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Medication Adherence for Psychotropic and Non-Psychotropic Medication in Patients with Bipolar Disorder and Medical Morbidities

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Abstract

Objective—This descriptive study assessed the relationship between non-adherence to psychotropic and non-psychotropic medications in 88 patients non-adherent to bipolar treatment.

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

Results—The majority was female with Type I bipolar disorder, 49% had hypertension, 39% hyperlipidemia, 69% smoked, average BMI was 34, and 64% were obese. Median number of days with missed doses was 53.57% (IQR= 38.10–73.40%) and 33.93% (IQR= 13.81–51.91%) for psychotropics and non-psychotropics, respectively. There is a significant difference between non-adherence to psychotropic and non-psychotropic medication for past week ($Z=-4.11$, $p<.001$) and past month ($Z=-4.19$, $p<.001$). More global psychopathology related to non-psychotropic non-adherence.

Conclusions—Psychotropic adherence was worse than non-psychotropic adherence, yet both were poor. Improving adherence to CV medications is a reasonable pathway to improve CV health in this population.

Keywords

medication adherence; medical morbidity; psychotropic medication; non-psychotropic medication; bipolar disorder

Disclosures and Conflicts of Interest

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Adherence is 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.” Non-adherence to psychotropic medication is known to be a significant problem in the treatment of bipolar disorder (1). Non-adherence estimates for bipolar medications range from 20% to 60% (1), depending on how non-adherence is measured, and is associated with negative consequences including increased rates of relapse, poor treatment response, hospitalization, violence, incarceration, suicidal behavior, and elevated healthcare costs (2).

Individuals with serious mental illness including bipolar disorder are three times more likely to die prematurely than the general population and have a life expectancy that is shortened by 10–30 years (3). Approximately three-fourths of all deaths in individuals with bipolar disorder result from chronic medical illness and more than two-thirds die of cardiovascular (CV) related disorders (4). CV risk factors include hypertension, diabetes, elevated lipids, smoking, alcohol, obesity, inactivity, and metabolic syndrome, and it has been well documented that those with bipolar disorder have notably higher rates of these risk factors than the general population (4).

Non-adherence in bipolar disorder extends to all medication types; however, the data are sparse regarding the relationship between medication taking behavior for psychotropic and non-psychotropic medication in the same individual in this population (5). Furthermore, the results are inconsistent on adherence to psychotropic and non-psychotropic medication in other psychiatric populations (5, 6). Finally, few studies have looked at adherence to non-psychotropic medications in individuals known to be non-adherent to their psychotropic medications. The current study describes medical morbidities and CV risk factors in individuals who are non-adherent with their medications for bipolar disorder and assesses the relationship between adherence to psychotropic and non-psychotropic medications in these individuals. It was hypothesized that patients with bipolar disorder who are non-adherent to psychotropic medication would also be non-adherent to non-psychotropic medication.

Methods

These descriptive data are part of a larger, NIMH-funded randomized controlled trial testing a psychosocial intervention intended to promote bipolar medication adherence versus an educational control in poorly-adherent individuals with bipolar disorder. Study inclusion criteria include having either type I or type II bipolar disorder as confirmed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (7), bipolar disorder for 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 non-adherence with current bipolar medication treatment for either the past week or past month as measured by the Tablets Routine Questionnaire (8). The 20% cutoff was chosen based on the expert consensus guidelines on adherence in patients with serious mental illness (9). 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 non-adherence.

Past week non-adherence was utilized as recall for shorter periods are likely to be more accurate. Past month non-adherence was utilized to capture individuals who are adherent for relatively short periods of time but may have more difficulty adhering for longer periods of time. Study inclusion criteria were purposely broad in order to be generalizable to real-world patients with bipolar disorder. Only individuals who were unable to participate in study procedures, unable/unwilling to provide informed consent, and those at immediate risk of harm to self or others were excluded. In the current descriptive study, the data analysis focused on baseline data and did not assess intervention effects.

Tablets Routine Questionnaire (TRQ) – This self-report measure identifies non-adherence for the past 7 and past 30 days (2). It correlates with past week and past month non-adherence and has been shown to correlate highly with lithium levels (10). The percentage of days with missed doses of a given medication was assessed for each foundational oral bipolar medication prescribed for ≥3 months. For individuals who were on ≥1 foundational medication, an average was calculated in order to gather information on the full bipolar disorder treatment regimen. We did not track non-adherence to antidepressant drugs as they are often prescribed sporadically to target acute symptoms and are not considered to be maintenance medication for bipolar disorder. Non-adherence was calculated for each non-psychotropic medication prescribed ≥3 months. Additionally, average non-psychotropic past week and past month non-adherence was calculated. Data on comorbid medical conditions were collected using 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 ≥30. The Brief Psychiatric Rating Scale (BPRS) measured global psychopathology (12), the Montgomery-Asberg Depression Rating Scale (MADRS) measured depression symptoms (13), and Young Mania Rating Scale (YMRS) measured mania symptoms (14). Total scores on the BPRS range from 18 to 126 and total scores on both MADRS and YMRS range from 0–60.

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 demographics and clinical characteristics were summarized with descriptive statistics. Wilcoxon Signed-Rank Tests were conducted to compare within-subject non-adherence to psychotropic and non-psychotropic medications. Two-tailed Spearman correlation coefficients were calculated for non-adherence to psychotropic with non-psychotropic medications and number of medications prescribed with TRQ. Additional two-tailed Spearman correlation coefficients were calculated for non-psychotropic TRQ with number of psychiatric hospitalizations, years of illness, and BPRS. Mann-Whitney U tests were run comparing CV risk factors with years of illness and global psychopathology (BPRS). All statistical analyses were performed using IBM SPSS Statistics 22.

Results

Participants had a mean age of 46.16 ± 8.98 and mean years of education was 12.25 ± 2.16. The majority was female (73%), African-American (65%), disabled (56%) with Type I bipolar disorder (74%). Participants evidenced moderate global psychopathology (BPRS M= 36.56 ± 8.39; median = 37.00, IQR = 31.25–42.00), depression (MADRS M= 20.88 ± 8.94, median= 21.00, IQR= 15.50–27.00), and mania (YMRS M= 8.97 ± 5.10, median= 8.00, IQR= 5.00–11.00). Average psychiatric hospitalizations was 5.14 ± 8.99 (median= 3.00, IQR= .75–5.00). Mean age of bipolar disorder onset was 19.84 ± 9.58 (median= 18.00, IQR= 13.75–24.25). There were missing data on BMI (N=16), smoking, hypertension, and hyperlipidemia (N=11) as these variables were added after the start of data collection.

The most prevalent health problems were: hypertension (49%), rheumatologic diseases (49%), respiratory diseases (42%), hyperlipidemia (39%), and diabetes (27%). With regard to additional CV risk factors, 69% were smokers with an average of 9.77 ± 7.48 cigarettes smoked daily and 13% were abusing alcohol. Average BMI was 33.81 ± 8.71 and 64% (45/70) were obese. Among individuals with ≥1 chronic medical condition (N=73), 54% had hypertension, 43% had hyperlipidemia, 72% were smokers, 66% were obese, 30% had diabetes, and 13% were abusing alcohol.

The median number of prescribed foundational bipolar medications was 1 (IQR= 1.00–2.00, M=1.50 ± .84) with 66% on one drug, 24% on two drugs, and the remaining 10% on ≥3. Twenty-five individuals (28%) were not taking any non-psychotropic medications and 10 (11%) were taking ≥6. Of those prescribed non-psychotropics (N=63), 35 (56%) were taking antihypertensives and 45 (71%) were taking either antihypertensives, diabetes or cholesterol medications, or a combination thereof. Of those diagnosed with ≥1 chronic medical condition (N=73), the number of prescribed non-psychotropic medications ranged from 0 to 10 with a median of 3 (IQR= 2.00–5.00) M=3.33 ± 1.77). Fifteen (21%) people with ≥1 medical conditions were not taking any psychotropic medications and 9 (12%) were taking ≥6. Of those prescribed non-psychotropics (N=63), 57% indicated that they had trouble taking them regularly.

The median number of days with missed bipolar medication doses was 53.57% (IQR= 38.10–73.40%), when averaging past week and past month. Of those taking non-psychotropic medications, the median of days with missed doses was 33.93% (IQR= 13.81–51.91%), when averaging past week and past month. There is a significant difference between patient non-adherence to psychotropic and non-psychotropic medication for past week (Z= −4.11, p<.001) and past month (Z= −4.19, p<.001) (see Table 1).

There was no significant correlation between psychotropic and non-psychotropic non-adherence for past week (r_s=.16, df= 60, p=.23) but there was a trend for past month (r_s=.23, df= 59, p=.08). There were no significant correlations either between number of bipolar medications prescribed and psychotropic non-adherence for past week (r_s= −.04, df= 86, p=.74) or month (r_s=.08, df= 83, p=.47) or between number of non-psychotropic medications prescribed and non-psychotropic non-adherence for past week (r_s= −.10, df= 60, p=.45) or month (r_s= −.09, df= 59, p=.50).

Correlations between psychiatric hospitalizations and non-psychotropic TRQ for past week (r_s=.28, df= 58, p=.03) and past month (r_s= .25, df= 57, p=.05) were significant, as was BPRS with non-psychotropic non-adherence for past month (r_s=.26, df= 59, p=.04) with a trend for past week (r_s=.23, df= 60, p=.07). Years of illness was greater in individuals with diagnosed hypertension (Median=31.0, IQR=23.00–36.50) than in 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 with foundational medication for bipolar disorder ranged from 50–57%, while poor adherence with non-psychotropic medication ranged from 30–38%. The literature regarding the relationship between non-adherence to psychotropic versus non-psychotropic medication in bipolar patients is sparse and inconsistent in other psychiatric populations. Dolder et al. (6) found adherence was equally problematic for antipsychotic and somatic medications in individuals with serious mental illness while Okwembe et al. (5) found that adherence for non-psychotropics was not consistently better or worse than psychotropic medication. The results of our study indicated that adherence to psychotropic and non-psychotropic medication are not highly associated. We did find that adherence to non-psychotropic medications, although somewhat better than adherence to bipolar medications, was still low and thus is a reasonable target for intervention. Furthermore, non-psychotropic non-adherence was related to number of psychiatric hospitalizations and global psychopathology. This suggests that mental health instability may impact one's ability to manage non-psychotropic medication regimens. It is also possible that adherence for non-psychotropics was better than psychotropic adherence given that patients were recruited for a trial to address non-adherence 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 are similar to those found in the literature for the bipolar population (15) and much greater than for the general population (4).

While this study did not gather participants' reasons for differences in taking psychotropic and non-psychotropic medications, one participant volunteered that he made a point to consistently take his HIV medication but no other medications on a regular basis. Additionally, the majority of participants reported difficulty taking their non-psychotropic 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 as the trial participants were largely urban, African-American female research volunteers recruited for being non-adherent to their psychotropic medication. Additionally, reasons for non-adherence to each type of medication were not collected and we relied on the available literature to determine factors that predict non-adherence. Finally, the self-report non-

adherence data may lack reliability. In the future, it will be important to include at least one other method to measure adherence such as pill counts or electronic monitoring devices.

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

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Table 1

Adherence Characteristics to Psychotropic and Non-Psychotropic Medication in Poorly-Adherent Patients with Bipolar Disorder

Adherence Characteristics	N	Mean	SD	Median	Interquartile range
Past week average TRQ* for bipolar medications	88	60.26	25.80	57.14	42.86–76.79
Past month average TRQ for bipolar medications	85	54.96	24.71	50.00	33.33–70.00
Past week average TRQ for non-psychotropic medications	62	40.38	30.10	37.86	14.29–57.14
Past month average TRQ for non-psychotropic medications	61	33.94	26.30	30.00	13.33–46.67

* Tablets Routine Questionnaire, possible scores range from 0–100, with higher scores indicating more non-adherence

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