Originals

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Profile of bipolar disorder outpatients: a cross-sectional study in the Madrid Community

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Introduction. The purpose of this cross-sectional study is to obtain a sociodemographic, clinical, psychosocial functioning and therapeutic profile of bipolar outpatients in the Madrid Community.

Methods. A total of 115 outpatients were consecutively recruited by 10 psychiatrists.

Results. Mean time between initial symptoms and an accurate bipolar diagnosis was of 7.6 years. A depressive episode was the onset of the illness in most patients independently of clinical subtype. Syndromal or subsyndromal symptoms were present in 47% of the patient population, dominating the depressive polarity (33.1%). A subjectively reduced perception of quality of life was associated to the presence of depressive symptoms and a worse clinical outcome last year. More than half of the patients (58.2%) were overweight or obese. Lithium was the most frequently used mood stabilizer (71.3%), whereas 41% of the patients were taking at least three psychotropic drugs.

Conclusions. Results of this study widely confirm previous data on bipolar disorder. Reduction in quality of life of bipolar patients associated to depressive symptoms must be highlighted. It is necessary to optimize treatments in bipolar disorder in order to improve prognosis.

Key words:
Bipolar disorde. Cross-sectional. Mood stabilizer. Depression. Quality of life.

Perfil de los pacientes ambulatorios con trastorno bipolar: un estudio transversal en la Comunidad de Madrid

Introducción. El propósito de este estudio transversal es obtener un perfil de las características sociodemográficas, clínicas, de funcionamiento psicosocial y pautas tera-

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péuticas de los pacientes con trastorno bipolar atendidos de forma ambulatoria en la Comunidad de Madrid.

Metodología. Un total de 115 pacientes fueron incluidos en el estudio de forma consecutiva por 10 psiquiatras.

Resultados. Desde el inicio de los síntomas hasta recibir un diagnóstico correcto de trastorno bipolar habían transcurrido una media de 7,6 años. La depresión fue la forma de inicio de la enfermedad en la mayoría de los pacientes independientemente del subtipo. El 47% de los pacientes, presentaba alguna sintomatología clínica sindrómica o subsindrómica, siendo depresiva la más predominante (33,1%). Una percepción subjetiva reducida de la calidad de vida se asoció a la presencia de síntomas depresivos y a una peor evolución el año previo. Más de la mitad del total de los pacientes (58,2%) se encontraban en una situación de sobrepeso u obesidad. El litio fue el estabilizador del humor más utilizado (71,3%), aunque el 41% de los pacientes recibía al menos tres psicofármacos.

Conclusiones. Los resultados obtenidos en este estudio confirman en gran medida buena parte de los datos conocidos en la actualidad sobre el trastorno bipolar. Destaca la disminución en la calidad de vida de los pacientes bipolares relacionada con la presencia de síntomas depresivos. Se hace necesario optimizar los tratamientos en el trastorno bipolar para mejorar así su pronóstico.

Palabras clave:
Trastorno bipolar. Transversal. Estabilizador del estado de ánimo. Depresión. Calidad de vida.

INTRODUCTION

Bipolar disorder is a serious mental disorder characterized by alternance or concurrence of depressive and manic symptoms that may be accompanied by psychotic symptoms with intercurrent periods without major affective episodes. However, far from the classical manic-depressive concept, increasingly more data exist that show a different course. The presence of clinical symptoms that do not meet criteria for a major affective disorder during the disease course is more frequent than their total absence[1,2]. This also has a negative repercussion on the patient's quality of life[3].

The life prevalence of bipolar disorder ranges from 2% to 5%, depending on the diagnostic criteria considered. There is also growing agreement among the experts that the symptoms may be seen within a more extensive bipolar clinical spectrum[4-6].

The idea that the bipolar disorder does not cause deterioration in the different life spheres of the patient is not always true[7,8], the evolution and prognosis of the disease undergoing great variability related with the number of previous episodes and severity/intensity of the symptoms and to the treatment response and compliance. In addition, bipolar disorder supposes an important personal and social cost, it being the seventh cause of discapacity among women from 15 to 44 years of age[9].

Several drugs and even different drug groups may be involved in its treatment because of the concurrence of different symptoms. Lithium is considered to be the primary treatment and gold standard of mood stabilizers[10]. Lamotrigine[11] or valproate[12] stand out among the new stabilizers as preventive drug in depressive phases or in the treatment of mania, respectively, although other anti-seizure drugs may also be useful. Use of antipsychotics are often necessary, the atypical ones being preferable to the classical ones since the former do not induce depressive phases. Besides being effective in the treatment of mania, some may also be effective in prevention of relapses[13] and treatment of depressive symptoms[14,15]. Using antidepressants, at least in single drug therapy, is debatable, although necessary in many cases because they may induce mood swings[16]. On the other hand, many patients with this disease may also benefit from complementary treatments such as psychotherapy and, above all, the psychoeducation groups that have been demonstrated to improve the course of the disorder[17].

This study has aimed to obtain an image of the situation of the Bipolar disorder patient who is receiving out-patient treatment in the Madrid Community. The study was performed by obtaining information on the subject's sociodemographic and clinical characteristics, psychosocial functioning level in its usual context and the diagnostic guidelines and therapeutic approach practiced by the psychiatrists in the community.

There is little epidemiological information on the clinical situation and natural history available for bipolar disorder patients and the treatments they receive in Spain. The findings of this study carried out in the Madrid Community may be representative of those that could be found in the rest of Spain.

METHODS

This is an observational, cross-sectional, descriptive and multicenter study within the Madrid Community area in the out-patient clinics of medical psychiatric specialists that aimed to obtain information on the current situation of patients with bipolar disorder. The study is not interventionist since it is a purely observational cross-sectional study of the situation of the patients with bipolar disorder.

The inclusion period duration was two months (May and June 2006). Ten psychiatrists working full time (n = 3) or part time (n = 7) in out-patient clinics and dedicated to the treatment of bipolar disorder patients participated in it. An attempt was made to obtain a representation of most of the Madrid Community health care areas so that the patients included would belong to the different social-health care profiles of that community. During the case collection period, starting at the moment when the investigator decided to initiate the study, he/she consecutively enrolled the first 12 patients who fulfilled the inclusion criteria. This enrolment method is a limitation of the study, although other more correct forms of doing it would have meant having previous knowledge about the population to be studied that currently does not occur.

The study protocol was approved by the ethics committee of one of the participating sites (Hospital Universitario Príncipe de Asturias of Alcalá de Henares).

Patients

The study included patients from both genders, over 18 years of age, diagnosed of type I, II or non-specified bipolar disorder according to DSM-IV-TR criteria, who agreed to participate in the study after signing an adequate informed consent, that guarantee preservation of confidentiality, after they had been informed of the voluntary nature of their participation and the study objectives.

Only those patients who had previously been included in any other intervention study or those patients who, being candidates, refused to participate, were excluded.

Measurement variables and instruments

According to the previously established objectives, information regarding the sociodemographic, life habits, previous background of the disease and clinical condition and current treatment variables were gathered during a single variable.

In addition, the Modified Clinical Global Impression Scale for bipolar disorder (CGI-BP-M)[18] made up of three subscales (range: 1-7) of depression, mania and global, was used. The global subscale evaluates the severity of the disorder the previous year while the depression and mania ones consider the symptoms currently present.

The Drug Attitude Invention (DAI)[19] was used in order to know the subjective impression of these patients regarding the psychodrugs they were being treated with. The version used contains 10 items, six of which considered the response to be correct if the patient considered it to be true and four if the patient considered it to be false. The correct answer was scored as + 1, while the incorrect one was –1. Total score is the sum of the 10 scores, so that a positive score represents a subjective attitude that is also positive towards the medication while a negative one implies a negative opinion about the medication.

Quality of life was evaluated using part two of the Spanish version of the EuroQol (EQ-5D)20, called Visual Analogue Scale (VAS). This consisted in a 20 cm long graph in the form of a thermometer whose end points are labeled as «the worse possible health condition» and the «best possible health condition» with scores going from 0 to 100, respectively. The patients have to make a mark indicating their health condition.

Statistical analysis

A descriptive analysis was then performed using the necessary techniques for the quantitative and qualitative variables.

Calculation of the sample size for a descriptive study of this type was done by trying to answer the question: How many patients are needed to detect reliably the proportion of patients who have certain sociodemographic, clinical or therapeutic characteristics, beginning with prevalence in the general population for the bipolar disorder of 2%-5%? The minimum *n* value needed for an admissible error of 0.04 would be 114.

Two groups were established to make the comparative analysis. Those patients diagnosed of bipolar disorder type I were included in one group and the patients diagnosed of type II bipolar disorder and not otherwise specified bipolar disorder (NOS) were included in a second group. Those subtypes already diagnosed were included in the latter group since they were considered as a population more related with the bipolar spectrum versus the classical manic-depressive disorder represented by type I.

In addition, a linear regression model was made, using the total score on the VAS on the health condition as dependent variable. Independent variables were age, gender, clinical subtype, toxic habits, years of disease evolution, time without treatment, number of drug treatments, adverse events, other therapies and current clinical condition. This last variable was reconverted into six «dummy» variables, with the absence of symptoms as reference and the remaining ones: presence of hypomania, mixed or depression episode, subsyndromal depressive or manic symptoms and global CGI-BP-M score.

RESULTS

A total of 115 patients from 10 out-patient psychiatric clincs were included in this study. Nine investigators contributed 12 patients each while one investigator contributed 7 patients until completing the total sample required. A total of 76 patients were type I bipolar subjects (66.1%), 33 type II (28.7%) and 6 were diagnosed of not otherwise specified bipolar disorder (5.2%). Table 1 shows the sociodemographic characteristics of the total sample. No statistically significant differences between the two bipolar typologies esta-

Table 1	Sociodemographic characteristics of the bipolar patient population of the study		
Characteristics	Total (n = 115)	Bipolar I (n = 76)	Bipolar spectrum (n = 39)	P value (n = 39)
Gender: feminine (N) (%)	68 (59.6)	47 (61.8)	21 (55.3)	0.547*
Age (mean) (DS)	49.2 (14.6)	49.6 (12.4)	48.3 (18.2)	0.700**
Civil status civil (N) (%)				0.328***
Single	43 (37.4)	28 (36.8)	15 (38.5)	
Married	50 (43.5)	32 (42.1)	18 (46.2)	
Widow(er)	8 (7.0)	4 (5.3)	4 (10.3)	
Separated/ divorced	14 (12.2)	12 (15.8)	2 (5.1)	
Living arrangement (N) (%)				0.891***
Along	17 (14.9)	11 (14.7)	6 (15.4)	
Family of origin	34 (29.8)	23 (30.7)	11 (28.2)	
Own family	62 (54.4)	40 (53.3)	22 (56.4)	
Others	1 (0.9)	1 (1.3)	0 (0.0)	
Study level (N) (%)				0.460***
Illiterate	1 (0.9)	0 (0.0)	1 (2.6)	
Primary	32 (28.3)	23 (30.7)	9 (23.7)	
Secondary	42 (37.2)	28 (37.3)	14 (36.8)	
University	38 (33.6)	24 (32.0)	14 (36.8)	
Work situation (N) (%)				0.108***
Student	3 (2.6)	1 (1.3)	2 (5.1)	
Active	46 (40.0)	30 (39.5)	16 (41.0)	
Unemployed	10 (8.7)	7 (9.2)	3 (7.7)	
Temporary work disability	8 (7.0)	2 (2.6)	6 (15.4)	
Disability	9 (7.8)	8 (10.5)	1 (2.6)	
Pensioner	26 (22.6)	18 (23.7)	8 (20.5)	
Others	13 (11.3)	10 (13.2)	3 (7.7)	

*Fisher's exact test. **Student's T test. ***Chi square.

blished for the analysis were observed. A tendency (p=0.108) towards a greater percentage of patients who were employed but with temporary incapacity was observed in the bipolar spectrum patient subgroup (15.4%) compared to the bipolar patients I (2.6%), who more frequently had permanent work incapacity (10.5% vs 2.6%).

Disease background

The data regarding the disease background are shown in table 2. Mean time was 7.6 years from when the symptoms initiated to when an adequate and specific treatment was prescribed for the bipolar disorder, there being no difference between the two subpopulations, stands out. On the contrary, there was a tendency (p=0.105) towards a longer mean time of evolution from the diagnosis of the disease in type I (14.6 years) than in the bipolar spectrum (11.1 years).

Except for the mean number of manic episodes, greater in the bipolar I subjects (4.0) than in those of the spectrum (0.3, at the expense of NOS bipolar disorders, possibly due to atypical episodes, i.e., less duration than that required for the diagnosis), no statistically significant differences were observed between the two groups of bipolar patients as well. This greater number of manic episodes leads to a greater mean number of admissions among type I bipolar subjects (4.1 vs 1.1).

Depression was the disease debut form in most of the patients, regardless of the subtype, although it was slightly greater among bipolar spectrum patients (76.9% vs 61.3%). On the contrary, a first manic episode was significantly more frequent (p=0.002) among bipolar I patients (37.3%) than among those of the spectrum (10.3%).

Rapid cycling phenomenon also has a similar frequency of appearance in both subtypes of bipolar patients during the disease evolution. In most of the cases (66.6%), this initiation of the acceleration of the cycling was spontaneous or this could not be associated to any identifying precipitating factor, such as substance abuse (4.8%) or use of antidepressants (23.8%). Furthermore, no relationship could be established between the development of rapid cycling and some factors considered as risk such as polarity of the first episode, prolonged time without treatment or thyroid dysfunction.

Current clinical situation

Approximately half of the patients (47%) had some clinical syndromal or subsyndromal symptoms when the study was performed (table 3). The predominant symptom was depressive (33.1%), which can also be observed in the CGI subscales where it can be seen that 13% of the patients were at least moderately depressive while only 3.5% were mode-

| Table 2 | Characteristics of the history of the disorder in the bipolar patient population of the study |

Characteristics	Total (n=115)	Bipolar I (n=76)	Bipolar spectrum (n=39)	P value
Years of evolution (mean) (SD)	21.1 (12.4)	21.4 (11.8)	20.5 (13.6)	0.690**
Years from diagnosis (mean) (SD)	13.4 (11.2)	14.6 (11.6)	11.1 (10.0)	0.105**
Years without treatment (mean) (SD)	7.6 (8.8)	7.9 (9.1)	7.2 (8.2)	0.737**
Polarity first episode (N) (%)				0.002*
Depression	76 (66.7)	46 (61.3)	30 (76.9)	
Mania	32 (28.1)	28 (37.3)	4 (10.3)	
Hypomania	3 (2.6)	0 (0.0)	3 (7.7)	
Mixed	3 (2.6)	1 (1.3)	2 (5.1)	
Total number of episodes (mean) (SD)	16.7 (23.6)	16.5 (20.5)	17.1 (20.9)	0.902**
Distribution episodes (mean) (SD)				
Mania	2.8 (3.7)	4.0 (3.9)	0.3 (1.7)	<0.001**
Hypomania	5.8 (12.1)	5.1 (8.4)	7.1 (17.4)	0.394**
Depression	7.4 (12.6)	6.5 (12.6)	9.0 (12.5)	0.322**
Mixed	0.8 (2.2)	0.9 (2.3)	0.6 (1.9)	0.596**
Rapid cycling (N) (%)				0.999*
Passed	7 (6.1)	5 (6.6)	2 (5.1)	
Current	14 (12.2)	8 (11.6)	6 (15.4)	
Total number of admissions (mean) (SD)	3.1 (4.3)	4.1 (4.8)	1.1 (2.2)	<0.001**
Distribution admissions (mean) (DE)				
Mania	2.1 (3.3)	2.9 (3.8)	0.4 (1.1)	<0.001**
Depression	0.8 (1.8)	0.9 (1.8)	0.6 (1.8)	0.510**
Mixed	0.2 (0.7)	0.3 (0.8)	0.1 (0.2)	0.043**
Number of suicide attempts (mean) (SD)	0.7 (1.7)	0.7 (1.7)	0.7 (1.8)	0.957**
Family background (N) (%)				
Bipolar	33 (28.7)	22 (28.9)	11 (28.2)	0.999*
Affective	29 (25.2)	21 (27.6)	8 (20.5)	0.499*
First generation	43 (37.4)	28 (36.8)	15 (38.5)	0.999*
Second generation	23 (20.0)	17 (22.4)	6 (15.4)	0.465*

*Fisher exact test. **Student's *t* test.

Table 3	Current clinical characteristics in the bipolar patient population of the study			
Characteristics	Total (n = 115)	Bipolar I (n = 76)	Bipolar spectrum (n = 39)	P value
Current clinical symptoms (N) (%)				0.516*
Depressive episode	14 (12.2)	8 (10.5)	6 (15.4)	
Hypomanic episode	9 (7.8)	7 (9.2)	2 (5.1)	
Manic episode	0 (0.0)	0 (0.0)	0 (0.0)	
Mixed episode	2 (1.7)	2 (2.6)	0 (0.0)	
Manic subsyndromal symptoms	5 (4.3)	4 (5.3)	1 (2.6)	
Depressive subsyndromal symptoms	24 (20.9)	13 (17.1)	11 (28.2)	
Without symptoms	61 (53.0)	42 (55.3)	19 (48.7)	
CGI-BP global (mean) (SD)	2.8 (1.5)	2.8 (1.5)	2.7 (1.4)	0.823**
CGI-BP depression (mean) (SD)	1.9 (1.3)	1.8 (1.3)	1.8 (1.3)	0.381**
CGI-BP mania (mean) (SD)	1.3 (0.7)	1.4 (0.8)	1.2 (0.5)	0.540**
VAS (mean) (SD)	71.6 (23.1)	71.8 (23.2)	71.1 (23.2)	0.874**
DAI (mean) (SD)	4.8 (4.3)	5.3 (4.1)	3.7 (4.1)	0.072**

*Chi square. **Student's *t* test.

rately manic. No differences were observed regarding the predominant clinical symptoms among the two subpopulations of patients. In regards to the CGI subscale, it was seen that one out of every three patients (36%) had presented at least one moderate state of severity of the disease in the previous year.

Comorbidity with another psychiatric disorder was detected in 7% of all the patients, personality disorders being the most frequent ones (2.6%). In regards to medical disease, thyroid or parathyroid endocrine disorders were the most frequent (15.7%), followed by metabolic disorders (diabetes, dyslipidemias, etc.) in 9.6% of the cases and by arterial hypertension (7.8%). The remaining medical diseases appeared in less than 5%.

In the linear regression analysis used to evaluate score on the VAS scale on health condition, a final model in which a lower perception of quality of life was explained by the current presence of a depressive, mixed or subsyndromal depressive episode was obtained and a higher score on the CGI-BP (worse evolution the previous year) was observed.

Life habits

Table 4 shows the data regarding the life habits of the patients and that they performed scarce physical activity (77.9%).

Table 4	Life habits of the bipolar patient population of the study			
Characteristics	Total (n = 115)	Bipolar I (n = 76)	Bipolar spectrum (n = 39)	P value
BMI (mean) (SD)	26,8 (5,3)	27,0 (5,0)	26,2 (5,9)	0,439**
Distribution by BMI (N) (%)				0,809***
Thinness (< 18,5)	3 (2,7)	2 (2,7)	1 (2,8)	
Normality (18,5-24,9)	43 (39,1)	26 (35,1)	17 (47,2)	
Overweight (25-29,9)	40 (36,4)	30 (40,5)	10 (27,8)	
Obesity grade I (30-34,9)	16 (14,5)	11 (14,9)	5 (13,9)	
Obesity grade II (35-39,9)	6 (5,5)	4 (5,4)	2 (5,6)	
Morbid Obesity (≥ 40)	2 (1,8)	1 (1,4)	1 (2,8)	
Physical activity (N) (%)				0,451***
None	53 (46,9)	36 (48,6)	17 (43,6)	
Mild	35 (31,0)	20 (27,0)	15 (38,5)	
Moderate	18 (15,9)	14 (18,9)	4 (10,3)	
Intense	7 (6,2)	4 (5,4)	3 (7,7)	
Hours of usual sleep (N) (%)				0,298***
< 4 hours	1 (0,9)	0 (0,0)	1 (2,6)	
4-6 hours	8 (7,0)	5 (6,6)	3 (7,7)	
6-8 hours	73 (63,5)	46 (60,5)	27 (69,2)	
> 8 hours	33 (28,7)	25 (32,9)	8 (20,5)	
Substance consumption (N) (%)				0,723**
Tobacco	43 (37,4)	29 (38,2)	14 (35,9)	
Alcohol	9 (7,8)	4 (5,3)	5 (12,8)	
Caffeine	59 (51,3)	40 (52,6)	19 (48,7)	
Other toxics	1 (0,9)	1 (1,3)	0 (0,0)	
Alcohol + others	9 (7,8)	4 (5,3)	5 (12,8)	

*Fisher's exact test. **Student's *t* test. ***Chi square.

Table 5	Current drug treatments in the bipolar patient population of the study		
	Total n = 115	Bipolar I n = 76	Bipolar spectrum n = 39
Lithium (N) (%)	82 (71.3)	58 (76.3)	24 (61.5)
Anti-seizure (N) (%)			
Lamotrigine	32 (27.8)	19 (25.5)	13 (33.3)
Valproate	23 (20.0)	18 (23.7)	5 (12.9)
Otrhers	18 (15.7)	15 (19.7)	3 (3.9)
Antidepressants (N) (%)			
SSRI	14 (12.1)	8 (10.5)	6 (15.3)
SNRI	15 (13.1)	8 (10.5)	7 (17.9)
Heterocyclic	2 (1.8)	0 (0.0)	2 (5.2)
Others	3 (2.6)	1 (1.3)	2 (5.2)
Antipsychotics (N) (%)			
Classical	4 (3.5)	1 (1.3)	3 (7.7)
Olanzapine	23 (20.0)	16 (21.1)	7 (17.9)
Quetiapine	17 (14.8)	9 (11.8)	8 (20.5)
Risperidone	10 (8.7)	8 (10.5)	2 (5.1)
Others	6 (5.2)	4 (5.3)	2 (5.1)

Treatment

Practically all of the patients received a mood stabilizer (96.5%), lithium being the one used most (71.3%), followed by lamotrigine (27.8%) and valproate (20%). Lithium was also the treatment that had been maintained most during the evolution of the disorder (a mean of 131 months). Half of the patients also received an antipsychotic drug (49.6%), olanzapine and quetiapine being the ones used most.

The combination of treatment with a mood stabilizer and an antipsychotic drug was used the most (47.0% of the cases), while only 22.6% of the patients received single drug therapy. Two out of every five patients (41%) received at least three psychodrugs, with a mean of 2.5 drugs per patient. No differences were observed between the two subpopulations of patients as well.

The psychiatrist considered that there was almost total therapeutic compliance (75%-100%) in 76.5% of the cases, observing a tendency towards better compliance among type I bipolar patients (80.3% vs 69.2%; p=0.143). The patients with type I bipolar disorder also had a tendency (p=0.072) towards a better attitude regarding the medication according to the DAI scale (score of 5.3) than the patients of the bipolar spectrum (3.7 points on the DAI).

Sixty percent of the patients did not report having experienced adverse events associated with the drug, this difference not being statistically significant between the two

subpopulations. However, type I bipolar patients reported a significantly greater mean number of adverse events (0.8 vs 0.4). The most frequent adverse events were tremor (12.2%), sedation-drowsiness (12.2%), polyuria (8.7%) and gastrointestinal alterations (6.1%). The other adverse events appeared in less than 5%.

The patients of our sample received another non-pharmacological treatment (psychoeducation or psychotherapy) in 32.2% of the cases, there being a tendency towards a higher percentage in the case of type I bipolar subjects (38.2 vs 20.5 %).

DISCUSSION

The results obtained in this study largely confirm part of the data presently known on bipolar disorder. In addition, they provide some new data that may be suggestive of confirmation in later investigations.

There is a dominance of women in the type II bipolar patients. However, this does not only occur among this subgroup of patients but also among bipolar I patients where the difference is even greater. If we consider the epidemiology of type I bipolar disorder, with equality in the prevalence between both genders, it should be considered that many type I male bipolar patients are undiagnosed. This may be due to the presence of other manifestations from a different manic sphere than the classical one during the manic episode (delusional symptoms, substance abuse, sociopathic attitudes, etc.) or because they have not acquired enough awareness of the disease to facilitate therapeutic adhesion. In either case, the diagnosis and means aimed at adequate treatment of this group of patients who are not included in this study need to be improved, such as conducting a clinical follow-up.

As could be expected, the type I bipolar patients had a permanent work incapacity grade that was greater than patients in the bipolar spectrum. However, a larger percentage of patients in the bipolar spectrum had transient work incapacity. This would be a reflection of the effort to maintain work normality in these patients, only interrupting it by the presence of intercurrent depressive episodes. This difficulty to remain in the work world contrasts with the grade of previous preparation (one third of the patients had university studies). The severe personal and social harm that the bipolar disorder may generate can be deduced from these data.

Bipolar patients as a whole led sedentary life styles. This, together with the tendency to be overweight, the possible use of drugs that favor the appearance of metabolic syndrome and the elevated importance of metabolic disorders and arterial hypertension, means an increase in risk of cardiovascular diseases. Obesity (BMI $\geq$30 kg/m^2) was detected in 21.8% of the bipolar patients while this percentage is inferior in the general Spanish population (14.5%)[21]. In this sense, the necessary steps must be taken to decrease this risk factor among bipolar patients.

The tendency to make a correct diagnosis of bipolar disorder late in regards to the onset of the appearance of the symptoms is also confirmed[22]. In our study, this delay occurs at a mean time of more than 7 years. Undoubtedly, this period is too long and has a negative repercussion on the subsequent course of the disorder. In most of the cases, the first clinical episode is depressive. This makes it more difficult to distinguish the bipolar disorder from unipolar depression. Thus, we believe that the resources used to detect bipolar disorder should be improved when the clinician is dealing with a patient who has depressive symptoms since this may have a repercussion in an underdiagnosis of the bipolar disorder.

The frequency of patients recorded in our study in the current clinical situation of rapid cycling was 12.2%. This value is comparable to that detected in other studies in which the sample was obtained from non-specialized clinics[23].

A series of studies[1,2] that indicate that the evolution of bipolar disorder is very distant from the classical evolution in episodes with intermediate period of euthymia has appeared recently. Previously, on the contrary, the bipolar patients were symptomatic half of the time after the disease onset. The results of our study indicate the same, since only 53% of the patients were totally symptom free when their clinical condition was evaluated. The presence of a clinically characterized depressive episode in one out of every 10 of the patients included especially stands out. In addition, one out of every 5 patients had at least subsyndromal depressive symptoms. Finally, another datum reflecting the preponderance of any type of depressive symptoms in bipolar patients is the fact that they suffer a greater number of depressive episodes during the course of their disorder versus manic or hypomanic sphere patients. It is very important in the daily clinical practice to stress this predominance of the depressive symptoms since it is precisely the symptoms of this pole that cause the greatest deterioration in the bipolar patient's functioning[7,8]. In fact, in our study the presence of depressive symptoms was the variable that determined a perception of a greater deterioration in the quality of life. Thus, it is crucial to reduce the presence of the depressive symptoms that are so frequently found in the course of the disorder in order to improve this quality of life.

Regarding the medical comorbidity found in our study, its prevalence is similar to that mentioned in other studies in the bipolar out-patient populations, both in regards to specific disorders as well as their frequency[24]. On the contrary, the low comorbidity with substance abuse/dependence (alcohol and other abuse substances) detected in our study (16.5%) contrasts with the values that are close to 50% of the patients found in other studies25. The explanation for this difference can be found in the way that the patients were enrolled in our study, their being a bias towards patients with better awareness and knowledge of the disease and treatment adherence.

Lithium has traditionally been considered as the gold standard treatment for bipolar disorder. It was also the one used the most in our patient sample, both in larger number of patients and as being maintained continuously in time. In spite of everything, lithium is not effective in a large percentage of patients[26] so that new drugs must be introduced. This could probably explain why there were few patients in our sample who received this or another treatment as single drug therapy (22.6%) while two out of every five patients received at least three types of psychodrugs in combined treatment. These results confirm a common practice in our country that has been found in other studies[27] and should alert us to the difficulty of treating bipolar patients and to the risks of increasing side effects.

Therapeutic compliance is a complex phenomenon in which very different factors play a role, among them tolerability of the treatments. The type I bipolar patients in our sample tended to experience more adverse events even though the type or mean number of psychodrugs were similar in both subgroups. On the contrary, in this subgroup of patients, the investigator reported that there was higher treatment adherence and the patient him/herself subjectively also perceived the medication better. If we accept the limitation derived from the way that therapeutic compliance was evaluated, exclusively based on the psychiatrist's impression, the explanation regarding this better acceptance and perception of the treatment between type I bipolar patients may be found in the fact that these patients had better awareness of the disease. This awareness of this disease may be derived from the presence of more disruptive clinical episodes which have greater repercussion, such as mania among type I bipolar subjects or because a greater percentage of these patients received psychoeducation on the disease and the treatment.

It must also be taken into account that most of the adverse events reported have been related with the treatment with lithium salts (tremor and polyuria). Thus, consideration should be given to using another type of treatment with better global tolerability that would avoid the frequently reported appearance of sedation. All this undoubtedly would have a repercussion on better treatment compliance.

This study has limitations because of the method used to select the sample. However, it would have been necessary to have previous knowledge of the real epidemiology of the patient with bipolar disorder seen in the daily clinical practice in order to use any other selection form. This type of selection undoubted includes a bias towards a sample of patient with better disease awareness and better treatment adherence.

Accepting this limitation makes it possible to drawn conclusions of interest for the daily clinical practice. In the first place, the need to improve some aspects of the care that would help make an earlier diagnosis of the disorder at the onset of the symptoms stands out. In addition, offering

psychoeducation to the entire group of bipolar patients may make it possible to improve their evolution by increasing treatment adherence and capacity to detect and control the subsyndromal symptoms.

Other collateral aspects to keep in mind about the clinical care given to bipolar patients refer to the monitoring of cardiovascular risk factors. The need to continue to search for new treatments or combinations of known one to improve effectivity, trying to reach the objective of total absence of symptoms, also stands out. One of the main findings of this study is the decrease of quality of life of the bipolar patients related with the presence of depressive symptoms. Thus, greater emphasis must be placed on performing treatments that prevent the appearance of depressive polarity symptoms.

Finally, because of minimum clinical differences that appear to exist between the different subtypes of bipolar patients, none of these subtypes should be considered as minor, even those of the spectrum.

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