

Assessment of Treatment Adherence in Patients with Bipolar Disorder

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ABSTRACT:

Assessment of treatment adherence in patients with bipolar disorder

Objective: Non-adherence with medication is very common in patients with Bipolar Disorder (BD) and is the most frequent cause of recurrence. The aim of this study was to assess treatment adherence and related demographic and clinical factors in patients with bipolar disorder.

Method: A total of 107 inpatients who had been followed between the years of 2006-2013 were analyzed retrospectively. Patients were recalled and the treatment adherence of 85 bipolar patients in euthymic period were evaluated with Morisky Medication Adherence Scale. The Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) Axis II (SCID-II) was used to determine the comorbidity of personality disorders. Well, moderately, and poorly adherent patients were compared with respect to clinical and socio-demographic variables and functionality scores.

Results: The rate of moderately and poorly adherent patients was 70.6% of the sample. Married patients and patients with social support were more adherent. The rate of previous suicide attempt was higher in well adherers. Comorbidity with personality disorders, alcohol and substance use, and the type of treatment were not associated with adherence.

Conclusions: The results of this study have shown that being single and lacking social support were the factors that have the most significant effect on treatment adherence. Good adherers may have a better outcome, so patients with BD especially who do not have efficient social support should be monitored for treatment adherence closely.

Keywords: adherence, bipolar disorder, morisky scale

Journal of Mood Disorders (JMood) 2017;7(4):185-90



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Date of received:

June 13, 2017

Date of acceptance:

November 06, 2017

Declaration of interest:

M.O.K., N.K., L.T., N.O., M.E.D., M.G.: The authors reported no conflicts of interest related to this article.

INTRODUCTION

Bipolar disorder (BD) is a life-long, disabling psychiatric disorder and can cause significant morbidity and mortality. Treatment is a necessity to minimize the frequency of manic or depressive episodes, to reduce the severity of symptoms, to prevent patients from negative consequences of disorder, and to improve their functionality and quality of life (1). The first-line treatment for BD is pharmacotherapies and effective medications combined with psychotherapies prove a relatively normal and productive life in 60-80% of patients. The efficacy of medications is directly related with adherence (2).

Medication adherence can be defined as the degree to which a patient correctly follows and applies medical advice (3,4). Both the patient and the health-care provider affect adherence, and a positive physician-patient relationship is the most important factor in improving adherence (3). Adherence to medical regimen has positive effects on the prognosis and is associated with lower costs of treatment. On the other hand, non-adherence is a major obstacle to the effective delivery of health care especially in chronic diseases (3-7). Estimates from the World Health Organization (WHO) indicate that only about 50% of patients with chronic diseases living in developed countries follow treatment recommendations (3).

Non-adherence to the medical regimen is a very common clinical problem in the management of patients with BD. 60% of patients with BD reported that they withdraw from medication in six months (1). More than one-third of bipolar patients discontinue the medication at least twice and nine of ten bipolar patients admitted they discontinue the medication at least once in their lives (8). Non-adherence is explained by “lack of insight” or as a symptom of disease for patients with mental disorders, but these conditions give limited information about medication adherence (9). Major barriers to compliance in patients with mental disorders include age, gender, marital status, substance use, psychotic symptoms, personality disorders, lack of insight and knowledge, chronicity of disorder, poor social support, fear of stigmatization, the poor quality of information available about treatment, the complexity of medication regimens, concerns about side effects, lack of comprehension of treatment benefits, and poor communication or lack of trust between the patient and his or her clinician (10).

There is a clear association between adherence with medication regimens and factors such as relapse, hospitalization and re-hospitalization rates; cost of treatment; incidence of suicides and so morbidity and mortality (11-15). Noncompliance is the most frequent cause of recurrence in patients with BD (16). Although most patients withdraw from medication during maintenance treatment, there are limited studies about medication adherence in euthymic bipolar patients. Knowledge of the factors associated with non-adherence and interventions that enhance adherence would result in gain in clinical management of these patients to achieve a better outcome.

The aim of this study was to assess the continuity of patients with BD to their appointments after discharge in euthymic phase, and related socio-demographic and clinical factors.

METHODS

Study Setting and Subjects

The bipolar patients who admitted to inpatient clinic of Cukurova University Medical School's Department of Psychiatry between the dates of January 1st, 2006 and December 31st, 2013 were included in the study. After the approval of the study protocol by institutional review

board, written informed consent was obtained from all patients. To be included in the current study, all patients had to be more than 18 years and take lower than 7 and 13 points from Young Mania Rating Scale (YMRS) and Hamilton Depression Rating Scale (HAM-D) respectively. Patients who were discharged before treatment completed or partially recovered were also excluded. Because of administration of self-report scales, necessity of giving a written consent and to provide more adequate information, all participants were required to have at least primary or higher level education. Of the 107 bipolar patients enrolled, due to these factors the resulting sample size was limited to 85 patients.

Procedures and Assessment Instruments

All interviews for study were made by the same psychiatrist (Dr. Karaytug). Patient assessment was completed in two phases and lasted in approximately 45-60 minutes in each one. In the first phase, a demographic data form for socio-demographic features and another for clinical characteristics of BD was filled by staff psychiatrist to obtain socio-demographic variables of patients (i.e., age, gender, marital status, education, socioeconomic status, employment, physical illnesses) and clinical characteristics of BD (i.e., age of onset, number of episodes, type of episodes, seasonality, hospital admission, medication, suicide attempt, and administration of electroconvulsive therapy). Also the clinical records of all patients were evaluated.

To exclude the presence of manic and depressive episodes YMRS and HAM-D were administered to all patients. YMRS is an 11-item, multiple choices questionnaire that is used to assess the severity of manic symptoms (17). HAM-D is a multiple item instrument evaluating the severity of depression and recovery by asking about mood, feelings of guilt, suicidal ideation, insomnia, agitation or retardation, psychic and somatic anxiety, weight loss, somatic symptoms, and insight (18). The validity and reliability of Turkish version of YMRS and HAM-D have been conducted (19,20).

In the second phase all eligible patients completed 4-item Morisky Medication Adherence Scale (MMAS-4). MMAS-4 is self-report questionnaire that assesses medication adherence developed by Morisky et al. The reliability and validity of its Turkish version in patients with

Table 1: Socio-demographic characteristics of bipolar patients and comparison of socio-demographic features according to MMAS-4

	n	%	Poor	Moderate	Good	p
Mean age (years) (mean±SD)	36.9±13.5		36.8±15.4	38.1±12.9	35.6±12.1	0.8
Gender						
Female	44	51.8	16 (36.4)	13 (29.5)	15 (34.1)	0.538
Male	41	48.2	15 (36.6)	16 (39)	10 (24.4)	
Marital status						
Married	41	48.2	9 (22)	17 (41.5)	15 (36.6)	0.027
Single/divorced	44	51.8	22 (50)	12 (27.3)	10 (22.7)	
Education level						
Elementary school	30	35.3	12 (40)	7 (23.3)	11 (36.7)	0.277
Higher education	55	64.7	19 (34.5)	22 (40)	14 (25.5)	
Place of residence						
City center	66	77.6	25 (37.9)	24 (36.4)	17 (25.8)	0.380
Others	19	22.4	6 (31.6)	5 (26.3)	8 (42.1)	
Employment						
Employed	30	35.3	12 (40)	12 (40)	6 (20)	0.363
Unemployed	55	64.7	19 (34.5)	17 (30.9)	19 (34.5)	
Social support available	55	64.7	9 (16.4)	25 (45.5)	21 (38.2)	<0.001
			22 (73.3)	4 (13.3)	4 (13.3)	
Family history for psychiatric disorders	44	51.8	16 (36.4)	15 (34.1)	13 (29.5)	1.000
History of physical disorders	16	18.8	4 (25)	9 (56.9)	3 (18.8)	0.116

*SD: Standard Deviation

BD has been reported by Bahar et al. and test-retest reliability coefficients were found to range between 0.64 and 0.96 (21,22). In addition personality disorders were evaluated by the Structured Clinical Interview for DSM-IV, Axis II (SCID-II) (23). Finally, the sample group were then divided into three groups (well/ moderate/ poorly adherent) according to MMAS-4 score and compared with respect to several clinical and socio-demographic variables and functionality scores as were measured by Global Assessment of Functioning Scale (GAF).

Statistical analysis

Descriptive statistical analyses were carried out for the evaluation of demographic and clinical characteristics of the sample. The Chi-square test and Fisher's exact test were used to analyze categorical variables and the student t-test was used for the comparison of parametric continuous variables. ANOVA was used for testing three groups or variables for statistical significance. All P values were two-tailed, and statistical significance was set as $p < 0.05$. Also the correlations between scales were measured.

RESULTS

The sample included 85 patients (44 females, 41 male) and

the mean age was 36.9 ± 13.5 years. 64.7% of our sample had mid or high level education, 51.8% were single, 77.6% lived in a city center and 64.7% were unemployed. For statistical purpose, patients with mid and high education level, patients who have been divorced and never married were dealt as a single group; and housewives, students, and retired patients assessed with unemployed group. 64.7% of patients reported to have sufficient social support.

Medication adherence was good in 29.4% ($n=25$) of bipolar patients, was moderate in 34.1% ($n=29$) and poor in 36.5% (31).

The statistically significant difference between sociodemographic characteristics of patients with poor, moderate or good adherence according to MMAS-4 point were found to be related to marital status and the presence social support. Patients who were married and had social support found to be more adherent ($p < 0.05$). There were no statistically significant differences between the other sociodemographic characteristics like gender, age, and education level ($p > 0.05$). The detailed socio-demographic features of bipolar patients and comparison of socio-demographic features of groups with poor, moderate, and good adherence were presented in Table 1.

The effects of clinical features of BD on treatment adherence have been determined. The majority of our sample was diagnosed as BD type I (98.3%), 63.5% of the

Table 2: The clinical features of bipolar patients and comparison of clinical features according to MMAS-4

	Mean±SD	Poor	Moderate	Good	p
Number of episodes	3.85±2.06	4.0±2.2	4.1±2.2	3.2±1.4	0.201
Mania-Hypomania	2.50±1.84	2.4±1.7	2.9±2.1	2.0±1.4	0.211
Depression	1.50±1.70	1.5±1.5	1.6±2.2	1.2±1.0	0.553
Mixed	0.04±0.26	0.06±0.3	0.03±0.1	0.04±0.2	0.898
Duration of BD (year)	11.07±7.92	11.9±8.9	12.6±8.8	8.2±4.1	0.098
Number of hospital admissions		2.1±1.3	2.3±1.7	2.0±1.2	0.797
	n (%)	Low	Moderate	High	p
BPD types					
BPD I	84 (98.8)	31 (36.9)	29 (34.5)	24 (28.6)	0.297
BPD II	1 (1.2)	0 (0)	0 (0)	1 (100)	
First Diagnosis					0.340
Depression with psychotic features	17 (20)	9 (52.9)	4 (23.5)	4 (23.5)	
Major Depression	38 (44.7)	15 (39.5)	12 (31.6)	11 (28.9)	
Mania	29 (34.1)	7 (24.1)	13 (44.8)	9 (31)	
Psychosis	1 (1.2)	0 (0)	0 (0)	1 (100)	
Administration of ECT	23 (27.1)	8 (34.8)	9 (39.1)	6 (26.1)	0.829
Inter-episodes					0.407
Full remission	54 (63.5)	18 (33.3)	20 (37)	16 (29.6)	
Partial remission	28 (32.9)	13 (46.4)	8 (28.6)	7 (25)	
No remission	3 (3.5)	0 (0)	1 (33.3)	2 (66.7)	
History of suicide attempt	18 (21.2)	3 (16.7)	6 (33.3)	9 (50)	0.05
Rapid cycling	1 (1.2)	28 (41.8)	23 (34.3)	16 (23.9)	
Presence of psychotic symptoms	42 (49.4)	0 (0)	1 (100)	0 (0)	0.376
Mood-stabilizers		13 (31)	16 (38.1)	13 (31)	0.564
Lithium	46 (54.1)	18 (39.1)	15 (32.6)	13 (28.3)	0.858
Valproic acid	22 (25.8)	6 (27.3)	9 (40.9)	7 (31.8)	0.563
Carbamazepine	6 (7)	2 (33.3)	3 (50)	1 (16.7)	0.653
Lamotrigine	1 (1.4)	0 (0)	0 (0)	1 (100)	0.297
Combination of mood-stabilizers	10 (11.7)	5 (50)	2 (20)	3(30)	0.540

sample group achieved a full remission of the episodes, nearly one half of patients had episodes with psychotic symptoms. There were no statistically significant differences between the groups with poor, moderate and good adherence in terms of rapid cycling, psychotic symptoms, type and number of episodes, duration of disorder, number of hospital admissions, and administration of ECT. The prevalence rate of suicide attempt was 21.2% in bipolar patients. Patients who attempted suicide were found to be marginally more adherent ($p=0.05$). In our study all patients were using a mood stabilizer. Lithium were the most frequently used mood stabilizer followed by valproic acid. There was no statistically significant difference between treatment adherence and the drug used. Clinical characteristics of BD and comparison of poorly, moderate and well adherent groups are presented in Table 2.

There were no statistically significant differences

between the groups in comorbidity of personality disorders, functioning scores and alcohol and substance use. Table 3 shows the comorbidity of personality disorders and GAF scores of sample group and their effects on treatment adherence.

DISCUSSION

Non-adherence with medication is commonly seen and remains to be a substantial problem in the treatment of patients with BD. In this study, we aimed to describe treatment adherence and related socio-demographic and clinical factors in a group of euthymic bipolar patients and found that 70.6% of these patients to be moderately or poorly adherent to medication recommended by the clinicians.

In the literature, the rate of non-adherence with medication of patients with BD ranges between 20 to 60%

Table 3: Comparison of comorbidity and GAF scores according to MMAS-4

	n (%)	Poor	Moderate	Good	p
Alcohol-substance use	8 (9.4)	5 (62.5)	2 (25)	1 (12.5)	0.257
Personality disorders	15 (17.6)	6 (40)	3 (20)	6 (40)	0.402
GAF Score					0.168
(91-100)	7 (8.2)	0 (0)	3 (42.9)	4 (57.1)	
(61-90)	47 (55.3)	18 (38.3)	14 (20.8)	15 (31.9)	
(51-60)	31 (36.5)	13 (41.9)	12 (38.7)	6 (19.4)	

(24,25). The rate of poorly adherent patients in our study was 36.5% and this result is in agreement with previous studies. In the literature, medication adherence in BD is associated with being male and caucasian, side or insufficient effects of medications used, the presence of a comorbid substance use disorder or personality disorder, treatment with combinations of mood stabilizers, the complex interaction of illness, patient, drug, physician attitude, and prevailing cultural attitude and non-adherence is found to result in greater severity of episodes, poor outcome, increased risk of relapse, re-hospitalization, suicide and greater utilization of healthcare services, increased mental health expenditures and so the poorer quality of life, stigmatization, and functional impairment (26-31). In our study the statistically significant differences between poorly, moderately, and well adherers were only in variables of marital status and the presence of social support. Patient who were married and declared to have social support were better adherers. We found no association between other demographic, clinical and medication-related factors and treatment adherence which was measured by MMAS-4. Although past studies suggest that nonadherence is predictive for suicidality, we surprisingly found treatment adherence was marginally better in patients who attempted suicide before ($p=0.05$) (32). Attempting suicide and its consequences may have raised awareness about the disorder, these patients may be observed more closely by the clinician and supported more by their family. The high rate of treatment adherence in suicide attempters may be due to these factors. We found no statistically significant differences between the groups in comorbidity of personality disorders and GAF scores. The variability in rates and differences in studies are likely to be the consequence of the differences between

methodology used, study settings and designs, the definition and assessment of adherence, the patient samples included, and the phase of disorder.

The study has a number of limitations. Our study was performed in a tertiary level hospital on a small sample group who were admitted in our inpatient clinic and have been followed in our outpatient clinic after hospital discharge. Adherence was measured by MMAS-4 and the effects of the patients' beliefs, their relationship with clinician and comorbid psychiatric disorders (except substance-alcohol use and personality disorders) on adherence cannot be excluded, so it is difficult to generalize our results to all patients with BD.

In conclusion, non-adherence in BD is a complex phenomenon influenced by multiple factors and despite the introduction of new medications, the rates of non-adherence seemed to be stable over the years. The studies in this area are limited and the results of them are inconsistent. In this study, treatment adherence of euthymic bipolar patients was found to be associated only with social support and being married. The results of the studies in the literature are far to give the critical demographic and clinical factors to predict or determine non-adherence in BD. Non-adherence concluded with poor outcome, impairment in functioning and quality of life. Further research is needed to determine what factors most significantly contribute to medication adherence in patients with BD. Special care should be given to enhance treatment adherence to reduce adverse consequences of BD and to improve health outcome of bipolar patients.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References:

1. Isik E, Isik U. Çocuk, Ergen, Erişkin ve Yaşlılarda Depresif ve Bipolar Bozukluklar. Ankara: Rota Tıp Kitapevi; 2013.
2. Sofuoğlu S, Turan MT. Antipsikotik ilaç tedavisinde uyum problemleri: Bunların ekstrapiramidal yan etkilerle ilişkisi. *Anadolu Psikiyatri Dergisi*. 2000;1(2):100-6.
3. World Health Organization. Adherence to Long-Term Therapies: Evidence for Action. Geneva: World Health Organization; 3. 2003
4. Wright EC. Non-compliance-or how many aunts has Matilda? *Lancet* 1993;342(8876):909-13. [\[CrossRef\]](#)
5. Frank E, Perel JM, Mallinger AG, Thase ME, Kupfer DJ. Relationship of pharmacologic compliance to long-term prophylaxis in recurrent depression. *Psychopharmacol Bull*. 1992;28(3):231-5.
6. Buckley P, Cannon M, Larkin C. Abuse of neuroleptic drugs. *Br J Addict*. 1991;86(6):789-90. [\[CrossRef\]](#)
7. Riley W, Velligan D, Sajatovic M, Valenstein M, Safren S, Lewis-Fernandez R, et al. Adherence to psychiatric treatments. *CML Psychiatry*. 2009;20(4):89-96.
8. Colom F, Vieta E, Tacchi MJ, Sanchez-Moreno J, Scott J. Identifying and improving non-adherence in bipolar disorders, Bipolar Disord. 2005;7(Suppl.5):S24-S31. [\[CrossRef\]](#)
9. Crowe M, Wilson L, Inder M. Patients' reports of the factors influencing medication adherence in bipolar disorder – an integrative review of the literature. *Int J Nurs Stud*. 2011;48(7):894-903. [\[CrossRef\]](#)
10. Johnson FR, Ozdemir S, Manjunath R, Hauber AB, Burch SP, Thompson TR. Factors that affect adherence to bipolar disorder treatments: A stated-preference approach. *Med Care*. 2007;45(6):545-52. [\[CrossRef\]](#)
11. Roy R, Jahan M, Kumari S, Chakraborty PK. Reasons for drug non-compliance of psychiatric patients: A centre based study. *Journal of the Indian Academy of Applied Psychology*. 2005;31(1-2):24-8.
12. Svarstad BL, Shireman TI, Sweeney JK. Using drug claims data to assess the relationship of medication adherence with hospitalization and costs. *Psychiatr Serv*. 2001;52(6):805-11.
13. Miaso AI, Monteschi M, Giacchero KG. Bipolar affective disorder: Medication adherence and satisfaction with treatment and guidance by the health team in a mental health service. *Rev Lat Am Enfermagem*. 2009;17(4):548-56. [\[CrossRef\]](#)
14. Kripalani S, Risser J, Gatti ME, Jacobson TA. Development and evaluation of the Adherence to Refills and Medications Scale (ARMS) among low-literacy patients with chronic disease. *Value Health*. 2009; 12(1):118-23. [\[CrossRef\]](#)
15. Zeber JE, Copeland LA, Good CB, Fine MJ, Bauer MS, Kilbourne AM. Therapeutic alliance perceptions and medication adherence in patients with bipolar disorder. *J Affect Disord*. 2008;107(1-3): 53-62. [\[CrossRef\]](#)
16. Colom F, Vieta E, Martínez-Arán A, Reinares M, Benabarre A, Gastó C. Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *J Clin Psychiatry*. 2000;61(8):549-55. [\[CrossRef\]](#)
17. Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatry*. 1978;133:429-35. [\[CrossRef\]](#)
18. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62. [\[CrossRef\]](#)
19. Karadağ F, Oral T, Aran-Yalçın F, Erten E. Young Mani Derecelendirme Ölçeğinin Türkiye'de geçerlik ve güvenilirliği. *Türk Psikiyatri Dergisi*. 2001;13(2):107-14.
20. Akdemir A, Örsel SD, Dağ İ, Türkçapar MH, İşcan N, Ozbay H. Hamilton depresyon derecelendirme ölçeği (HDDO)'nin geçerliliği, güvenilirliği ve klinikte kullanımı. *Psikiyatri Psikoloji Psikofarmakoloji Dergisi*. 1996;4(4):251-9.
21. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24(1):67-74. [\[CrossRef\]](#)
22. Bahar G, Savaş HA, Ünal A, Savaş E, Kaya H, Bahar A. Morisky tedavi uyum ölçeğinin iki uçlu duygudurum bozukluğu için geçerlilik ve güvenilirlik çalışması. *Anadolu Psikiyatri Derg*. 2014; 15(2):141-49. [\[CrossRef\]](#)
23. First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS. The Structured Clinical Interview for DSM IV Axis II Personality Disorders (SCID-II). Washington DC: American Psychiatric Press, 1997.
24. Scott J. Predicting medication non-adherence in severe affective disorders. *Acta Neuropsychiatr* 2000;12(3):128-130. [\[CrossRef\]](#)
25. Bech P, Vendsborg P, Rafaelsen OJ. Lithium maintenance treatment of manic-melancholic patients: Its role in the daily routine. *Acta Psychiatr Scand*. 1976;53(1):70-81. [\[CrossRef\]](#)
26. Keck PE JR, McElroy SL, Strakowski SM, Stanton SP, Kizer DL, Balistreri TM, et al. Factors associated with pharmacologic noncompliance in patients with mania. *J Clin Psychiatry*. 1996;57(7):292-7.
27. Johnson RE, McFarland BH. Lithium use and discontinuation in a health maintenance organization. *Am J Psychiatry*. 1996;153(8):993-1000. [\[CrossRef\]](#)
28. Keck PE Jr, McElroy SL, Strakowski SM, Bourne ML, West SA. Compliance with maintenance treatment in bipolar disorder. *Psychopharmacol Bull*. 1997;33(1):87-91.
29. Jamison KR, Akiskal HS. Medication compliance in patients with bipolar disorder. *Psychiatr Clin North Am*. 1983;6(1):175-92.
30. Colom F, Vieta E, Martínez-Arán A, Reinares M, Benabarre A, Gastó C. Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *J Clin Psychiatry*. 2000;61(8):549-55. [\[CrossRef\]](#)
31. Chakrabarti S. Treatment-adherence in bipolar disorder: A patient-centered approach. *World J Psychiatry* 2016;6(4): 399-409. [\[CrossRef\]](#)
32. Gaudio BA, Weinstock LM, Miller IW. Improving treatment adherence in bipolar disorder: A review of current psychosocial treatment efficacy and recommendations for future treatment development. *Behav Modif*. 2008;32(3): 267-301. [\[CrossRef\]](#)