of onset is an independent predictor of suicidal behavior or it increases risk via its association with other factors such as severity of bipolar disorder, more comorbidities with axis I and II disorders, more physical and sexual abuse and more rapid cycling.[48,57]

4) Polarity of episodes

Depression episodes are strongly correlated to suicide attempts in the literature. Oquendo et al., in an inpatient sample, found that twice as many attempters presented with a current episode of depression or mixed states when compared with non-attempters.[30] Additionally, the subjective and clinical severity of depression was higher in attempters and they had more than twice as many lifetime episodes of depression when compared to non-attempters. Oquendo et al. evaluated 44 bipolar patients (21 attempters and 23 non-attempters) and found that attempters had more than twice as many depressive episodes, more suicidal ideation, fewer reasons for living, higher frequency of family members with suicidal behavior and higher levels of lifetime aggression.[17] Hawton et al. found that a preponderance of depressive symptoms and mixed states were associated with higher risk for suicide attempts.[45] Leverich et al. found that suicide attempters had more prior hospitalizations for depression, more suicidal thoughts during depressive episodes and greater family history of substance abuse and suicide attempts.[48] Marangell et al., in a large prospective study, using a univariate analysis found that patients with more severe depressive symptoms were more likely to attempt or complete suicide over the follow-up period.[35] Chaudhury et al., in a mixed sample of bipolar type I and type II, demonstrated that patients who had a first mood episode of depression had eight-fold greater odds of suicide attempts, had more severe course of illness and more alcohol misuse and psychotic episodes.[58] In several studies, the number of hospitalizations for depression was also an independent predictive risk factor.[48,49,55]

Although the severity of depression is a risk factor as well, studies have previously shown that prior suicidal behavior does not appear to be related only to the objective severity of depression, i.e., the clinician's rating of how severe is the depression as measured by depression rating scales such as the Montgomery-Asberg Depression Rating Scale (MADRS)[59] and the Hamilton Depression Rating Scale (HAM-D).[60] Instead, evaluating subjective reports of depression severity (the patient's rating of how severe the depression is as measured by self reported instruments such as the Beck Depression Inventory),[61] hopelessness and perceived reasons for living might provide clinicians with a better indicator of the level of risk for suicidal behavior.[42] More pronounced suicidal ideation and greater subjective report of depression severity have been shown to increase the risk for future suicidal acts in bipolar patients.[34] Valtonen et al., in a study which evaluates the prevalence and risk factors for suicidal behavior during different phases of bipolar disorder, found that in mixed states, the subjective severity of depression predicted suicide attempts.[36]

It has been also suggested that suicide risk may increase during periods of rapid changes in mood state, occurring mainly

at the beginning and end of episodes.[40] Other studies suggest an association between a history of suicide attempts and increasing severity of depressive and manic episodes.[48,57] In a cross-sectional study comparing patients in manic and mixed states, Scharzmann et al. found no differences in the number of suicide attempts during episodes between the two groups.[62]

Mixed states are also associated with suicide attempts. Dilsaver et al. found in a cross-sectional study that patients with depressive mania had higher rates of suicidality when compared to patients with pure mania.[20] Goldberg et al. found a significant relationship between suicidal ideation and dysphoric mania and a relationship between suicide attempts and non remission of mixed mania.[22,23] Strakowski[25] and Sato[63] also found an association between suicidality and mixed mania. Johnson[32] found that mixed state was a predictor of future suicidal acts.

The literature is inconsistent about psychotic episodes as a risk factor. Oquendo et al. demonstrated that attempters had a trend towards fewer psychotic symptoms compared to non-attempters.[30] Johnson et al. found no differences in psychotic symptoms between attempters and non-attempters.[32] Grunebaum et al., in a study with a mixed sample of patients with major depression, schizophrenia and bipolar disorder, found no evidence that the presence of delusions distinguished patients with or without a history of suicide attempts.[64]

5) Rapid cycling

Rapid cycling (i.e. four episodes or more in one year) was related to greater suicidality in numerous studies. Coryell et al., comparing patients with and without rapid cycling, found that patients with rapid cycling had more attempts with higher intent and more attempts with higher lethality.[65] During the follow-up period, patients with rapid cycling had two-fold more attempts, and these attempts were at least three times more lethal and had a higher degree of intent in comparison to patients without rapid cycling.

Other studies did not find a relationship between rapid cycling and suicide attempts,[33,57] although rapid cycling was associated with other risk factors for suicidal behavior, such as early age of onset, more depressive episodes, and family history of bipolar disorder.

6) Comorbidity with Axis I and Axis II disorders

Comorbidity is common among patients with bipolar disorder. McElroy et al. found that 65% of patients with bipolar disorder have at least one lifetime comorbidity, 42% have experienced two or three lifetime comorbidities and 24% have three or more lifetime comorbidities.[66] Suppes et al. observed in a sample of 261 patients (81% bipolar type I) that 65% had a lifetime co-occurring Axis I comorbidity, and 41% had a history of substance abuse and 44% an anxiety disorder.[57]

The presence of Axis I comorbidity is correlated with suicide completion and suicide attempts in bipolar disorder, being the strongest associations between suicidal behavior and Axis I comorbidities found with anxiety disorders, eating disorders, and alcohol and drug abuse disorders.[45,48]

The relationship between suicidal behavior in Bipolar Disorder in the presence of comorbid anxiety disorders is the subject of considerable controversy in the literature. Simon et al. in a sample of 469 bipolar patients showed that 51.2% had lifetime anxiety comorbidity and 30.5% had current anxiety comorbidity. Of the patients with current anxiety comorbidity, 60% had history of suicide attempts and among patients with lifetime comorbidity, 40% had history of suicide attempts.[67] Lifetime anxiety comorbidity showed an odds ratio of 2.45 to suicide attempts, even after controlling for alcohol and substance abuse and bipolar state. In the group without anxiety, the rates of suicide attempt were around 27% for current anxiety and 20% for lifetime anxiety. A meta-analysis[50] showed that the risk for suicide attempts is increased in the presence of comorbidity with anxiety disorders. Dilsaver et al.[68] also found that 57.9% of patients with depressive mania and intra-episodic panic disorder had been suicidal during the study with scores in the Schedule for Affective disorders and Schizophrenia (SADS)[69] suicide subscale higher than 3 (i.e. mild suicidality) having all patients suicide ideation according to SADS. On the other hand, other studies have failed to demonstrate the association of suicide attempts and anxiety disorders[32,33,38] and some have reported a protective effect of anxiety.[19,70]

There have been reports of an association between suicidal behavior and alcohol and drug abuse in the context of bipolar disorder, but this has not been consistently replicated. Many studies found a positive association between alcohol use and suicide attempts and suicidal ideation in bipolar disorder.[17,49] Tondo et al. found that substance abuse raises suicide risk more than two-fold regardless the comorbid psychiatric disorder.[6] Vieta et al. observed that among 129 bipolar patients in remission, 31% had comorbidity, and these patients showed higher rates of mixed states, depressive episodes and suicide attempts.[71] Goldberg noted that the presence of alcohol abuse or dependence led to an approximately four-fold increased risk for suicidality above and beyond the effects of mixed states and dysphoric mania.[23] Simon et al. observed that comorbidity with substance abuse was significantly related to the risk of suicide attempts, but not to suicide completion in a bipolar sample.[72]

On the other hand, some studies did not find an association between alcohol and suicide attempts.[33,34,54] Also, alcohol and drugs can interact with numerous risk factors related to suicide attempts. They may be triggers of an attempt and can be linked to insomnia, mixed states, worsening of depressive episodes, higher hopelessness, higher levels of impulsivity and aggression, all of which can lead to suicidal behavior.

Fawcett et al. noted some risk factors that can lead to suicidal behavior despite the presence of a diagnosable comorbidity (see Table 1).[38] The acute risk factors (factors that are associated with suicide attempts in the first year after study entry) and chronic risk factors (the ones associated with suicide attempts between 2 and ten years of follow-up) should be a target for the clinician's intervention.

Axis II disorders play a major role in suicidal behavior, particularly with cluster B disorders (borderline personality disorder, antisocial personality disorder, histrionic personality disorder and narcissistic personality disorder). It seems that personality disorders may have effects on suicidality above and beyond effects of additional illness burden, loss of social support, poor health care and more frequent negative events. Axis II disorders also seem to be associated with more aggression and impulsive behaviors. Garno et al. in a mixed

Table 1 - Acute and chronic risk factors for suicide behavior

Acute risk factors for suicide attempts (until 1 year after entry in the study)	Chronic risk factors for suicide attempts (between 2-10 years of follow-up)
Alcohol abuse	Hopelessness
Anhedonia	Suicidal ideation (persistent plan)
Psych anxiety/panic attacks	
Diminished concentration	
Global insomnia	

Adapted from Goodwin and Jamison, 2007.[38]

sample of 100 bipolar type I and type II patients found that 30% had a comorbidity with cluster B (17% with borderline personality disorder) and that patients with this comorbidity had more lifetime suicide attempts, even after controlling for severity of depression, substance abuse, and physical and sexual abuse.[73] Oquendo et al. also found a correlation between comorbidity with cluster B and suicide attempts among bipolar individuals.[42] Leverich et al. found that attempters had greater prevalence of Axis II disorders (especially borderline personality disorder) and a greater number of negative stressors.[48]

Based on the same sample, Galfalvy[34] and Grunebaum[55] also showed higher rates of comorbidity with borderline personality disorders in bipolar suicide attempters. Valtonen et al.[29,33] found both in retrospective and prospective studies that personality disorders (clusters A, B and C) were associated with suicide attempters. Nakagawa et al., in a multiple regression analysis, showed that comorbidity with cluster B was associated with past suicidal behavior and severity of suicidal ideation.[70]

In a recent study about borderline personality symptoms and risk for death by suicide, McGirr et al. showed that patients who completed suicide, borderline personality disorder symptoms were less likely to include affective instability and paranoid ideation-dissociative symptoms, suggesting that these symptoms could be associated with suicide attempts but not with death by suicide.[74] These findings support the proposition that suicide attempts and death by suicide in patients with borderline personality and other disorders are phenomenologically distinct.

7) Impulsiveness, hostility, aggressiveness and hopelessness

Impulsiveness, hostility and aggressiveness are risk factors for suicidal behavior in different psychiatric samples. Suicidal individuals typically exhibit higher levels of those traits, suggesting that they are related to a common underlying behavioral dimension, which is crucial to suicide risk.[16] In a study comparing depressed suicide attempters from New York City, USA and Madrid, Spain, Baca-Gracia et al. observed that attempters from New York made attempts of greater lethality and reported more lifetime aggressive behavior than did depressed attempters in Madrid, suggesting that the greater lethality of suicidal behavior in NYC compared to Madrid is related to higher aggression levels.[75]

Brezo et al. in a systematic review about personality traits and its correlates with suicidal behavior demonstrated that the traits that seem to be more useful in predicting history of suicide attempts were aggression, anxiety, neuroticism, extroversion, impulsivity, hostility, and psychoticism.[76] In suicide ideators, neuroticism, psychoticism, introversion, perfectionism and hopelessness are the most common traits.

In bipolar suicide attempters, aggression and hostility variables are associated with past suicide attempts and some studies have shown they also predict suicidal behavior in this population.[34,42] Lifetime aggressiveness is reported to be also higher in previous attempters.[30,55] Impulsivity seems to play a different role in bipolar patients. In other psychiatric conditions (e.g., major depression), impulsivity is associated with suicide attempts. In bipolar disorder, some studies[31,77] did not find differences in the level of impulsivity as measured by the Barrat Impulsiveness Scale. This may be explained by the elevated impulsiveness intrinsic to bipolar disorder, which mitigates the utility of impulsiveness as a marker for suicide risk.

In suicide attempters, studies about the role of hopelessness as a predictive risk factor for suicidal behavior have shown conflicting results. Three studies demonstrated that hopelessness is an independent risk factor for suicide attempts,[29,33,34] even in different phases of bipolar disorder[36] and predicted mortality by suicide.[38] Prospective studies have reported hopelessness to be associated with suicide attempts in the short-term. Others have found that hopelessness is only significantly associated with suicidal behavior in subjects with alcohol or substance use.[78] Furthermore, some authors suggest that hopelessness can be integrated into a pessimism factor, which can include other measures such as subjective depression, reasons for living and suicidal ideation, and may be a better predictor of future suicide attempts.[42]

8) Physical and sexual abuse

A reported childhood history of abuse is associated with higher rates of mood disorders and suicidal behavior in adulthood. This can also be associated with higher levels of impulsiveness and higher rates of comorbidity with personality disorder, both risk factors for suicidal behavior.[77]

There are mixed results in the literature regarding this important issue. Leverich et al. found that attempted suicide was associated with a history of early physical abuse and early sexual abuse when these patients were compared to a control group.[48] These patients also showed an earlier age of onset. Suppes et al. observed that 23% of patients in the Stanley Foundation Bipolar treatment Outcome Network reported both physical and sexual abuse during childhood and adolescence and these patients were more likely to have a history of suicide attempts.[57] Oquendo et al., in a comparison of attempters and non-attempters with major depressive episode (21% bipolar), observed that previous attempters were more likely to report a childhood history of abuse.[42] Grunebaum et al. evaluated 96 patients with bipolar disorder and observed that the percentage of attempters reporting a history of physical or sexual abuse was twice as much as among non-attempters, although this variable was not retained in the regression analysis.[55]

One interesting point about physical and sexual abuse is that in a family study the rates of childhood abuse were higher in probands with a family history of suicidal behavior[79,80] and a history of sexual abuse in either the parents[81] or the offspring predicted suicidal behavior in offspring.[79]

9) Family history

Several family studies have found that the higher risk of suicidal behavior conferred holds true even after controlling for the effects of psychiatric disorders. Of note, familial transmission of the risk for suicidal acts was found to be independent from the familial transmission of psychiatric disorders.[82] In a study comparing offspring of non-attempters versus offspring of attempters, Brent et al.[79] found that offspring of attempters had six-fold increased risk of suicide attempts. Based on the same sample but using a prospective method, Melhem et al. observed that the offspring of probands who had made suicide attempts had a higher rate of suicide attempts in comparison to the offspring of probands who did not[81] (relative risk = 6.5; $p = 0.040$). In this study, mood disorder and impulsiveness-aggressiveness in the offspring were related to suicide attempts.

Hawton et al. showed that family history of suicide was associated with suicide attempts in patients.[45] Lopez et al. found a positive relation between family history for affective disorders and suicide attempters.[49] Galfalvy et al. reported a correlation between family suicidal acts and early suicide attempts.[34] Romero et al. observed that patients in a mixed sample of bipolar disorder and schizoaffective disorder, bipolar subtype, with positive family history for suicide completion had more lifetime suicide attempts and had a trend for more severe suicidal ideation.[83]

However, there are disagreements between studies. Oquendo et al. also found that family history rates for suicide and suicide attempts did not differ between attempters and non-attempters, although this was a cross-sectional study with a small sample and in which family members were not directly interviewed.[30]

In conclusion, bipolar disorder and suicide attempts can be related to several different risk factors, such as comorbidity with Axis I disorders (especially anxiety disorders, eating disorders and substance abuse disorders) and axis II disorders (especially borderline personality disorder), impulsivity, aggressiveness, early sexual or physical abuse, family history of suicide behavior, disease features (rapid cycling, depressive or mixed episodes, worsening of symptoms such as insomnia or anxiety), female gender and past suicide attempts. The clinician should investigate these risk factors for each patient and should reassess them periodically with the patient and family. When new risk factors for suicide attempts appear, such as worsening symptomatology or interpersonal problems, the clinician should reassess suicide ideation. It is also possible that assessment of severity of episode, levels of impulsivity, hopelessness, aggressiveness, hostility, presence of substance use, anxiety and insomnia may assist the clinician in identifying risk factors. Aggressive treatment of symptoms and management of modifiable risk factors may prevent future suicide attempts.

Suicide risk assessment

Suicide risk assessment and intervention has three key elements: clinical assessment of intent and overall suicide risk, intensive treatment of acute symptoms associated with increased risk and a careful clinical follow-up of patients with suicide risk factors, with renewed attention to comorbidities and underlying affective disorder.

In terms of assessment of suicidal ideation and suicide intention, the goal is to arrive at an overall qualitative estimate of the patient's risk of suicide regarding both acute and chronic risk factors (see Table 1). First, the clinician should compile a complete history of past suicide attempts, including severity of suicide ideation at the time of the attempt, number of attempts, lethality, circumstances of each attempt, clinical consequences and impact of the attempt for the patient and the family. This is a key issue because the strongest predictor of future suicide attempt is past attempt.

Of interest, studies show there is a breakdown in communication between patients and clinicians during the months preceding suicide, with clinicians frequently failing to ask explicit questions and patients often evading or denying their real intentions.[84] Isometsa et al. in a psychological autopsy study of 571 patients who died from suicide found that only 30% of inpatients and 39% of outpatients had communicated their intent to mental health providers.[85] Weeke studying the clinician's evaluations of patients who later killed themselves reported that only 13% were assessed as "seriously suicidal", 58% were assessed as "suicide possible not likely" and 28% as "suicide quite unexpected".[86] These findings underscore the importance of directly asking about suicide ideation and suicide intent, although direct inquiry may not uncover suicidal ideation, especially in cases where the patient is determined to hide the information from the clinician.

Some scales have been translated into Portuguese and can be used in clinical settings to assess the risk of suicidal behavior:

1) Scale for Suicidal Ideation: evaluates the presence of suicidal ideation, its intensity and suicide plans at current time and in the two weeks prior to the evaluation. Suicidal ideation refers to patients with a score $\geq$ 6 on the Scale for Suicidal Ideation.[12]

2) Beck Depression Inventory: a self report instrument to assess subjective severity of depression over the past week. The possible range of scores is 0 to 63, with scores higher than 19 indicating at least a moderate depressive episode.[62]

3) Beck Hopelessness Scale: evaluates the degree of hopelessness over the past week. The possible range of scores is 0 to 20, and scores equal to, or higher than, 9 indicated significant hopelessness.[87]

Conclusion

Bipolar disorder is the psychiatric condition associated with highest lifetime risk for suicide attempts and suicide completion. Thus it is crucial for the clinician to understand the relationship between suicidal behavior and the course of the disease, as well as the effects of risk factors.

In clinical practice, the patient should be evaluated and some of key risk factors for suicidal ideation and suicidal behavior discussed above should be assessed. Some of these risk factors can vary over time, which require reassessment. Some cross-sectional studies have assessed major risk factors for suicide ideation and suicide attempts, but only a few prospective studies have been reported. Further prospective studies are fundamental to understand the link between suicidal ideation and suicide attempts in bipolar disorder. These can lead to better prevention strategies, which is the ultimate goal of these studies.

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Lena Nabuco de Abreu	USP	-	-	-	-	-	-
Beny Lafer	USP**	FAPESP*** CNPq***	APA/AstraZeneca Young Minds in Psychiatry International Awards***	Astra-Zeneca*	-	-	-
Enrique Baca-Garcia	Autonomous University of Madrid NYS Psychiatric Institute Columbia University	-	-	-	-	-	-
Maria A. Oquendo	Columbia University	NIMH NIAAA	Astra-Zeneca* Pfizer* Janssen*	Astra-Zeneca*	Bristol Myers Squibb*	-	-

** Modest*
*** Significant*
**** Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.*
Note: USP = Universidade de São Paulo; FAPESP = Fundação de Amparo à Pesquisa do Estado de São Paulo; CNPq = de Desenvolvimento Científico e Tecnológico; NIDA = National Institute of Drug Abuse; NIAAA = National Institute on Alcohol Abuse and Alcoholism;
For more information, see Instructions for authors.

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