

Sharing of Noninjection Drug-Use Implements as a Risk Factor for Hepatitis C

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ABSTRACT

This study examined sharing noninjection drug implements as a risk factor for hepatitis C (HCV) infection among women drug users ($n = 123$) with no history of drug injection. Participants were street-recruited from East Harlem, New York City, between October 1997 and June 1999. Participants were administered a survey measuring risk factors for HCV. Prevalence of HCV and HIV infections was 19.5% and 14.6%, respectively. Multiple logistic regression determined significant associations between sharing noninjection drug-use implements and HCV infection. “Ever shared both oral and intranasal noninjection drug implements” was independently

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associated with HCV infection [Odds ratio (OR) 2.83; Confidence interval (CI) 1.04, 7.72; $p=0.04$]; "ever shared noninjected heroin implements with an injector" was a trend (OR 3.06; CI .85, 10.79; $p=0.08$). The strongest association between sharing noninjection drug-use implements and HCV infection was found among HIV positive individuals ($\chi^2=8.8$, 1 d.f., $p<0.01$). These findings, if supported by future research, indicate a need to reassess policies regarding HCV infection.

Key Words: Risk factors for HCV infection; HCV infection and drug use; HCV and HIV co-infections.

INTRODUCTION

Hepatitis C virus (HCV) is the single most important cause of liver disease worldwide (Amarapurkar, 2000). In the United States the prevalence of HCV among the general population is about 1.8% (Amarapurkar, 2000). Primarily transmitted through blood-to-blood contact, it is endemic among injection drug users (IDUs) and hemophiliacs transfused prior to 1992. About 60% of infections are attributable to syringe sharing among IDUs (Alter, 1999), and another important proportion of infections is linked to the sharing of equipment used to prepare drugs for injection (Hagan et al., 2001).

Several studies have reported very low levels of nonparenteral HCV transmission through sexual contact and sharing household implements (Ackerman et al., 2000), and recent data show HCV viral titers in low quantities in nonserologic body fluids such as semen, vaginal fluids, and saliva (Ackerman et al., 1998). Some estimates indicate about 10% to 12% of infections cannot be accounted for by any recognized source (Flamm et al., 1998; Murphy et al., 2000), most of which occur among individuals of low socioeconomic status (Alter, 1999).

In a previous study, we documented an unexpectedly high prevalence of HCV infection among drug-users who reported never injecting. Participants in this study were recruited in two neighborhoods in New York City: East Harlem and the Lower East Side of Manhattan. The prevalence of HCV ranged from 5% to 29%, according to age, gender, and location (Tortu et al., 2001). This finding raised the possibility of noninjection drug-related HCV transmission among this population.

In New York City, illegal noninjected drugs such as heroin and cocaine are administered orally, via pipes, or intranasally, through straws

or rolled bank notes. These implements are often shared, and may come into contact with blood or other bodily fluids in the nose and/or mouth, thus serving as conduits through which HCV and other pathogens can travel from person to person. Conry-Cantilena et al. (1996) reported intranasal cocaine use as a significant risk factor for HCV infection among U.S. blood donors, but did not measure implement sharing. In a recent case-control study of 1797 blood donors, Murphy et al. (2000) evaluated a series of risk factors for HCV infection, including use of "inhaled drugs." Although drug inhalation was a significant risk factor in univariate analysis (even when controlling for IDU status), it did not retain significance in the final multiple regression model reported by these authors. However, the variable "inhaled drugs" does not necessarily involve the exchange of bodily fluids, such as when vapors from cooked heroin are inhaled (i.e., "chasing the dragon"), nor does it measure the *sharing* of noninjection implements.

In the present study, we documented the prevalence of HCV and HIV among women drug users who reported never injecting and examined the association between HCV infection and possible risk factors for HCV, including pre-1992 transfusion, lifetime number of sex partners, and sharing noninjection drug-use implements with both IDUs and non-IDUs. Other putative risk factors, including surgical or dental procedures, tattooing, acupuncture, and body piercing, were not measured because most studies have shown no association between these and HCV infection in U.S. populations (Alter, 1999).

METHODS

Study Protocol

Using targeted sampling methods (Watters and Biernacki, 1989) and participant referrals, over 600 women drug users were recruited between October 1997 and June 1999 for a study on social factors associated with risk for HIV/AIDS. Women were at least 18 years old, heterosexually active at least once in the previous 6 months, and used injected or noninjected heroin, cocaine or crack in the last 30 days. Drug use was verified by urinalysis. Participants were aware that urinalysis results were available before the interview, thus enhancing the validity of self-reports (Hamid et al., 1999). All participants reviewed and signed informed consents. Structured interviews were conducted, and participants were paid \$25. All were offered counseling and testing for HIV and HCV infections.

Sample Description

For this report, we examined a subsample of 123 women who underwent voluntary hepatitis and HIV testing and had no history of drug injection. Each completed a supplemental questionnaire on possible risk factors for HCV, in addition to other survey items. Demographic characteristics were: mean age, 37.8 years; 54% African-American, 45% Puerto Rican; 50% high-school graduates; 11% homeless; 79% ever incarcerated; 85% ever used crack, 62% ever used noninjected heroin, 85% ever used noninjected cocaine; 59% reported 10 or more lifetime sex partners; and 14.6% tested HIV positive on the basis of saliva testing.

Validity of Injector Status

Never-injector status was based on self-report and interviewer observations. Numerous items regarding injection drug use were embedded in different sections of the survey. Four respondents were excluded from the subsample because of conflicting responses regarding injector status, past or present. Also, our interviewers have had extensive experience with injectors, and were instructed to look for signs of injection (e.g., needle track marks). Both self-reported injectors and noninjectors were accepted into the original sample from which the subsample was drawn; thus, there was no reason for participants to misrepresent their injector status to get into the study.

Survey and Hepatitis C Testing

Survey topics included: demographics, drug use history, current drug use, and possible risk factors for HCV infection, including sexual history, history of blood transfusion, use of noninjection drug implements (i.e., straws, rolled bank notes, pipes, etc.), and sharing noninjection implements with nonIDUs and IDUs. Hepatitis C testing was conducted using the ELISA (Abbott HCV EIA 2.0; Abbott Laboratories, Abbott Park, IL) procedure for encoded antigens (recombinant c100-3, HC-31, and HC-34).

Data Analyses

A case-control analysis was used to determine risk factors associated with HCV infection using published statistical software (SAS 8.0; PASS 6.0, NCSS). Inferential tests of significance were evaluated at $\alpha = 0.05$. In univariate analysis, the unadjusted chi-square statistic was used to assess the association between HCV status and categorical dichotomous variables (including continuous variables recoded as such). For 2×2 tables in which cells had expected counts of less than 5, a two-tailed Fisher's Exact test was used. For ordinal variables composed of three or more categories, the Mantel-Haenszel statistic was used to test for significant trends. Variables significant at ≤ 0.15 in the univariate analysis were retained in the multivariate analyses. Multiple logistic regression was used to test for significant associations between noninjection drug-use implement sharing and HCV status, while controlling for other known or potential sources of HCV infection. Several model-building methods were applied in the multiple regression analyses of the main effects. Incremental tests for significance were used to assess effects of interaction terms.

Power analysis revealed that with 80% power, the chi-square tests could detect medium to large effect sizes ($w \geq 0.23$) as defined by Cohen (1988); and the multiple logistic regression test achieved 80% power to detect an Odds Ratio (OR) of 3.0 or greater.

RESULTS

Of 123 drug users in the sample, 24 (19.5%) tested anti-HCV positive. Demographic and drug use characteristics of the sample are presented in Table 1. No statistically significant differences between cases and controls on demographic characteristics were found. However, it should be noted that observed effect sizes between demographic characteristics and HCV status were small (generally $OR \leq 1.5$), and our sample size may have lacked sufficient power to detect significant associations in chi-square tests. Similarly, two variables representing known or suspected risk factors for HCV transmission—lifetime number of sex partners and blood transfusion prior to 1992—had effect sizes too small to detect in this analysis. However, a significant association was detected between HIV and HCV infections, measured by saliva and blood test results. The likelihood that HIV-positive women were infected with HCV was 4.5 times that of HIV-negative women [95% confidence

Table 1. Selected demographic and drug use history. $n = 123$ female never-injectors.

Characteristic	%
Age	
Under 30	9.8
30 to 39	52.8
40 or over	37.4
Race/ethnicity	
African-American	53.7
Hispanic	44.7
White	1.6
Graduated high school	50.4
Homeless	10.6
Lifetime incarceration record	
None	28.5
Less than 1 year	52.0
1 year or more	19.5
Ever have sexually transmitted disease	44.7
HIV positive	14.6
Number lifetime male sexual partners	
Less than 10	41.5
10-99	43.9
100 or more	14.6
Ever used crack	84.6
Ever used non-injected heroin	61.8
Ever used non-injected cocaine	85.4
Last 30 days drugs used	
Crack only	39.8
Non-injected heroin only	14.6
Non-injected cocaine only	14.6
Crack and NI heroin	13.0
Crack and NI cocaine	7.3
NI heroin and NI cocaine	5.7
Crack, NI heroin, and NI cocaine	4.9

interval (CI): 1.54, 13.34; $p = 0.008$, Fisher's Exact]. Univariate analyses of noninjection drug-use implement sharing revealed two variables that were significantly associated with HCV infection: a) ever shared noninjected heroin implements with an injector; b) ever shared both intranasal and oral drug-use implements.

Multiple logistic regression analyses tested for significant independent associations between noninjection implement sharing and HCV infection, while controlling for other potential routes of HCV transmission. Logistic regression models were specified on the basis of theoretical or etiological considerations to include only variables representing known or suspected routes of transmission, and factors that may facilitate HCV transmission.

Five noninjection drug implement sharing variables with p values ≤ 0.15 in the univariate analyses, shown in Table 2, were entered into the main effects model (see Table 3). They included: a) ever shared crack implements, b) ever shared noninjected cocaine implements, c) ever shared noninjected heroin implements with an injector, d) ever shared any oral implements, and e) ever shared both oral and intranasal implements. Lifetime number of male sex partners and having received a pre-1992 blood transfusion were included as covariates. Choice of model selection technique (hierarchical, simultaneous, forward, backward, or stepwise) had no effect on final model specification. Two implement sharing risk factors were retained from the main effects model: "ever shared both oral and intranasal drug implements" was independently associated with HCV infection (OR 2.83; CI: 1.04, 7.72; $p=0.04$); and "ever shared noninjected heroin implements with an injector" was a trend (OR 3.06; CI .85, 10.79; $p=0.08$).

In the second phase of the analysis, main effects and interaction terms between each of two implement-sharing variables and HIV serostatus were entered into the model incrementally. A likelihood ratio test was used to determine whether the increment in the proportion of variance accounted for by addition of the interaction terms was statistically significant. Inclusion of the combined effects of sharing oral/intranasal implements and HIV seropositivity added significant explanatory power to the main effects model (Likelihood ratio test: $\chi^2=8.8$, 1 d.f., $p<0.01$). Similarly, the combined effects of sharing noninjected heroin implements with an injector and HIV seropositivity provided a significant increase in the proportion of explained variance in HCV serostatus, when added to the main effects model (Likelihood ratio test: $\chi^2=4.39$, 1 d.f., $p<0.05$). The main effects comprising the interaction terms were not significantly associated.

DISCUSSION

This study produced several provocative findings. First, data suggest that sharing noninjection drug-use implements (both orally and

Table 2. Noninjection implement sharing risk behavior by hepatitis C blood test results. *n* = 123 female never-injectors.

Risk factor	No. HCV- positive/ No. tested	% HCV positive	OR (95% CI)	<i>p</i> ^a
Ever shared crack implements	—	—	2.12 (0.77, 5.80)	0.14
No	6/47	12.8	—	—
Yes	18/76	23.7	—	—
With injector	—	—	1.45 (0.42, 4.97)	0.51
No	20/107	18.7	—	—
Yes	4/16	25.0	—	—
Ever shared heroin implements	—	—	1.25 (0.51, 3.06)	0.63
No	13/72	18.1	—	—
Yes	11/40	21.6	—	—
With injector	—	—	4.38 (1.32, 14.57)	0.02
No	18/110	16.4	—	—
Yes	6/13	46.2	—	—
Ever shared cocaine implements	—	—	2.21 (0.81, 6.05)	0.12
No	6/48	12.5	—	—
Yes	18/75	24.0	—	—
With injector	—	—	0.57 (0.67, 4.88)	1.0
No	23/115	20.0	—	—
Yes	1/8	12.5	—	—
Ever shared oral implements	—	—	2.12 (0.77, 5.80)	0.14
No	6/47	12.8	—	—
Yes	18/76	23.7	—	—
With injector	—	—	1.04 (0.27, 4.00)	1.0
No	21/108	19.4	—	—
Yes	3/15	20.0	—	—
Ever shared intranasal implements	—	—	1.99 (0.68, 5.79)	0.20
No	5/39	12.8	—	—
Yes	19/84	22.6	—	—
With injector	—	—	2.34 (0.71, 7.64)	0.17
No	19/108	17.6	—	—
Yes	5/15	33.3	—	—
Shared both intranasal and oral implements	—	—	3.44 (1.31, 9.03)	0.01
No	7/65	10.8	—	—
Yes	17/58	29.3	—	—
With injector	—	—	2.91 (0.46, 18.47)	0.25
No	22/118	18.6	—	—
Yes	2/5	40.0	—	—

Note: CI, confidence interval; OR, odds ratio.

^a*p* values are for χ^2 except for "With Injector" items, which are for Fisher's Exact Test.

Table 3. Multiple logistic regression models for predictors of antiHCV serostatus. *n* = 123 female never-injectors.

Main effects entered			
Number of lifetime male sex partners			
Pre-1992 blood transfusion			
Ever shared noninjected crack implements			
Ever shared noninjected cocaine implements			
Ever shared noninjected heroin implements with an injector			
Ever shared any oral drug-use implements			
Ever shared both oral and intranasal drug-use implements			
Main effects retained	Adjusted OR (95% CI)	<i>p</i>	
Ever shared both oral and intranasal drug-use implements	2.83 (1.04, 7.72)	0.04	
Ever shared noninjected heroin implements with injector	3.06 (0.87, 10.70)	0.08	
Likelihood ratio test for significant increment of variance accounted for by effect modifiers	-2 Log likelihood	χ^2 (d.f.)	<i>p</i>
Main effects model	111.64	—	—
Modifier I: HIV serostatus \times oral and intranasal implement sharing	102.84	8.8 (1)	< 0.01
Modifier II: HIV serostatus \times shared noninjected heroin implements w/IDU	107.25	4.4 (1)	< 0.05

Note: OR, odds ratio; CI, confidence interval.

intranasally) may be a risk factor for HCV infection. This finding may explain the higher than expected prevalence of HCV observed in this sample. Also, the trend demonstrating an association between HCV infection and sharing noninjection heroin implements with an IDU may indicate a route of infection that bridges IDU and non-IDU populations. Finally, the strong association observed between HIV and HCV seropositivity among women reporting no history of injecting drugs indicates that HIV may facilitate the transmission of HCV through noninjecting routes (Filippini et al., 2001; Giuliani, 1997). Our finding that the joint effects of noninjection drug-use implement sharing and HIV seropositivity significantly added to the explanatory power of the main effects model supports this hypothesis.

Study's Limitations

Although our findings are compelling, this study is not without limitations. The cross-sectional design obviates causality inferences. Specifically, the timing of HCV infection is unknown in relation to reported risk behaviors. Also, the use of self-reported behavior may have introduced bias. However, in a recent review, Darke (1998) concluded that self-reports are sufficiently reliable and valid to afford accurate descriptions of drug use behavior. Moreover, drug testing by urinalysis, when conducted prior to a survey, dramatically increases the validity of such data (Hamid et al., 1999). The generalizability of our findings to noninjectors in other geographical locations is unknown and will require additional research.

Abbott Laboratories reported that specificity of the HCV test used is high, with a false positive rate of 0.17%. The false negative rate was estimated at 27.27%. Thus, the antiHCV prevalence reported here might be underestimated. Finally, as previously noted, the small sample size may lack sufficient power to detect significant associations between HCV infection and other risk factors. The limited number of participants in this study precluded the use of matched case-control methodology. Given these limitations, our findings must be interpreted carefully and confirmed by prospective studies. Nevertheless, our results are intriguing and suggest that noninjection drug-use implement sharing among substance users may be an important risk factor for hepatitis C transmission.

Implications

If substantiated by further research, our findings have a number of relevant implications.

- First, there is the need to reassess blood donor screening criteria to include noninjection as well as injection drug use practices.
- In addition, HCV screening procedures that exclude substance users with no history of injection drug use will need to be reevaluated. Such screening criteria may exclude a substantial number of HCV-infected individuals.
- Finally, prevention programs will need to include noninjection implement sharing as a potential risk factor for HCV transmission. Given the important consequences of these findings, more research on this topic is warranted.

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RESUMEN

Este estudio examinó el compartimiento de implementos de drogas no inyectadas como factor de riesgo para la infección de Hepatitis C (HCV) entre mujeres usuarias de droga ($n = 123$) sin historial de inyección de droga. Las participantes fueron reclutadas en las calles de Harlem Oriental, NYC, entre octubre 1997 y junio 1999. Las participantes fueron administradas una entrevista midiendo los factores del riesgo para HCV. La frecuencia de HCV e infecciones de VIH fueron de 19.5% y 14.6%, respectivamente. Múltiples retrocesos logísticos determinaron las asociaciones significativas entre compartir implementos de uso de drogas no inyectadas e infección de HCV. “Alguna vez compartió implementos para el uso de droga no inyectada ambas orales e internasales” se asoció independientemente con la infección de HCV (OR 2.83; CI 1.04, 7.72; $p = 0.04$); “compartió alguna vez implementos para el uso de heroína no inyectada con un inyector” fué una tendencia (OR 3.06; CI .85, 10.79; $p = 0.08$). La asociación más fuerte entre compartir implementos para el uso de drogas no inyectada e infección de HCV fue encontrada entre individuos positivos de VIH ($\chi^2 = 8.8$, 1 D.F., $p < 0.01$). Estas conclusiones, si las apoyamos con investigación futuras, indican una necesidad de revalorar las normas con respecto a la infección de HCV.

RÉSUMÉ

Cette étude a examiné le partage d'instruments d'utilisation de drogues de non-injectées comme facteur de risque pour l'infection de

l'hépatite C (HCV) parmi les femmes utilisatrices de drogues ($n = 123$) qui n'avaient pas d'histoire d'injection de drogue. Les participants furent recrutées dans les rues de Harlem Est à New York City entre octobre 1997 et juin 1999. Un questionnaire qui mesure les facteurs de risque de HCV fut administré. La prévalence du HCV et du VIH étaient 19,5% et 14,6%, respectivement. La régression logistique multiple a déterminé des associations significatives entre le partage d'instruments d'utilisation de drogues de non-injectées et l'infection de HCV. "Avoir partagé des instruments oraux et intranasaux de drogues non-injectées" était indépendamment associés à l'infection du HCV (OR 2.83; CI 1.04, 7.72; $p = 0.04$); "avoir partagé des instruments d'utilisation d'héroïne non-injectées avec un injecteur" était une tendance (OR 3.06; CI .85, 10.79; $p = 0.08$). L'association la plus forte entre le partage d'instruments de drogue non-injectées et l'infection de HCV a été trouvée parmi les individus positifs pour le VIH ($\chi^2 = 8.8$, 1 d.f., $p < 0.01$). Ces résultats, s'ils sont soutenus à l'avenir, indiquent un besoin de réévaluer des pratiques concernant l'infection de HCV.

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