

The Pattern of Adherence in Patients with Bipolar I Disorder; an Eight Weeks Study

Ali Sharifi MD * , Amir Shabani, MD * , Masoud Ahmadzad-Asl, MD •*

(Received: 5 July 2009; Accepted: 29 Sep 2009)

Objectives: Non-adherence limits the effectiveness of medications among patients with bipolar disorder. Many studies have investigated the predicting factors of non-adherence. This paper aims to present the pattern of adherence in patients with bipolar I disorder (BID).

Methods: Seventy six patients with BID enrolled in a prospective study. The Medication Possession Ratio (MPR) was used to evaluate patients' adherence to medications, and repeated measure analysis was performed to reveal the pattern of variations. A Persian translation of Drug Attitude Inventory (DAI-10) (shortened version) was used to assess the attitude of patients toward medications.

Results: the repeated measure analysis revealed that the adherence to medications successively decreased ($p < 0.001$). Age, gender, marital status, educational level, comorbid substance abuse did not alter the pattern.

Conclusion: There is a decreasing pattern in the adherence to medications among BID patients, regardless of known predicting factors of non-adherence. It means even fully adherent patients could potentially become non-adherents during the course of maintenance treatment.

Iranian Journal of Psychiatry and Behavioral Sciences (IJPBS), Volume 3, Number 2, Autumn/Winter 2009: 39-43.

Keywords: Adherence • Bipolar Disorder • Compliance • Pharmacotherapy

Introduction

The fourth edition of the diagnostic and statistical manual of mental disorders (DSM-IV), defines Bipolar I Disorder (BID) as "having a clinical course of one or more manic episodes and, sometimes, major depressive episodes". The life-time prevalence of BID is estimated to be 0-2.4% (1) The prevalence of the disorder is equal in both sexes, and has been assumed to have an earlier onset compared to other mood disorders (1). Dual medical treatment (pharmacotherapy in addition to psychotherapy) is considered the main principle of treating a BID patient, but non-adherence is the most common limit to gain the optimal effectiveness of medications

among patients (2). The non-adherence is prevalent among bipolar patients; the range has been reported from 18% to 52% or 20% to 60% (3, 4) There are researches showing that even more than 60% of bipolar patients are at least partially non-adherent to medications (5, 6). The wide range of reports are mainly because of discrepancies in the definition of adherence or assessing non-adherence in different studies, rather than socio-economic or geographical factors (7,8). Many studies have been conducted to determine the predicting factors of adherence. Medication side effects (3, 9-11), youth (9, 12, 13), negative attitude toward medications (3,11,14-17), and co-morbid substance abuse (9, 13,14,18-20), are well known predictors of non adherence. This paper aims to present the pattern of adherence in BID patients.

Materials and Method

Seventy six patients with confirmed diagnosis of maniac episode of bipolar I

Authors' affiliations : * Tehran Psychiatric Institute, Mental Health Research Centre, Iran University of Medical Sciences and Health Services.

Corresponding author : Masoud Ahmadzad-Asl. Tehran Psychiatric Institute, Mansouri St, Niyayesh St, Sattarkhan Ave, Tehran, Iran.
Tel: +98 21 66551655
Email: m.ahmadzad@gmail.com

disorder, enrolled in an observational, prospective and longitudinal study, conducted in Iran Psychiatric Hospital, Tehran, Iran. The patients were to be older than 18, speak Farsi, resident in Tehran, Karaj or suburbs, and give their consent to participation.

Each enrolled patient was followed every two weeks for eight weeks. The four follow up visits were free of charge and were to be held in outpatient setting, unless the patients had to be admitted due any medical/ psychiatric indication. The Phone call reminder program designed to remind patients for their visits was helpful to have all enrolled patients for all 4 follow up visits.

A valid Persian Translation of the Structured Diagnostic Interview for DSM-IV (SCID) (21) was the instrument for diagnosis. A Persian translation of Drug Attitude Inventory (DAI-10) (shortened version) was used to assess the attitude of patients toward medications. Patients and/or their companions were asked for number of token medication doses depending on the patients' cognitive or mood condition and cooperation. Medication possession ratio (MPR), defined as number of token medication doses to all prescribed doses during eight weeks of follow up and was used as the measure for compliance or the extent to which patients take medications as prescribed by their psychiatrist. According to MPR scores patients were categorized to good adherent (MPR score \geq 80), moderately adherent (MPR score 50-80) and poorly adherent (MPR score $<$ 50).

Demographic characteristics of patients, including their age, gender, marital status, educational level and co-morbid substance abuse were extracted from their medical records or during follow up interviews.

SPSS 16 software was used to compare adherent and non-adherent groups statistically and estimate the correlation coefficient between variables. A repeated measure analysis on 4 successive data was performed to reveal the pattern of variations in drug adherence during the follow up period.

Results

According to MPR scores 22 patients (28.9%) had poor adherence to their

medications. Eleven (14.5%) and 43 (56.6%) were classified in "moderate" and "good" adherence categories respectively.

Age, gender, marital status, educational level, co-morbid substance and hospitalization to relapse index ($\frac{\text{hospitalization}}{\text{relapse}}$) had no significant difference among patients of three mentioned adherence categories (Table 1).

Table 1. Patients' Characteristics by Compliance

Category	Compliance Category			Total (n)	
	Poor	Moderate	Good		
Gender	Male	13	7	25	45
	Female	9	4	18	31
	Total	22	11	43	76
Marriage	Single	9	5	21	35
	Married	11	6	15	32
	Divorced	2	0	7	9
	Total	22	11	43	76
Comorbid substance abuse	Yes	5	4	13	22
	No	17	7	30	54
	Total	22	11	43	76
Education	Illiterate	0	2	2	4
	Elementary school	5	1	7	13
	Junior high school	7	2	11	20
	High school	5	3	1	9
	Diploma	4	2	17	23
	University degree	1	1	5	7
	Total	22	11	43	76
Mean Age (SD)	31(1.9)	38.09(3.8)	32.88(1.6)		
Mean hospitalization to relapse index (SD)	0.99(0.1)	0.59(0.08)	0.84(0.3)		

A repeated measure analysis revealed that, the adherence to medications successively decreased ($p < 0.001$) (Figure 1). The repeated measure analysis was performed, including gender, marital status, educational level, and co-morbid substance abuse as covariates, to compare the adherence patterns among specific groups of patients (e.g., males vs. females). The results revealed no significant difference in the pattern.

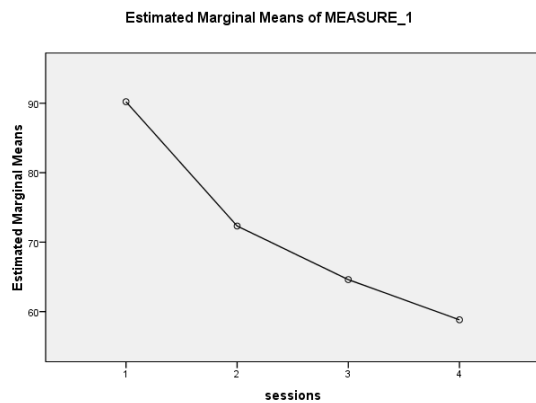


Figure 1. The Pattern of Adherence to Medications in 4 Successive Follow up Sessions.

There was a significant difference in patients' attitude toward taking their medications between well, moderately and poor adherent groups ($p=0.02$). The attitude had no correlation with the compliance, during the first two weeks ($p>0.05$). But there was a direct correlation between positive attitude and medication adherence in week 4 (Spearman's $\rho=0.239$, p value= 0.038), week 6 (Spearman's $\rho=0.319$, p value= 0.005) and week 8 (Spearman's $\rho=0.264$, p value= 0.02).

Discussion

The majority of studied patients were moderately or good adherent to their medications; while some other studies report a higher rate of non-adherence (5,6). The duration of follow up period (2 months in the present study, compared to 6-24 months in others) could be an explanation to the low non adherence rate (4, 22), as it has been shown that recently diagnosed patients are more adherent to their medications (11). The most comparable study in design and setting, published in 2007, reported the non adherence prevalence to be 38.1% with a male to female ratio of 1.7 (23).

The non-adherence appears to start from the early stages of maintenance therapy in the study population; as the repeated measure analysis revealed a significant decrease in MPR score at week 4, compared to week 2 of follow up period. That could be explained by "late adherence" phenomenon; i.e., some

patients show initial resistance to accepting their disorder and deny their need for treatment (4).

There are contradictory findings about the correlation of socio-demographic variables and treatment adherence. Some previous studies claim that treatment non-adherence is associated with substance abuse (3, 9, 14, 18, 19, 22), being unmarried (22, 24), male gender (13, 22, 24), young age (9, 12, 13, 22) and low level of education (22). While some others did not report age (4, 25), gender (3, 4, 26), and marital status (3, 4, 26) to be associated with adherence. The present findings revealed no significant relationships either. But since the study was not to determine the predicting factors of non adherence, there might be some limitation to generalize these findings.

This study revealed a decreasing pattern in the adherence to medications among bipolar I disorder patients, regardless of known predicting factors of non adherence. It means although the level of adherence might be different regarding some socio-demographic factors, but the decline pattern is similar. In another word, even fully adherent patients with no predicting factor of non-adherent could potentially become moderately adherents or non-adherents during even a short course of maintenance treatment. Therefore, the compliance of BID patients should be assessed regularly. Psychiatrist should be aware of risk factors that could lead to acute episode relapses and inquire their patients about them. Education for patients and families about the long course of the disorder and importance of maintenance therapy should be integrated in to the treatment plans. Other treatments such as targeted psychotherapy could also be included (27).

The attitude toward taking the medications is one of the most important predictors of adherence (3,14,15, 28-31). Well adherent study patients had a more positive attitude toward medications, compared to the two other groups. Moderately adherent patients also had a more positive attitude compared to poor adherent patients. The present study revealed no correlation between attitude and adherence during the first two weeks, but a direct correlation during the rest of follow up period. The fact that many patients resist medication

routines and tend to take their medications "on demand", might be an explanation to why there is a gradual change in attitude and compliance concordantly.

The study has some limitations regarding the short course of follow up period. Further studies could evaluate patients for more potential determinants of adherence such as socio-economic factors, family history, receiving psychotherapy and patient/family education.

References:

1. Sadock BJ, Sadock VA, editors. Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences, Clinical Psychiatry. Philadelphia: Lippincott Williams & Wilkins; 2007.
2. Jackson WC. The importance of facilitating adherence in maintenance therapy for bipolar disorder. *J Clin Psychiatry* 2008; 69(1): e3.
3. Scott J, Pope M. Non-adherence with mood stabilizers: prevalence and predictors. *J Clin Psychiatry* 2002; 63(5):384-90.
4. 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):24-31.
5. 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.
6. Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. *Psychiatr Serv* 2007; 58(6):855-63.
7. Colom F, Vieta E. Non-adherence in psychiatric disorders: misbehaviour or clinical feature? *Acta Psychiatr Scand* 2002; 105(3):161-3.
8. Lingam R, Scott J. Treatment non-adherence in affective disorders. *Acta Psychiatr Scand* 2002; 105(3):164-72.
9. Baldessarini RJ, Perry R, Pike J. Factors associated with treatment non-adherence among US bipolar disorder patients. *Hum Psychopharmacol* 2008; 23(2):95-105.
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.
11. Fleck DE, Keck PE, Corey KB, Strakowski SM. Factors associated with medication adherence in African American and white patients with bipolar disorder. *J Clin Psychiatry* 2005; 66(5):646-52.
12. Sajatovic M, Blow FC, Kales HC, Valenstein M, Ganoczy D, Ignacio RV. Age comparison of treatment adherence with antipsychotic medications among individuals with bipolar disorder. *Int J Geriatr Psychiatry* 2007; 22(10):992-8.
13. Azorin JM, Kaladjian A, Adida M, Hantouche E, Hameg A, Lancrenon S, et al. Toward the delineation of mania subtypes in the French National EPIMAN-II Mille Cohort. Comparisons with prior cluster analytic investigations. *Eur Arch Psychiatry Clin Neurosci* 2008; 258(8):497-504.
14. Sajatovic M, Gnacio RV, West JA, Cassidy KA, Safavi R, Kilbourne AM, et al. Predictors of non-adherence among individuals with bipolar disorder receiving treatment in a community mental health clinic. *Compr Psychiatry* 2009; 50(2):100-7.
15. Rosa AR, Marco M, Fachel JM, Kapczinski F, Stein AT, Barros HM. Correlation between drug treatment adherence and lithium treatment attitudes and knowledge by bipolar patients. *Prog Neuropsychopharmacol Biol Psychiatry* 2007; 31(1):217-24.
16. Yen CF, Chen CS, Yang SJ, Ko CH, Yen JY, Huang CF. Relationships between insight and psychosocial adjustment in patients with bipolar I disorder. *Bipolar Disord* 2007; 9(7):737-42.
17. Clatworthy J, Bowskill R, Rank T, Parham R, Horne R. Adherence to medication in bipolar disorder: a qualitative study exploring the role of

- patients' beliefs about the condition and its treatment. *Bipolar Disord* 2007; 9(6):656-64.
18. Manwani SG, Szilagyi KA, Zablotsky B, Hennen J, Griffin ML, Weiss RD. Adherence to pharmacotherapy in bipolar disorder patients with and without co-occurring substance use disorders. *J Clin Psychiatry* 2007; 68(8):1172-6.
 19. DelBello MP, Hanseman D, Adler CM, Fleck DE, Strakowski SM. Twelve-month outcome of adolescents with bipolar disorder following first hospitalization for a manic or mixed episode. *Am J Psychiatry* 2007; 164(4):582-90.
 20. Baethge C, Hennen J, Khalsa HM, Salvatore P, Tohen M, Baldessarini RJ. Sequencing of substance use and affective morbidity in 166 first-episode bipolar I disorder patients. *Bipolar Disord* 2008; 10(6):738-41.
 21. Sharifi VAS, Mohammadi MR, Amini H, Kaviani H, Semnani Y, Shabani A, et al. A Persian translation of the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: psychometric properties. *Comprehensive Psychiatry* 2009; 50(1):86-91.
 22. Berk M, Berk L, Castle D. A collaborative approach to the treatment alliance in bipolar disorder. *Bipolar Disord* 2004; 6(6):504-18.
 23. Shabani A, Eftekhar M. Non-compliance after first episode of manic or mixed state: a 17 months follow-up. *Iranian Journal of Psychiatry and Behavioral Sciences* 2007; 1(2):46-49.
 24. Gonzalez-Pinto A, Mosquera F, Alonso M, Lopez P, Ramirez F, Vieta E, et al. Suicidal risk in bipolar I disorder patients and adherence to long-term lithium treatment. *Bipolar Disord* 2006; 8(5 Pt 2):618-24.
 25. Perlick DA, Rosenheck RA, Clarkin JF, Maciejewski PK, Sirey J, Struening E. Impact of family burden and affective response on clinical outcome among patients with bipolar disorder. *Psychiatr Serv* 2004; 55(9):1029-35.
 26. Colom F, Vieta E, Martinez-Aran A, Reinares M, Benabarre A, Gasto C. Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *J Clin Psychiatry* 2000; 61(8):549-55.
 27. 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.
 28. Mitchell AJ. Adherence behaviour with psychotropic medication is a form of self-medication. *Med Hypotheses* 2007; 68(1):12-21.
 29. Kessing LV, Hansen HV, Bech P. Attitudes and beliefs among patients treated with mood stabilizers. *Clin Pract Epidemiol Ment Health* 2006; 2:8.
 30. Taj R, Khan S. A study of reasons of non-compliance to psychiatric treatment. *J Ayub Med Coll Abbottabad* 2005; 17(2):26-8.
 31. Strauss JL, Johnson SL. Role of treatment alliance in the clinical management of bipolar disorder: stronger alliances prospectively predict fewer manic symptoms. *Psychiatry Res* 2006; 145(2-3):215-23.