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Assessment of hepatitis C monitoring adherence after viral eradication in veterans with substance use to improve care and surveil reinfection

Miranda L. Stratton, PharmD[1]; Elayne D. Ansara, PharmD, BCPS, BCPP[2]; Amanda P. Ifeachor, PharmD, MPH, BCPS[3]; Kelly K. Houck, PharmD, BCPS[4]; Suthat Liangpunsakul, MD, MPH[5]; Katie J. Binger, PharmD, BCPP[6]

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Abstract

Introduction: Hepatitis C virus (HCV) incidence rates are rising for patients with substance use and/or SUDs. Guidelines provide monitoring recommendations to ensure remission after successful treatment. The study's objective was to identify gaps in follow-up for patients with documented substance use and/or SUD through assessment of adherence to guideline-recommended HCV RNA lab 12 months post-treatment.

Methods: Patients treated for HCV through the Veteran Health Indiana Hepatitis C Pharmacy Clinic were retrospectively evaluated. Subjects were categorized based on the provider assigned for follow-up care after 12-week sustained virologic response (SVR12) labs (primary care provider [PCP] or HCV provider). The primary outcome was HCV RNA obtained 11 to 13 months post-treatment. Secondary outcomes were HCV RNA detected post-treatment, substance use, engagement in substance use treatment, and engagement with social work.

Results: Two hundred forty-one patients were included in the HCV provider cohort and 139 in the PCP cohort. Forty-one patients did not have a specified clinic for follow-up treatment, and 20 patients did not achieve SVR12. Sixty-one patients (28%) in the HCV provider cohort completed a 12-month HCV RNA within 11 to 13 months post-treatment vs 15 patients (11%) in the PCP cohort ($P \leq .01$). One patient had HCV RNA detected post-treatment.

Discussion: This study reveals inadequate HCV post-treatment follow-up for patients with substance use and/or SUD. SUD is a chronic disease that requires continued monitoring to prevent complications. Further studies are needed to identify reinfection rates and improvements of care in this population.

Keywords: hepatitis C virus, veterans, monitoring, substance use disorder

[1] (Corresponding author) Clinical Pharmacy Practitioner – Mental Health, Veteran Health Indiana, Indianapolis, Indiana, miranda.stratton@va.gov, ORCID: https://orcid.org/0000-0003-3057-4331; [2] Clinical Pharmacy Practitioner – Mental Health, Veteran Health Indiana, Indianapolis, Indiana, ORCID: https://orcid.org/0000-0001-9835-0305; [3] Clinical Pharmacy Practitioner – Ambulatory Care (Gastrointestinal/Hepatitis C Virus Clinics), Veteran Health Indiana, Indianapolis, Indiana, ORCID: https://orcid.org/0000-0002-3986-8849; [4] Facility Pain Management, Opioid Safety, and Prescription Drug Monitoring Program (PMOP) Coordinator, Veteran Health Indiana, Indianapolis, Indiana, ORCID: https://orcid.org/0000-0003-4800-5671; [5] Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana and Associate Chief of Staff for Research service and Hepatologist, Gastroenterology Section, Medicine Service, Veteran Health Indiana, Indianapolis, Indiana, ORCID: https://orcid.org/0000-0002-6504-8123; [6] Clinical Pharmacy Practitioner – Mental Health, Veteran Health Indiana, Indianapolis, Indiana, ORCID: https://orcid.org/0000-0002-2031-5646

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Introduction

Liver disease secondary to hepatitis C virus (HCV) is associated with significant morbidity and mortality.[1] The success rate of HCV eradication has increased to 95% with the development of direct-acting antiviral (DAA) therapy.[2] Despite this advancement, the incidence of acute infection continues to rise in part due to the opioid epidemic. There were 1952 cases of HCV with risk factor information reported to the Centers for Disease Control and Prevention (CDC) in 2019, and 67% reported intravenous substance use, which is consistent with 2018 data (72%).[1] Barriers prevent access to treatment for patients with underlying mental health disorders and SUD regardless of high transmission rates.[3] At a large medical institution, Jain and colleagues[4] identified that only 13.6% of patients with any mental health or SUD received HCV treatment compared with 21.6% of patients without either disorder. The study notes insurance restrictions, provider bias, provider lack of knowledge of DAA therapy's impact on mental health disorders, and patient failure to follow up as barriers to HCV treatment.[4] The American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) HCV guidelines include recommendations to treat patients with concomitant SUD, which is mirrored in the Department of Veterans Affairs guidelines.[5-7] Patients with no ongoing risk factors for HCV infection post-treatment do not warrant repeat HCV RNA testing after 12-week sustained virologic response (SVR12) achievement unless unexplained hepatic dysfunction develops.[5,6] Patients with active SUD who achieve SVR12 are recommended to complete a quantitative HCV RNA lab at least 12 months post-treatment and annually thereafter to ensure SVR and identify cases of reinfection.[5,6]

HCV reinfection rates after achievement of SVR among patients who use substances vary significantly. A meta-analysis by Hajarizadeh and colleagues[8] finds an average reinfection rate of 5.9/100 person-years among patients with any substance use and 6.2/100 person-years for those injecting substances. There was a substantially lower reinfection rate among those using medications for opioid use disorder, such as buprenorphine or methadone, with an average of 3.8/100 person-years.[7] Another study[9] has similar findings that emphasize the positive impact therapeutic interventions can have on HCV reinfection rates.

The Veteran Health Indiana (VHI) Hepatitis C Pharmacy Clinic provides guideline-driven treatment and monitoring. Patients are followed by the team, which consists of physicians, nurse practitioners, pharmacists, a social worker, and a nurse. The clinic is responsible for obtaining HCV RNA at the end of HCV treatment and 12 weeks after treatment completion to assess for SVR12. Pharmacists perform drug therapy management (compliance, lab monitoring, drug interaction assessments) during HCV treatment. If SVR12 is achieved, the patient is either followed by an HCV provider (if patient has cirrhosis or another liver comorbidity) or is discharged back to the patient's primary care provider (PCP). The PCP is instructed to repeat an HCV RNA 12 months post-treatment though it is unclear if this test is completed.

This study is a continuation study from the Ifeachor and colleagues study, "HCV eradication in veterans with underlying mental health disorders and/or substance use."[10] The objective of this study was to identify gaps in follow-up care for patients successfully treated for HCV with documented substance use and/or SUD through assessment of provider adherence to guideline-recommended HCV RNA 12 months post-treatment. The impact of the study could be invaluable considering the potential to improve quality of care and reinfection surveillance in this at-risk population.

Methods

This retrospective chart review assessed patients who completed interferon-free HCV treatment in the VHI Hepatitis C Pharmacy Clinic from August 17, 2013 to August 17, 2017. The primary outcome was HCV RNA lab obtained 11 to 13 months after treatment completion. This timeline was created to allow for flexibility in appointment scheduling. Secondary outcomes included the following within 24 months post-treatment: HCV RNA detection, substance use reported, engagement in social work services, and initiation of substance use treatment through the Substance Use Disorder Recovery Program (SUDRP) before, during, or within 24 months post-treatment. Eligibility criteria included: age $\geq$18 years old, completed SVR12, and documented substance use or SUD within 6 months prior to HCV treatment initiation. Patients were excluded if they did not complete HCV treatment or died within 13 months of completing HCV treatment. Data collected included demographic information, documented substance use and/or SUD, HCV RNA tests post-treatment, high-risk behaviors for HCV infection, toxicology results, designated follow-up clinic, and support by social work and/or SUDRP. SUDRP is a VHI outpatient clinic that provides medication management, social work, and psychotherapy services for patients with SUD. Substance use was documented based on patient report, urine drug screen (UDS) results, and/or liquid chromatography mass spectrometry (LCMS) results. SUDRP engagement was defined as completion of at least 1 clinic appointment. Social work involvement was defined as at least 1 social work note that involved coordination of substance use treatment or psychotherapy related to substance use. Social work services were

TABLE 1: Baseline demographics of the study cohort stratified by designated follow-up provider type

Demographic	HCV Provider (n = 241)	PCP Group (n = 139)	*P* Value
Gender, n (%)			
Male	232 (96.3)	137 (98.6)	.20
Race, n (%)			
White	142 (58.9)	71 (51.1)	.13
Black	85 (35.3)	63 (45.3)	.05
Other/unknown	14 (5.8)	5 (3.6)	.34
Age, y			
Mean ± SD	61.1 ± 5.6	61.5 ± 6.5	.93
Baseline substance use, n (%)[a]			
Alcohol	210 (87.1)	112 (80.6)	.08
Cannabis	106 (44.0)	77 (55.4)	.03
Opioid	33 (13.7)	14 (10.1)	.30
Stimulant	42 (17.4)	25 (18.0)	.89
Other/unspecified	35 (14.5)	22 (15.8)	.73

HCV = hepatitis C virus; PCP = primary care provider.

[a]Percentages do not add up to 100% because some patients had multiple different types of substance use.

documented based on involvement post-treatment as this would seemingly have the biggest impact on reinfection rates.

This study was approved by the Indiana University IRB and the VHI Research Advisory Board. Study data were collected and managed using REDCap electronic data capture tools hosted at VHI.[11,12] Descriptive statistics were utilized to assess data. Statistical analysis was performed using a Student *t* test for unpaired data for continuous variables and χ^2 tests for categorical variables.

Results

Of 466 patients who were screened, 25 patients were excluded for the following reasons: died within 13 months post-treatment (n = 14); failed to complete SVR12 or took the test at an outside facility (n = 9); and delayed SVR12 to 10 or more months post-treatment, which negated the need for 12-month HCV RNA (n = 2). Of the 441 patients who met eligibility criteria, 61 patients were not included in analysis because they either did not have a specified clinic for follow-up treatment (n = 41) or did not achieve SVR12 (n = 20). Two-hundred forty-one patients were included in the HCV provider cohort and 139 in the PCP cohort. Table 1 shows baseline demographic characteristics and documented substance use, which were similar in both groups.

For the primary outcome, 61 patients (25%) in the HCV provider cohort completed the 12-month HCV RNA within 11 to 13 months post-treatment versus 15 patients (11%) in the PCP cohort ($P \leq .01$; see Table 2). One-hundred thirty-nine (57.7%) patients in the HCV provider group completed at least one HCV RNA within 11 to 24 months after treatment versus 31 patients (22.3%) in the PCP group ($P \leq .01$). Of the 170 total patients who had at least one HCV RNA drawn within 11 to 24 months post-treatment, 1 patient had a viral load detected, indicating possible reinfection. Reasons why the lab was not drawn are shown in Table 3.

UDS and LCMS results collected as well as substance use documented per patient report post-HCV-treatment are displayed in Table 4. Some patients had documented use and/or positive toxicology test results for multiple substances via multiple routes of use. The majority of patients from both cohorts had documented substance use post-treatment. The most common substance used was alcohol and most common route of use was oral ingestion.

Both groups had strong engagement in SUDRP services (HCV provider group: n = 112 [49.8%]; PCP group: n = 56 [40.3%]; $P = .24$), and most of the patients initiated SUDRP services prior to HCV treatment (HCV provider group: n = 100 [41.5%]; PCP group: n = 53 [38.1%]; $P = .52$). Comparatively, ~20% of patients from each cohort were involved with social work services post-treatment (HCV provider group: n = 52 [21.6%]; PCP group: n = 27 [19.4%]; $P = .62$).

Discussion

This study evaluated rates of quantitative HCV RNA monitoring in patients with substance use and SUD who

TABLE 2: HCV RNA labs collected

Outcome	HCV Provider Group (n = 241), n (%)	PCP Group (n = 139), n (%)	*P* Value
Primary:			
Completed HCV RNA lab within 11 to 13 mo post-treatment	61 (25.3)	15 (10.8)	<.01
Secondary:			
Completed HCV RNA lab within 11 to 24 mo post-treatment	139 (57.7)	31 (22.3)	<.01

HCV = hepatitis C virus; PCP = primary care provider.

TABLE 3: Reasons for failure to collect HCV RNA lab within 11 to 13 months post-treatment

Reason	HCV Provider Group (n = 180), n (%)	PCP Group (n = 124), n (%)	*P* Value
Lab not ordered or appointment not scheduled	75 (41.7)	52 (41.9)	.96
Lab not recommended by HCV provider at SVR12 appointment	28 (15.6)	66 (53.2)	<.01
Provider recommended lab outside of 11 to 13 mo post-treatment	32 (17.8)	5 (4.0)	<.01
Scheduled, patient did not show	19 (10.6)	...	...
Appointment cancelled	8 (4.4)	...	...
Not scheduled, patient never attended 3-mo HCV follow-up appointment	4 (2.2)	...	...
Not scheduled, patient relocated	2 (1.1)	...	...
Other	12 (6.6)	1 (0.81)	<.01

HCV = hepatitis C virus; PCP = primary care provider; SVR12 = 12-week sustained virologic response.

TABLE 4: Secondary outcome: substance use post-treatment

Substance Use	HCV Provider Group	PCP Group	*P* Value
UDS and/or LCMS results, n (%)[a]			
n	62	33	
Amphetamines	13 (21.0)	5 (15.2)	.49
Barbiturates	2 (3.2)	2 (6.1)	.51
Benzodiazepines	14 (22.6)	4 (12.1)	.22
Cannabinoids	46 (74.2)	28 (84.8)	.23
Cocaine	11 (17.7)	9 (27.2)	.28
Methadone	10 (16.1)	3 (9.1)	.34
Opiates	30 (48.4)	15 (45.5)	.79
Phencyclidine	1 (1.6)	...	...
Patient-reported type, n (%)			
n	241	139	
Alcohol	117 (48.5)	72 (51.8)	.54
Cannabis	62 (25.7)	52 (37.4)	.02
Opioid	13 (5.4)	4 (2.9)	.25
Sedative, hypnotic, or anxiolytic	7 (2.9)	3 (2.2)	.66
Stimulant	14 (5.8)	11 (7.9)	.43
Other	2 (0.8)	1 (0.7)	.91
Unspecified	1 (0.4)	1 (0.7)	.69
None	89 (36.9)	42 (30.2)	.16
Patient-reported route of use, n (%)			
n	152	97	
Oral ingestion	118 (77.6)	77 (79.4)	.23
Inhalation	42 (27.6)	34 (35.1)	.10
Intravenous	4 (2.6)	1 (1.0)	.44
Intranasal	2 (1.3)	...	...
Unspecified	40 (26.3)	24 (24.7)	.87

HCV = hepatitis C virus; LCMS = liquid chromatography mass spectrometry; PCP = primary care provider; UDS = urine drug screen.

[a]Results shown in this table do not include positive results for any medications documented as prescriptions at the time of the test.

completed HCV treatment and achieved SVR12 stratified by the type of follow-up provider, HCV provider versus PCP. Significant gaps were identified in post-HCV treatment care by HCV providers and PCPs alike. Although patients followed by HCV providers had a higher rate of completing an HCV RNA 12 months post-treatment, only 20% of the entire population met this standard. There are many possible reasons for the disparity, including lack of recommendations by HCV providers to PCPs during transitions of care. In fact, 66 of the 124 patients (53.2%) from the PCP cohort who did not have the HCV RNA drawn on time either did not have a documented recommendation from the HCV provider in the HCV clinic discharge note or the HCV provider stated the lab was not needed, which does not align with AASLD/IDSA guidelines for patients with ongoing risk factors for HCV.[5]

Of the 170 patients between both cohorts who were reassessed for HCV viral load within 24 months after HCV treatment, only 1 patient had a possible reinfection. The patient's original HCV genotype was 1b although the viral load post-treatment was not assessed for genotype. No substance use was documented within 24 months post-treatment; however, the patient did report unprotected sexual activity, which could have put this patient at risk for reinfection. Given the low number of possible reinfections, no correlation could be identified between engagement in SUDRP or social work services and reinfection rates. There was also missing data beyond SVR12 for some patients due to patients transferring care outside of VHI; therefore, a true reinfection rate cannot be determined. Previous studies[8,9,13] suggest engagement of these services would lower rates of substance use, thus decreasing the likelihood of HCV reinfection.

The large sample size was a strength of this study. Additionally, the cohorts had minimal differences in demographic information, which enhances the quality of the data comparisons between groups. Data was collected

up to 24 months after treatment completion, which allowed for more data to be analyzed. Furthermore, missing data was limited given the comprehensive medical record system shared by both primary and specialty care.

Study limitations include that it was a chart review in a single health care facility. Human error in missing or incorrectly categorizing data is possible. Data was excluded from outside facilities to ensure assessment of VHI clinic practices alone and may have excluded data from patients who intermittently received care at VHI. The population sizes differed greatly between the 2 groups and the sample was almost entirely male, which decreases the generalizability of the data analysis to each cohort. The data collection period was 2013-2019, which limited assessment for reinfection to within 24 months post-treatment and does not account for patients recently treated in the clinic.

The VHI HCV clinic is well-established with very high rates of patients achieving SVR, yet this is the first study at our site to examine what happens beyond this point. This study reveals the significant inadequacy of HCV post-treatment follow-up for patients with substance use and/or SUD despite enrollment in an organized clinic. Study findings identify future opportunities that may improve the quality of follow-up care patients with SUD receive. First, standardizing the lab scheduling process so the 12-month HCV RNA is scheduled earlier, such as at the final treatment appointment when SVR care is scheduled, may improve the admittedly low rate of HCV RNA completion found in this study. Second, training PCPs on guideline-recommended HCV RNA monitoring even after successful treatment may increase awareness that patients with SUD can become reinfected. CDC guidelines for bloodborne pathogen surveillance among persons who use substances recommend annual screenings for infections, such as viral hepatitis, which reinforces the need for routine monitoring.[14] Third, incorporating substance use treatment referrals into the standardized intake process for patients treated with HCV may decrease rates of future substance use and subsequent HCV reinfection. This avenue may also lead to more formal engagement in social work services. Pharmacists can support these initiatives by providing education about HCV surveillance and identifying patients for substance use treatment referrals.

As guidance for HCV treatment becomes more inclusive of patients with ongoing substance use, it is important that treatment clinics examine gaps in care and the extent of support services in place. HCV, SUD, primary care, and mental health clinics should collaborate to improve the quality of care for this population. Substance use is a chronic condition that involves periods of relapse and remission as part of the disease course, which bolsters the need for continuous surveillance for diseases such as HCV. Further research is needed at additional facilities so best practices for identifying and preventing reinfection can be established.

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