Prevalence and Clinical Implications of Interactive Toxicity Beliefs Regarding Mixing Alcohol and Antiretroviral Therapies among People Living with HIV/AIDS

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Abstract

Alcohol use is a barrier to medication adherence. Beyond the cognitive effects of intoxication, people living with HIV/AIDS who believe that alcohol should not be mixed with their medications may temporarily stop taking medications when drinking. To examine the effects of alcohol-treatment beliefs on HIV treatment adherence. People living with HIV/AIDS who were receiving treatment ($n = 145$) were recruited from community and clinical services during the period between January 2006 and May 2008 to complete measures of substance use and alcohol-antiretroviral (ARV) interactive toxicity beliefs (e.g., alcohol breaks down HIV medications so they will not work). Medication adherence was monitored using unannounced telephone-based pill counts. Forty percent of participants were currently using alcohol and nearly one in four drinkers reported stopping their medications when drinking. Beliefs that mixing alcohol and medications is toxic were common among drinkers and nondrinkers, with most beliefs endorsed more frequently by non-drinkers. Hierarchical regression analysis showed that stopping ARVs when drinking was associated with treatment nonadherence over and above quantity/frequency of alcohol use and problem drinking. Beliefs that alcohol and ARVs should not be mixed and that treatments should be interrupted when drinking are common among people living with HIV/AIDS. Clinicians should educate patients about the necessity of continuing to take ARV medications without interruption even if they are drinking alcohol.

Introduction

ANTIRETROVIRAL MEDICATIONS effectively suppress HIV replication and improve the health of people living with HIV/AIDS. Optimal HIV treatment outcomes require close adherence to medication regimens.[1,2] Lapses in antiretroviral (ARV) adherence allow HIV to replicate and develop selective genetic resistance, therefore limiting the clinical benefits of treatment. Among known barriers to HIV treatment adherence are medication side effects, depression, and psychoactive substance use.[3,4] Although periodically missing doses of ARV medications can diminish their effectiveness, extended interruptions in therapy, such as occurs during drug holidays or ceasing treatment to "cleanse toxins," pose the greatest threats for developing drug resistance.[5]

Alcohol use is among the factors that have been established to interfere with consistent HIV treatment adherence. Studies show temporal and dose-response relationships between alcohol consumption and missed HIV medications,

with nonbinge drinkers missing more doses than nondrinkers, and binge drinkers missing more doses than nonbinge drinkers.[5] Nonadherence to treatment is commonly associated with even low levels of alcohol use, including drinking quantities beneath an individual's threshold for intoxication.[6] Alcohol intoxication effects memory, attention, and other basic cognitive functions that are obviously linked to missing medications. Less studied is how alcohol interrupts treatment when individuals believe they should stop taking their medications to avoid mixing them with alcohol. Beliefs that mixing alcohol with medications will lead to adverse reactions (interactive toxicity beliefs) result in patients deliberately interrupting ARV therapy. For example, Altice et al.[7] found that one in three prison inmates receiving ARVs stated that they would stop taking their medications if they started taking street drugs. Decisions to stop treatment were based on inmates' beliefs that mixing illicit drugs with ARVs would lead to adverse drug reactions. Interactive toxicity beliefs may stem from early reports of what were

indeed adverse drug interactions between the first protease inhibitors and street drugs or they may stem form the more generally held belief not to mix any prescription medications with recreational drugs. Regardless of their origins, research findings suggest that patient-initiated treatment interruptions occur in response to unfounded interactive toxicity beliefs.

Alcohol use among people living with HIV/AIDS is associated with poorer prognosis, but the nature of this relationship is complex. Although alcohol use itself may have direct ill effects on health, medication non-adherence that co-occurs with alcohol use at least partially accounts for the poor health of people who are taking ARVs and drink alcohol.[8] In a qualitative interview study of interactive toxicity beliefs regarding ARVs and alcohol among people living with HIV/AIDS, Sankar et al.[9] found that nearly all patients (85%) believed that ARVs should not be mixed with alcohol. Indeed, half of the participants in their study indicated that they would not take any of their ARV medications if they had been drinking. Participants commonly believed that mixing alcohol and ARVs would "break down" ARVs and make them ineffective, that mixing the two was toxic, and that alcohol would make HIV disease worse. Sankar et al.[9] found that heavier drinkers were less likely to believe that mixing alcohol and ARVs was harmful, and were therefore less likely to stop taking their medications when they had been drinking.

While some of the nonadherence to medications observed in people who drink may therefore result from cognitive impairment from intoxication, nonadherence may also be the result of purposive decisions to stop taking medications while drinking.[7,9] Importantly, the implications of multiple missed doses that can occur with treatment lapses during periods of drinking may be far direr than a single missed dose that may occur while intoxicated. In the current study we investigated the prevalence of ARV-alcohol interactive toxicity beliefs in a sample of people living with HIV/AIDS. Specifically, we examined toxicity beliefs associated with drinking alcohol among men and women currently treated with ARVs. In addition, we investigated the associations among alcohol use, interactive toxicity beliefs, and HIV treatment adherence. We hypothesized that compared to nondrinkers; drinkers would view fewer adverse outcomes from mixing alcohol and ARVs. We also hypothesized that stopping ARV therapies when drinking would be associated with HIV treatment non-adherence over and above alcohol use itself.

Methods

Participants

Men and women were recruited from AIDS service organizations, health care providers, social service agencies, and infectious disease clinics in inner-city areas of Atlanta, Georgia. Recruitment relied on provider referrals and word-of-mouth chain contacts. Interested persons phoned our research program to schedule an appointment to participate. The study entry criteria were age 18, proof of positive HIV status using a photo ID and matching ARV prescription bottle, and currently taking ARV medications. Data were collected between January 2006 and May 2008. Demographic characteristics of the sample are shown in Table 1.

TABLE 1. CHARACTERISTICS OF NONDRINKERS AND DRINKERS LIVING WITH HIV/AIDS RECEIVING ANTIRETROVIRAL TREATMENTS

	Nondrinkers (n = 85)		Drinkers (n = 60)		
	n	%	n	%	χ^2
Men	52	61	49	82	
Women	33	39	11	18	6.9[a]
African American	77	91	57	95	
White	5	6	3	5	
Other ethnicities	3	3	0		2.2
Married	14	16	19	32	4.5*
AIDS diagnosis	57	67	41	68	0.3
Marijuana	10	12	15	25	4.5*
Cocaine	11	13	14	24	2.7
	M	SD	M	SD	t
Age	46.1	5.9	43.3	6.5	2.8[a]
Education	11.9	1.7	12.9	2.4	2.9[a]
Years HIV-positive	13.2	6.2	13.8	5.9	0.6
ARV adherence	68.6	23.1	60.0	28.9	1.9[b]

[a]$p < 0.01$.
[b]$p < 0.05$.
ARV, antiretroviral.

Measures

Measures were collected using an instructor guided self-administration procedure in groups of 4 to 8 persons. Participants where shown page by page how to complete the study measures by using a projected facsimile of the instruments, assuring that instructions for each assessment instrument was carefully described and that participants were given privacy with minimal demand characteristics when responding. Participants who experienced difficulty reading the measures were interviewed (less than 10%). Participants completed surveys assessing demographic and health information, substance use, and interactive toxicity beliefs. HIV treatment adherence was monitored using unannounced telephone-based pill counts.

Demographic and health characteristics. Participants were asked their age, years of education, income, ethnicity, and employment status. We assessed HIV related symptoms using a previously developed and validated measure concerning experience of 14 common symptoms of HIV disease.[10] Participants also indicated whether they had ever been diagnosed with an AIDS-defining condition, and their most recent CD4 cell count and viral load.

Substance use. Participants completed the Alcohol Use Disorder Identification Test (AUDIT[11]), a 10-item self-report instrument that includes quantity and frequency of alcohol use that was designed to identify individuals for whom the use of alcohol places them at risk for developing alcohol-related problems. AUDIT scores range from 0 to 40, and scores of 8 or above are sensitive in identifying individuals who may be at risk or who are experiencing alcohol problems.[12] The first item of the AUDIT asks "how often do you have a drink containing alcohol." This item was used to

classify participants as those who do not drink (responded never) and those who do drink (responded with some frequency of current drinking). Participants also indicated whether they had used marijuana, cocaine, and other drugs in the previous four months.

Interactive toxicity beliefs. Participants were asked the degree to which they agree with five beliefs related to mixing alcohol and ARVs. These indicator beliefs were derived from the findings of previously published qualitative research that investigated beliefs about alcohol use and their influence on ARV adherence among people living with HIV/AIDS.[9] Interactive toxicity beliefs reflected the potential adverse outcomes of mixing alcohol and ARVs, including risks for nonadherence after drinking, worsening HIV infection as a result of drinking, and interference of alcohol with ARV effectiveness. The exact interactive toxicity belief indicator items are presented in Table 2. Interactive toxicity beliefs were responded to on four-point scales, $1 =$ strongly disagree, $4 =$ strongly agree. Because the response mid-point was highly skewed to the third position on all items (range of skew -0.83 to -2.08, range of kurtosis $= -0.44$ to 3.81), we used the "strongly agree" response category to indicate belief endorsement.

ARV adherence. Participants enrolled in this study were taking ARVs and consented to monthly unannounced telephone-based pill counts. Unannounced pill counts have been demonstrated reliable and valid in assessing HIV treatment adherence when conducted in participants' homes[13] and on the telephone.[10,14] Following an office-based training in the pill counting procedure, participants were called at an unscheduled time by a phone assessor. Repeated pill counts occurred over 21 to 35 day intervals and were conducted for each of the ARV medications participants were taking. Pharmacy information from pill bottles was also collected to verify the number of pills dispensed between calls. Adherence was calculated as the ratio of pills counted relative to pills prescribed and dispensed. Two consecutive pill counts were necessary for computing adherence. Adherence data reported here represents the percentage of pills taken as prescribed in the four months following the office-based assessment averaged across time and ARV medications.

Data analyses

We first conducted descriptive analyses for the sample that included comparisons between participants who reported current drinking and those who stated that they were not currently drinking alcohol. To test our first hypothesis that drinkers would view fewer adverse outcomes from mixing alcohol and ARVs (i.e., fewer endorsements of interactive toxicity beliefs) compared to nondrinkers, we used univariate and multivariate logistic regression analyses with drinking/non-drinking groups entered as the dependant variable predicted by interactive toxicity beliefs, reporting odds ratios and 95% confidence intervals (95% CI). To test our second hypothesis, that the inclination to stop ARV therapies when drinking would be associated with HIV treatment nonadherence over and above alcohol use, we examined the association of alcohol use and stopping ARVs when drinking on HIV treatment adherence using a hierarchical linear regression model. In this analysis AUDIT scores and interrupting treatment when drinking were entered as predictors of HIV treatment adherence. Finally, we explored the association between interactive toxicity beliefs and participant demographic and health characteristics. All hypothesis tests controlled for participant gender, age, and education and significance was defined as $p < 0.05$.

Results

Among the 145 study participants, 100 were men, 44 women, and 1 male-female transgender person. The sample was primarily African American ($n = 135$, 93%) with 8 (6%) white, and 3 (1%) participants other ethnicities. The mean age was

TABLE 2. ALCOHOL-ANTIRETROVIRAL INTERACTIVE TOXICITY BELIEFS AMONG NONDRINKERS AND DRINKERS LIVING WITH HIV/AIDS RECEIVING ANTIRETROVIRAL TREATMENTS

	Nondrinkers (n = 85)		Drinkers (n = 60)					
	n	%	n	%	OR[a]	95% CI	OR[b]	95% CI
People are more likely to miss taking their medications if they have been drinking alcohol.	57	67	24	40	3.1[c]	1.5–6.1	2.1	0.9–4.9
Alcohol and HIV medications should never be mixed.	70	82	37	62	2.9[c]	1.3–6.2	0.8	0.3–2.5
Drinking alcohol can make HIV worse by harming the immune system.	66	78	28	47	4.2[c]	2.0–8.6	3.3[d]	1.1–10.6
Alcohol breaks down HIV medications so they will not work right.	50	59	20	33	2.8[c]	1.4–5.7	1.3	0.5–3.3
A person should stop taking their HIV medications if they are going to be drinking.	17	20	15	25	0.8	0.4–1.7	0.3[d]	0.2–0.9

[a]Model adjusted for demographic characteristics.
[b]Model includes all belief indicators and demographic characteristics.
[c]$p < 0.01$.
[d]$p < 0.05$.
OR, odds ratio; CI, confidence interval.

44.9 (standard deviation [SD] = 6.3) and the mean years of education was 12.3 (SD = 2.1). Participants indicated an average of 13.5 years (SD = 6.2) since testing HIV positive. The average number of HIV symptoms experienced was 4.3 (SD = 3.6), and 98 (67%) had been diagnosed with an AIDS-related condition. Half of participants (n = 72) had been hospitalized for an HIV-related health problem, 60% (n = 87) had CD4 cell counts below 200. The mean percent of pills taken as prescribed over the subsequent months was 64.7 (SD = 26.1, median = 71.1%)

In terms of alcohol use, 41% (n = 60) of participants reported currently drinking alcohol. Among those who drink, their mean AUDIT score was 4.5 (SD = 4.4), with 18% (n = 11) of participants scoring over 8 on the AUDIT, indicating possible problem drinking. Most drinkers (n = 53, 89%) drank at least monthly and 11% (n = 7) drank weekly. In terms of drinking quantity, 20% (n = 12) drank three or four drinks on typical drinking occasions, with only three participants usually consuming five or more drinks. Table 1 presents the demographic characteristics of non-drinkers and drinkers. Comparisons showed that drinkers were more likely to be men, younger, better educated, and married. Drinkers were also more likely to report recent marijuana use and had poorer ARV treatment adherence.

Prevalence of interactive toxicity beliefs

Results showed that 18% (n = 11) of drinkers reported occasionally stopping ARV medications when they are drinking. We also found that 31% (n = 26) of non-drinkers and 25% (n = 15) of drinkers indicated that they would plan to stop taking their ARVs if they were drinking, a non-significant difference, OR = 0.9, 95% CI 0.4–2.3. Table 2 shows the interactive toxicity beliefs held by nondrinkers and drinkers. Overall, participants commonly believed that mixing alcohol and ARVs would lead to adverse outcomes. A majority of participants believed that people are more likely to miss medications when drinking, that alcohol and ARV medications should never be mixed, and that drinking alcohol can make HIV worse by harming the immune system. It was also common for participants to believe that alcohol "breaks down" ARVs and interferes with their effectiveness, with nondrinkers holding these beliefs significantly more often than drinkers. In an adjusted regression model, results showed that nondrinkers were significantly more likely to believe that alcohol worsens HIV and were less likely to believe that a person should stop taking their ARVs if they are

going to drink. In exploratory analyses, we did not find associations between interactive toxicity beliefs and participant demographic and health characteristics.

Interactive toxicity beliefs and HIV treatment adherence

An initial linear regression model showed that alcohol use (AUDIT scores), controlling for demographic characteristics, predicted HIV treatment nonadherence, $\beta = -0.168$, $t = 2.01$, $p < .05$, $R^2 = 0.036$. In a second model, we performed a hierarchical linear regression to test the association between stopping treatment when drinking and HIV treatment nonadherence. Demographic characteristics were entered in the first block, followed by AUDIT scores, and finally stopping ARV medications when drinking. Results are shown in Table 3. Having stopped medications while drinking significantly predicted HIV treatment nonadherence over and above all other factors. The entire model accounted for 9.9% of the variance in treatment nonadherence. Stopping treatment while drinking contributed 4.6% to the explained variance above the other factors, representing a significant change in R^2. Thus, stopping HIV treatment when drinking was associated with nonadherence, over and above global use of alcohol.

Discussion

The current study found that 2 of 5 people receiving ARV treatments in our community sample were currently drinking alcohol, with one third drinking at least two to four times a month and 1 in 5 drinkers typically consuming 3 or more drinks. In addition, 1 in 4 drinkers reported using marijuana and/or cocaine. We extended previous research to show that beliefs regarding adverse outcomes from mixing alcohol and ARV mediations are commonly held among people living with HIV/AIDS.[7,9] We also found that drinkers are less likely to hold interactive toxicity beliefs, although they are likely to stop taking ARVS when drinking. More than one in five people taking ARVS who also drink alcohol reported stopping their medications when drinking and these self-reported data were consistent with an objective measure of treatment adherence. These results parallel previous research showing that greater specificity in assessing context dependant alcohol use affords greater predictive power than global alcohol use.[15]

TABLE 3. HIERARCHICAL LINEAR REGRESSION PREDICTING HIV TREATMENT ADHERENCE

	B	SE	β	t	R^2	$R^2\Delta$	FΔ
Block 1: Participant characteristics						0.027	
Gender	0.010	.052	0.02	0.2			
Age	0.005	.004	0.12	1.3			
Race	0.042	.052	0.07	0.8			
Education	−0.010	0.013	−0.078	0.7			
Block 2: Alcohol use (AUDIT scores)	−0.013	0.008	−0.165	1.7[a]	0.053	0.025	2.9[a]
Block 3: Stopping medications while drinking	0.161	0.067	0.240	2.4[b]	0.099	0.046	5.6[b]

[a]$p < 0.1$.
[b]$p < 0.05$.

Interactive toxicity beliefs were endorsed by a majority of our participants. These beliefs may serve a protective function for some people with HIV who abstain from drinking while receiving treatment, with over 80% of nondrinkers stating that alcohol and ARVs should not be mixed and 80% stating that alcohol worsens HIV infection by adversely affecting the immune system. In addition, 1 in 4 nondrinkers stated that they would plan to interrupt their ARV treatment if they were to drink. Among drinkers, alcohol use below an individual's level of intoxication can lead to treatment nonadherence,[6] with interactive toxicity beliefs potentially accounting for at least some of these lapses in doses. We found that poorer treatment adherence was associated with ceasing mediations while drinking over and above frequency, quantity, and problems associated with drinking. The potential for patients to deliberately interrupt treatment when drinking alcohol therefore adds to the deleterious effects of alcohol intoxication on HIV treatment adherence.

The current study findings should be interpreted in light of their methodological limitations. First, the study utilized a nonrepresentative convenience sample of men and women living with HIV/AIDS. Participants were recruited from multiple community and clinical services in a major metropolitan area. Caution is therefore warranted in generalizing these finings to other populations. Second, the study is limited by its reliance on self-reported alcohol use and drinking practices in relation to medications. The validity of self reported drinking is often questioned, suggesting that the degree of drinking reported by our participants should be considered a lower-bound estimate of their true drinking. Our measure of interactive toxicity beliefs was also limited by ceiling effects. Future research should use a broader range of responses when assessing these sensitive behaviors and beliefs to afford greater variability. Another potential limitation is our definition for non-adherence to treatment. Research shows that different regimens of ARVs have varying resistance profiles and several regimens are forgiving of missed doses.[16,17] Our use of a standard criterion for nonadherence across regimens may therefore have overestimated the implications of nonadherence. Finally, we relied on cross-sectional data for our self-report measures with prospective data only available for our measure of treatment adherence. With these study limitations in mind, we believe that our results have important implications for HIV treatment adherence counseling.

Patients may deliberately stop taking their ARV medications when they believe that mixing alcohol and medications is harmful. People living with HIV/AIDS should be advised that excessive drinking as well as other drug use does indeed have harmful health effects and that medications are more difficult to adhere to when intoxicated.[18] Patients should also be educated that there are no known adverse health effects from mixing alcohol and ARV medications and patients who drink should be routinely counseled that it is essential to continue taking their medications even when drinking. Patient education should emphasize that missing medications when drinking, for whatever reason, threatens the long-term benefits of treatment. We recommend that patient assistance directly address alcohol use as a barrier to adherence and directly dispel misconceptions and false beliefs that lead people to stop taking their ARVs when drinking.

Author Disclosure Statement

No competing financial interests exist.

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