Adherence to Psychotropic and Nonpsychotropic Medication Among Patients With Bipolar Disorder and General Medical Conditions

Jennifer B. Levin, Ph.D., Michelle E. Aebi, M.A., Curtis Tatsuoka, Ph.D., Kristin A. Cassidy, M.A., Martha Sajatovic, M.D.

Objective: This study assessed the relationship between nonadherence to psychotropic and nonpsychotropic medications for 88 patients nonadherent to medication treatment for bipolar disorder.

Methods: This descriptive study was part of a clinical trial promoting medication adherence. Nonadherence was defined as ≥20% of days with missed doses.

Results: A majority of the sample was female and had type I bipolar disorder; 49% had hypertension, 39% had hyperlipidemia, and 69% smoked; average body mass index was 34, and 65% were obese. The median proportion of days with missed doses was 53.6% (interquartile ratio [IQR]=38.10%–73.40%) for psychotropic medications and 33.93% (IQR=13.81%–51.91%) for nonpsychotropic medications. There was a significant difference between nonadherence to psychotropic and nonpsychotropic medication for the past week ($z=-4.11$, $p<.001$) and past month ($z=-4.19$, $p<.001$). More global psychopathology was associated with nonpsychotropic nonadherence.

Conclusions: Psychotropic adherence was worse than nonpsychotropic adherence, yet both were poor. Improving adherence to cardiovascular medications is a reasonable pathway to improve cardiovascular health in this population.

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Adherence has been defined by the World Health Organization as "the extent to which a person's behaviour—taking medication, following a diet, and/or executing lifestyle changes[—]corresponds with agreed recommendations from a health care provider" (1). Nonadherence to psychotropic medication is known to be a significant problem in the treatment of bipolar disorder (2). Nonadherence estimates for medications for bipolar disorder range from 20% to 60% (2), depending on how nonadherence is measured, and is associated with negative consequences, including increased rates of relapse, poor treatment response, hospitalization, violence, incarceration, suicidal behavior, and elevated health care costs (3).

Individuals with serious mental illness, including bipolar disorder, are three times more likely than the general population to die prematurely and to have a life expectancy that is shortened by ten to 30 years (4). Approximately three-fourths of all deaths of individuals with bipolar disorder result from chronic medical illness, and more than two-thirds die of cardiovascular-related disorders (5). Cardiovascular risk factors include hypertension, diabetes, elevated lipids, smoking, alcohol misuse, obesity, inactivity, and metabolic syndrome, and people with bipolar disorder are known to have notably higher rates of these risk factors compared with the general population (5).

Nonadherence in bipolar disorder extends to all medication types; however, data are sparse regarding the relationship between medication-taking behavior for psychotropic and nonpsychotropic medication by the same individual in this population (6). Furthermore, the results are inconsistent on adherence to psychotropic and nonpsychotropic medication in other psychiatric populations (6,7). Finally, few studies have looked at adherence to nonpsychotropic medications among individuals known to be nonadherent to their psychotropic medications. This report describes general medical comorbidities and cardiovascular risk factors of individuals who are nonadherent in regard to use of their medications for bipolar disorder. The study assessed the relationship between adherence to psychotropic and nonpsychotropic medications among these individuals. We hypothesized that patients with bipolar disorder who are nonadherent to psychotropic medication would also be nonadherent to nonpsychotropic medication.

METHODS

These descriptive data are part of a larger, randomized controlled trial funded by the National Institute of Mental Health and intended to promote bipolar medication adherence. The trial tested a psychosocial intervention versus an

educational intervention (control group) with poorly adherent individuals with bipolar disorder. Study inclusion criteria included having either type I or type II bipolar disorder, as confirmed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; 8); bipolar disorder of at least two years' duration; treatment with at least one evidence-based medication to stabilize mood for at least six months (lithium, anticonvulsant, or antipsychotic mood stabilizer); and 20% or more nonadherence to current bipolar medication treatment for either the past week or past month, as measured by the Tablets Routine Questionnaire (TRQ; 9). The 20% cutoff was chosen on the basis of expert consensus guidelines on adherence by patients with serious mental illness (10).

Demographic and clinical data, including substance abuse history, were collected via an interview-based demographic questionnaire and the SCID. Data were gathered for both past-week and past-month self-reported nonadherence. Past-week nonadherence was used because recall over shorter periods such as this one is likely to be more accurate than recall over a longer period. Past-month nonadherence was used to identify individuals who are adherent for relatively short periods but may have difficulty adhering for periods of a month or longer. Study inclusion criteria were purposely broad in order to be generalizable to typical patients with bipolar disorder. Only individuals who were unable to participate in study procedures, who were unable or unwilling to provide informed consent, and who were at immediate risk of harm to self or others were excluded. In this descriptive study, the data analysis focused on baseline data and did not assess intervention effects.

The TRQ is a self-report measure for identifying nonadherence for the past seven and past 30 days (3). It correlates with past-week and past-month nonadherence and has been shown to correlate highly with lithium levels (9). The proportion of days with missed doses of a given medication was assessed for each foundational oral bipolar medication prescribed. For individuals who were taking one or more foundational medications, an average was calculated in order to gather information on the full bipolar disorder treatment regimen. We did not track nonadherence to antidepressant drugs because they are often prescribed sporadically to target acute symptoms and are not considered to be maintenance medication for bipolar disorder. Nonadherence was calculated for each nonpsychotropic medication prescribed. In addition, average nonpsychotropic past-week and past-month nonadherence was calculated. Data on comorbid medical conditions were collected with the self-report version of the Charlson Comorbidity Index (11).

Self-report data were gathered via structured interview to identify the presence or absence of hypertension, hyperlipidemia, diabetes, smoking, number of daily cigarettes, and body mass index (BMI). Obesity was defined as having a BMI of ≥30. The Brief Psychiatric Rating Scale (BPRS) measured global psychopathology (12), the Montgomery-Asberg Depression Rating Scale (MADRS) measured depression symptoms (13), and the Young Mania Rating Scale (YMRS) measured mania symptoms (14). Total scores on the BPRS range from 18 to 126 and total scores on both the MADRS and the YMRS range from 0 to 60; higher scores on the three scales indicate more severe symptoms.

The study was approved by the local institutional review board, and all study participants provided written informed consent. Data were collected between October 2012 and November 2014.

Sample demographic characteristics and clinical characteristics were summarized with descriptive statistics. Wilcoxon signed-rank tests were conducted to compare within-subject nonadherence to psychotropic and nonpsychotropic medications. Two-tailed Spearman correlation coefficients were calculated for nonadherence to psychotropic and nonpsychotropic medications, as measured by the TRQ, and for number of medications prescribed. Additional two-tailed Spearman correlation coefficients were calculated for nonadherence to nonpsychotropic medications, with number of psychiatric hospitalizations, years of illness, and BPRS score. Mann-Whitney U tests were run for comparing cardiovascular risk factors with years of illness and global psychopathology (BPRS scores). All statistical analyses were performed with IBM SPSS Statistics 22.

RESULTS

Participants had a mean±SD age of 46.16±8.98; education averaged 12.25±2.16 years. Most participants were female (73%, N=64) and African American (71%, N=60) and had type I bipolar disorder (74%, N=65); 56% (N=49) were unable to work because of a disabling condition. Participants had moderate global psychopathology (BPRS score of 36.56±8.39, median=37.00, interquartile ratio [IQR]= 31.25–42.00), depression (MADRS score of 20.88±8.94, median=21.00, IQR=15.50–27.00), and mania (YMRS score of 8.97±5.10, median=8.00, IQR=5.00–11.00). On average, each participant had 5.14±8.99 lifetime psychiatric hospitalizations (median=3.00, IQR=.75–5.00). Mean bipolar disorder age of onset was 19.84±9.58 (median=18.00, IQR=13.75–24.25). Data were missing for some individuals for BMI (N=14) and for smoking, hypertension, and hyperlipidemia (N=11) because these variables were added after the start of data collection.

The most prevalent health problems were hypertension (49%, N=38), rheumatologic diseases (49%, N=43), respiratory diseases (42%, N=37), hyperlipidemia (39%, N=30), and diabetes (27%, N=24). With regard to additional cardiovascular risk factors, 69% (N=53) were smokers, with an average of 9.77±7.48 cigarettes smoked daily, and 13% (N=10) were abusing alcohol. Average BMI was 33.81±8.71, and 65% (47 out of 72) of the sample were obese. Among individuals with one or more chronic medical conditions (N=73), 54% (N=35) had hypertension, 43% (N=28) had hyperlipidemia, 72% (N=47) were smokers, 66% (N=41) were obese, 30% (N=22) had diabetes, and 13% (N=9) were abusing alcohol.

TABLE 1. Medication adherence among patients with bipolar disorder and poor adherence[a]

Adherence characteristic	N	M	SD	Median	Interquartile range
Bipolar disorder medications					
Past week average	88	60.26	25.80	57.14	42.86–76.79
Past month average	85	54.96	24.71	50.00	33.33–70.00
Nonpsychotropic medications					
Past week average	62	40.38	30.10	37.86	14.29–57.14
Past month average	61	33.94	26.30	30.00	13.33–46.67

[a] As reported on the Tablets Routine Questionnaire, on which possible scores range from 0 to 100, with higher scores indicating more nonadherence

The median number of prescribed foundational bipolar medications was 1 (IQR=1.00–2.00, M=1.50±.84), with 66% (N=58) taking one drug, 24% (N=21) two drugs, and the remaining 10% (N=9) taking three or more medications. Twenty-five individuals (28%) were not taking any nonpsychotropic medications, and ten (11%) were taking six or more. Of 63 persons prescribed nonpsychotropics, 35 (56%) were taking antihypertensives and 45 (71%) were taking antihypertensive, diabetes, or cholesterol medications or a combination thereof. Of the 73 individuals with one or more chronic medical conditions, the number of prescribed nonpsychotropic medications ranged from 0 to 10, with a median of 3 (3.33±1.77, IQR=2.00–5.00). Fifteen (21%) people with one or more chronic medical conditions were not taking any psychotropic medications, and nine (12%) were taking six or more. Of the 63 persons prescribed nonpsychotropics, 57% (N=36) indicated that they had trouble taking them regularly.

The median proportion of days with missed bipolar medication doses was 53.6% (IQR=38.10%−73.40%) when we averaged past-week and past-month data. Of those taking nonpsychotropic medications, the median proportion of days with missed doses was 33.93% (IQR=13.81%−51.91%) when we averaged past-week and past-month data. There was a significant difference between patient nonadherence to psychotropic and nonpsychotropic medication for past week ($z=-4.11$, $p<.001$) and past month ($z=-4.19$, $p<.001$) (Table 1).

There was no significant correlation between psychotropic and nonpsychotropic nonadherence for past week, but there was a trend for past month ($r_s=.23$, df=59, $p=.08$). There were no significant correlations between number of bipolar medications prescribed and psychotropic nonadherence for either the past week or the past month or between number of nonpsychotropic medications prescribed and nonpsychotropic nonadherence for the past week or the past month.

Correlations between psychiatric hospitalizations and nonpsychotropic TRQ for the past week ($r_s=.28$, df=58, $p=.03$) and the past month ($r_s=.25$, df=57, $p=.05$) were significant, as was the correlation between BPRS score and nonpsychotropic nonadherence for the past month ($r_s=.26$, df=59, $p=.04$) with a trend for the past week ($r_s=.23$, df=60, $p=.07$). The total years of illness was greater for individuals with diagnosed hypertension (median=31.0, IQR=23.00–36.50) than for those without hypertension (median=25.0, IQR=15.00–29.50; $U=470.5$, $p=.01$).

DISCUSSION AND CONCLUSIONS

In this well-characterized sample of 88 patients with bipolar disorder, poor adherence to foundational medication for bipolar disorder ranged from 50% to 57%, whereas poor adherence to nonpsychotropic medication ranged from 30% to 38%. The literature regarding the relationship between nonadherence to psychotropic versus nonpsychotropic medication among patients with bipolar disorder is sparse and is inconsistent with other psychiatric populations. Dolder and colleagues (7) found that adherence was equally problematic for antipsychotic and somatic medications among individuals with serious mental illness. Okwemba and colleagues (6) found that adherence to nonpsychotropics was not consistently better or worse than adherence to psychotropic medication. The results of our study indicated that adherence to psychotropic and adherence to nonpsychotropic medication were not highly associated. We found that adherence to nonpsychotropic medications, although somewhat better than adherence to bipolar medications, was still low and thus is a reasonable target for intervention. Furthermore, nonpsychotropic nonadherence was related to number of psychiatric hospitalizations and global psychopathology. This suggests that mental health instability may affect one's ability to manage nonpsychotropic medication regimens. It is also possible that adherence to nonpsychotropics was better than psychotropic adherence, given that patients were recruited for a trial to address nonadherence to bipolar medications.

Top medical conditions in our poorly adherent sample were hypertension, rheumatologic and respiratory conditions, hyperlipidemia, and diabetes. Reported rates of hypertension, hyperlipidemia, and cigarette smoking in this sample were similar to those found in the literature for the bipolar population (15) and much greater than for the general population (5).

Although this study did not gather participants' reasons for differences in taking psychotropic and nonpsychotropic medications, one participant volunteered that he made a point to consistently take his HIV medication, but no other medications, on a regular basis. In addition, most participants reported difficulty taking their nonpsychotropic medications regularly. Future research on personalized adherence enhancement approaches should include qualitative methods to provide specific reasons why one may or may not take a given type of medication.

Notable limitations of the study include a potential lack of generalizability because the trial participants were largely urban, African-American, female research volunteers recruited for being nonadherent to their psychotropic medication. In addition, reasons for nonadherence to each type of medication were not collected, and we relied on the available literature to

determine factors that predict nonadherence. Finally, the self-reported nonadherence data may lack reliability. In the future, it will be important to include at least one other method, such as pill counts or electronic monitoring devices, to measure adherence.

Although these participants were preselected for psychotropic nonadherence, there may be some patients with bipolar disorder who are adherent to psychotropics and nonadherent to nonpsychotropics, or alternatively, adherent to both types. However, our sample was selective and possibly biased, thus limiting generalizability. Despite this, the high rates of cardiovascular factors in our sample suggest that addressing poor adherence to cardiovascular medications is an area worth targeting to reduce cardiovascular risk and premature mortality in bipolar disorder.

AUTHOR AND ARTICLE INFORMATION

Dr. Levin and Dr. Sajatovic are with the Department of Psychiatry and Dr. Tatsuoka is with the Department of Neurology, Case Western Reserve University School of Medicine, Cleveland, Ohio (e-mail: jennifer.levin@uhhospitals.org). Dr. Levin, Dr. Tatsuoka, and Dr. Sajatovic are also with the Neurological and Behavioral Outcomes Center, University Hospitals Case Medical Center, Cleveland, where Ms. Aebi and Ms. Cassidy are with the Department of Psychiatry.

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