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BRIEF REPORT

Impact of Co-occurring Drug Use, Hazardous Alcohol Use, and Mental Health Disorders on Drug Use Patterns in People With HIV and Hepatitis C Virus Infection

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Drug use, hazardous alcohol use, and mental health disorders are prevalent among people with HIV and hepatitis C virus (HCV) infection. Co-occurrence of alcohol use and depression negatively impacts substance use patterns. Nevertheless, HCV treatment provides a promising opportunity to identify and address co-occurring drug use, hazardous alcohol use, and mental health disorders.

Keywords. hazardous alcohol use; hepatitis C virus; HIV; mental health disorder; substance use.

People with HIV (PWH) are disproportionately affected by hepatitis C virus (HCV) infection [1]. Among people who use drugs (PWUD), particularly among people who inject drugs, this burden is even greater, with HCV prevalence exceeding 50% in many settings [2]. PWUD also have a high prevalence of co-occurring mental health disorders [3], which has been linked to riskier behaviors, leading to HIV and HCV exposure [4].

Chronic HCV infection is associated with significant morbidity and mortality due to complications of cirrhosis, which are exacerbated by HIV coinfection and ongoing alcohol use [5]. With the recent advent of safe, highly effective direct-acting antivirals (DAAs), the risk of these liver complications is lowered with HCV cure [6]. In real-world cohorts, the effectiveness of DAAs is similar in people who use drugs and those who do not [7]. In some instances, HCV treatment initiation has been associated with reduction in hazardous substance use behaviors, including reduced sharing of injection equipment [8]. HCV treatment is a promising opportunity to engage PWUD, many of whom are broadly marginalized from the health care system and are disparately burdened by infectious diseases. There is, however, limited information on substance use behaviors and changes in this behavior during DAA treatment [8].

The present study assessed substance use at enrollment and describes the substance use patterns of PWH who initiated HCV treatment in a randomized trial of HCV treatment among PWUD [9].

METHODS

This study reports data collected from participants enrolled in the CHAMPS study, a randomized trial that compared usual care with peer support or cash incentive strategies for increasing uptake of HCV treatment among PWUD [9]. Between August 2015 and October 2016, PWH with active HCV genotype 1 infection and no evidence of engagement in HCV care were enrolled, linked to HCV providers, and offered treatment with ledipasvir/sofosbuvir.

At enrollment and subsequent visits, participants completed interviewer-administered surveys encompassing demographic, behavioral, and health information and provided blood and urine samples. Among these questionnaires, participants completed the Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item questionnaire evaluating depressive symptoms within the past week; a cutoff score of ≥16 was used to identify depressive symptoms [10]. Urine toxicology results were used to evaluate opiate and cocaine use. Self-reported drug use was obtained by asking about any use of heroin or cocaine within the previous 30 days. Self-reported alcohol use was determined through the 10-question Alcohol Use Disorders Identification Test (AUDIT); hazardous alcohol use was defined as a score ≥8 for males and ≥4 for females [11].

Patient Consent

The study design and all study procedures were approved by the Johns Hopkins School of Medicine Institutional Review Board and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

Drug Use Definition

Drug use within the past 30 days was defined as either self-report of heroin or cocaine use within the past 30 days or a positive urine test result for either codeine, morphine, or benzoylecgonine (cocaine metabolite). Participants who did

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not report use of heroin or cocaine and did not test positive were classified as not having used drugs in the past 30 days. Drug use pattern was defined using a comparison of drug use at enrollment and HCV treatment week 6. Participants were categorized into 4 groups based on patterns of drug use: (1) ongoing active drug use (positive at enrollment and week 6); (2) persistent drug use abstinence (negative at enrollment and week 6); (3) change from inactive to active drug use (negative at enrollment and positive at week 6); (4) change from active to inactive drug use (positive at enrollment and negative at week 6). Additional analyses compared drug use at 6 weeks with self-reported drug use at 12 weeks.

Statistical Analysis

Demographic, substance use, and health characteristics at enrollment were compared by drug use pattern. Categorical variables were compared using chi-square tests, and continuous variables were compared using an independent *t* test. An analysis of variance for continuous variables and Kruskal-Wallis for categorical variables were used when comparing across the 4 substance use pattern groups. Analyses were conducted using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Of 144 PWUD enrolled in the study, 110 started HCV treatment with the DAA regimen. Among those 110 participants, 100 had data on self-reported drug use and urine toxicology at both enrollment and the week 6 visit. About half (48%) used drugs within 30 days of enrollment, and the median age (interquartile range) was 55 (51.0–59.3) years (Table 1). Among the 48 participants who used drugs, substances used included opioids alone in 16 (33%), cocaine alone in 19 (40%), and a combination of opioids and cocaine in 13 (27%). The majority were Black/African American (92%) and male (58%). Unemployment was prevalent (80%), and approximately half (56%) had obtained a high school diploma. There were 18 participants (18%) with concurrent hazardous alcohol use and depression.

At enrollment, participants with recent substance use were more likely to report depressive symptoms (70.8% vs 51.9%; $P = .05$) and hazardous alcohol use (35.4% vs 15.4%; $P = .02$) compared with those without recent use. Participants with recent substance use also showed a trend toward being more likely to have co-occurring depressive symptoms and hazardous alcohol use (25.0% vs 11.5%; $P = .08$) compared with those without recent use.

During HCV treatment, most participants had ongoing active drug use (36%) or persistent drug use abstinence (46%) (Table 2). However, 12% of participants transitioned from active to inactive drug use, whereas 6% transitioned from inactive to active drug use. The majority (11/12; 92%) of participants who transitioned to inactive drug use reported abstinence from substance use at 12 weeks. Despite only 25% of all participants having hazardous alcohol use at enrollment, they represented a significantly higher proportion (41.7%) of the participants with ongoing active drug use ($P = .04$).

DISCUSSION

Our data highlight that drug use, hazardous alcohol use, and depression symptoms commonly co-occur among people with HIV and HCV [12]. In our study of PWUD, 18% of participants had co-occurring hazardous alcohol use and depressive symptoms. Drug use, hazardous alcohol use, and mental health disorders are an interconnected burden, with one condition often inflaming the other [13]. While it is encouraging that most participants in this study achieved HCV cure, the high prevalence of co-occurring substance use and mental health disorders warrants attention. Persistent active drug use, especially in the setting of co-occurring mental health disorders, has been associated with an increased risk of HCV re-infection [14]. HCV care programs should address these interrelated conditions by incorporating valid screening tools for the identification of drug use and hazardous alcohol use and mental health problems, such as the AUDIT and PHQ-9. HCV care should also include referrals to indicated services and access to medications, such as naltrexone and buprenorphine, with proven effectiveness for treatment of alcohol and opioid use disorders.

Within this cohort of PWH with high levels of substance use at HCV treatment initiation, it is encouraging that 12% transitioned from active to inactive drug use during HCV treatment. Among a population that is often marginalized from the health care system, HCV treatment may provide an avenue to engage in care and receive additional psychosocial support and treatment. Changes in substance use behaviors have been identified within other cohorts of people receiving HCV treatment, although data are mostly limited to the pre-DAA era [8]. These data provide further evidence for engagement in HCV treatment as an opportunity to address the interrelated burden of problematic substance use, hazardous alcohol use, and mental health disorders among people with HIV and HCV. HIV care settings in particular provide an opportunity to provide long-term support and treatment for substance use and mental health disorders.

With a disproportionate percentage (42%) of participants with ongoing drug use at the 6-week visit reporting hazardous alcohol use at enrollment, this research draws particular attention to the significant role of alcohol use in perpetuating other substance use. Traditionally, in HCV settings, alcohol use has been viewed as a risk factor that can exacerbate liver-related complications among people with HCV [5]. This research extends those findings to include recognition of the interrelatedness of alcohol and drug use and to address alcohol use as both a risk factor for progression of liver disease and a risk factor for continued use of other substances.

This study has limitations. Determination of substance use incorporated results of urine toxicology testing, which has a

Table 1. Characteristics of Participants who Started HCV Treatment at Baseline by Substance Use in the Past 30 Days

Characteristic	Total, No. (%)	Substance Use in the Past 30 Days (Self-report and Urine Tox) No. (%)	No Substance Use in the Past 30 Days (Self-report and Urine Tox) No. (%)	*P* Value
Total	100	48	52	
Intervention group				.63
Usual care	19 (19.0)	8 (16.7)	11 (21.2)	
Usual care + peer	42 (42.0)	19 (39.6)	23 (44.2)	
Usual care + incentives	39 (39.0)	21 (43.8)	18 (34.6)	
Age, median (IQR), y	54.9 (51.0–59.3)	54.6 (51.2–58.4)	55.3 (50.7–60.6)	.54
Gender				.46
Male	58 (58.0)	26 (54.2)	32 (61.5)	
Female	42 (42.0)	22 (45.8)	20 (38.5)	
Race				.11
Black/African American	92 (92.0)	42 (87.5)	50 (96.2)	
White	8 (8.0)	6 (12.5)	2 (3.9)	
Completed high school/obtained GED				.65
No	44 (44.0)	20 (41.7)	24 (46.1)	
Yes	56 (56.0)	28 (58.3)	28 (53.9)	
Insurance				**.008**
Medicaid	54 (54.0)	**28 (58.3)**	**26 (50.0)**	
Medicaid & Medicare	24 (24.0)	**16 (33.3)**	**8 (15.4)**	
Medicare, Tricare, other government	13 (13.0)	**3 (6.3)**	**10 (19.2)**	
Private	9 (9.0)	**1 (2.1)**	**8 (15.4)**	
Unemployed				.19
No	20 (20.0)	7 (14.6)	13 (25.0)	
Yes	80 (80.0)	41 (85.4)	39 (75.0)	
Depressive symptoms				**.05**
No (CES-D <16)	39 (39.0)	**14 (29.2)**	**25 (48.1)**	
Yes (CES-D ≥16)	61 (61.0)	**34 (70.8)**	**27 (51.9)**	
Self-reported hazardous alcohol use				**.02**
No (Male AUDIT <8/Female AUDIT <4)	75 (75.0)	**31 (64.6)**	**44 (84.6)**	
Yes (Male AUDIT ≥8/Female AUDIT ≥4)	25 (25.0)	**17 (35.4)**	**8 (15.4)**	
Depressive symptoms and hazardous alcohol use at baseline				.08
Neither or only 1	82 (82.0)	36 (75.0)	46 (88.5)	
Both (CES-D >16 + (Male AUDIT ≥8/ Female AUDIT ≥4))	18 (18.0)	12 (25.0)	6 (11.5)	
Alcohol use[a]				.06
PEth <50 ng/mL	64 (68.1)	27 (58.7)	37 (77.1)	
PEth >50 ng/mL	30 (31.9)	19 (41.3)	11 (22.9)	
Prescribed medication for opioid use disorder in past 3 mo				**.0008**
Methadone	22 (22.0)	**19 (39.6)**	**3 (5.8)**	
Buprenorphine	11 (11.0)	**3 (6.3)**	**8 (15.4)**	
Naltrexone	3 (3.0)	**0**	**3 (5.8)**	
None	64 (64.0)	**26 (54.2)**	**38 (73.1)**	
Receiving antiretroviral therapy	98 (98.0)	46 (95.8)	52 (100.0)	.14
Undetectable HIV viral load (<200 copies/mL)	86 (86.0)	40 (83.3)	46 (88.5)	.46
CD4 count, cell/mm^3	509 (349–804)	432 (298–830)	562 (415–797)	.22
Liver stiffness (n = 96), kPa				.38
≤8	66 (68.8)	36 (75.0)	30 (62.5)	
8.1–11.9	19 (19.8)	7 (14.6)	12 (25.0)	
≥12	11 (11.5)	5 (10.4)	6 (12.5)	

Bold text indicate statistical significant differences in the drug use groups.

Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; CES-D, Center for Epidemiologic Studies Depression Scale; HCV, hepatitis C virus; IQR, interquartile range; PEth, phosphatidylethanol.

[a]PEth data missing for 6 participants (4 in the no substance use group and 2 in the substance use group).

Table 2. Characteristics of Participants who Started Treatment by Substance Use Pattern (Difference in Substance Use Status [SR and UTOX] at Baseline vs Week 6 Visit)

Characteristic	Total, No. (%)	No Change (Persistent Drug Use Abstinence) No. (%)	No Change (Ongoing Active Drug Use) No. (%)	Change From Inactive to Active Drug Use No. (%)	Change From Active to Inactive Drug Use No. (%)	*P* Value
Total	100	46	36	6	12	
Intervention group						.95
Usual care	19 (19.0)	9 (19.6)	6 (16.7)	2 (33.3)	2 (16.7)	
Usual care + peer	42 (42.0)	21 (45.7)	14 (38.9)	2 (33.3)	5 (41.7)	
Usual care + incentives	39 (39.0)	16 (34.8)	16 (44.4)	2 (33.3)	5 (41.7)	
Age, median (IQR), y	54.9 (51.0–59.3)	55.3 (51.0–60.2)	53.9 (50.9–58.9)	57.0 (48.1–63.6)	56.3 (54.6–58.0)	.73
Gender						.65
Male	58 (58.0)	28 (60.9)	21 (58.3)	4 (66.7)	5 (41.7)	
Female	42 (42.0)	18 (39.1)	15 (41.7)	2 (33.3)	7 (58.3)	
Race						.22
Black/African American	92 (92.0)	45 (97.8)	32 (88.9)	5 (83.3)	10 (83.3)	
White	8 (8.0)	1 (2.2)	4 (11.1)	1 (16.7)	2 (16.7)	
Insurance						.15
Medicaid	54 (54.0)	24 (52.7)	21 (58.3)	2 (33.3)	7 (58.3)	
Medicaid & Medicare	24 (24.0)	7 (15.2)	12 (33.3)	1 (16.7)	4 (33.3)	
Medicare, Tricare, other government	13 (13.0)	8 (17.4)	2 (5.6)	2 (33.3)	1 (8.2)	
Private	9 (9.0)	7 (15.2)	1 (2.8)	1 (16.7)	0	
Unemployed						.25
Yes	80 (80.0)	34 (73.9)	29 (80.6)	5 (83.3)	12 (100.0)	
No	20 (20.0)	12 (26.1)	7 (19.4)	1 (16.7)	0	
Receiving antiretroviral therapy	98 (98.0)	46 (100.0)	35 (97.2)	6 (100.0)	11 (91.7)	.30
Undetectable HIV viral load (<200 copies/mL) at enrollment	86 (86.0)	40 (87.0)	29 (80.6)	6 (100.0)	11 (91.7)	.53
Undetectable HIV viral load (<200 copies/mL) at 12 mo after enrollment	90 (90.0)	42 (91.3)	31 (86.1)	6 (100.0)	11 (91.7)	.71
CD4 count, cell/mm^3	509 (349–804)	534 (403–765)	426 (335–804)	854 (643–1108)	466 (225–909)	.22
Depressive symptoms (baseline)						.27
No (CES-D <16)	39 (39.0)	22 (47.8)	11 (30.6)	3 (50.0)	3 (25.0)	
Yes (CES-D ≥16)	61 (61.0)	24 (52.2)	25 (69.4)	3 (50.0)	9 (75.0)	
Depressive symptoms (6-wk FU)						.68
No (CES-D <16)	46 (46.9)	23 (52.3)	14 (38.9)	3 (50.0)	6 (50.0)	
Yes (CES-D ≥16)	52 (53.1)	21 (47.7)	22 (61.1)	3 (50.0)	6 (50.0)	
Alcohol use[a]						.17
PEth <50 ng/mL	64 (68.1)	32 (74.4)	20 (58.8)	5 (100.0)	7 (58.3)	
PEth >50 ng/mL	30 (31.9)	11 (25.6)	14 (41.2)	0	5 (41.7)	
Self-reported hazardous alcohol use						**.04**
No (Male AUDIT <8/Female AUDIT <4)	75 (75.0)	**39 (84.8)**	**21 (58.3)**	**5 (83.3)**	**10 (83.3)**	
Yes (Male AUDIT ≥8/Female AUDIT ≥4)	25 (25.0)	**7 (15.2)**	**15 (41.7)**	**1 (16.7)**	**2 (16.7)**	
Depressive symptoms and hazardous alcohol use at baseline						.27
No (neither or only 1)	82 (82.0)	41 (89.1)	26 (72.2)	5 (83.3)	10 (83.3)	
Yes (CES-D >16 + (Male AUDIT ≥8/Female AUDIT ≥4))	18 (18.0)	5 (10.9)	10 (27.8)	1 (16.7)	2 (16.7)	
Prescribed medication for opioid use disorder in past 3 mo						**.0004**
Methadone	22 (22.0)	**3 (6.5)**	**15 (41.7)**	**0**	**4 (33.3)**	
Buprenorphine	11 (11.0)	**5 (10.9)**	**3 (8.3)**	**2 (50.0)**	**0**	
Naltrexone	3 (3.0)	**2 (4.3)**	**0**	**1 (16.7)**	**0**	
None	64 (64.0)	**36 (78.3)**	**18 (50.0)**	**2 (33.3)**	**8 (66.7)**	
SVR						.18
Yes	96 (96.0)	42 (91.3)	36 (100.0)	6 (100.0)	12 (100.0)	
No	4 (4.0)	4 (8.7)	0	0	0	

P value for comparison of drug use patterns from chi-square tests for categorical variables and Kruskal-Wallis test for continuous variables. Figures in bold indicate statistically significant differences between drug use groups.

Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; CES-D, Center for Epidemiologic Studies Depression Scale; HCV, hepatitis C virus; IQR, interquartile range; PEth, phosphatidylethanol; SR, self report; SVR, sustained virologic response; UTOX, urine toxicology.

[a]PEth data missing for 6 participants.

relatively short window (1–5 days from use) for detection of heroin and cocaine [15]. However, we also incorporated self-report of substance use in the determination of substance use category. Participants included may represent a population more connected to the health care system due to HIV care linkage. It is likely that the issues of hazardous substance use, mental health disorders, and HCV are more severe within populations that are less engaged in the health care system. This reality would make engaging patients receiving HCV treatment in comprehensive services more critical, underscoring the findings of this research. Although this study was limited to PWH receiving care within a single urban infectious disease clinic, these issues of co-occurring mental health and substance use disorders are prevalent among people chronically infected with HCV and are likely reflective of diverse settings [16]. Furthermore, drug use data were limited to only week 6 of HCV treatment. However, these patterns still underscore the potential role of HCV treatment in shaping drug use behavior. Future research should examine the impact of systematic integrated substance use and mental health disorder screening and care on long-term outcomes for PWUD receiving HCV care.

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