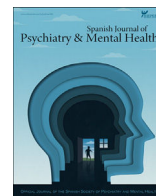




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Spanish Journal of Psychiatry and Mental Health

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Original article

Fatal suicidal behavior in Bipolar II patients after their first hospitalization[☆]

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ARTICLE INFO

Article history:

Received 22 September 2021

Accepted 28 December 2021

Available online xxx

Keywords:

Bipolar II disorder

Fatal suicide behavior

First hospitalization

Violent suicide attempt

ABSTRACT

Introduction: Bipolar disorder, especially Bipolar II disorder, is a mental disorder with high risk of fatal suicide behavior (FSB). The aim of this study was determine rate and risk factors of FSB in a cohort of Bipolar II patients followed after their first hospitalization.

Material and methods: We recruited all Bipolar II patients according DSM-IV criteria who were hospitalized for first time in our Psychiatric unit between 1996 and 2016 ($N = 59$). We collected clinical variables during their first hospitalization and identified all patients with FSB during follow-up until 31st December 2020. We compared baseline variables between Bipolar II patients with FSB and the ones without FSB.

Results: The average age at FSB was 45.5 years old and there was a 2-year gap on average between the first psychiatric hospitalization and completed suicide. FSB was characterized by a violent act (83% of cases). When we compared Bipolar II patients who died by suicide with who died by other causes or they are alive, only a history of previous violent suicide attempt ($p < 0.05$) was detected as a risk factor significantly associated with FSB. 10% of Bipolar II inpatients died by suicide, all of them in the first five years after the first hospitalization and usually by a violent method.

Conclusions: Bipolar II disorder has a high rate of completed suicide. History of a previous violent suicide attempt is a predictor of completed suicide.

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Introduction

Bipolar disorder is a mental disorder with the highest risk of died by suicide,¹ reaching a suicide rate up to 30 times higher than general population.² Suicide behavior in bipolar disorder is influenced by multiple variables.^{3–6} Although there is no coincidence between all studies, many indicate an increased risk of fatal suicide behavior (in our study we use the acronym FSB in Bipolar II Disorder versus Bipolar I Disorder.^{7–11} As we know from previous studies, psychiatric hospitalization in itself suggests an additional severity and a greater risk of died by suicide in affective disorders^{12,13} compared to affective patients who have never been hospitalized. Although there are some studies focused on suicide behavior in Bipolar II

patients, the majority of them include mixed samples of Bipolar I and Bipolar II patients with non-fatal suicide behavior.^{14–17} There is no previous study that analyses FSB and risk factors in a specific sample of Bipolar II followed long-term after their first hospitalization. Bipolar II disorder is a valid and reliable diagnosis¹⁸ but has been understudied¹⁹ and may be different from Bipolar I disorder.^{20,21} For this reason, we consider this study of great interest in relation to prevalence and risk factors of completed suicide in a cohort of Bipolar II patients followed for a long period of time after their first hospitalization.

Material and methods

We have selected all patients diagnosed with Bipolar II Disorder, according to DSM-IV criteria, who were admitted for first time in their life in our Psychiatric Hospitalization Unit, between January 1st, 1996 and December 31st, 2020. All patients agreed to participate in this study. Ethical and legal considerations ensure the protection of the anonymity of patients.

[☆] This research has not received specific aid from public sector agencies, commercial sector or non-profit entities.

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<https://doi.org/10.1016/j.rpsm.2021.12.007>

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Table 1
Baseline and final characteristics of the 6 Bipolar II patients who died by suicide.

Sex	Basal age	Basal phase	Previous suicide attempt	1st degree relative with FSB	Basal lithium treatment	Age at FSB	Days after discharge	Phase at FSB	Method of FSB	Treatment at FSB	Days since last visit and specialist
Man	49	Hypomania	No	No	No	49	237	Depression	Carbon monoxide	Lamotrigine	30 Psychiatrist
Man	31	Depression	Yes (violent)	No	No	33	758	Depression	Hanging	Olanzapine Lamotrigine Risperidone	3 Psychiatrist
Woman	54	Depression	Yes (no violent)	No	No	57	1061	Depression	Hanging	Venlafaxine Mirtazapine	125 General Doctor
Woman	51	Depression	No	No	No	51	42	Depression	Jumping	Fluoxetine Quetiapine	22 Psychiatrist
Man	28	Depression	Yes (violent)	No	No	33	1753	Depression	Hanging	None	180 General Doctor
Man	47	Depression	No	No	No	49	840	Depression	Hanging	Lamotrigine Citalopram	63 Psychiatrist

Clinical variables are systematically collected at first hospitalization using a specific database. Our hospital is a public general hospital that provides healthcare to a specific catchment area of the Manresa and its suburbs. After hospital discharge, these patients underwent outpatient follow-up at Mental Health Centre and we have been collecting the study variables until December 31st, 2020. Database was updated retrospectively when their death occurred.

One of the advantages of the Hospital's and Mental Health Centre at our place is that they cover the whole population of the area around Manresa city (Catalonia, Spain) and that all suicides are identified either by the hospital or by the administration, so there is no risk of false negatives. Moreover in Catalonia there is computer Medical access to the shared Clinical History of all the inhabitants of the community with a public health card (all patients included in the study had this card) and it immediately reflects the death of patients when it occurs. Therefore, despite the fact that a few patients moved to other areas of Catalonia, we were able to follow the evolution and detect the death of all the patients included in the study.

Using SPSS statistical package and using the Chi-square test for categorical variables and Student's *T*- and Mann–Whitney *U* for continuous variables (parametric and non-parametric respectively), we compared baseline variables collected on first admission between Bipolar II patients with FSB and those without FSB. In same way, we compared other powerful evolutionary variables between the two groups of patients, such as rehospitalizations and non-lethal suicide attempts that occurred throughout the follow-up.

Results

After a long follow-up of a cohort of 59 Bipolar II patients, almost 10% (6 of 59 patients) of them died by suicide.

Table 1 summarizes the baseline and final characteristics of 6 Bipolar II patients who died by suicide. Of these, 66% were male and 33% had a history of previous violent suicide attempts. On the contrary, none of them had a family history of first degree with completed suicide. Five of them were admitted for depression and one for hypomania with comorbidity with alcohol abuse.

Regarding the characteristics of these patients at time of FSB (Table 1) it should be noted that 83% (5 of the 6 cases) made FSB by a violent method; four by hanging and one by jumping. The mean age of completed suicide was 45.5 years (range between 33 and 57 years), while the mean age of first admission was 43.3 years. Therefore, the average period between admission and FSB was only 2.14 years (range between 43 and 1753 days). All patients who died by suicide were in a depressive phase (without mixed elements) and

only one of them had associated psychotic symptoms. None of the 6 patients was treated with lithium carbonate either on admission or during their follow-up, they were receiving other treatments for their depressive phase (antidepressants, lamotrigine), except one who dropped out treatment and follow-up. Finally, it should be noted that the mean time from the last visit to completed suicide was about 2 and a half months, varying between only 3 days and a maximum of 6 months.

In our cohort, 33% of patients had a previous violent suicide attempt. When we compared Bipolar II patients with FSB at baseline with the ones without FSB (Table 2), we detected that only previous history of a violent suicide attempt was significantly associated ($p < 0.05$) with FSB. Curiously, if we included non-violent suicide attempts, we saw that this relationship was not significant in any group. The history of suicide attempt is around 50%.

The male difference between Bipolar II with FSB (66%) and Bipolar II patients without FSB (28%) failed to achieve statistical significance.

Comorbidities such as personality disorder or substance-use disorder also had no statistical significance.

Cholesterol levels in first hospitalization showed no significant differences between Bipolar II patients who died by suicide and those who are still alive or did not died by suicide Age variable also showed no significant difference.

No patients of the sample (with or without FSB) had antecedents of completed suicide at familiar of first degree. When we analyzed any familiar history of FSB (included second or higher degree), we found that there were more antecedents in non-suicidal Bipolar II patients (14%) than in suicidal Bipolar II (0%). Although this difference is not significant (Table 2).

The average follow-up for Bipolar II patients with FSB was 13.3 years, slightly longer than Bipolar II patients without FSB (12.5 years), but this difference was not significant (Table 3).

In Table 3, we can also see that none of the six patients who died by suicide required re-entry since their first hospitalization. This represented a significant difference ($p < 0.027$) with patients who did not die by suicide, as more than 50% of these required another hospitalization. None of the six patients died by suicide made any suicide attempt during this period, compared to 26% of patients who did not die by suicide, but this difference did not prove significant.

Discussion

Our study highlights the finding of a very high rate of completed suicide in Bipolar II patients who made a first hospital income.

Table 2

Basal comparison (in their first admission) between Bipolar II patients with fatal suicide behavior (FSB) and those with non-fatal suicide behavior (NFSB).

Basal variables (on first admission)	FSB (N=6)	NFSB (N=53)	p FSB vs NFSB
<i>Categorical (chi square)</i>			
Any previous suicide attempt	3 (50%)	31 (58.5%)	p = 0.5
Previous violent suicide attempt	2 (33%)	2 (3.8%)	p = 0.048
First Grade Family history with FSB	0 (0%)	0 (0%)	p = 0.8
Second Grade Family history with FSB	0 (0%)	7 (13%)	p = 0.45
Male gender	4 (66%)	15 (28.3%)	p = 0.078
Depressive onset polarity	6 (100%)	48 (88.7%)	p = 0.63
Depressive phase	5 (83%)	31 (58.5%)	p = 0.23
Absence of psychotic symptoms	6 (100%)	45 (85%)	p = 0.65
Comorbidity with personality disorder	0 (0%)	22 (41.5%)	p < 0.075
Comorbidity with substance abuse	2 (33%)	19 (36%)	p = 1
Lithium treatment	0 (0%)	16 (30.2%)	p = 0.17
Treatment with antiepileptics (lamotr/valp)	3 (50%)	29 (54.7%)	p = 1
Antidepressant treatment	5 (83%)	30 (57%)	p = 0.21
<i>Continuous (Student's t)</i>			
Age	43.33	43.17	p = 0.98
Cholesterol level	178	177	p = 0.97
Duration of first admission in days	24	19	p = 0.19

Table 3

Follow-up comparison between Bipolar II patients with fatal suicidal behavior (FSB) and non-fatal suicidal behavior.

Follow-up variables	FSB (N=6)	NFSB (N=53)	p FSB vs NFSB
<i>Categorical (Chi-square)</i>			
Any rehospitalization	0 (0%)	27 (50.9%)	p < 0.027
Any non-lethal suicide attempt	0 (0%)	14 (26.4%)	p = 0.3
<i>Continuous (Mann-Whitney U)</i>			
Mean years of follow-up	13.2	12.4	p = 0.74
Mean number of re-admissions	0	1.63	p < 0.024
Mean number of days of re-hospitalization	0	35.8	p < 0.029
Average number of non-fatal suicide attempts	0	0.36	p = 0.27

This rate is 116 times higher than that of the general population in our health area and is the highest rate found in a clinical study. Also, this rate is twice as high as the percentage of completed suicide obtained in a the same period in a mixed Bipolar I (80%) and Bipolar II (20%) cohort, indicating a greater relative risk of death by suicide in Bipolar II patients who have been admitted as compared to Bipolar I patients who have required an hospitalization.¹¹ This increased risk of completed suicide is probably due to the fact than on many occasions basal polarity and/or dominant polarity is depressive. This data so high of completed suicides do not appear to be related to poor access to mental health service. All completed suicides in our regions are reported and investigated.

Our study notes that Bipolar II patients died by suicides had a previous violent suicide attempt at the start of the study, unlike Bipolar II patients without completed suicide. The association between a violent suicide attempt and Bipolar Disorder is a differentiating factor compared to unipolar Depression²² and occurs especially in men.^{23,24}

As previous studies,^{25,26} a high percentage of all hospitalized Bipolar II patients showed an initial or predominant depressive polarity or the reason for hospitalization was for depressive symptomatology, but we found no significant differences between patients with FSB and patients with NFSB. Perugi et al.,²⁷ described that initial depressive polarity is associated with suicidal behavior, especially with suicide attempts, but only in the sample of Bipolar I patients.

In relation to cholesterol variable, our study matches in a previous study.²⁸ Cholesterol levels were similar in both groups (Bipolar II patients with FSB and Bipolar II patients with NFSB).

Relative to gender, although the difference was not significant as in other studies,^{12,29} probably due to the small sample size, there was a clear tendency to increase the risk of completed suicide ($p < 0.08$) in male sex (20% of men died by suicide versus 5%

of women). However, if we compare the proportion of males and females who died by suicide in the general population, we found a high percentage of women in our study, so it may be the case that bipolar disorder reduces sex differences in relation to completed suicide, even if women adhere better to treatment.³⁰

The fact of not finding an association between a family history of suicide and an increased risk of suicide attempts³¹ or FSB,³² could be owed to our small sample size or that they play a more decisive role as a suicide factor in Bipolar I patient and not in Bipolar II patients.

In our study comorbidity with Personality Disorder showed no significant difference in Bipolar II patients who died by suicide. Previous studies indicate an increased risk of suicidal behavior in bipolar patients with Personality Disorder,³³ but significant association occurs with suicide attempts,³⁴ especially with multiple suicide attempts,³⁵ whereas in case of FSB there is no significant increased risk of suicide in Bipolar patients with Personality Disorder.³²

A remarkable fact is that suicidal Bipolar II patients perform completed suicide fairly soon after discharge (mean 2.14 years) and all hospitalized Bipolar II patients who died by suicide did so within the first five years after their first hospitalization. Most Bipolar II patients were admitted for a depressive phase. It has been shown that patients who complete suicide after hospitalization do so much more quickly when admission is due to depressive symptoms than when it is due to manic symptoms, as in Bipolar I patients.²⁹

On the other hand, Bipolar II patients who died by suicide did not need rehospitalization and did not make further suicide attempts from hospital discharge to FSB. Most likely, it may be due to a previous violent suicide attempt, which determines the mortality of the attempt. Therefore, previous studies agree on higher lethality of suicide attempts in Bipolar II patients, as well as a lower percentage of patients who make repetitive suicide attempts³⁴ and a lower

proportion of patients with suicide attempts compared to deaths from suicide⁸ than patients with unipolar Depression or Bipolar I patients. In our study, recurrence of non-fatal suicide behavior results in new rehospitalization, but is not associated with FSB.

Finally, it should be noted that none of FSB patients were prescribed lithium. Lithium has antisuicidal properties, and is nevertheless rarely used for that particular purpose.^{36,37} Lithium might not have been chosen in those patients because they had depressive predominant polarity and type II bipolar disorder. This might have driven the choice of an anticonvulsant drug as mood stabilizer. Other treatments may not protect against suicide.³⁸ Although lithium is backed by scientific evidence as the gold standard treatment for bipolar disorder, in recent years there has been a downward trend in its use. Perez de Mendiola et al.,³⁹ found that one of the main reasons for not prescribing it in our country was the tolerability profile.

It is very important that patients have information with scientific evidence about lithium treatment. An expert consensus was made to create an information sheet for patients with bipolar disorder being treated with lithium, with information agreed by a group of experts from different areas of healthcare.⁴⁰

Our study has some limitations, such as a limited sample size and data extrapolation to Bipolar II patients who only have outpatient follow-up or have gone through multiple admissions.

Conclusions

Bipolar II patients who were followed up after their first hospitalization had fatal suicidal behavior, early and by a violent method. The suicide rate was more than 100 times higher than that of the general population. They did not require hospital readmission nor attempted any non-fatal suicide attempt after discharge.

The previous history of a violent suicide attempt is a powerful and significant predictor of suicide death in Bipolar II patients after their first hospitalization.

Conflict of interests

The authors declare that they have no conflict of interest.

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