BRIEF REPORT

SUICIDE ATTEMPTS IN BIPOLAR DISORDER PATIENTS

Maurizio Pompili, Leonardo Tondo, Alessandro Grispini, Eleonora De Pisa, David Lester, Gloria Angeletti, Letizia Buonocore, Paolo Girardi, and Roberto Tatarelli

Summary

Object: The risk of completed suicide is very high among bipolar disorder (BPD) patients. The risk of attempted suicide is not as well-quantified, but attempting suicide is the most important factor for predicting the risk of subsequent completed suicide.

Method: We retrospectively evaluated 88 patients diagnosed with bipolar I, bipolar II, or unipolar depression. Of these, 44 had made at least one suicide attempt, and were matched for age, sex and diagnosis with 44 patients who had never attempted suicide.

Results: In the univariate contrasts, suicidal patients were more likely to be men, single, ill for a long period of time, bipolar, substance abusing, and unemployed. In a logistic regression analysis, only length of illness and unemployment were statistically significant.

Conclusions: Our results support previous finding in the literature but suggest that length of illness and unemployment are two important variables involved in the precipitation of suicide attempts in bipolar and unipolar patients. Length of illness is a trait-dependent risk factor (unchangeable) while unemployment is a state-dependent risk factor (which can potentially be modified).

Limitations: The study findings may not generalize to other samples, settings, and treatment programs.

Keywords: Suicide Attempts – Bipolar Disorder – Prevention

Declaration of interest: None

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A call to action to prevent suicide has been launched by WHO and by many governments worldwide. A number of preventive strategies have been proposed, but their effectivenss has rarely been tested or verified. New strategies to identify persons at risk for suicidal behavior have been proposed recently, imitating programs for the early detection of cardiovascular disorders (Knox et al. 2004). Persons who attempt suicide, particularly those who make violent or potentially lethal attempts, resemble closely in clinical and psychological characteristics those who commit suicide (Mann 2002).

Suicidal behavior in patients diagnosed with bipolar (manic-depressive, BPD) or major depressive disorders (MDD) has been investigated extensively (Goodwin & Jamison 2006; Lester 1993; Baldessarini et al. 2006a, b). The lifetime prevalence of DSM-IV BPD type I (with mania and often psychotic features) is at least 1%, and the total prevalence of bipolar syndromes may by as high as 5% if type II BPD with relatively liberal hypomania criteria and cyclothymia are included (Kessler et al. 2005, Goodwin & Jamison 2006).

Guze and Robins (1970) analyzed 17 long-term studies and found that the median proportion of deaths ascribed to suicide among persons considered to have a major affective disorder was approximately 15% (mean 30.6% ± 18.3%; range, 12%–60%) of all deaths.

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In a similar analysis of 27 studies, Goodwin and Jamison (1990) found that an average of 19% of deaths in BPD patients were due to suicide. Recent estimates in samples of never-hospitalized patients with affective disorders of moderate severity have suggested lifetime suicide rates of only 6% or less (Inskip et al. 1998, Blair-West et al. 1999, Bostwick & Pankratz 2000, O'Leary et al. 2001). Even this moderate rate is nearly nine-times the estimated lifetime risk in the international general population, of 0.70% ([0.014%/year x 50]; WHO 2003), and among ever-hospitalized BPD or MDD patients. The risk is approximately 20-times that in the general population, and averages about 0.4%/year—higher than in any psychiatric or medical disorder. Moreover, all of these estimates almost certainly underestimate suicidal risk, owing to difficulties in determining suicide as a cause of death, with even greater uncertainties in ascertaining suicide attempts and differentiating them from accidents. Tondo et al. (2003) surveyed suicide rates associated with BPD (usually type I, with mania), and found an overall average standardized mortality ratio (SMR), or risk as compared to persons of the same sex and similar age in the general population, of over 22, and a pooled, weighted mean rate of 0.4%/year (based on 823 suicides among 21,484 persons-at-risk for an average of 9.93 years, in 28 studies), which is about 28-times greater than in the general population (0.40 versus 0.014). In the general population, as well as in recurrent MDD patients (Blair-West et al. 1999), suicide rates are several times higher in men than in women, but in BPD patients the risk, by sex, is nearly 1:1 (Ahrens et al. 1995, Tondo et al. 2003, Baldessarini et al. 2006). In their seminal study, Avery and Winokur (1978) reported in the 1970s that 45%–70% of suicide victims had a mood disorder and that 19%–42% of suicides had made at least one previous suicide attempt. Finally, 10% of patients who had made a suicide attempt died by suicide within 10 years (Table 1).

Beautrais (2001) suggested that completed suicides and serious suicide attempts form two overlapping populations. Her data suggested that the risk factors and life processes that lead to completed suicide are similar for those making serious suicide attempts. Suicide attempts are highly prevalent in BPD patients and often related to substance abuse, a family history of affective disorders and severe depressive episodes. Patients hospitalized during depressive episodes also have a significantly higher frequency of prior suicide attempts (Lopez et al. 2001). Moreover, BPD is associated more frequently with a history of suicide or suicide attempts than are most DSM-IV psychiatric disorders, other than MDD (Chen & Disalver 1996). Kuo et al. (2001) and Goldsmith et al. (2002) suggested that a history of suicide attempts is a strong predictor of new attempts. Fagiolini et al. (2004) investigated suicide attempts and ideation in patients with type I BPD and reported that severity of BPD and higher body mass index (BMI) were correlated with a history of attempted suicide. They stressed that suicide risk may be a transient event preceded by severe suicidal ideation lasting only a few minutes or hours. Michaelis et al. (2003) reported that BPD patients who made a single suicide attempt were more likely than those who made multiple suicide attempts to demonstrate high suicidal intent in their first attempt.

Rihmer and Pestality (1999) and Rihmer and Kiss (2002) supported the notion that bipolar II patients are at higher risk of suicide when compared with bipolar I patients or patients with recurrent MDD. Valtonen et al. (2005) investigated a sample of patients with bipolar I and II disorders and found that the vast majority of patients had attempted suicide, had suicidal ideation or had both. They found a remarkably similar prevalence of suicidal acts in types I and II BPD, indicating that BPD-II disorder is not a milder form of BPD. Indeed, Tondo et al. (2006) recently found that suicidal risk, by diagnosis, ranked: BP-II > BP-I > MDD. In an ongoing investigation of 60 reports based on suicide attempts in more than 70,000 subjects, Tondo et al. (2006) found an annual risk of 2.13%/year vs. 2.86%/year in BPD patients and major affective disorder (MAD) patients, respectively; whereas the attempt risk was 26.1% vs. 21.8%, respectively. The male:female ratio was 1.37 in BPD and 0.85 in MAD patients.

Sokero et al. (2003) reported that, in their sample of suicidal patients, those who had made suicide attempts had more severe depression and functional

Table 1. *Risk factors for suicide in bipolar disorder* (adapted from Baldessarini et al. 2006)

- Early in the course of illness
- Younger age
- Depressive, mixed dysphoric-irritable states
- Caucasian ethnicity
- Being unmarried
- Previous depression
- Previous dysphoric-agitated states
- Hopelessness
- Previous suicide attempts
- Substance or alcohol abuse
- Impulsivity
- Stressful life events (deaths, divorce, separations, scandals, etc)
- Suicidal ideation
- Limited access to support or clinical services

disability and had a higher prevalence of psychotic features and comorbid disorders. They also noted the presence in these subjects of alcohol dependence or abuse. Sakamoto and Fukunaga (2003) found that depression was significantly more likely to improve one week after admission among suicidal patients with major depression following a unipolar course at the time of the suicide attempt than among nonsuicidal unipolar patients, whereas bipolar patients, both with and without a suicide attempt, demonstrated no significant improvement after one week when compared with baseline.

Materials and Methods

Suicide attempts were evaluated retrospectively in 88 patients with DSM-IV bipolar I, bipolar II, or major depressive disorders who sought outpatient treatment in 1998–2003 and were followed through 2004 at the "Rome E" psychiatric clinic (a branch of the Italian National Mental Health Service). Of these, 44 had made at least one suicide attempt, and they were matched for age, sex and diagnosis with 44 patients from the same outpatient psychiatric clinic who had never attempted suicide.

Diagnoses were based on clinical records and semistructured interviews at intake in accordance with DSM-IV criteria, and at clinical follow-up assessments on an average of every 6.5 weeks. Illness history was determined retrospectively during interviews with patients and family members and by reviewing clinical records and notes provided by referring physicians. Cases with uncertain diagnosis were excluded. All patients signed an informed consent following the procedure of a local IRB. Statistical analyses included bivariate analyses (χ^2, Fisher's exact test, ANOVA) and multivariate logistic regression. We used commercial microcomputer programs (Stata®, Stata Corporation, College Station, TX; Statview-5®, SAS Institute, Cary, NC). Comparisons with two-tailed $p > 0.05$ at stated degrees-of-freedom were considered not significant (NS).

Results

A total of 88 patients met the study criteria. Thirty-two were men and 56 women. There were 44 in the case group and a similar number in the control group. Diagnosis was bipolar I (n=44), bipolar II (n=20), and major depression (n=24). During this period of time, suicidal patients had made an average of 1.6 (±1.4) suicide attempts. Sixty-five percent of the patients were women, 25% married, 32% lived alone, 32% were unemployed, and 49% had more than 8 years of education. As for clinical characteristics, 50% of the patients had a diagnosis of BP-I disorder, 23% of BP-

Table 2. *Characteristics of major bipolar and unipolar patientswith or without suicidal attempts*

Measures	Suicide Attempts (N = 44)	Controls (N = 44)	Statistics	p
Women (%)	49.1	50.9	Fisher's exact	0.99
Age (years; m±SD)	61.64±15.98	62.25±15.6	F = 0.33	0.86
Married (%)	38.1	61.9	Fisher's exact	0.45
Living alone (%)	50.0	50.0	$\chi^2 = 3.07$	0.22
Unemployment (%)	68.2	31.8	$\chi^2 = 4.30$	0.04
Education ≤8 years (%)	51.4	48.6		0.99
Bipolar I (%)	52.4	47.6	$\chi^2 = 0.24$	0.88
Bipolar II (%)	50.0	50.0		
Unipolar (%)	46.1	53.9		
Years ill (m±SD)	24.09±9.44	15.78±7.92	F = 13.43	0.0005
Substance use disorder (%)	80.0	20.0	Fisher's exact	0.05
Long-term treatment (%)	53.8	46.1	$\chi^2 = 1.47$	0.23

Table 3. *Multivariate logistic regression model comparing patients with suicide attempts vs. controls (constant factor)*

Measures	OR	95% CI	χ^2	p
Illness years	0.90	0.83 to 0.98	6.22	0.01
Unemployment	4.43	1.07 to 18.3	4.22	0.04

OR = odds ratio; CI = confidence interval

II, and 30% of MDD. Substance abuse was present in 12% of the patients, and 74% of the patients were treated with a mood stabilizer.

In the univariate contrasts (see Table 2), suicidal patients were more likely to be ill for a longer period of time (p=0.0005), to be unemployed (p=0.04), and to have a substance abuse disorder (p=0.05). In a logistic regression, only length of illness and unemployment were statistically significant (Table 3).

Discussion

Bipolar disorder is associated with a very high risk of suicide and relatively lethal attempts, especially early in the illness when sustained clinical interventions, and even the diagnosis, may not have been established.

The focus of this paper was to review issues related to suicide attempts in bipolar patients and to present preliminary new findings derived from a comparison between patients with a lifetime history of suicide attempts and patients who had never attempted suicide. We found that the effects of age, sex, unemployment and substance abuse confirmed previous reports (Tondo et al. 2003, Baldessarini and Tondo 2005, Baldessarini et al. 2006, Tondo et al. 2006). Specifically, in the univariate contrasts, suicidal patients were more likely to have a longer period of illness, to be unemployed and to have a substance abuse disorder but, in a logistic regression, only length of illness and unemployment were statistically significant. Length of illness may be viewed as a trait-dependent risk factor (unchangeable) and unemployment as a state-dependent risk factor (which can potentially be modified). The lack of significant effects in the multivariate logistic regression may reflect the limited sample size (n=44 per group), as well as effects of matching for age, sex, and diagnosis.

Patients with affective disorders, particularly bipolar disorders, have a high suicide risk compared to those with other psychiatric and medical disorders. Approximately 48% of patients with bipolar disorder make at least one suicide attempt (Goodwin and Jamison 1990). The majority of suicides among patients with bipolar disorder occur in association with the depressed phase, and most are carried out within the first few years after illness onset (Tsuang and Woolson 1977, Weeke et al. 1979, Johnson and Hunt 1979). Bipolar manic-depressive disorders are prevalent, often severe and disabling illnesses, with greatly increased early mortality due to accidents and complications of comorbid substance abuse and medical illnesses, but particularly due to suicide. Suicide rates in bipolar disorder patients average 0.4% per year, or at least 25 times higher than in the general population (0.014% per year). Suicidal acts often occur early in the illness, in association with severe depressive and dysphoric-agitated mixed phases, and following repeated, severe depressions. The high lethality of their suicide attempts is suggested by the much lower ratio of attempted to completed suicide among bipolar manic-depressive disorder patients (5:1) as compared to the general population (about 20:1) (Baldessarini et al. 2006a). Consideration of risk factors helps to identify patients at increased risk for suicide, but ongoing clinical assessment is essential to limit the risk of suicide.

Reliance on routine screening of patients at risk for suicide for the risk factors reviewed earlier can be helpful, but this has uncertain power to predict specific risk and its timing in individual patients (American Psychiatric Association 2003). Such unpredictability may be particularly challenging in the assessment of patients with bipolar disorder, owing to the effects of rapid shifts in mood (lability), reactivity to losses or other stressors, impulsivity, behavioral control and the disinhibiting effects of commonly abused central depressants including alcohol and sedatives.

Studies reporting on the association of lithium treatment and suicide in bipolar disorder and other major affective disorders, including several prospective, randomized, and controlled trials, have consistently found lower rates of completed and attempted suicide during lithium maintenance treatment than without it (Baldessarini et al. 2006b).

A comprehensive meta-analysis of studies of lithium adds additional support to the impression that lithium has major beneficial effects for both completed and attempted suicide. These effects are found consistently across almost all trials reported over the past three decades, including trials involving randomization and double-blind assessments (Baldessarini et al. 2006b). This larger analysis considered a total of 45 reports involving 53,472 patients with bipolar disorder or more broadly defined manic-depressive disorder (including unipolar recurrent major depressive and schizoaffective disorder), treated and evaluated for an average exposure of nearly 348,000 person-years with or without lithium. Risks for both completed and attempted suicide were reduced by nearly fivefold, or 80%. Anticonvulsants, modern antipsychotics, and less-toxic modern antidepressants are widely employed in the treatment of bipolar disorder, but their potential ability to limit suicide risk either is unsupported by preliminary evidence or requires study (Baldessarini et al. 2006). Despite intensive efforts, effective prediction and prevention strategies have remained elusive, suggesting that our understanding of the interplay of factors that result in suicide remains incomplete. Clearly more knowledge about suicide among patients with bipolar disorders is needed. Further studies should address, in addition to the various factors involved, the role played by depressive and dysphoric-agitated mixed phases of bipolar disorder, substance abuse, anxiety disorders, impulsivity, lack of insight, and poor treatment adherence.

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