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Are High-Lethality Suicide Attempters With Bipolar Disorder a Distinct Phenotype?

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Abstract

Because Bipolar Disorder (BD) individuals making highly lethal suicide attempts have greater injury burden and risk for suicide, early identification is critical. BD patients were classified as high- or low-lethality attempters. High-lethality attempts required inpatient medical treatment. Mixed effects logistic regression models and permutation analyses examined correlations between lethality, number, and order of attempts. High-lethality attempters reported greater suicidal intent and more previous attempts. Multiple attempters showed no pattern of incremental lethality increase with subsequent attempts, but individuals with early high-lethality attempts more often made high-lethality attempts later. A subset of high-lethality attempters make only high-lethality attempts. However, presence of previous low-lethality attempts does not indicate that risk for more lethal, possibly successful, attempts is reduced.

Keywords

attempt; bipolar disorder; high-lethality; suicide

INTRODUCTION

Bipolar Disorder (BD) is associated with excess mortality from suicide and high rates of attempted suicide. Meta-analysis of 28 studies generated a pooled suicide rate of .397% per year, nearly 28 times higher than the international suicide base rate in the general population (.0143%), and representing approximately a 19.8% lifetime risk of death by suicide in BD (Tondo, Isacson, & Baldessarini, 2003). For non-fatal suicide attempt, in community samples the rate in BD is 29% (Chen & Dilsaver, 1996) and as high as 50% among psychiatric in- and outpatients (Valtonen, Suominen, Mantere et al., 2005). It has yet to be resolved as to whether there is differential risk for suicidal behavior in BD I and BD II, with some studies identifying differences (Coryell, Andreasen, Endicott et al., 1987; Rihmer, Barsi, Aratooó et al., 1990; Serretti, Mandelli, Lattuada et al., 2002) and others not (Michaelis, Goldberg, Singer et al., 2003; Valtonen, Suominen, Mantere et al., 2005; Valtonen, Suominen, Mantere et al., 2006).

Multiple clinical and demographic factors have been associated with suicide attempt in bipolar disorder, including being unmarried, early traumatic stressors, more hospitalizations

for depression, mixed affective states and rapid cycling disorder, a course of increasing severity of mania, early onset of disorder, comorbid anxiety disorder, abuse of alcohol and/or drugs, suicidal ideation, and family history of suicide or suicide attempts (reviewed in Hawton, Sutton, Haw et al., 2005). Suicide attempts vary considerably in type, intent, and medical severity of sequelae. In mood disorder samples, it has been noted that individuals who make high-lethality non-fatal suicide attempts, that is attempts resulting in a high level of medical damage, are more similar in clinical and behavioral characteristics to those who die by suicide than to those who make low-lethality attempts (Fawcett, Scheftner, Clark et al., 1987; Placidi, Oquendo, Malone et al., 2001). In a register study, individuals who made higher lethality suicide attempts were also more likely to eventually die by suicide than those who made lower-lethality attempts (Suokas & Lonnqvist, 1991).

Identifying clinical and behavioral characteristics of high-lethality suicide attempters is important for targeting interventions at individuals at risk for greater morbidity due to suicidal acts and who may have higher risk for eventual suicide death. Moreover, given the indications of similarities with those who die by suicide, it may also be informative regarding risk factors for suicide death in bipolar disorder. In this study, we examine bipolar suicide attempters to determine if there are identifiable characteristics in seriousness and frequency of suicidal behavior and/or in clinical features that distinguish high- and low-lethality suicide attempters. Should such differences appear, they may indicate different suicidal phenotypes within Bipolar Disorder, with differing levels of risk for suicide completion.

METHODS

Subjects

One hundred and forty six bipolar subjects presenting for treatment at two university hospitals in New York and Pittsburgh with an episode of depression (84%), mixed states (12%), mania or hypomania (4%) were recruited into studies associated with our Conte Center for the Neurobiology of Suicidal Behavior. Patients were informed that we were interested in learning about the underlying biology and clinical characteristics associated with suicidal behavior. For this analysis, we selected those bipolar participants who had a lifetime history of suicide attempts. Patients were classified into the high- or low-lethality group based on the lethality of their most lethal suicide attempt. Lethality of suicide attempts was assessed using the Lethality Rating Scale which rates attempts based on actual objective medical sequelae of the attempt: from 0 for minimal medical damage to 8 for completed suicide. Attempts rating 4 or more were considered high-lethality, since this score indicates that medical inpatient treatment for the sequelae of the attempt was required. As there was little difference between methods used in high- and low-lethality groups (see below), classification of lethality was based solely on medical outcomes. High-lethality attempters had an average of 3.2 ± 2.1 (range 1–11) lifetime attempts, and low-lethality attempts 2.3 ± 1.5 (range 1–9). Suicide attempt methods were: overdose/poisoning (low-lethality (LL) attempters 76%, high-lethality (HL) attempters 86%), cutting (LL 11%, HL 4%), jumping (LL 7%, HL 2%), hanging (LL 1%), firearms (LL 1%, HL 2%), immolation (LL 3%), and drowning (HL 2%). Twenty-two subjects had made a suicide attempt within a month of study admission, 10 subjects made an attempt between 2 to 7 months after initial study evaluation, and the remainder a median of 3.5 years prior assessment (range 2 months to 41 years). Subjects met DSM III-R criteria for Bipolar Disorder (Bipolar I: 64%, Bipolar NOS: 36%). Exclusion criteria included rapid-cycling, neurological illness, or active medical conditions. All subjects provided written informed consent.

Measures

Clinical and diagnostic assessments were made using our previously described method (Oquendo, Galfalvy, Russo et al., 2004). Axis I and Axis II disorders were diagnosed with Structured Clinical Interviews, SCID-I for DSM-III-R and SCID II DSM-III-R. Information on past suicide attempts was recorded on the Columbia Suicide History Form (Oquendo, Halberstam, & Mann, 2003), which constructs a chronology of all prior suicide attempts, including data on type of attempt (actual, ambiguous, aborted, etc.), method used, triggering event if any, and medical consequences of each attempt. A suicide attempt was defined as a self-destructive act with intent to end one's life. Once it was determined that the self-destructive behavior was associated with at least some intent to die, attempt lethality was assessed using the Lethality Rating Scale (Beck, Beck, & Kovacs, 1975) described above. Suicidal ideation was rated using the Scale for Suicidal Ideation (SSI; Beck, Kovacs, & Weissman, 1979), a 19-item instrument assessing frequency, intensity of suicidal thoughts and availability of lethal means. Total scores were based on 19 items rating ideation in the 2 weeks prior to interview. Suicidal intent was rated using the Suicidal Intent Scale (SIS; Beck, Schuyler, & Herman, 1974), a 19-item instrument that assesses constructs such as the individual's perception of the lethality of their method and efforts not to be discovered during the suicide attempt. Total scores were generated for the most lethal and most recent suicide attempt. Suicide attempts and completions in first-degree relatives were recorded using a family history questionnaire.

Lifetime aggression, hostility, and impulsivity were rated using the Brown-Goodwin Aggression Scale (Brown & Goodwin, 1986), Buss Durkee Hostility Inventory (Buss & Durkee, 1957) and Barratt Impulsivity Scale (Barratt, 1965). Current severity of depressive symptoms was assessed using the 17-item Hamilton Depression Rating Scale (HAM 17; Hamilton, 1960). Overall functioning was assessed with the Global Assessment of Functioning Scale (GAS; Endicott, Spitzer, Fleiss et al., 1976), and hopelessness with the Beck Hopelessness Inventory (BHI; Beck, Weissman, Lester et al., 1974). The Reasons for Living Inventory (Linehan, Goodstein, Nielsen et al., 1983) assessed protective factors against suicide. Life stressors during the preceding 6 months were measured using the St. Paul-Ramsey Scale (Lumry, 1978).

Statistical Methods

Subjects were classified into two groups based on having a history of either high-lethality or low-lethality attempts. Individuals who had made more than one attempt were classified according to the lethality of their most highly lethal attempt. The two groups were compared in terms of clinical, diagnostic, and demographic characteristics (excluding aggression, hostility and impulsivity scores) using Student's *t* test or Wilcoxon tests for continuous variables and Chi² statistics for categorical variables. All tests were two tailed. Comparison of lifetime aggression, hostility, and impulsivity in high-lethality and low-lethality suicide attempters were controlled for sex and age, using analysis of variance.

Correlations between lethality of attempt, age at the time of attempt, the number and lethality of previous attempts were tested in individual mixed effects logistic regression models that included a random subject effect. In model 1, high lethality was the response variable, and number of previous attempts was the independent variable. In model 2, for individuals with multiple attempts, high lethality was the response variable and lethality of previous attempts and age at time of attempt were the independent variables. Additionally, permutation analysis was performed whereby 2,000 random permutations of the data were generated in which the order of the lethality of suicide attempts for each individual was scrambled and Spearman correlation coefficient was computed. This analysis tested whether lethality increased with each subsequent attempt.

RESULTS

Demographics

Subjects with high-lethality attempts were older (37.4 ± 10.4 vs. 33.3 ± 9.9 , $t = 2.37$, $df = 113$, $p = 0.019$) and more likely to be married than low-lethality attempters (37.5% vs. 17% , $\chi^2 = 3.99$, $df = 1$, $p = 0.014$), but were not different on gender (48% male vs. 34% male, $\chi^2 = 2.14$, $df = 1$, $p = 0.144$) or any other demographic variable (data not shown). For individual attempts, older age at the time of attempt was associated with higher lethality when adjusted for a random subject effect ($OR = 1.5$ for each 10 years increase, $z = 3.0$, $p = .002$).

Acute and Comorbid Psychopathology

High-lethality attempters were more likely to be inpatients at the time of entry to the study than low-lethality attempters (Table 1), and remained so even after excluding recent attempters from the analysis (data not shown). The two groups did not differ in severity of depressive symptoms and both had high, but similar, lifetime rates of alcohol and/or substance use disorders, severity of life stressors, and rates of childhood abuse (Table 1).

Aggression and Other Trait Characteristics

There was no difference in lifetime aggression, impulsivity, or hostility scores, and there were similar rates of comorbid cluster B personality disorder (CBPD) in high- and low-lethality attempter groups (Table 1).

Course of Illness

High-lethality attempters had a greater number of prior psychiatric hospitalizations than low-lethality attempters (adjusted for age and number of attempts) despite the fact that the two groups did not differ in number of depressive episodes, or age of onset of first depressive, manic, or hypomanic episode (Table 1).

Suicidal Behavior

High-lethality attempters had greater suicide intent at the time of the most lethal attempt than low-lethality attempters, and had made a greater number of previous attempts (Table 2). The two groups did not differ in terms of suicidal ideation in the 2 weeks prior to study entry, or in suicide related factors such as hopelessness and reasons for living. There was no difference in rates of suicide attempt or suicide in first-degree relatives (Table 2).

Repeat Suicide Attempt and Lethality

In model 1, the number of previous attempts did not predict high-lethality at the next attempt ($OR = 1.06$, $z = 0.6$, $p = 0.580$). Permutation analysis did not find a pattern of increasing lethality with each subsequent attempt (Spearman Correlation = 0.05480678 , p -value = 0.4305). These two findings combined suggest that the lethality of the next attempt cannot be predicted based on the number of earlier attempts and that lethality does not automatically increase at each subsequent attempt. However, model 2 showed that for multiple attempt individuals who had made an early attempt of high lethality, there was significant likelihood that any subsequent attempts would also have high lethality ($OR = 2.6$, $z = 2.8$, $p = .006$). That model also showed that age at time of attempt was not a significant correlate of high lethality (age: $OR = 1.25$, $z = 1.2$, $p = .220$) once lethality of early of attempt is considered.

DISCUSSION

Risk factors for suicidal behavior in Bipolar Disorder have been identified primarily through studies comparing bipolar suicide attempters with either bipolar non-attempters or normal controls. To our knowledge, this is the first study to focus on characteristics of bipolar suicide attempters who may be at greater risk for suicide by comparing high- and low-lethality bipolar suicide attempters, the former group perhaps more closely resembling those who die by suicide.

Lethality and Trait Characteristics

There were no differences in impulsivity, aggression, or hostility in high- and low-lethality bipolar suicide attempters. Studies in MDD have found greater impulsivity in low-lethality suicide attempters compared to high-lethality attempters, and greater aggression associated with higher lethality attempt (Fawcett, Scheftner, Clark et al., 1987). We also found high and similar levels of comorbid cluster B personality disorders in the high and low-lethality groups, consistent with reports that CBPD is associated with greater risk for suicidal behavior when comorbid with Bipolar Disorder (Garno, Goldberg, Ramirez et al., 2005) and MDD (Hansen, Wang, Stage et al., 2003). CBPD, particularly borderline personality disorder, is associated with impulsivity and aggression, carries a high risk of suicide attempt (Gunderson, 1984), and has a 3–9% rate of completed suicide (Brodsky, Malone, Ellis et al., 1997). The high prevalence of comorbid CBPD in both the high- and low-lethality attempter groups may have resulted in a ceiling effect in this sample for aggression and impulsivity.

Psychopathology, Course of Illness, and Lethality

Suicidal behavior in BD has been associated with psychosis at time of illness onset (Tsai, Kuo, Chen et al., 2002), mixed episodes at onset and during the course of illness (Khalsa, Salvatore, Hennen et al., 2007), and rapid cycling (Coryell, Solomon, Turvey et al., 2003). A psychological autopsy study of 31 BD I suicides, found suicides were more likely to be in a depressed episode at death (Isometsä, Henriksson, Aro et al., 1994), while depressive phase at baseline predicted suicide attempt in an 18 month follow-up prospective study (Valtonen, Suominen, Mantere et al., 2006). We found that measures of acute psychopathology in terms of depression and psychosis did not distinguish high- and low-lethality attempters. Nonetheless, given the cross-sectional study design, and that the majority of participants had not made a suicide attempt during the episode we assessed, we cannot rule out such associations becoming apparent over time.

High-lethality attempters had a greater number of psychiatric hospitalizations but a similar number of depressive episodes compared to low-lethality attempters. The higher number of hospitalizations may reflect greater medical damage sustained in higher lethality attempts. Hoyer, Olesen, and Mortensen (2004), reported that multiple hospital admissions increased the risk of suicide by 3.8 fold compared to a single admission in the year prior to death. Psychological autopsy found more frequent hospitalizations and longer treatment histories in bipolar suicides compared to MDD suicides, however no information was available on prior suicide attempts (Isometsä, Henriksson, Aro et al., 1994). Clearly, more data regarding the association between lethality of suicidal behavior and hospitalization is needed to clarify the relationship between these variables.

Lethality and Characteristics Suicidal Behavior

High-lethality attempters had higher suicidal intent than low-lethality attempters for their most lethal attempt. This is consistent with reports that greater suicide intent has an effect on lethality in MDD (Oquendo, Placidi, Malone et al., 2003; Placidi, Oquendo, Malone et al., 2001), psychosis (Hamdi, Amin, & Mattar, 1991), and in a general hospital sample (Diaz,

Baca-Garcia, Diaz-Sastre et al., 2003), although not all studies agree that the effect is robust (Nielsen, Stenager, Brahe et al., 1993). Suicidal ideation was not different between the two groups, however it was assessed only for the 2 weeks prior to entering the study and most of the participants had not made a suicide attempt in the current episode.

In addition to having higher intent at the time of their most lethal attempt, high-lethality attempters had made more past attempts. This is in contrast to findings by Michaelis et al., that bipolar attempters with high intent at their first attempt are less likely to make multiple attempts than those with low intent (Michaelis, Goldberg, Singer et al., 2003). That study did not assess the relationship between lethality, intent, and number of suicide attempts, so direct comparisons with our study are difficult. In a military sample of young adult suicide attempters with varied psychiatric diagnoses, Pettit, Joiner and Rudd (2004) found that lethality of current attempt was not associated with number of previous attempts.

In this study, lethality of suicide attempt was greater in those with multiple attempts and 61% of those who had made two or more attempts had variation in lethality of attempts. Examining the relationship between lethality and order of suicide attempts, we found there was no linear progression from lower to higher lethality attempts, whereby lethality increased incrementally with each successive attempt. Rather, we identified a pattern showing that individuals with multiple past attempts who had made an early high-lethality attempt had a significant likelihood of subsequent high-lethality attempts. In contrast, for individuals with multiple past attempts and whose early attempt was of low lethality, subsequent attempts do not inevitably escalate in lethality, but importantly, in this group, future attempts will not necessarily remain low-lethality. That is, the presence of prior low-lethality attempts does not protect against the likelihood of a future high-lethality attempt. This pattern of attempt lethality suggests a possible high-lethality suicide attempt phenotype, one which potentially is more telling with respect to completed suicide. In contrast, we were unable to identify a low-lethality phenotype, as the low-lethality group likely contains a mix of future high-lethality attempters as well as individuals who have a low-lethality phenotype. This lack of a clearly defined low-lethality group may explain the lack of discernible clinical and trait differences between the high- and low-lethality suicide attempter groups. Identifying and clinically characterizing a low-lethality phenotype group would better allow a comparison.

Limitations

This cross-sectional, retrospective study did not assess psychopathology at the time of most lethal suicide attempt. Recall bias is an issue in all retrospective studies, and in this study where for some participants the most lethal attempt took place a considerable time before study assessment, recalling intent and perceptions of distant events is less than ideal. The sample size is modest and comprises mainly bipolar individuals in a depressed or mixed episode seeking treatment at a tertiary referral center. Thus, the sample may not be representative of the full spectrum of BD. Although there may be differential risk for suicidal behavior in BD I versus II (Coryell, Andreasen, Endicott et al., 1987; Rihmer, Barsi, Aratooó et al., 1990; Serretti Mandelli, Lattuada et al., 2002) not all studies agree (Michaelis, Goldberg, Singer et al., 2003; Valtonen, Suominen, Mantere et al., 2005; Valtonen, Suominen, Mantere et al., 2006). We pooled subjects with Bipolar I and NOS, which may blur important differences among subtypes. Further studies are required to examine possible differences in suicidal behavior related to subtype of BD. We have not taken treatment history into account, but studies in MDD (Oquendo, Kamali, Ellis et al., 2002) suggest few patients are adequately treated both before and after study entry. We used the medical consequences of the suicide attempt to classify attempters as having high- or low-lethality attempts. Alternate ways of viewing lethality, for example taking into account whether intervention to rescue the individual was likely or assessing injuries without

accounting for intent or rescuability may lead to different results. Finally, our sample included subjects with comorbid Cluster B personality and substance use disorders, both independently associated with aggression and suicidal behavior, which suggest caution in result interpretation.

CONCLUSIONS

In BD, it appears that risk for high-lethality attempts is greater in those with higher intent to die and greater number of suicide attempts. Future attempts in individuals who have made an early high-lethality attempt are likely to also be of high-lethality, while the lethality of future attempts in individuals with an early low-lethality attempt could not be predicted in this sample. Thus, the occurrence of minimally damaging suicide attempts does not ensure that future attempts will continue to be similarly low-risk. This key point underscores the need to remain alert to suicide risk even in those with a history of low-lethality attempts. Further research is necessary to determine if there are distinct subtypes of suicidal behavior in BD and if the relationships between impulsivity, aggression, and suicide attempt lethality observed in MDD are similar in Bipolar Disorder.

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TABLE 1

Comparison of Bipolar Patients Who Have Made High- and Low-Lethality Suicide Attempts: Clinical and Psychosocial Characteristics

	High lethality (n = 57)		Low lethality (n = 89)		Analysis		
	Mean (range) or %	±SD (n)	Mean (range) or %	±SD (n)	t(²)	df	Sig
Inpatient	69%	(39)	41.4%	(36)	9.81	1	0.002
Number of prior MDE	22.0 (0-100)	30.4	12.9 (0-99)	20.1	1559 [†]	-	0.112
Number of hospitalizations	6.6 (0-60)	9.8	2.9 (0-20)	3.4	1362 [†]	-	0.003
Age of onset of 1st MDE	19.1 (4-46)	10.7	16.8 (5-48)	8.7	-1.26	96.8	0.210
Age of onset of 1st manic episode	22.3 (6-48)	10.0	20.7 (7-49)	7.4	-0.80	65.0	0.428
Cluster B personality	42.1%	(16)	49.2%	(31)	0.24	1	0.626
Lifetime alcohol or substance use disorders	60.5%	(26)	4.5%	(49)	0.06	1	0.812
Hamilton Depression Scale (17 Item) *	18.9 (4-31)	6.1	19.1 (3-32)	6.7	0.23	123.6	0.818
Global assessment scale	43.7 (20-80)	11.9	46.3 (25-90)	10.4	1.28	99.2	0.202
History of childhood abuse	51.9%	(27)	48.1%	(37)	0.06	1	0.801
Life events (St. Paul Ramsey)	4.3 (2-6)	1.0	4.3 (1-6)	1.0	-0.30	84.5	0.767
Trait Characteristics							
Barratt Impulsivity Scale	60.9 (22-98)	20.2	67.7 (32-95)	15.5	2.70		.103
Brown-Goodwin Aggression Scale	21.3 (11-36)	6.3	22.1 (10-39)	6.3	.467		.496
Buss Durkee Hostility Inventory	40.6 (18-69)	11.9	44.7 (23-65)	11.6	3.02		.085

* Note. Assessed for the 2 weeks prior to study entry.

[†] Wilcoxon rank-sum non-parametric test.

TABLE 2

Comparison of Bipolar Patients Who Have Made High- and Low-Lethality Suicide Attempts: Characteristics of Suicidal Behavior

	High lethality (n = 57)		Low lethality (n = 89)		Analysis		
	Mean (range) or (%),	±SD (n)	Mean (range) or (%),	±SD (n)	t (²)	df	Sig
Family history of suicide	3.7%	(2)	9.6%	(8)	(0.94)	1	0.333
Family history of suicide attempt	16.7%	(9)	19.3%	(16)	(0.03)	1	0.873
Age at 1st suicide attempt	24.3 (7-52)	11.6	22.6 (7-58)	10.7	-0.90	110.3	0.369
Number of suicide attempts	3.2 (1-11)	2.1	2.3 (1-9)	1.5	-2.91	91.5	0.005
Time between 1st and most lethal suicide attempt (years)	5.6 (0-31)	8.5	3.8 (0-29)	6.7	-0.89	111.1	0.374
Suicidal Ideation 2 weeks prior to study entry	15.3 (0-32)	11.0	12.6 (0-31)	9.7	-1.31	87.2	0.194
Suicide Intent Scale for most lethal attempt	18.3 (8-27)	4.7	14.4 (0-26)	5.5	-4.30	122.26	<0.001
Measures associated with Suicidal Behavior							
Beck Hopelessness Scale (current)	10.5 (0-20)	5.9	11.7 (1-20)	5.4	1.11	88.7	0.269
Reasons for Living Scale (current)	144.5 (63-282)	43.7	146.7 (52-256)	42.5	0.26	95.1	0.792