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Why do persons with bipolar disorder stop their medication?

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Abstract

Objective—Non-adherence to maintenance medication regimens is a major problem, limiting outcomes for many persons with bipolar disorder. The aim of this paper is to determine the most relevant aspects of adherence *attitudes* in a sample of bipolar patients selected for problems with adherence *behavior*.

Methods—Among a larger sample of bipolar disorder patients participating in a prospective follow-up study (N=140), a subsample of patients were selected for non-adherent *behavior* defined as missing ≥ 30% of medication during the past month (n=27; 19.3%). Adherence *attitudes* were assessed with the Rating of Medication Influences scale (ROMI), a self-reported attitudinal

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measure assessing reasons for and against adherence. Multiple logistic regression models for non-adherence vs. adherence were estimated with each of the 19 ROMI items in the model, while controlling for sex, age, ethnicity, education, duration of illness, and substance abuse.

Results—Mean score of ROMI items corresponding to reasons for treatment adherence was greater among adherent participants, whereas the mean score of ROMI items corresponding to reasons for treatment non-adherence was greater among non-adherent participants.

The ROMI item identifying that the individual believes that medications are unnecessary had the strongest influence for non-adherence (p<.0001). This was followed by ROMI items corresponding to no perceived daily benefit (p=.0008), perceived change in appearance (p=.0057), and perceived interference with life goals (p=.0033). The ROMI item identifying fear of relapse was the strongest predictor for adherence (p=.0017).

Conclusions—Non-adherent patients with bipolar disorder differ from adherent patients with bipolar disorder on reasons for adherence and non-adherence. Utilization of tools that evaluate medication treatment attitudes, such as the ROMI or similar measures, may assist clinicians in the selection of interventions that are most likely to modify future treatment adherence.

Keywords

Bipolar disorder; treatment adherence; Rating of Medication Influences (ROMI); compliance

Introduction

Among populations with bipolar disorder (BPD), treatment non-adherence is known to occur in approximately 40% of individuals, and poor or partial adherence is generally associated with poor illness outcomes.[1,2] Factors associated with treatment non-adherence among individuals with BPD are varied, and include demographic variables such as gender and age, illness-specific features such as illness severity or comorbidity, and subjective variables surrounding the illness experience.[2,3] Not surprisingly, attitudes towards illness and treatment are a critical determinant of medication adherence among populations with serious mental illness.[4–11]

The Rating of Medication Influences (ROMI) scale was one of the first subjective quantitative measures developed to assess attitudinal factors that influence adherence with neuroleptic treatment in seriously mentally ill individuals.[12] The Health Belief Model (HBM), a conceptual framework developed to assess health behavior, served as the theoretical basis for ROMI development. The ROMI has been demonstrated to be a reliable and valid measure of salient attitudes and influences for schizophrenia patients taking antipsychotic medications.[12] The ROMI is divided into 2 subscales, reasons for adherence (ROMI-A) and reasons for non-adherence (ROMI-NA). Each item covers a specific aspect known to influence medication adherence. For example, specific ROMI-A items include perceived benefit from medication, positive influence of family members, and positive influence of a clinician. Likewise, examples of ROMI-NA items include the perception that medication has no benefit, feeling stigmatized, or distress from medication side effects. Scaling of individual items ranges from 0 (“no influence) to 2 (“strong influence”). While the ROMI has been widely utilized in psychotic populations there is still a rather limited

literature on how the ROMI may differentiate adherent vs. non-adherent populations with bipolar disorder.[13,14]

The aim of this analysis was to evaluate self-reported attitudes regarding medication adherence in patients selected for non-adherent behavior. Non-adherent behavior was determined by a self-reported treatment adherence among 140 individuals with bipolar disorder being treated with mood stabilizing medications in a community mental health clinic (CMHC).

Methods

This analysis was part of a larger, prospective study, conducted by this group of investigators[15] to examine factors associated with treatment non-adherence among individuals receiving treatment for bipolar disorder in a CMHC. The study was approved by the local Institutional Review Board (IRB). In the larger study, subjects received treatment as usual in the CMHC. While the larger, on-going study followed participants over a six-month period, this analysis was confined to baseline study data.

All study subjects met the following inclusion criteria: 1) a clinical diagnosis of BPD Type I or Type II determined by a standardized diagnostic interview, the Mini-International Neuropsychiatric Interview (MINI),[16] 2) illness of at least two years duration, 3) an index depressive episode, 4) prescribed medication to stabilize mood for at least six months, and, 5) willingness to participate in baseline and follow-up psychiatric interviews, 6) providing written, informed consent to study participation.

Measures

In addition to standardized psychiatric diagnostic evaluation (MINI) and assessment of baseline demographic variables, study participants completed a variety of baseline measures that included the 19-item version of the Rating of Medication Influences (ROMI) which, as noted above, evaluates separate subscales on reasons for treatment adherence and reasons for treatment non-adherence. The interviewer-rated items have good inter-rater agreement (kappa > .60) with kappa coefficients ranging from .75 to 1.0 for Reasons for Adherence items, and .63 to 1.0 for Reasons for Non-Adherence items.

Treatment adherence was evaluated with the Tablet Routines Questionnaire (TRQ),[17] a brief, self-report instrument which has been validated among populations with bipolar disorders.[17–19] A revised version[14] has a specificity for non-adherence of 90%. The TRQ identifies a clinically relevant population of “non-adherent” individuals, who miss 30% or more of their medication in the last month. The TRQ does not separate medications by individual compound. In instances where an individual was prescribed multiple medications, an average of missed medications was calculated based upon their self-report.

Substance abuse was evaluated with the Addiction Severity Index/ASI,[20] and bipolar symptoms were evaluated with the Brief Psychiatric Ratings Scale/BPRS,[21] and the Hamilton Depression Rating Scale /HAM-D.[22]

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. As there have been reports of clinical and illness-related variables being associated with non-adherence in bipolar populations,[23] sex, age, ethnicity, education, duration of illness, and substance abuse were included as covariates in the models. To evaluate the strongest factors in attitudes towards treatment, multiple logistic regression models for non-adherence vs. adherence were estimated with each of the 19 ROMI items in the model, while controlling for sex, age, ethnicity, education, duration of illness, and substance abuse.

Results

Nearly 20% (N=27. 19.3%) of study participants were non-adherent compared to just over 80% (N= 113, 80.7%) who were adherent with medication treatment. On average, individuals had been ill for just over 20 years, and minority representation (mostly African-American) was consistent with the overall psychiatric population served by the CMHC. Most individuals had completed high school and some individuals had some college-level education.

Participants classified as non-adherent did not differ with regards to most demographic and clinical factors such as age, education, ethnicity and gender compared to adherent participants. Furthermore, adherent and non-adherent individuals did not differ with regards to duration of illness or symptom severity as measured by the BPRS and the HAM-D. However, the mean score for ASI-drug severity was significantly higher for the non-adherent individuals (Mean ASI drug severity = 4.0, SD ± 3.55) compared to the adherent group (mean ASI drug severity =2.0, SD ± 3.15, t=−2.94, df=134, p=0.004).

As expected, the mean score of ROMI items corresponding to reasons for treatment adherence was lower among the non-adherent group (mean ROMI- A = 8.5, SD ± 4.06) compared to adherent participants (mean ROMI-A = 10.2 SD ± 3.11, t=2.27, df=137, p=0.02), whereas the mean score of ROMI items corresponding to reasons for treatment non-adherence was greater among non-adherent participants (mean ROMI-NA= 6.6, SD ± 4.62) compared to adherent participants (mean ROMI-NA= 2.3, SD ± 2.58, t=−4.42 df=28, p=0.0001).

Table 1 demonstrates scores for each of the 19 ROMI items comparing individuals who were non-adherent with medications vs. those who were adherent with medications. Treatment non-adherence was associated at the P=0.01 level with the following ROMI items: no perceived daily benefit, perception that medications are unnecessary, perceived treatment interfering with life goals, perceived change in appearance and substance abuse. The perception of never being ill and of perceived undesirable side effects was associated with

treatment non-adherence at the P=0.05 level. Considering those ROMI items corresponding to reasons for treatment adherence, perceived daily benefit, fear of relapse, and perceived side effect relief were found to be associated with treatment adherence at the P=0.01 level. Outside influences was found to be associated with treatment adherence at the P=0.05 level.

Logistic regression models for non-adherence vs. adherence, controlling for sex, age, ethnicity, education, duration of illness, and substance abuse were calculated separately for each of the 19 ROMI items in order to evaluate the ROMI items that are the strongest predictors for non-adherence. The ROMI item identifying that the individual believes that medications are unnecessary has the strongest influence for non-adherence (Odds Ratio (OR): 15.1, 95% Confidence Interval (CI): 3.8, 60.9, p<.0001). This is followed by ROMI items: no perceived daily benefit (OR: 5.8, 95% CI: 2.0, 17.2, p=.0008), perceived change in appearance (OR: 4.9, 95% CI: 1.6, 15.1, p=.0057), and perception of interfere with life goals (OR: 4.6, 95% CI: 1.6, 13.4, p=.0033). The ROMI item identifying fear of relapse was the strongest predictor for adherence (OR: 7.8, 95% CI: 2.0, 30.3, p=.0017).

Discussion

This cross-sectional analysis of medication adherence attitudes and behavior in a CMHC-treated population with bipolar disorder (N=140) demonstrated that approximately one in five individuals are non-adherent with prescribed bipolar medication treatments. In common with other reports on bipolar populations, except for substance abuse severity, demographic and clinical variables did not appear to differ between adherent and non-adherent individuals.[15]

The focus of this report was attitudes towards medication treatment among non-adherent patients with bipolar disorder. Several self-rated and interviewer-administered rating scales have been developed to evaluate adherence attitudes. These scales measure a variety of conceptual domains including subjective response to medication, insight and awareness of the disease and intended treatment affect, and factors influencing adherence behavior such as environmental and financial constraints. The use of attitudinal rating scales allows for the examination of potential reasons for medication adherence and non-adherence, and can ultimately help influence the development of new strategies for promoting adherence.

Evaluation of treatment adherence attitudes utilizing the ROMI identified that among non-adherent bipolar patients reasons for non-adherence were greater in number than reasons for adherence, compared to adherent bipolar patients. These findings support the theoretical foundation of the ROMI, which was developed drawing heavily from the Health Belief Model[24]. Furthermore, these findings highlight the importance of subjective attitudes in predicting treatment adherence.

Despite the potential utility of the Health Belief Model in assessing subjective attitudes to help improve treatment adherence, the majority of previous research into non-adherence in bipolar disorder has focused on objective factors including demographic variables, clinical severity, and treatment factors such as dosing, and the presence of side effects. There is only a very limited literature on the use of the ROMI in assessing subjective aspects of treatment

adherence and non-adherence in populations with bipolar disorder.[14] Adams and Scott report that among a group of individuals suffering from severe affective disorders, fear of relapse and greater perceived severity of illness was strongly associated with treatment adherence.[14]

In the study reported here fear of relapse was the strongest predictor for adherence. (OR: 7.8, 95% CI: 2.0, 30.3, p=.0017). Perhaps even more important than predictors of adherence, is identification of those factors that pose barriers to adherence—reasons for non-adherence. In our study, the belief that that medications are unnecessary had the strongest influence for non-adherence. (OR: 15.1, 95% CI: 3.8, 60.9, p<.0001). Additional important reasons for non-adherence were lack of perceived benefit of medications, negative effects on physical appearance and medication-related interference with achieving one's life goals.

An understanding of reasons for non-adherence (and adherence) for a specific individual may allow for the use of interventions that can be "customized" for that individual and which take advantage of the individual's strengths. For example, Miklowitz and colleagues[25] have demonstrated that family-focused psychoeducation improves treatment adherence in patients with bipolar disorder. It may be that individuals who have limited insight into the severity and the perceived negative impact of bipolar illness on their lives would be particularly good candidates for a therapeutic approach that involves family and significant others. Our group has had preliminary positive effects on treatment adherence as measured by the TRQ (p=.015) using a modular, tailored psychosocial intervention that identifies and addresses the specific reasons for non-adherence in a given patient with bipolar disorder (Customized Treatment Adherence Enhancement (CAE) in bipolar disorder. NIMH. R34MH078967-01, Sajatovic). For individuals with experienced side effects or fear of specific side effects, discussion with prescribing clinicians, and possible adjustment/ switching of pharmacologic treatments may be an important factor in minimizing non- or partial adherence.

The primary limitation of this study is the use of self-report for adherence assessment. In the current study, non-adherence was found to be 20% compared to prior studies suggesting rates of 40%.[1,2] Previous research has shown that patient self-report may overestimate adherence.[26] While self-report may under-report non-adherence, it is generally accepted that individuals who state that they are non-adherent can be believed.[27] Self-report has been shown to have a specificity as high as that of plasma measurement and electronic event monitoring techniques.[26] Ultimately, the use of self-report may have led to confounding in that attitudes among non-adherent individuals are being compared to attitudes among a mixed group of partially adherent, fully adherent individuals and possibly some non-adherent individuals. In addition results from this study may not generalize to more "extreme" non-adherent bipolar samples since the entire study sample in the current study was at least somewhat adherent given the participation in this study and willingness to at least accept ongoing medication prescriptions for their condition. Another limitation in the study is the cross-sectional design, which by definition fails to capture adherence behavior over a longitudinal time course.

In summary, non-adherent patients with bipolar disorder differ from adherent patients with bipolar disorder on reasons for adherence and non-adherence. Utilization of the tools that

evaluate treatment attitudes such as the ROMI or similar measures[12,14] may assist clinicians in the selection of interventions that are most likely to modify future treatment adherence.

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Table 1

Rating of Medication Influences (ROMI) scores among 140 individuals with BPD who are adherent vs. non-adherent with treatment as measured by the Tablets Routine Questionnaire (TRQ).

CHARACTERISTIC	Adherent (N=113)		Non-adherent (N=27)		Test Statistics
	N	%	N	%	
1. Perceived daily benefit	108	95.6	21	77.8	χ^2=9.53, df=1, p=.0020 **
2. Fear of relapse	105	92.9	18	66.7	χ^2=14.08, df=1, p=.0002 **
3. Side effect relief	84	74.3	13	48.1	χ^2=7.02, df=1, p=.0080 **
4. Fulfillment of life goals	90	79.6	17	63.0	χ^2=3.37, df=1, p=.0665
5. Deference to authority	88	77.9	21	77.8	χ^2=0.0001, df=1, p=.9912
6. Positive relation with clinical staff	88	77.9	17	63.0	χ^2=2.58, df=1, p=.1079
7. Outside positive opinion about taking medications	74	65.5	16	59.3	χ^2=.37, df=1, p=.5440
8. Outside opinion that current medication is better	47	41.6	12	44.4	χ^2=.07, df=1, p=.7875
9. Outside pressure/force	19	16.8	10	37.0	χ^2=5.43, df=1, p=.0198 *
Reasons for Non-Adherence					
10. No daily benefit	23	20.4	15	55.6	χ^2=13.66, df=1, p=.0002 **
11. Medications unnecessary	6	5.3	10	37.0	χ^2=21.67, df=1, p=<.0001 **
12. Never was ill	9	8.0	6	22.2	χ^2=4.63, df=1, p=.0314 *
13. Interferes with life goals	22	19.5	14	51.9	χ^2=11.96, df=1, p=.0005 **
14. Distressed by side effects	31	27.4	13	48.1	χ^2=4.34, df=1, p=.0372 *
15. Embarrassment/stigma	30	26.5	10	37.0	χ^2=1.17, df=1, p=.2784
16. Change in appearance	14	12.4	11	40.7	χ^2=11.94, df=1, p=.0005 **
17. Outside opposition to taking medications	18	15.9	7	25.9	χ^2=1.49, df=1, p=.2230
18. Access problems	23	20.4	13	48.1	χ^2=8.81, df=1, p=.0030 **
19. Substance abuse	14	12.4	9	33.3	χ^2=6.96, df=1, p=.0083 **

* = p<.05

TRQ= Tablets Routines Questionnaire. Non-adherence defined as missing 30% or more of prescribed bipolar medication treatment in the past week or past month.

** =p<.005