established in 2016

MAS JOURNAL of Applied Sciences

ISSN 2757-5675

DOI: http://dx.doi.org/10.52520/masjaps.v7i2id171

Research Article

Quality of Life And Disability of Patients With Bipolar Disorder According To Treatment Response

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Received: 15.01.2022 **Accepted**: 20.02.2022

Abstract

Bipolar Disorder (BD) is a lifelong, chronic mental illness with recurrent depressive, manic, hypomanic, or mixed episodes, with euthymic periods between episodes. The inadequate response is defined as the ineffectiveness of the drug from two different groups, despite being used sufficient dose and duration for the specific attack of the disease. BD is also related to impairment in functionality and disability. Most studies have demonstrated marked deterioration of quality of life and disability in patients with BD, even if they are clinically considered euthymic. Our study aims to determine the factors affecting the response to treatment and compare the quality of life and disability in patients with bipolar disorder. Our study included 150 patients with BD between 18-65 years who applied to the Dicle University Faculty of Medicine Psychiatry Clinic. Patients were divided into two groups according to treatment response. Sociodemographic Data Form, Clinical Global Impression Scale (CGI), Sheehan Disability Scale (SDS), World Health Organization Quality of Life Scale (WHOQOL-27) were applied to the participants. Inadequate response group had higher mood episodes, number of hospitalization, inadequate family support, non-adherence to treatment, suicide attempt, psychiatric comorbidity, late-onset treatment, and higher mean CGI-S and SDS subscales scores and lower mean WHOQOL-BREF 27 score. Inadequate response to treatment was associated with worse functionality and disability. Inadequate response related factors such as misdiagnosis, late diagnosis, late treatment, low adherence to treatment, missed psychiatric comorbidity, and inadequate family support should be minimized. Treatment should aim not only to remission symptoms but also aim complete functional recovery and no disability in work, social life, and family life/home responsibilities.

Keywords: Bipolar Disorder, treatment response, inadequate response to treatment, life quality, disability

INTRODUCTION

Bipolar Disorder (BD) is a lifelong, chronic mental illness with recurrent depressive, manic, hypomanic, or mixed episodes, with euthymic periods between episodes (Grande et al., 2016). The prevalence rate in BD is 9-15/100,000 for men and 7.4-30/100,000 for women. In recent years, studies including BD I and II show a lifetime prevalence rate of up to 5% (Merikangas et al., 2007; Rihmer and Angst, 2005). Although BD II is more common in women than men, when all subgroups are evaluated in BD, the female/male ratio is 1/1(Carta and Angst, 2005). The age of onset of BD peaks between the ages of 15-19, followed by the period between the ages of 20-24. There is a 5-10 year duration between first onset and first treatment ages (Lish et al., 1994). BD I and II are classified under the category of "Bipolar disorder and related disorders" in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-5). BD I is characterized by at least one manic episode. The manic episode may have been followed by hypomanic or major depressive episodes. In manic periods, symptoms such as inflated self-esteem or grandiosity, decreased need for sleep, increased talkativeness, racing thoughts are observed. According to DSM-5, the symptoms must persist for at least one week and cause significant impairment in functionality to diagnose a manic episode. In cases severe enough to require hospitalization, a diagnosis can be made without seeking time. The duration criterion for the hypomanic period is four days, and the impairment in functionality is not as severe as mania. There are no psychotic symptoms, and no hospitalization is required. Depressive episodes that can be seen in both BD I and II include symptoms such as depressive mood, loss of interest or pleasure, sleep disturbances, thoughts of death that have been present for at least 14 days and result in impaired functionality. BD II; is characterized by at least one hypomanic episode in addition to one or more major depressive episodes (APA, 2013). BD differs significantly between individuals regarding prognosis, outcome, and response to treatment. There are some prognostic factors for BD. Early-onset, advanced age, residual symptoms between episodes, co-diagnosis of mental disorder, more than ten manic episodes, mixed episodes, long depressive episodes, rapid cycling; adversely affect prognosis and treatment response (Gitlin et al., 1995). Male gender, low socioeconomic level, presence of a family history of the disease, being single, and being from races other than Caucasians are other poor prognostic factors (Goodwin and Ghaemi, 2003). However, the predominance of manic episodes, good compliance with treatment, long euthymic periods, positive family, work, and occupation conditions, and low expression of emotion in the family are positive prognosis indicators. These factors are associated with greater benefit from treatment (Leboyer et al., 2005). The number of recurrences and severity of the disease are the most important factors determining the course. It has been found that good response to treatment is associated with good clinical course and outcome. It is thought that early and successful treatment of the first disease period affects the course positively (Belmaker, 2004; Tohen et al., 2003). Despite treatment, patients tend to switch from one attack to another, and it is difficult to maintain a long euthymic period with typical treatment methods (Gitlin, 2006). Inadequate response to treatment is highly variable for different clinical

conditions in BD. It has been defined primarily for depressive episodes for both BD I and II. The inadequate response is defined as the ineffectiveness of the drug from two different groups, despite being used sufficient dose and duration for the specific attack of the disease (Özalp, 2015). The International Society defined resistance to treatment in **BD for Bipolar Disorders**

Acute mania: Despite 8-10 weeks of treatment; insufficient decrease in YMRS scores or significant increase in Montgomery Asberg Rating Scale (MADRS) or Hamilton Depression Rating Scale (HAM-D) scores or MADRS and HAM-D scores exceed 6.

Acute bipolar depression: Despite 10-12 weeks of treatment; insufficient decrease in MADRS and HAM-D scores or YMRS scores exceed 5

Maintenance period: Despite one year of treatment; no change in episode frequency or MADRS or HAM-D scores above 6 or YMRS scores above 7 between episodes (Tohen et al., 2009). Disability is defined as the impairment or loss of the ability to perform normal social functions or roles in the family, work, or social life (Zarate et al., 2000). Global Burden of Disease studies considered BD one of the leading causes of disability-adjusted life years worldwide for women and men (Murray and Lopez, 1997; WHO, 2008). Previous studies have shown that 75 percent of patients with BD have some degree of impairment (Goswami et al., 2006; Morgan et al., 2005). The grade of disability and impairment is greater in BD than in other mental disorders but lower than in schizophrenia (Gutierrez-Rojas et al., 2011). Good quality of life doesn't express just good health also consists of a person's physical, emotional, social, occupational, and spiritual well-being. The World Health Organization (WHO) has described the quality of life as "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns" (WHOQOL, 1995). Most studies have demonstrated marked deterioration of quality of life in patients with BD, even if they are clinically considered euthymic (Michalak, 2005). Our study aims to determine the factors affecting the response to treatment and compare the quality of life and disability in patients with BD according to treatment response.

MATERIALS and METHODS

Sample selection

Our study included 150 patients between 18-65 years who applied to the Dicle University Faculty of Medicine Psychiatry Clinic between October 2015 and January 2016 and were diagnosed with Bipolar Disorder I or II according to DSM-5 criteria. The participants signed an informed consent form. Inclusion criteria for the study were having been diagnosed with bipolar disorder for at least two years and still receiving at least one mood stabilizer and at least one antipsychotic treatment. The criteria for the duration of treatment were at least one year of maintenance therapy, at least 6 weeks for acute manic episode, and at least 12 weeks for acute depressive episode. Patients were divided into two groups according to treatment response.

Group 1: Patients who responded to treatment,

Group 2: Patients who responded inadequately to treatment

Ethics committee approval of the study Retrieved from the Dicle University Medical Faculty Non-Invasive Clinical Research Ethics Committee (Date: 25/12/2015, Number: 59).

Our study was carried out following the ethical principles of the Helsinki Declaration.

Assessment tools

Sociodemographic Data Form, Clinical Global Impression Scale (CGI), Sheehan Disability Scale (SDS), World Health Organization Quality of Life Scale (WHOQOL-27) were applied to the participants.

Sociodemographic Data Form

It is a form created by us to record the patients' sociodemographic features and clinical information.

Clinical global ımpression scale (CGI)

Guy developed it to evaluate the clinical course of all psychiatric disorders (Guy, 1976). It consists of 3 parts, including the severity of illness (CGI-S), Global Improvement (CGI-I), and Efficacy Index. Only CGI-S subscale was used in this study.

Hamilton depression rating scale (HAM-D)

It is a 17-item scale that measures the severity of depression in the patient and facilitates diagnosis and follow-up during treatment (Hamilton, 1960). The validity and reliability study of the Turkish form was performed by Akdemir et al. (2001).

Young mania rating scale (YMRS)

It was developed by Young et al. to assess the severity of manic episodes in bipolar patients (Young et al., 1978). It is a scale consisting of 11 items. Seven of the 11 items are in the five-point Likert type, and the other four items are in the nine-point Likert type. Turkish validity and reliability study of YMRS was done by Karadağ et al. (2002).

Sheehan disability scale (SDS)

The scale has five items, and it is a self-rated questionnaire. Disability was assessed in 3 fields; work/school, social life/leisure activities, and family life/home responsibilities by the SDS (Sheehan et al., 1996).

World health organization quality of life scale brief 27 (WHOQOL-BREF 27)

WHOQOL-BREF is the short form of WHOQOL-100 developed by the WHO. It consists of 26 questions evaluated as a five-point Likert scale (Whoqol Group 1998). It consists of 4 areas: physical, psychological, social, and environmental. Its Turkish validity and reliability were performed by Eser et al. in 1999 (Eser et al., 1999). Question 27 has been added to the Turkish version as a national environmental field and is used only in national studies.

Statistical method

The data obtained were evaluated in the "Statistical Packages for the Social Science" (SPSS) 24 program. Numerical values in the results were expressed as mean ± standard deviation. Descriptive information was given as percentage (%) and number (n). The conformity of the data to the normal distribution was evaluated with the Shapiro-Wilk test. We used the Student t-test for normally distributed data in two-group comparisons and the Mann-Whitney U test for non-normal distributed data. P-value of 0.05> was taken statistically significant.

RESULTS

There was no statistical difference between the two groups in terms of age, gender, marital status, education, socioeconomic status ($p>0,05$) (Table 1). Group 1 had significantly fewer mood episodes and higher adequate family support than Group 2. The rate of no hospitalization and treatment compliance were statistically significantly higher in Group 1 than Group 2 ($p<0,05$). Suicide attempt, psychiatric comorbidity, and late-onset treatment rates were statistically higher in group 2 ($p<0,05$) (Table 2). The mean CGI-S and SDS

subscales scores were statistically higher in Group 2 compared to Group 1. The mean WHOQOL-BREF 27 score was statistically higher in Group 1 than Group 2 (p<0,05) (Table 3).

Table 1. Sociodemographic features of individuals

	Group 1 (N=59)	Group 2 (N=91)	P Value
	Mean±SD	Mean±SD	
Age	31,86±9,46	30,89±9,20	,532
	N (%)	N (%)	
Gender			
Female	23 (39)	39 (42,9)	,763
Male	36 (61)	52 (57,1)	
Marital status			
Single	35 (59,3)	51 (56,0)	,692
Married	24 (40,7)	40 (44,0)	
Education			
≤ 8 years	26 (44,1)	39 (42,9)	,884
8 years<	33 (55,9)	52 (57,1)	
Socioeconomic status			
Low	10 (16,9)	27 (29,7)	,116
Middle	49 (83,1)	64 (70,3)	
High	-	-	

Table 2. Clinical features of individuals related to Bipolar Disorder

	Group 1 (N=59)	Group 2 (N=91)	P Value
	Mean±SD	Mean±SD	
The number of mood episodes	3,15±0,96	7,92±1,39	<0,001**
	N (%)	N (%)	
Suicide attempt			
Yes	12 (20,3)	42 (46,2)	,002**
No	47 (79,7)	49 (53,8)	
Psychiatric comorbidity			
Yes	21 (35,6)	59 (64,8)	<,001**
No	38 (64,4)	32 (35,2)	
Number of hospitalization			
Once in a year<	10 (16,9)	59 (64,8)	<0,001**
Once in a year	21 (35,6)	21 (23,1)	
None	28 (47,5)	11 (12,1)	
Late-onset treatment			
Yes	14	55	<0,001**
No	45	36	
Treatment compliance			
Yes	41	25	<0,001**
No	18	66	
Adequate family support			
Yes	59	41	<0,001**
No	-	50	

Table 3. Scale scores of patients with BD

	Group 1 (N=59)	Group 2 (N=91)	P Value
	Mean±SD	**Mean±SD**	
CGI-S	1,14±0,392	4,59±0,882	<0,001**
SDS			
Work	4,44±3,10	8,62±1,86	<0,001**
Social life	3,31±2,76	7,16±2,77	<0,001**
Family life/home responsibilities	2,27±1,42	7,51±2,69	<0,001**
WHOQOL-BREF 27	85,31±6,61	71,84±5,23	<0,001**

DISCUSSION

Our study involved two groups according to response to treatment. Groups were similar in terms of age, gender, marital status, education, socioeconomic status.

Group 1: Treatment responders. Group 2: Inadequate treatment responders Inadequate treatment response was associated with more hospitalizations, mood episodes, and less treatment compliance. Also, inadequate treatment responders had higher rates of suicide attempts, psychiatric comorbidity, late-onset treatment, and inadequate family support. Treatment response was related to higher quality of life and less disability in work, social life, and family life/home responsibilities. A significant part of bipolar patients show permanent subsyndromal symptoms, and most individuals with BD spend more than half of their lives symptomatic despite treatment. Even if this patient group goes into remission with treatment, it is difficult for them to reach full functionality or return to their premorbid functionality. In this study, factors associated with poor functioning and higher disability were categorized as sociodemographic (older age, male sex, poor premorbid adjustment), clinical (age of onset, number of episodes, number of hospitalizations, history of psychotic symptoms, persistent subclinical symptoms, rapid cycling, psychiatric and non- psychiatric comorbidities), cognitive (persistent cognitive dysfunctions), pharmacological (number of treatments, side effects of medicine) and environmental factors (social support and attitudes, family support and attitudes, health services, systems, and policies) (Sanchez-Moreno et al., 2009). Vieta et al. found that nearly half of the BD patients continue to experience difficulties in their functioning, including work impairment, family disturbances, marital and interpersonal problems. Psychiatric comorbidity, depressive episodes, psychotic symptoms, the number of attacks, illness duration, and an earlier age of onset were the factors related to poor functionality (Vieta, Colom &Martinez-Aran 2002). Deckersbach et al. have found that treatment was associated with significant improvements in functioning and quality of life in patients with BD. Responders showed better improvement in quality of life and functionality than non-responders (Deckersbach, Nierenberg &McInnis 2016). In our study, similar results were obtained with the literature. Inadequate treatment response was associated with less treatment compliance and higher rates of late-onset treatment. In this context, starting treatment early and maintaining treatment adherence will be beneficial in terms of improving functionality and quality of life in individuals with BD. In addition, psychiatric comorbidities stand out as a factor that reduces functionality and quality of life in patients with BD.

Therefore, comorbid psychiatric conditions should not be overlooked and should be treated. Latest longitudinal studies have shown significant relapse rates, residual symptoms, and functional impairment despite the treatment. In previos years, treatments had focused just on clinical remission. However, recently, the aim of treatment is not only clinical remission but also improvement of the functionality of the patients. Despite innovations and developments in BD treatments, it may still be insufficient in terms of patients' functionality and disability. Nearly half of euthymic bipolar patients who complied with a special program for BD had low functionality (Martinez-Aran et al., 2007). Even in treated euthymic patients, this low functioning is one of the main factors that explain why bipolar disorders, when measured in disability-adjusted life years, are one of the leading causes of non-fatal disease burden worldwide. It is known that psychoeducation and other psychosocial approaches to BD generally improve the outcome of the disease, and it has been reported that interventions focused on treatment compliance can yield positive results in this area. Patients with BD who can not reach total functional recovery may benefit from psychosocial rehabilitation (Colom et al., 2008). The cross-sectional design of the study, heterogeneity of the patient group with inadequate response to treatment, and the absence of a healthy control group are our limitations. The high number of patients is also the strength of our study. Since our hospital is a tertiary health center that also serves the surrounding provinces has made it easier for us to reach more patients who respond inadequately to treatment. As a result, BD is a disease that causes severe loss of functionality and disability. Inadequate response to treatment was associated with worse functionality and disability. Therefore, modifiable factors that may cause resistance to treatment should be considered. Factors such as misdiagnosis, late diagnosis, late treatment, low adherence to treatment, missed psychiatric comorbidity, and inadequate family support should be minimized. Treatment should aim not only to remission symptoms, complete functional recovery, and no disability in work, social life, and family life/home responsibilities.

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