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Hepatitis C Infection in Non-Treatment-Seeking Heroin Users: The Burden of Cocaine Injection

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Abstract

Background and Objectives—In heroin dependent individuals, the HIV epidemic has been controlled in countries where access to opioid maintenance treatment (OMT) and needle exchange programs (NEP) have been implemented. However, despite similar routes of contamination for both viruses, the prevalence of hepatitis C (HCV) infection remains high in drug users. The objective of this analysis was to identify the prevalence of HCV and the correlates of being HCV-positive in a sample of out-of-treatment heroin-dependent individuals.

Methods—Data were collected from five inpatient studies (n = 120 participants) conducted at the New York State Psychiatric Institute. A logistic regression was used to identify correlates of being HCV-positive at baseline.

Results—Among the 120 heroin-dependent volunteers, 42 were HCV-positive. Participants who had heavier alcohol use, a longer duration of heroin use, or who reported using heroin by injection were more likely to be HCV-positive. Interestingly, participants who had injected cocaine during the previous month had a ninefold greater risk of being HCV-positive compared to non-cocaine users and those who used cocaine by a non-injecting route.

Conclusions and Scientific Significance—These findings confirm the risk of being HCV-infected through intravenous drug use, especially with cocaine use. These results underscore the importance of rethinking interventions to prevent HCV infection with combined strategies using pharmacological approaches for cocaine dependence and tailored prevention for cocaine users.

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Declaration of Interest

The authors taking part in this study declare that they have nothing to disclose regarding funding or conflict of interest with respect to this manuscript.

INTRODUCTION

Since the identification of non-A, non-B hepatitis in 1982, currently known as hepatitis C virus (HCV) infection, a decline in its incidence by more than 90% has been observed in the United States.[1] However, the same study, conducted from 1982 to 2006 by Williams et al.,[1] showed that the incidence of HCV in the subpopulation of injecting drug users (IDUs) remains very high. Injection drug use is known to be a common source of both HCVand HIV infection, but it is unclear why the course of the HCV epidemic is so different from the HIV epidemic among IDUs.[2] Indeed, the HIV epidemic in drug users has shown a tremendous decline in the last decade mainly due to needle exchange programs (NEPs) and access to opioid maintenance treatment (OMT).[3,4] Surprisingly, although less than 10% of IDUs are infected with HIV, the prevalence of HCV is commonly more than 60% in the same population.[5,6] Moreover, a recent Swedish study conducted in a NEP setting showed that HIV prevalence and incidence remained low and hepatitis B (HBV) incidence declined because of vaccination, but transmission of HCV was persistently high.[7] Several reasons may underlie this phenomenon including the persistence of risky behaviors[8,9] and the higher rate of infectivity of HCV.[10] Injection drug use is a well-known risk factor for HCV infection.[11] Cocaine use is also a well established risk factor for HCV infection, particularly when it is used intravenously,[12–16] because it is associated with unsafe injecting practices,[17] and also when it is smoked or snorted.[18,19] It is known that access to OMT has a positive impact on injection cessation in heroin users[20,21] and on HIV outcomes.[22,23] However, in out-of-treatment current heroin users, few studies have shown the correlates of HCV infection in order to identify some effective interventions to target this population.

The objective of the present study was to identify the prevalence of HCV and to assess the correlates of being HCV-antibody-positive among heroin-dependent individuals who were enrolled in inpatient laboratory studies.

MATERIAL AND METHODS

Data Collection

For this post hoc analysis, we used the information collected during the consent visit before entering the study for participants enrolled in one of five experimental inpatient studies conducted between 2006 and 2010 at the Substance Use Research Center of the New York State Psychiatric Institute. All of these studies aimed to investigate the effects of opioids in non-treatment-seeking, opioid-dependent volunteers. More precisely, study #4,857 examined the reinforcing effects of oral prescription opioids in buprenorphine-maintained participants (n = 26), study #5,182 assessed the relationship between infusion duration and reinforcing effects of intravenous oxycodone in buprenorphine-maintained individuals (n = 19), study #5,518 compared the reinforcing effects of intravenous buprenorphine and the buprenorphine/naloxone combination (n = 15), study #5,725 evaluated a glial activation inhibitor, ibudilast, in heroin abusers under conditions of morphine maintenance and withdrawal (n = 41), and study #5,879 compared the reinforcing effects of intranasal buprenorphine and buprenorphine/naloxone in intranasal heroin abusers (n = 19). One recent paper summarized four of these studies.[24] For two of the studies (#5,182 and #5,518), the

design, objectives, and other study-related contingencies have been described in previous articles.[25,26] Manuscripts from the remaining three studies currently are in preparation.

Screening

After completing an initial telephone interview, eligible participants came into the hospital to provide consent to receive additional screening, which included completing detailed medical history and drug use questionnaires, unstructured clinical interviews with a psychologist and psychiatrist, and a medical evaluation conducted by a physician.

For this analysis, we used the data collected during an interview with a PhD-level staff member using the same standardized questionnaire for each study. It includes a set of questions concerning socio-demographic data, as well as recent and past drug use. The educational level was assessed using the highest grade or degree completed and the ethnicity was reported by the participant (Hispanic, Caucasian, African American, Asian, or other). Regarding the history of treatment for heroin dependence, we considered any reported opioid maintenance treatment or detoxification program during the lifetime as treatment. Heroin use was quantified by the number of bags used per day and described by the preferred route of administration. One street bag of heroin in New York City contains approximately 25 mg of pure heroin and costs $10.[25] Cocaine use was quantified by the number of days per month participants reported having used cocaine and described by the route of administration, alcohol use was quantified by the number of drinks ingested per month and tobacco use was quantified by the number of cigarettes smoked per day during the last month.

The diagnosis of HCV infection was based on analysis of plasma using the method of enzyme-linked immunosorbent assay (ELISA). Participants were asked about their HIV serostatus during the medical evaluation, but the presence or absence of HIV was not confirmed objectively. However, blood tests confirmed the absence of any other active diseases for example, HIV-related opportunistic infections. Urine drug toxicologies (using urine quick tests) were performed several times during screening to test for opioids, benzoylecgonine (cocaine metabolite), benzodiazepines, cannabinoids, and amphetamines. A naloxone challenge test or visual observation of opioid withdrawal symptoms was carried out on all potential participants to confirm current dependence on opioids. Participants who were requesting drug treatment, had a current major Axis I psychopathology other than opioid dependence (ie, schizophrenia or major depression), or met DSM-IV criteria for dependence on drugs other than opioids, nicotine, or caffeine were excluded from the study. Individuals on parole or probation, or with histories of significant violent behavior also were excluded.

Before admission, all participants signed consent forms that described the risks and benefits of participation and explained the overall aims of the study. For these studies, the common inclusion criteria required participants to be healthy volunteers, users of heroin, and not seeking treatment for their heroin dependence. All of the studies were approved by the New York State Psychiatric Institute’s Institutional Review Board.

Statistical Analyses

A logistic regression was used to identify factors associated with HCV-antibody-positive tests at baseline among the participants who were enrolled in the five studies. To avoid situations where strong confounding could hide important predictors of HCV-antibody-positive test, a liberal *p*-value of <.20 was defined in the bivariate analysis to select eligible factors for the multivariate model and then, a stepwise backward selection procedure was used, based on a *p*-value >.05 to identify the best multivariate model. The area under the curve (AUC) was calculated to determine model robustness for identifying correlates of HCV-antibody-positive test.

As some studies have tried to show that objective measurements such as urine drug tests are more reliable than self-reported data obtained through questionnaires or interviews, we decided to perform an ancillary analysis using urine drug toxicology for cocaine use instead of self-reported cocaine use to confirm the validity of self-reported drug use. First, we assessed the correlation between self-reported use and urinary toxicology results for each drug tested. Then, we replaced the self-reported drug use variable with the objective result of urine drug toxicology in the multivariate analysis to confirm the association with the outcome.

RESULTS

Sample Characteristics

As summarized in Table 1, among the 120 participants enrolled, 42 tested positive for HCV infection before entering the studies. All participants were asymptomatic and without signs of hepatic compromise just prior to admission into the hospital and throughout study participation, as transaminases greater than 2–3× normal were exclusionary. We would estimate that a significant majority of participants testing positive for HCV antibodies have a chronic HCV infection, but HCV RNA was not tested in the current studies to confirm the presence of live virus. As part of the medical screening interview, risks for HIV and hepatitis transmission were reviewed, and participants were required to be using adequate forms of contraception during study participation. Twelve percent (14) of the participants were female and the median age was 39 years [35–42]. Almost one-third (35, 35%) of the population reported being Caucasian, 24 (24%) were African American, and 42 (41%) were Hispanic. At baseline, 73 (61%) of the participants reported being intravenous heroin users and the remaining 47 (39%) were intranasal heroin users. Regarding cocaine use, although 53 participants reported no cocaine use, 21 reported smoking, 18 snorting, and 28 injecting cocaine during the previous month. Of those who used cocaine, the average self-reported number of days per month of cocaine use was 2.2 [0–16]. The average self-reported number of heroin bags used per day was 6 [4–10]. At baseline, the urine drug toxicology tests revealed that 15%, 57%, 25%, 28%, 23%, and 38% of the 120 participants were positive for, respectively, cannabis, cocaine (benzoylecgognine), benzodiazepines, oxycodone, buprenorphine, and methadone. By comparison, analysis of the self-reported use of drugs at baseline revealed that 24% and 53% of the 120 participants, respectively, endorsed current (within the past month) use of cannabis and cocaine.

Correlates of HCV-Antibody-Positive Test at Baseline

Table 1 shows the results of the bivariate analysis and Table 2 gives the correlates of being HCV-positive at enrollment. After the multivariate analysis, which consisted of adjusting all of the variables in the same model, participants who had a longer duration of heroin use, heavier alcohol use, and reported using heroin by injection were more likely to be HCV-positive. Interestingly, participants who had injected cocaine during the previous month had a ninefold greater risk of being HCV-positive compared to non-cocaine users or those who used cocaine by a non-injecting route. After calculating the area under the curve, the model showed an excellent discrimination [AUC = .83 (95% Confidence Interval (CI): .75–.91)].

We also performed a model using a continuous variable of cocaine use in terms of number of days used per month. This variable was significantly associated with HCV infection [odds ratio (95% Cl) = 1.21 (1.03–1.41); p = .02].

The self-reported cocaine use data were based on past-month use, while the cocaine urine drug toxicology results reflected use within the past 3–4 days. Nevertheless, in order to provide a rough confirmation of the self-reported cocaine use data, analyses also were performed using cocaine urine drug toxicologies. The first finding was that self-reported past-month cocaine use was strongly correlated with the cocaine urine toxicology results (Z = 5.69; $p < .001$). Second, when urine drug toxicology results were used instead of self-reported cocaine use in the final model, the results did not change compared to when self-reported cocaine use was examined.

CONCLUSIONS

This study shows a prevalence of HCV (35%) in this sample of heroin-dependent individuals that is lower than the prevalence found among injection drug users (80% or greater).[27] In addition, we identified the correlates of being HCV-antibody positive among our non-treatment-seeking heroin users. Not surprisingly, participants who reported being intravenous heroin users had a 3.5-fold greater risk of being HCV positive compared to intranasal heroin users as injecting is one of the main modes of disease transmission[28] and HCV has a higher rate of infectivity than HIV.[10] As the present study reveals, heroin users who have a longer heroin use career also are more likely to be HCV positive. This is consistent with the literature showing a higher prevalence of HCV infection in long-term injecting drug users.[29]

Alcohol use also appears to be associated with HCV positive serostatus. Indeed, a review by Bhattacharya and Shuhart[30] revealed that HCV infection is common among unselected alcoholics, with prevalence rates ranging from 14% to 36%. Alcohol's known psychological effects (ie, disinhibition, loss of judgment, mood elevation, or depression) can lead to engagement in high-risk sexual and drug-taking behaviors,[31] which in turn increase the probability of HCV transmission. The present findings emphasize the importance of tailoring prevention messages to those who use heroin in combination with other drugs, such as alcohol and cocaine, and to refer those who are HCV-positive to adequate care.

After adjusting for these latter important determinants, our results showed that HCV was more prevalent in individuals who also use cocaine and particularly among those who report cocaine injection. Specifically, cocaine injectors have a ninefold greater risk of being HCV positive, compared to non-cocaine users. This result endorses observations reported in previous studies about cocaine use as a risk factor of HCV transmission.[32–34] Although some data exist on the transmission risk through sharing of straws,[19] many of those who use cocaine when they initiate injection of drugs have a higher risk of HCV transmission because cocaine is typically used multiple times (three or more) during each injection event.[35] Also, our results showed that the more frequently the participant used cocaine during the previous month, the greater the risk of being HCV positive. Even though cocaine dependence, as defined by DSM-IV criteria, was exclusionary, the burden of cocaine use highlights the need for effective treatments for this disorder since no pharmacological treatment is available currently and it is known that cocaine use and especially dependence is highly correlated with risky drug taking behaviors in terms of frequency, quantity, and route of administration.[36,37]

The high prevalence of HCV compared to HIV found in the present study, as well as in other studies conducted in New York City,[38,39] raises concerns that preventive interventions, mainly developed to target HIV epidemics did not effectively reduce HCV transmission. Therefore, innovative strategies should be implemented to reduce the transmission of HCV in drug users. This suggestion was raised previously by Mateu-Gelabert et al.,[40] who described the importance of implementing new interventions focusing specifically on HCV transmission risk behaviors. These interventions for safer injection should also focus on the sharing of unsterile equipment which has been shown to be as risky as the sharing of syringes[41] and should be based on peer mentoring interventions.[42] In addition, to this preventive approach, it is urgent to develop therapeutic strategies for pathological conditions that increase HCV transmission, such as stimulant dependence and psychiatric comorbidities.

Some limitations of our analysis should be acknowledged. First, examination of self-reported drug use may be questionable because it may underestimate the true pattern of use. However, previous studies have demonstrated that it can be used as a reliable tool[43,44] and, in fact, a strong correlation between self-reported cocaine use and cocaine urine toxicology results was found in the present study. Because HIV serostatus also was collected through self-reports, its prevalence also may have been underestimated. However, as with self-reported drug use, several studies have shown the validity of self-reports on HIV outcomes in different contexts.[45,46] Nevertheless, because we did not confirm HIV status objectively, the present results should be viewed with some caution. It is important to note that because cocaine dependence was an exclusion criterion, it limited the enrollment of more at-risk individuals. A more representative sample would have included a higher number of at-risk cocaine users, which would have permitted a more powerful analysis of risk factors and HCV infection. In addition, the small sample size may explain the lack of association between non-intravenous cocaine use and HCV infection, as it is also known to be a risk factor.[18,19] Finally, the correlation between recent drug use and HCV serostatus must be interpreted carefully because the date of HCV contamination is unknown. That is, the causal link between drug use and HCV infection could not be established in the present study.

Our results underscore the importance of focusing on more targeted prevention strategies for HCV transmission, particularly in intravenous drug users, as well as stimulant and alcohol users. The identification of correlates of HCV infection is crucial in aiding public health decision makers to implement more adequate preventive interventions for drug users. Furthermore, innovative prevention strategies focusing on intravenous drug use and stimulant dependence should be developed to aid in the efforts to reduce transmission of HCV among heroin users.

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S. Comer, J. Jones, and P. Roux were involved in the study concept and design as well as the acquisition of data. Statistical analyses and interpretation of data were performed by L. Fugon and P. Roux. P. Roux was principally involved in the drafting of the manuscript under the supervision of S. Comer. We gratefully acknowledge the medical support of Drs. Sullivan, Manubay, Martinez, Mogali, Dakwar, Kalapatapu, and Herron, the nursing support of Ms. Tindall and Murray, and the technical support of Ms. Madera, Fogel, Bielaczyc, and Mr. Saccone and Lazar. We also thank all physicians, nurses, and research assistants who were involved in the studies and the entire heroin users who participated in these studies.

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TABLE 1

Factors associated with HCV-antibody-positive test at baseline

	Participants (%) or median [IQR]		Bivariate analysis	
	HCV−	HCV+	OR (95% CI)	*p*-value
Study protocol				
#4,857	21 (27)	5 (12)	1	
#5,182	8 (10)	11 (26)	5.78 [1.52–21.93]	.01
#5,518	8 (10)	6 (14)	3.15 [.75–13.29]	.12
#5,725	30 (39)	12 (29)	1.68 [.51–5.48]	.39
#5,879	11 (14)	8 (19)	3.05 [.80–11.60]	.10
Age	38 [35–41]	39 [34–44]	1.03 [.96–1.11]	.38
Gender				
Male	69 (89)	37 (88)	1	
Female	9 (11)	5 (12)	1.04 [.32–3.32]	.95
Years of education*	12 [12–13]	12 [11–12]	1.08 [.93–1.27]	.32
Race				
African American	21 (27)	10 (24)	1	
Caucasian or Hispanic	57 (73)	32 (76)	1.18 [.49–2.81]	.71
Employment				
No	67 (86)	38 (91)	1	
Yes	11 (14)	4 (9)	.64 [.19–2.15]	.47
Years of heroin use†	10 [7–16]	15 [8–20]	1.05 [1–1.11]	.06
Route of administration for heroin use‡				
Intranasal	39 (50)	8 (19)	1	
Intravenous	39 (50)	34 (81)	4.25 [1.75–10.34]	.001
Heroin bags per day‡,§	6 [4–9]	6.5 [4–10]	1.03 [.96–1.11]	.44
Alcohol use‡,§,¶	1 [0–3]	2 [0–12]	1.03 [1–1.06]	.08
Tobacco use‡,§,‖	10 [6–20]	13.5 [10–20]	1.04 [1–1.09]	.06
Cocaine use‡,§				
No cocaine use	41 (53)	12 (29)	1	
Smoking cocaine use	16 (20)	5 (12)	1.07 [.32–3.52]	.91
Intranasal cocaine use	14 (18)	4 (9)	.98 [.27–3.52]	.97
Intravenous cocaine use	7 (9)	21 (50)	10.25 [3.51–29.89]	$<10^{-3}$

Bivariate analysis based on a logistic regression model (n = 120).

*For each grade year increase;

†Per 1 year increase;

‡During the previous month;

§At the consent visit before entering the study (baseline visit);

¶Number of drinks per month;

[||]Number of cigarettes per day.

TABLE 2

Factors associated with HCV-antibody-positive test at baseline

	Multivariate analysis	
	aOR (95% CI)	***p*-value**
Years of heroin use*	1.10 [1.03–1.18]	.008
Route of administration for heroin use		
Intranasal	1	
Intravenous	3.49 [1.09–11.18]	.04
Alcohol use†,‡	1.05 [1.01–1.10]	.01
Cocaine use†		
No cocaine use	1	
Smoking cocaine use	1.09 [.27–4.37]	.90
Intranasal cocaine use	1.22 [.30–4.98]	.78
Intravenous cocaine use	8.52 [2.58–28.21]	$<10^{-3}$

Multivariate analysis based on a logistic regression model (n = 120).

*Per 1 year increase;

†At the consent visit before entering the study (baseline visit);

‡Number of drinks per month.