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Predictors of non-adherence among individuals with bipolar disorder receiving treatment in a community mental health clinic

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Abstract

Background—Subjective experience of illness is a critical component of treatment adherence in populations with bipolar disorder (BPD). This cross-sectional analysis examined clinical and subjective variables in relation to adherence in 140 individuals with BPD receiving treatment with mood stabilizing medication.

Methods—Non-adherence was defined as missing 30% or more of medication on the Tablets Routine Questionnaire (TRQ), a self-reported measure of medication treatment adherence. Adherent and non-adherent groups were compared on measures of attitudes towards illness and treatment including the Attitudes towards Mood Stabilizers Questionnaire (AMSQ), the Insight and Treatment Attitudes Questionnaire (ITAQ), The Rating of Medication Influences (ROMI), and the Multidimensional Health Locus of Control Scale (MHLC).

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Results—Except for substance abuse comorbidity, adherent individuals (N=113, 80.7%) did not differ from non-adherent individuals (N=27, 19.3%) on clinical variables. However, non-adherent individuals had reduced insight into illness, more negative attitudes towards medications, fewer reasons for adherence, and more perceived reasons for non-adherence compared to adherent individuals. The strongest attitudinal predictors for non-adherence were difficulties with medication routines (OR 2.2) and negative attitudes towards drugs in general (OR 2.3).

Limitations—Results interpretation is limited by cross-sectional design, self-report methodology and sample size.

Conclusions—Comorbid substance abuse, negative attitudes towards mood stabilizing medication, and difficulty managing to take medication in the context of one's daily schedule are primary determinants of medication treatment adherence. A patient-centered, collaborative model of care that addresses negative attitudes towards medication and difficulty coping with medication routines use may be ideally suited to address individual adherence challenges.

Keywords

Bipolar disorder; treatment adherence; compliance; subjective experience; attitudes towards treatment; mood stabilizers

Introduction

Medication treatment non-adherence among populations with bipolar disorder (BPD) is widespread and pervasive. A recent large-scale (N=3,681) study found that 40% of individuals with bipolar mania were partially or totally non-adherent with prescribed medication treatments [1]. The effects of medication non-adherence include symptoms worsening, reduced quality of life and in some cases, suicide. A recent study of suicidal behavior in relation to mood stabilizer treatment found a sixteen-fold greater suicidal behavior rate after medication discontinuation compared with mood stabilizer monotherapy continuation (55.9 vs. 3.5 events/100 patient years) among 405 individuals with bipolar disorder followed for a 3-year period, suggesting that commonly utilized mood stabilizing drugs (lithium, divalproex, carbamazepine) are protective against suicidal behavior [2]. Reduced adherence with mood-stabilizer therapy is also associated with greater use of mental-health related emergency room visits and inpatient hospitalizations [3].

Factors reported to be associated with treatment non-adherence among individuals with BPD include demographic variables specific to an individual such as gender, ethnicity, age, and illness-specific features such as illness severity or comorbidity. However, more mutable factors, such as attitudes towards illness and treatments, also contribute to non-adherence, [4, 5,6,7,8,9,10,11,12,13]. These factors can potentially be addressed in targeted psychosocial interventions, such as psychoeducation or social cognitive theory-based interventions that are used to supplement pharmacotherapy in bipolar disorder.

Individual perception of risks and benefits of medication treatment are known to affect treatment adherence in bipolar populations [14,15], and the experience of burdensome or intolerable side effects, complicated medication regimens, lack of knowledge of underlying illness and felt /experienced stigma in relation to mental illness are all known to have a negative effect on medication adherence [14,16,17,18,19,20,4]. Additionally, an individual's beliefs regarding controllability of one's health, or health locus of control is likely to affect illness experience [15]. Self-reported adherence with health treatment has been associated with personal health locus of control beliefs [21,22,23] with those individuals who perceive an internal locus of control being more likely to have good adherence with treatment compared to those individuals with an external locus of control. Finally, insight is another aspect of

subjective experience of illness worth special mention. Although “lack of insight” has more traditionally been associated with primary psychotic illness, such as schizophrenia, increasing attention is being paid to the often – severe deficits in insight seen in individuals with BPD [24].

Patients are described as “the final health care decision-makers”, and satisfaction with and perceived value of medication treatments among individuals with BPD are strong drivers of medication adherence/non-adherence [25]. Identification of predictors of adherence in populations with BPD, particularly those that are mutable, provides a starting place for focused adherence enhancement interventions. Previously published studies on adherence in bipolar populations have not generally included reasons for adherence as well as non-adherence or an assessment of locus of control, and many studies have not adjusted for clinical characteristics and illness severity [26]. The aim of this analysis was to examine the relationships between demographic and clinical variables, selected illness severity markers, and markers of subjective illness and treatment attitudes in relation to treatment adherence in a sample of 140 individuals with BPD being treated with mood stabilizing medications in a community mental health clinic (CMHC). The study focuses on individuals with bipolar depression, a population known to be particularly disabled.

Methods

This is a cross-sectional analysis of factors associated with treatment non-adherence among individuals receiving treatment for bipolar disorder in a CMHC. The analysis is part of a larger, prospective study on treatment adherence conducted by this group of investigators (K23 MH 065599-01, PI Sajatovic). This analysis was confined to baseline study data.

This analysis compared characteristics of individuals with BPD who were adherent and those who are non-adherent with treatment at a CMHC as defined by missing 30% or more of their medication on the self-reported Tablets Routine Questionnaire [TRQ,27,19]. In addition to standardized psychiatric diagnostic evaluation and assessment of baseline demographic variables, study participants also completed a variety of measures that evaluated illness severity (symptoms, substance abuse comorbidity and psychosocial supports), as well as their personal attitudes towards illness and treatment, insight into their disorder, reasons for adherence/non-adherence and perceived control over health.

All study participants met the following inclusion criteria: 1) Subjects had a clinical diagnosis of BPD Type I determined by a standardized diagnostic interview, the Mini-International Neuropsychiatric Interview (MINI) [28]; 2) Subjects had illness of at least two years duration; 3.) Subjects had an index depressive episode; 4) Subjects received treatment with medication to stabilize mood for at least six months (Mood stabilizing medications were: Lithium, lamotrigine, valproate, carbamazepine, oxcarbazepine, topiramate, gabapentin, aripiprazole, olanzapine, quetiapine, risperidone, clozapine, clonazepam. Medications, including atypical antipsychotics, could be utilized as either monotherapy or as part of a polytherapy regimen); and 5) Subjects were able to participate in psychiatric interviews and able to give written, informed consent to study participation. The study was approved by the local Institutional Review Board (IRB).

Specific Measures

Medication Treatment Adherence

Adherence was evaluated with the Tablet Routines Questionnaire [TRQ,26,19] a brief, self-report instrument which has been validated in populations with bipolar disorders [14,26]. The revised version by Adams and Scott [19] has specificity for non adherence of 90%. The TRQ

identifies “non-adherent” individuals, defined as those who miss 30% or more of their medication in the last month. A number of investigators have defined “good” adherence in seriously mentally ill populations, including those with BPD, as missing no more than 20% of medication [29,30,31], while Scott and Pope [14] have derived a clinically relevant definition of poor adherence in BPD as missing 30% or more of medications as identified by the TRQ. The conservative estimate of non-adherence as defined by Scott and Pope [14] was utilized in this study in order to maximize clinical relevance and focus on a population where non-adherence could be anticipated to be extensive enough to pose substantial risk for relapse.

Individuals were considered to be non-adherent if they self-reported missing 30% or more of prescribed medication in the past week. Weekly adherence (number of days medications were taken out of the past seven days) was calculated for each mood stabilizing medication, and then in cases of multiple medications, an average weekly adherence was calculated. Individuals who were unable to determine a percentage of adherence, but who self-reported missing 3 days or more of medication in the last week were also considered to be non-adherent. The TRQ does not separate medications by individual compound. In this analysis, in instances where an individual was prescribed multiple medications, an average of missed medications was calculated based upon their self-report.

Symptom severity variables and social supports

Overall psychopathology was evaluated with the Brief Psychiatric Rating Scale [BPRS, 32] and the Clinical Global Impression [CGI,33]. Depressive symptoms were evaluated with the 17-item version of the Hamilton Depression Scale [HAM-D,34]. Substance abuse comorbidity was assessed as a continuous measure using a portion of a standardized instrument, the Addiction Severity Index [ASI,35,36] items 1 through 14 of the Alcohol/Drug Index (ADI). The ASI evaluates both lifetime and past 30-day use of a wide variety of commonly abused substances. Psychosocial support was measured with the Interpersonal Support Evaluation List [ISEL,37], a 40-item self-report questionnaire that was developed to assess social support. The ISEL captures perceptions of resources provided by others. A total index is comprised of 4 subscales: tangible assistance (material aid), appraisal (availability of someone to talk to about life's problems), self-esteem (positive appraisal of self from others and positive comparison when comparing one's self with others), and belonging (people with whom one can do things.) Response for each item is coded on a four-point Likert scale ranging from definitely false to definitely true.

Subjective attitudes to illness and treatment

Attitudes toward medication treatment were evaluated with the Attitude toward Mood Stabilizers Questionnaire (AMSQ), a modification of the Lithium Attitudes Questionnaire [38] which evaluates an individual's attitudes towards mood stabilizing medication [14,19]. The AMSQ has seven subscales that represent key attitudinal domains with respect to adherence including 1.) opposition to prophylaxis, 2.) denial of therapeutic effectiveness, 3.) fear of side effects, 4.) difficulty with medication routines, 5.) denial of illness severity, 6.) negative attitude towards drugs in general, and 7.) lack of information about mood stabilizers [38,14]. Higher scores on each subscale represent more negative attitudes toward mood stabilizers. The AMSQ has been used by other investigators to predict adherence in BPD [14] and have been noted to improve with psychoeducational programs for BPD [27].

Reasons for adherence/non-adherence were evaluated using the Rating of Medication Influences (ROMI), a standardized assessment of selected reasons for compliance and non-compliance with medications [39]. Insight was evaluated with the Insight and Treatment Attitudes Questionnaire (ITAQ), an 11-item rating scale to evaluate patient recognition of illness and need for treatment in psychiatric illness. The ITAQ has been widely utilized in both

populations with schizophrenia and bipolar disorder [40,41,42,43]. Each ITAQ item is scored on a 0 to 2 scale (0 = no insight, 2 = good insight), and the scale has high inter-rater reliability ($r=0.82$, $p<.001$) [44]. Locus of control was assessed with the Multidimensional Locus of Control (MHLC), an 18-item instrument that measures three dimensions of locus of control of reinforcement as it pertains to health (internal, IHLC: external-chance, CHLC: and external powerful others, PHLC) [45]. The MHLC has been utilized to study locus of control in populations with severe affective illness where treatment adherence has been a focus of evaluation [19]. Scoring is from 6-36 with higher scores indicating stronger beliefs.

Statistical analysis

Individuals who self-identified as non-adherent with medications (missing 30% or more of prescribed treatments) were compared to individuals who self-identified as adherent with treatment. Descriptive statistics were used to characterize demographic and clinical characteristics of patients with BPD who were adherent and those who were non-adherent with treatment. Chi-square analysis and t-tests were used to test statistical significance for categorical and continuous variables, respectively. Multiple logistic regression models were used to compare clinical characteristics, severity markers and attitudinal variables of adherent and non-adherent groups. As there have been reports of clinical and illness-related variables being associated with non-adherence in bipolar populations [26], sex, age, ethnicity, education, duration of illness, symptom rating scores, and substance abuse were included as covariates in the models. To evaluate the strongest factors in attitudes towards treatment, a logistic model for non-adherence vs. adherence was estimated with AMSQ subscales 1 through 7 in the model, while controlling for sex, age, ethnicity, education, duration of illness, BPRS, HAM-D, CGI scores, and substance abuse.

Results

Table 1 demonstrates characteristics of individuals with BPD who were adherent ($N=113$, 80.7%) and those who are non-adherent ($N=27$, 19.3%) with treatment. There were no significant differences in age, gender, ethnicity, education, or duration of illness. Individuals who were non-adherent had more substance use comorbidity ($p=.0039$), while depressive and psychotic psychopathology was not significantly different between adherent and non-adherent individuals. Global psychopathology (CGI score) was statistically greater ($p=.0183$) for non-adherent individuals, but appeared to be of marginal clinical difference (CGI mean for adherent individuals was 4.9 compared to 5.3 for non-adherent individuals).

In contrast to the relative similarities on clinical characteristics and illness severity among adherent and non-adherent individuals, there were substantial and significant differences in illness and treatment attitudes between the two groups. Individuals who were non-adherent with prescribed medication had significantly more negative attitudes towards mood stabilizers ($p<.0001$), reduced insight into illness ($p=.0039$), fewer reasons for adherence ($p=.0248$) and more reasons for non-adherence compared with adherent individuals ($p=.0001$). Additionally, non-adherent individuals more often perceived an external locus of control compared to adherent individuals ($p=.0422$).

In addition to overall more negative attitudes towards mood stabilizing medications, there were differences in specific negative attitudes among adherent vs. non-adherent individuals with BPD. Except for the AMSQ subscale for denial of therapeutic effectiveness, non-adherent individuals had significantly higher mean scores in the AMSQ subscales ($p<.01$) indicating more negative attitudes toward mood stabilizers, with differences in mean scores ranging from 0.3 to 1.8. Controlling for the effects of clinical characteristics and illness severity in a multiple logistic model for non-adherence vs. adherence, subscales of the AMSQ that appeared most predictive for non-adherence were negative attitudes towards drugs in general (Odds ratio,

OR= 2.3, 95% CI=(1.08, 4.8), $p=.0305$) and difficulty with medication routines (OR=2.2, 95% CI=(1.36, 3.6), $p=.0014$). Domains with the construct of negative attitudes towards medications included feeling that relief from personal stress was more important than taking medications, believing that “most people” would not be in favor of taking a mood stabilizer and feeling that taking a mood stabilizer was an “artificial” way to keep stable. Domains with the construct of medication routines included difficulty fitting medication-taking into daily schedule, needing to be reminded to take medication/forgetting medication and difficulty remembering to take medication if daily routine changes for any reason.

Looking at the strongest predictor of non-adherence in each of the 3 main domains (demographic, severity/social support variable, and attitudes/subjective experience) and overall, logistic regression models for non-adherence vs. adherence were calculated separately for each domain and an overall model with all factors in the model. None of the demographic factors appeared to have significant relationship with treatment adherence. Substance abuse, measured by ASI score, was the only significant clinical predictor ($p=.0479$), while AMSQ ($p=.0246$) was a significant attitudinal predictor. There was a trend for statistical significance for the ROMI compliance score ($p=.0568$), and ROMI non-compliance score ($p=.0869$) among the attitudinal factors.

Discussion

These data demonstrate a relatively high prevalence of treatment non-adherence among individuals with BPD receiving treatment at a CMHC, and suggest that comorbid substance abuse, negative attitudes towards mood stabilizing medication, and difficulty managing to take medication in the context of one's daily schedule are primary determinants of medication treatment adherence. In this CMHC-treated sample, approximately 1 in 5 individuals identified themselves as being non-adherent with mood stabilizing medications to a clinically significant degree (missing 30% or more medications in the recent past).

Treatment non-adherence sharply increases personal, social and financial costs among individuals with BPD [46,47]. Begley and colleagues [46] noted that health care costs for severe/relapsing BPD (often characterized by non-adherence with prescribed treatments and comorbid substance misuse) is approximately \$264,785 per person compared with \$11,720 for individuals who experiences only a single manic episode [46]. Similarly, Durrenberger and colleagues [48] reported that over a 6- year period, the cost of care for one non-adherent patient with frequent manic relapses was equal to that for 13 adherent individuals. Identification of potentially changeable variables that are associated with treatment non-adherence in bipolar populations offers the potential to design interventions that address these areas of concern, and potentially to minimize the negative consequence for individuals with bipolar disorder who are at risk for stopping their medication treatments.

In common with some other investigators [20], our study found few demographic or clinical variables that are clearly associated with non-adherence among patients with BPD. Identifying individuals at risk for future non-adherence thus goes beyond the need to focus on any specific age, gender or ethnic sub-groups. An exception to the similar demographic and clinical findings between adherent vs. non-adherent patients with BPD is more substance use among those who are non-adherent. Alcohol and other substance use disorders complicate the course of and prognosis of BPD [49,50], and in most instances, treatment adherence is reduced among individuals with BPD who abuse substances [51,49]. Large, epidemiological surveys of the general U.S. population have found BPD to have the highest association with alcohol or other psychoactive substance use disorders compared to other Axis I psychiatric disorders [52,53]. Unfortunately, substance use comorbidity among patients with bipolar disorder may be under-recognized, and is often not addressed within the context of treatment for bipolar disorder. It

has been demonstrated that individuals with more serious mental illness (including bipolar disorder) and co-existing substance use disorders are extensive users of costly crisis/emergency room care and inpatient services [54]. However, the literature on evidence-based treatments for individuals with bipolar disorder and substance abuse is quite limited [55].

Our study findings suggest that individuals who are non-adherent have negative attitudes towards medications, have difficulty managing medication routines and have more perceived reasons for non-adherence compared to adherent individuals. These are likely shaped by how the individual interprets and personally experiences bipolar illness. Models of health behaviors, such as the Health Belief Model [56] focus on determinants of adherence as a product of an individual's health beliefs. The fact that there was little symptom difference between adherent and non-adherent individuals in the study presented here supports the notion that adherence attitudes may be relatively independent of symptoms (particularly in the case of bipolar depression) and are more a product of the individual's established health beliefs. Perceptions of susceptibility to illness, perceived severity of illness, the benefits of treatment, the costs and burdens of treatment as well as cues to action all factor into treatment adherence outcomes [57,16].

In the population presented here, the strongest attitudinal predictors for non-adherence were difficulties with medication routines (OR 2.2) and negative attitudes towards drugs in general (OR 2.3). Individuals had difficulty always remembering to take medications, easily forgot their medication if they had a change in daily routine, and at times needed reminding by others to take their medications. Negative attitudes included the notion that taking medication for someone with BPD was not indicated or normal, and that the disorder might be best managed in other, perhaps non-pharmacological ways. These represent areas in which specific therapeutic interventions may be of benefit. The complexity of a treatment regimen can often affect treatment adherence [58]. For example, adherence may improve when an individual is prescribed a pill that can be taken once daily rather than in divided daily dosing [59]. When frequency of drug regimen is not modifiable, timing of medication can be matched to an individual's activities of daily living to improve adherence. Misinterpretation of common medication instructions can be addressed to improve treatment adherence. For example, Eraker [60] noted that only 36% of patients correctly interpreted the meaning of "every six hours". In addition to careful review of medication instructions, adherence aids such as pill boxes/pill reminders and pre-set dose alarms [60] can be helpful. Compensatory strategies to enhance functioning in patients with schizophrenia have been successfully utilized by Velligan and colleagues [61], and many of these methods appear likely to benefit bipolar patients with functional deficits as well [62].

Inadequate or incorrect understanding of illness and treatment needs are not uncommon in populations with serious mental illness, including individuals with BPD [63,64], and lithium knowledge has been demonstrated to be correlated with serum lithium levels [65]. One study of psychiatric inpatients found that more than half of psychiatric inpatients did not know the condition for which they were being treated, the names of the medications prescribed, or the role the medications had in addressing the illness [66]. Lack of communication or poor treatment alliance with providers may result in perpetuation of false beliefs regarding prescribed medications, which if addressed, could result in improved adherence [67]. For example, fear of becoming "addicted" or dependent upon mood stabilizing medications may become an issue that affects adherence for some individuals with BPD [13]. Psychosocial interventions that enhance knowledge and understanding of BPD, such as the Psychoeducational approach refined by Colom and colleagues [68] may simultaneously improve both treatment adherence and more global illness outcomes.

The literature suggests that concerns over medication adverse effects is a major reason for non-adherence [4,25], and that fear of side effects may play a larger role in treatment non-adherence among patients with BPD compared to the actual side effects themselves [19]. Recent studies in large populations of individuals with bipolar disorder noted that non-adherence rates are remarkably similar across a wide variety of medications including traditional mood stabilizers and atypical antipsychotics [69,70]. The medication concerns perceived by an individual may play a more important role in determining adherence rather than the specific type of medication prescribed. A recent survey of 233 members of the Manic Depression Fellowship [71] noted that over 60% of individuals were dissatisfied with information about the risks of side effects with their medication treatments. Clear and readily understandable information on medication treatments with ample opportunity to provide feedback and address ongoing medication concerns may improve treatment adherence.

There is evidence to suggest that exploration of an individual's beliefs about bipolar illness and then implementing a therapy that directly addresses these beliefs may lead to changes in treatment planning and improve attitudes and adherence to mood stabilizers [72,73]. This study found that non-adherent individuals more often had a strong powerful external locus of control compared to adherent individuals, contrasting with some previous reports in bipolar populations which found that adherence was more often associated with dependence on others or being more readily controlled/affected by others [18,19]. However, this study also did not evaluate specific qualities of the types of social environment individuals in this sample experienced. It is possible that external or social influences may have not been supportive of medication taking in this group of individuals with BPD—a recent qualitative analysis by this group of investigators found that up to 40% of patients with BPD reported that family members or others specifically advised them against taking medications [6]. An approach like Bauer and colleagues' [74,75] Collaborative Care Model (CCM), in which individuals with BPD are actively involved in care planning/self-management is associated with better outcomes than more traditional medical-model care. A CCM approach may also promote positive and constructive alliances with care providers that enhance adherence in individuals with external locus of control. Likewise, family-focused therapy that includes education, communication training and problem-solving skills training for individuals with bipolar disorder is associated with better medication compared to less intensive crisis management [76].

Our study has a number of important limitations including cross-sectional design and relatively small sample size. It is very likely that our analysis identified only a “lower boundary” of non-adherence given the possible under-detection of non-adherence when relying upon self-report. Additionally, expressed attitudes towards medication and adherence as evaluated on rating scales may not identify actual attitudes that individuals may be reluctant to share. Interpretation of study results can not be extrapolated to all bipolar populations who are non-adherent. Our study did not specifically focus on recruiting individuals who are non-adherent, and the most non-adherent patients are unlikely to volunteer to participate in a research study. Additionally, while adherent vs. non-adherent populations in this sample did not appear to differ substantially on symptoms, the study enrolled only individuals with bipolar depression, and it is possible that if individuals with mania were included the findings would have been different.

Conclusions

There are significant differences between adherent vs. non-adherent individuals with BPD, including such potentially changeable factors as substance abuse, level of comfort in coping with medication concerns/side effects, attitudes towards medication, and individual reasons for adherence/non-adherence. A patient-centered, collaborative model of care may be ideally suited to address specific and individual vulnerability to treatment non-adherence.

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Table 1

Characteristics of 140 individuals with BPD who are adherent vs. non-adherent with treatment as measured by the Tablets Routine Questionnaire (missing 30% or more of medications)

Characteristic	Adherent N= 113 (80.7%)	Non-adherent N=27 (19.3%)	Test Statistics
<i>Demographic factors</i>			
Age (in years), mean (SD)	43.1 (11.18)	40.8 (11.65)	ns
Education (in years), mean (SD)	13.8 (2.84)	12.7(2.16)	ns
Ethnicity, n (%)			ns
Caucasian	67(59.3)	11 (40.7)	
African-American	18 (15.9)	8 (29.6)	
Other	28 (24.8)	8 (29.6)	
Gender, n (%)			
Male	57 (50.4)	13 (48.2)	ns
Female	56 (49.6)	14 (51.8)	
<i>Severity/social support variables</i>			
Duration of illness (in years), mean (SD)	22.5 (11.44)	22.4 (12.41)	ns
BPRS total score, mean (SD)	42.1 (8.95)	44.6 (9.46)	ns
HAM-D total score, mean (SD)	22.4 (6.95)	25.0 (5.87)	ns
CGI score, mean(SD)	4.9 (0.81)	5.3 (0.79)	t=-2.39 df=130 p=0.0183 *
ASI score – drug, mean (SD)	2.0 (3.14)	4.0 (3.55)	t=-2.94 df=134 p=0.0039 **
ISEL score – overall, mean (SD)	71.2 (22.70))	67.3 (21.95)	ns
<i>Attitudes and Insight</i>			
AMSQ total score, mean (SD)	3.5 (3.35)	9.0 (3.67)	t=-7.50 df=138 p<.0001 **
ITAQ total score, mean (SD)	20.1 (2.55)	17.2 (4.68)	t=3.12 df=30 p=0.0039 **
ROMI reasons for compliance score, mean (SD)	10.2 (3.11)	8.5 (4.06)	t=2.27 df=137 p=0.0248 **

Characteristic	Adherent N= 113 (80.7%)	Non-adherent N=27 (19.3%)	Test Statistics
ROMI reasons for non-compliance score, mean (SD)	2.3 (2.58)	6.6 (4.62)	t=-4.42 df=28 p=0.0001 **
MHLC Internality, mean (SD)	18.3 (5.37)	19.4 (5.74)	t=-0.86 df=126 p=0.3942 ^{ns}
Powerful other, mean (SD)	20.9 (5.88)	23.6 (6.82)	t=-2.05 df=126 p=0.0422 *
Chance, mean (SD)	23.2 (5.98)	21.2 (7.79)	t=1.44 df=126 p=0.1534 ^{ns}

BPRS= Brief Psychiatric Rating Scale, HAM-D= Hamilton Depression Scale, AMSQ= Attitudes Toward Mood Stabilizer Questionnaire, ISEL= Interpersonal Support Evaluation list, ASI= Addiction Severity index, CGI=Clinical Global Impression, ROMI=Rating of Medication Influences, ITAQ= Insight and Treatment Attitudes Questionnaire, MHLC= Multidimensional Health Locus of Control Scale

*
p < 0.05;

**
p < 0.01;

^{ns}
not significant.