Bipolar disorder is associated with HIV transmission risk behavior among patients in treatment for HIV

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Abstract

This study examined HIV transmission risk behavior among 63 patients with bipolar disorder (BD), major depressive disorder (MDD), and no mood disorder (NMD); half had substance use disorders (SUDs). Patients with BD were more likely than others to report unprotected intercourse with HIV-negative partners and < 95% adherence to antiretroviral medications. In multivariate models, BD and SUD were independent predictors of both risk behaviors. Participants with poorer medication adherence were more likely to have detectable HIV viral loads and unprotected intercourse with HIV-negative partners. Patients with BD deserve careful evaluation and HIV prevention services to reduce HIV transmission risk behaviors.

Keywords

HIV/AIDS; bipolar disorder; HIV transmission risk behavior; mood disorders; substance dependence

INTRODUCTION

The advent of antiretroviral (ARV) medication has dramatically increased survival and quality of life for HIV-infected persons, and HIV/AIDS is now considered a chronic illness. While many individuals adopt risk reduction practices following HIV diagnosis, a substantial proportion engages in behaviors associated with HIV transmission, including unprotected intercourse with HIV-negative partners and poor adherence to antiretroviral (ARV) medications. Poor ARV medication adherence reduces the likelihood of obtaining and maintaining HIV viral suppression, increasing the risk of transmitting HIV to sex partners (1). Thus, the co-occurrence of poor ARV medication adherence and unprotected intercourse increases the risk of HIV transmission to others.

Mood disorders are disproportionately common among HIV patients and may contribute to HIV transmission risk behavior. A report from the National Epidemiologic Survey of Alcohol and Related Disorders found that the 12-month prevalence of major depressive disorder (MDD) and bipolar disorder (BD) among HIV-infected respondents was 9.0% and 10.8%, respectively, compared to 6.2% and 3.7% among HIV-negative respondents (2).

While the relationship between depression and HIV risk behavior has been extensively studied, far less is known about HIV risk behavior among persons with BD.

BD is a severe mood disorder characterized by cyclical shifts in mood, alternating between mania and depression. The constellation of manic symptoms, including euphoria, grandiosity, hypersexuality, impulsivity, and poor judgment, often results in risky behaviors. The co-occurrence of substance use disorders (SUDs), which are disproportionately high among persons with BD, may contribute to HIV risk behavior (3). While there is some evidence from HIV-negative samples that mania may be associated with sexual risk behavior (4), there has been very little research on HIV transmission risk behavior among HIV-infected persons with BD. In one recent study, HIV patients with BD were less adherent to ARV medications compared to those without BD, but sexual risk behavior was not reported (5).

The present study examined rates of HIV transmission risk behavior, specifically unprotected intercourse with HIV-negative partners and poor ARV medication adherence, among HIV patients with BD compared to HIV patients with MDD or no mood disorder (NMD). Our primary hypothesis was that these risk behaviors would be highest among patients with BD and lowest among patients with NMD. Second, we hypothesized that BD and SUD would be independent predictors of HIV transmission risk behavior, and that patients with co-occurring BD and SUD would have the highest prevalence of these behaviors. Third, we hypothesized that patients with poor adherence to ARV medications would be more likely to have detectable HIV viral loads and to engage in unprotected intercourse with HIV-negative partners, increasing the likelihood of HIV transmission to others.

METHOD

Participants and procedures

This case-control study examined HIV transmission risk behavior among three groups of HIV-infected adults defined by lifetime history of mood disorder: BD I, II, or NOS; recurrent MDD; or NMD. These groups were stratified such that approximately half of the participants in each group had a current SUD. The BD group served as the index, and for each participant with BD, a proportionate number of participants were subsequently enrolled in the MDD and NMD groups. Participants were excluded for psychotic disorders (though several had mood disorders with psychotic features), acute intoxication, and/or severe psychiatric distress.

Data collection occurred between December 2009 and September 2011. Participants were recruited via flyers posted in the waiting rooms of infectious diseases clinics and via participant referral. Following a brief telephone screening, individuals were scheduled for a 2-hour in-person screening. After a complete description of the study to participants, written informed consent was obtained. Participants then completed a psychiatric evaluation. Eligible participants returned for a 3-hour in-depth assessment, including clinical interviews, questionnaires, and neuropsychological testing. Assessments were administered in private offices by trained research assistants with bachelors or masters degrees. Participants were compensated $25 and $50 for each visit, respectively. This study was approved by the Institutional Review Board at the Medical Center.

Measures

Psychiatric diagnoses—The Mini International Neuropsychiatric Interview for BD studies, a widely used and well validated diagnostic instrument, was used to identify DSM-

IV mood, anxiety, and psychotic disorders (6). Participants with BD or MDD reported their age at first mood episode, number of mood episodes, history of suicide attempts, lifetime inpatient and outpatient psychiatric treatment, past and current use of psychiatric medications, and mood episodes in the past 12 weeks. Module E of the Structured Clinical Interview for DSM-IV was used to identify alcohol and drug use disorders (7). Urine toxicology screens were used to verify recent use of cannabis, cocaine, amphetamines, opioids, and benzodiazepines. Information from participants' medical records was used to corroborate data collected during the study visit. All cases were reviewed during group supervision with the principal investigator, a licensed clinical psychologist, and diagnoses were made by consensus.

Sexual risk behavior—The Timeline Follow-back method, which utilizes a calendar to facilitate recall, was used to assess sexual behavior in the past 3 months (8). For each occasion of vaginal or anal intercourse, participants indicated the HIV status of their partner and whether or not a condom was used. Partners of unknown status were categorized as negative. We computed the number of days on which participants engaged in unprotected intercourse with an HIV-negative partner.

Medication adherence—A visual analogue scale (VAS) was used to assess adherence to ARV and psychiatric medications (9). Participants were asked to "put a cross on the line showing your best guess about how much of each medication you took in the past 4 weeks." The VAS tool obtains estimates that parallel unannounced ARV pill counts and predicts HIV viral load (9). Mean percent adherence across all ARV and psychiatric medications were computed.

HIV disease characteristics—Participants provided information on date of HIV diagnosis, indicators of disease progression, and treatment history. Data on medical diagnoses, current medications, and lab results were abstracted from participants' medical records. This included the HIV RNA viral load and CD4+ T-cell count most proximate to the study visit. An undetectable viral load was defined as < 400 copies/mL.

Data analysis

Data anlaysis was conducted in three steps using SPSS 19.0. First, we compared the groups on rates of HIV transmission risk behavior using χ^2 tests. Sexual risk was defined as any unprotected intercourse with HIV-negative partners in the past 3 months. Poor ARV medication adherence was defined as < 95% adherence in the past month. Second, we used generalized linear modeling to examine the independent relationships of BD and SUD to HIV risk behavior. Sexual risk was defined as number of days of unprotected intercourse with HIV-negative partners. Negative binomial regression was used to account for potential overdispersion in this variable. Poor ARV adherence was defined as percent missed doses. The BD*SUD interaction term was added in a separate step to the final regression models. Third, we examined the relationships between ARV medication adherence, HIV viral load, and sexual risk using t and χ^2 tests.

RESULTS

The sample included 63 patients with BD (n= 22), MDD (n= 21), and NMD (n= 20). Participants were 65.1% male and 90.5% African American. They had a mean age of 45.3 years (SD= 7.05) and a mean of 12.54 (SD=2.53) years of education. The majority (84.1%) were currently unemployed, with 55.6% on disability. Most (89.9%) were currently single, and 55.6% identified as heterosexual. Participants had been diagnosed with HIV for 6 months to 29 years (M= 11.8, SD= 7.2), with a mean age at diagnosis of 33.5 years (SD=

8.3). Nearly all (98%) were prescribed ARV medications, and 37% were diagnosed with AIDS. Current CD4+ T-cell counts ranged from 37 to 1,497 (M= 536.1, SD= 320.2), and 32% had a detectable HIV viral load. By design, approximately half had current substance dependence (88% cocaine, 21% alcohol, 18% cannabis). The groups were comparable on demographic and HIV disease characteristics, except that NMD patients were significantly older ($F_{(60,2)}$= 5.12, p < .01).

Among patients with BD and MDD, all had experienced recurrent mood episodes, 91% had their first episode before being diagnosed with HIV, and 84% had a mood episode in the past 12 weeks. Patients with BD had an earlier age of onset of illness [14.3 (6.4) vs. 23.1 (10.2); $t_{(39)}$= 3.36, p= .002], and were more likely to have had 5 mood episodes (95% vs. 68%; $\chi^2_{(1)}$= 5.56, p= .018), a previous suicide attempt (73% vs. 24%; $\chi^2_{(1)}$= 10.29, p= .001) ,and an inpatient psychiatric hospitalization (77% vs. 29%; $\chi^2_{(1)}$= 10.24, p= .001). Most participants (88%) were currently prescribed psychiatric medications. Participants with BD were more likely to be prescribed mood stabilizers (41% vs. 0%; $\chi^2_{(1)}$= 10.87, p= .001) and atypical antipsychotics (64% vs. 5%; $\chi^2_{(1)}$= 16.40, p < .001), and participants with MDD were more likely to be prescribed antidepressants (91% vs. 68%; $\chi^2_{(1)}$= 3.23, p= .072). Adherence to psychiatric medications was poor in both groups (M= 69.58, SD= 38.88); 16% had not filled their prescriptions in the past month.

Patients with BD were more likely than patients with MDD/NMD to report unprotected intercourse with HIV-negative partners (32% vs. 7%, $\chi^2_{(1)}$= 6.44, p= .011). Among participants who reported this behavior, patients with BD did so on more days than patients with MDD/NPD [17.3 (SD= 19.5) vs. 4.7 (SD= 4.7)]. In a multivariate regression, BD and SUD were independently associated with days of unprotected intercourse with HIV-negative partners (Table 1). Furthermore, the BD*SUD interaction was significant, suggesting that the relationship between BD and unprotected intercourse was greater among participants with compared to without SUD.

Patients with BD also reported taking their ARV medications less frequently than those with MDD/NMD [M= 83.5% (21.9) vs. 92.8% (13.3); $t_{(58)}$= 2.05, p= .045), and they were more likely to report poor (< 95%) adherence (67% vs. 32%, $\chi^2_{(1)}$= 6.90, p= .009). In a multivariate regression, BD and SUD were independently associated with percent adherence (Table 1). The BD*SUD interaction was not significant.

As expected, adherence to ARV was poorer in participants with detectable viral loads compared to undetectable viral loads [M= 70.8% (34.7) vs. 93.9% (9.9); $t_{(60)}$= 4.05, p < .001]. Patients with BD were more likely than those with MDD/NMD to have detectable viral loads (41% vs. 15%; $\chi^2_{(1)}$= 5.50, p= .020). Furthermore, adherence to ARV medications was poorer among participants who reported unprotected intercourse with HIV-negative partners compared to those who did not [M= 72.5% (36.8 vs. 89.6% (18.9); $t_{(60)}$= 2.20, p= .032]. Thus, participants who engaged in risky sexual behavior were also more likely to have detectable viral loads, increasing the likelihood of HIV transmission.

Finally, we examined the relationships between HIV transmission risk behavior, psychiatric symptoms, and adherence to psychiatric medications. Participants who reported any unprotected intercourse with HIV-negative partners had greater symptoms of mania [1.41 (0.91) vs. 0.73 (0.66); $t_{(60)}$= 2.82, p= .007] and depression [1.54 (1.07) vs. 0.86 (0.83); $t_{(60)}$= 2.24, p= .029]. Similarly, participants who reported < 95% ARV adherence had greater symptoms of mania [1.02 (0.81) vs. 0.65 (0.62); $t_{(59)}$= 2.08, p= .042] and depression [1.21 (0.98) vs. 0.73 (0.74); $t_{(59)}$= 2.19, p= .033]. Furthermore, adherence to psychiatric medications was poorer among participants who engaged in unprotected interecourse with HIV-negative partners compared to those who did not [44.7% (44.1) vs. 77.3% (34.4);

t(36)= 2.33, p=.026] and among participants who reported < 95% adherence to ARVs compared to those who did not [57.2% (39.2) vs. 83.9% (35.2); t(35)= 2.17, p= .037], and it was negatively correlated with manic symptoms among patients with BD (r= −0.46, p= .043). These findings suggest that treatment of psychiatric symptoms may decrease HIV transmission risk behavior among HIV patients with BD.

DISCUSSION

We found that HIV patients with BD were more likely than those with MDD or NMD to engage in HIV transmission risk behavior. Specifically, one third of patients with BD reported unprotected intercourse with HIV-negative partners, and nearly two thirds reported < 95% adherence to ARV medications. Patients with co-occurring BD and SUD were at highest risk for these behaviors, with each disorder contributing significantly in multivariate models. Patients who engaged in unprotected intercourse were also more likely to be poorly adherent to ARV medications, which was associated with higher HIV viral loads, thus increasing the risk of transmission to others.

While previous research with HIV-negative samples supports a relationship between BD and risky sex, our study is among the first to examine HIV transmission risk behaviors in HIV-positive patients with BD. Symptoms of mania, including euphoric mood, grandiosity, increased energy, and impulsivity, may lead to risk behavior. Hypersexuality is one potential symptom of mania and may play a contributing role, but hypersexuality does not itself constitute a manic episode nor does it necessarily lead to sexual risk behavior. Acute mania is unlikely to fully explain the relationship between BD and risk behavior (4). Impulsivity, a core feature of BD, may make patients with BD more vulnerable to risky behavior. Previous research has found that patients with BD are more impulsive than controls even during periods of euthymia (10). As expected, patients with SUD were more likely to engage in HIV transmission risk behavior, but BD remained significantly associated with HIV transmission risk behavior even after accounting for SUD in the multivariate models. In fact, the co-occurrence of BD and SUD may have a synergistic relationship, at least on sexual risk behavior. Further research is needed to elucidate the mechanisms underlying the relationship between BD and HIV risk behavior, and the exacerbating role of SUD.

BD typically requires long-term treatment with mood stabilizing medications to prevent recurrence of manic and depressive episodes. Previous research with HIV-infected persons with BD has found that those who fill their prescriptions for psychiatric medications in a given month are more likely to fill their ARV medications in the subsequent month (11). In this study, we found that better adherence to psychiatric medications was associated with lower HIV transmission risk behaviors, lending support to the hypothesis that mental health treatment is an important component of HIV prevention.

Unfortunately, many persons with BD are not connected with the mental health system and receive sub-optimal psychiatric treatment (12) . In our sample, over a quarter of BD patients were not taking mood stabilizers. HIV clinics may provide an important opportunity to link patients with psychiatric disorders to mental health treatment. However, this puts a heavy burden on HIV care providers who may not have formal training in psychiatric assessment. In general medical settings, assessment of mood elevation is not routine practice, and BD is often mistaken as unipolar depression (12). Utilization of brief screeners and consultation-liasion services may facilitate the identification and monitoring of mania among HIV patients, but integration of mental health and substance abuse treatment within HIV clinics has the greatest potential to improve medical outcomes and reduce HIV transmission risk behavior.

Our results should be interpreted in light of several limitations. First, our sample size was fairly modest, but yielded robust results. Second, due to the cross-sectional design, it is not possible to infer causality or direction of effects. Third, we recruited a convenience sample, and results may not generalize to the broader population of HIV patients with mood disorders. Additional research with larger, more diverse samples and longitudinal designs is needed to replicate and extend these findings.

Our study also had several noteworthy strengths. First, we conducted in-depth assessments with participants, utilizing clinical interviews, self-report questionnaires, and medical record review to establish psychiatric diagnoses, and we used well-validated measures of risk behavior. Second, we included biological measures of HIV viral load to corroborate self-reports of ARV adherence. Third, we enrolled two comparison groups – patients with recurrent MDD of comparable severity and patients with no history of mood disorders. In addition, we stratified the groups equally by SUD, so that we were able to test the independent relationships of BD and SUD with HIV transmission risk behaviors. Our findings lay the groundwork for a prospective study of HIV patients with mood disorders to identify the relationship between psychiatric symptoms, active substance abuse, and psychiatric treatment on HIV transmission risk behavior.

HIV patients with BD, particularly those with co-occurring SUD, appear to be at high risk for engaging in behaviors associated with transmission of HIV to others. Patients presenting for HIV care require careful psychiatric evaluation, ongoing monitoring of mood symptoms, and access to high-quality mental health treatment. Adjunctive HIV prevention interventions may be necessary to support HIV risk reduction. With a few exceptions, the efficacy of secondary prevention interventions have not been tested among persons with mood disorders. Targeted interventions that address the unique challenges associated with BD have the potential to improve health outcomes in this high risk group, while also reducing the continued spread of HIV within vulnerable populations.

Acknowledgments

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Table 1

Summary of multivariate regression models predicting HIV transmission risk behavior

	Days of unprotected intercourse with HIV-negative/unknown partners			Percent missed doses of ARV medications		
	Beta (SE)	Wald χ^2	p-value	B (SE)	Wald χ^2	p-value
Univariate models						
Bipolar disorder	2.47 (0.40)	37.35	< .001	12.03 (6.05)	3.95	.047
Substance use disorder	1.80 (0.40)	20.41	< .001	14.05 (5.56)	6.39	.011
Multivariate model						
Bipolar disorder	2.11 (0.42)	24.73	< .001	12.29 (5.73)	4.59	.032
Substance use disorder	1.06 (0.50)	5.52	.019	14.25 (5.36)	7.05	.008
Bipolar disorder* Substance use disorder	3.63 (0.93)	15.37	< .001	16.16 (11.14)	2.11	.15

Note: All models controlled for age.