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Can Intranasal Drug Use Reduce HCV Infection among Injecting Drug Users?

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Abstract

Background—Preventing HCV infection among people who inject drugs is a difficult public health challenge. We examined the potential role of intranasal drug use in reducing HCV acquisition.

Methods—Subjects were recruited from IDUs entering the Beth Israel drug detoxification program from 2005–2010. A structured interview was administered and serum samples were collected for HCV testing.

Results—726 active injecting drug users were recruited from 2005 – 2010. HCV prevalence was 71%, 90% reported recent heroin injection and 44% reported recent intranasal heroin use. In a multiple logistic regression analysis, being HCV seropositive was associated with more years injecting, Latino ethnicity, previous testing for HCV, and recent injection of speedball, and negatively associated with recent intranasal use of heroin (AOR = .52, 95% CI .33–.82) and intranasal use of speedball (AOR = .41, 95% CI .31–.80). The association between intranasal heroin use and lower HCV seroprevalance was observed among both new injectors and persons with long injecting histories (16+ years since first injection).

Conclusion—Encouraging intranasal use as an alternative to injection among persons currently injecting drugs may be a viable strategy for reducing HCV transmission.

Keywords

injecting; non-injecting; intranasal drug use; HCV

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1. Introduction

Hepatitis C virus (HCV) infection in people who inject drugs or injecting drug users (IDUs)¹ again present a very difficult challenge to public health systems. HCV is efficiently transmitted via parenteral exposure to infectious blood, and the prevalence of HCV infection in IDU populations typically ranges between 40–90%, depending on geographic location and years injecting drugs (Gerberding, 1994; Hagan et al., 2008). Most studies of HCV incidence among IDUs show rates from 20–40 infections/100 person-years (Hagan et al., 2010; Hagan et al., 2001; Lucidarme et al., 2004; Maher et al., 2006; Semaan et al., 2010; Semaan and Leinhos, 2007; van den Berg et al., 2007).

Acute HCV infection results in chronic infection in 70–80% of cases, and 20–25% of those with chronic infection will develop liver disease, including cirrhosis, liver failure or hepatocellular carcinoma (Burke and Cox, 2010). In the US, it is expected that HCV-related mortality will surpass HIV-related mortality in the coming years (Deuffic-Burban, 2010), since no vaccine exists to prevent HCV infection (Grebely and Dore, 2011). Treatment for HCV infection is costly, and IDUs are less likely to receive care and treatment of the infection than other patients (Grebely et al., 2009; Stoove et al., 2005). Thus, the prevention of primary HCV infection among IDUs is a public health issue of major importance.

There have been a moderate number of studies of HCV prevention among IDUs, both at the population level and at the individual level. Interventions to reduce HIV transmission, most notably syringe exchange programs, were implemented in many high-income countries in the early to mid-1990s. A meta-analysis of pre-1995 versus post-1995 HCV prevalence studies in high income countries did find statistically significantly lower prevalence among IDUs in the post-1995 studies. The effect was modest, however, approximately 10% lower prevalence when controlling for duration of injecting (Hagan et al., 2007).

Hagan and colleagues (Hagan et al., 2011) have also recently conducted a meta-analysis of individual-level HCV prevention studies, in which HCV incidence among participants in various interventions was compared to HCV incidence among IDUs who did not participate in the intervention. This meta-analysis included 26 eligible studies of behavioral interventions, substance use treatment, syringe access, syringe disinfection, and multi-component interventions (in which the intervention group subject simultaneously participated in more than one intervention). Only the combined intervention category showed a statistically significant pooled effect size. However, there were only two studies in this category, so that additional studies are needed to more fully examine the effectiveness of combined interventions.

HCV is sufficiently easy to transmit that it can be transmitted through sharing of injection preparation equipment (filters, cookers, rinse water) in addition to sharing needles and syringes (Hagan et al., 2001). Gillies and colleagues (Gillies et al., 2010) recently conducted

¹* The term “persons who inject drugs” emphasizes that these individuals should be considered persons first and that they are much more than the behavior of injecting drug use, and would therefore be a better term for describing this group. However, this paper addresses official classification of HIV transmission routes, so that we will use the current standard terms injecting drug use and injecting drug users and the abbreviation IDU. We do want to emphasize that HIV prevention for persons who inject drugs should be based on full consideration of their human rights.

a meta-analysis of studies of the provision of clean injection preparation equipment to IDUs as a method for reducing HCV transmission. They included 13 studies in their final analysis and concluded that “The evidence to demonstrate that the provision of sterile non-N/S injecting paraphernalia reduces HCV transmission or modifies injecting risk behaviours is currently limited by an insufficient volume and quality of studies”(Gillies et al., 2010).

There clearly is a great need for new methods for reducing HCV transmission among IDUs. We report here that intranasal drug use among persons who are also injecting drugs may have a substantial and persistent protective effect against HCV infection.

2. Methods

2.1 Subject recruitment

The data reported here are derived from data collected from drug users entering the Beth Israel Medical Center drug detoxification program in New York City. The methods for this “Risk Factors” study have been previously described in detail (Des Jarlais et al., 2009; Des Jarlais et al., 2007a), so only a summary will be presented here. The Beth Israel detoxification program serves the city as a whole, and approximately half of its patients live in Manhattan, one quarter in Brooklyn, one fifth in the Bronx, and the remainder (i.e., 5%) live elsewhere. Patients enter the program voluntarily.

2.2 Data collection

Research staff visited the general admission wards of the program in a preset order and examined all intake records of a specific ward to construct lists of patients admitted within the prior 3 days. All of the patients on the list for the specific ward were then asked to participate in the study. Among patients approached by our interviewers, willingness to participate was more than 95%. After all of the patients admitted to a specific ward in the three-day period had been asked to participate and interviews had been conducted among those who agreed to participate, the interviewer moved to the next ward in the preset order. Because there was no relationship between assigning patients to wards and the order that the staff rotated through the wards, these procedures would yield an unbiased sample of persons entering the detoxification program.

A structured questionnaire covering demographics, drug use, sexual risk behavior, and use of HIV prevention services was administered by a trained interviewer. Most drug use and HIV risk behavior questions referred to the 6 months prior to the interview. Subjects were queried about using different drugs by different routes of administration, so that it was possible to determine if the same drug was being used through different routes of administration. Questions included the frequency of the use of different drugs and different routes of administration in the previous 6 months. For the analyses presented here, each drug by route of administration was dichotomized into yes/no and total frequency of injecting was dichotomized into less than daily and daily or more frequently. Subjects were also asked if they had ever been in methadone maintenance, had ever been tested for HIV (prior to the test administered in this study), and had ever been tested for HCV (again prior to test

administered in this study). The questionnaire included date of birth and age when illicit drugs were first injected to determine the number of years of injecting.

After completing the interview, each participant was seen by an HIV counselor for pretest counseling for both HIV and HCV and specimen collection. HIV testing was conducted at the New York City Department of Health Laboratory by using a commercial, enzyme-linked, immunosorbent assays (EIA) test with Western blot confirmation (BioRad Genetic Systems HIV-1-2+0 EIA and HIV-1 Western Blot, BioRad Laboratories, Hercules, CA). Samples were tested for HCV antibody with the Ortho HCV enzyme immunoassay (EIA) 3.0 (Ortho-Clinical Diagnostics, Inc., Raritan, NJ). Samples with optical density values of > 8.0 were considered positive, samples with values of 1.0 to 8.0 were confirmed with radioimmune blotting assay (RIBA) (Chiron RIBA HCV 3.0 Strip Immunoblot Assay, Novartis Vaccines and Diagnostics, Inc. Emeryville, CA) and samples with values < 1.0 were considered negative.

Serial cross-sectional data have been collected in the project since 1990. We did permit individuals to participate in the study in different years. For the analyses reported here, however, we used only the first interview from persons who participated more than once.

Both injecting and non-injecting drug users were recruited into the study, but only data from injecting users (subjects who reported injecting in the month prior to entry into the detoxification program) are analyzed in this report.

2.3 Data analyses

Univariate predictors of being HCV seropositive were first identified, and multivariate logistic regression was then used to develop a theoretically informed model of factors independently associated with being HCV seropositive. The statistical software packages SAS, version 9 (SAS Institute, Inc., Carey, NC), and Stata, version 11 (StataCorp, College Station, TX), were used for analyses.

2.4 Ethical approval

The study was approved by the Beth Israel Medical Center's Institutional Review Board. The Centers for Disease Control determined that the study did not require approval by its Institutional Review Board.

3. Results

3.1 Description

Seven hundred and twenty-six (726) active injecting drug users participated in the study between 2005 and 2010. HIV prevalence was 16% and factors associated with HIV status will be reported in a separate publication. Demographic characteristics, drug use behaviors and HCV serostatus are presented in Table 1. There was considerable variety in the patterns of drug use. Heroin injected by itself was by far the most commonly injected drug, with 91% of the subjects reporting heroin injection in the 6 months prior to the interview; 55% reported injecting cocaine by itself, 47% reported injecting speedballs (heroin and cocaine in combination), and 77% reported injecting daily or more frequently. The subjects also

reported considerable non-injecting drug use: 44% reported intranasal heroin use, 20% reported intranasal cocaine use, 11% reported intranasal speedball use, and 37% reported smoking crack cocaine.

3.2 Factors associated with HCV prevalence

HCV seroprevalence was significantly higher among Latino/as, older subjects, subjects with longer injection histories, subjects who reported daily injecting, injecting cocaine and injecting speedball (cocaine and heroin mixed together) in the six months prior to the interview, and significantly lower for IDUs who reported intranasal use of heroin and intranasal use of speedball in the 6 months prior to the interview. HCV serostatus was not associated with recent intranasal cocaine use or recent smoking of crack cocaine.

Intranasal use of heroin and intranasal use of speedball were both significantly associated with lower HCV prevalence, but 44% of the subjects reported intranasal heroin use and only 11% reported intranasal speedball use, so that intranasal heroin use would appear to be the more important pattern.

We examined whether participation in various HIV/HCV prevention services was associated with HCV serostatus. As shown in Table 2, participation in the HIV/HCV prevention programs was associated with higher HCV seroprevalence.

Four classes of variables (length of injecting career, demographic characteristics, use of prevention services, and recent drug use behaviors) were associated with HCV serostatus in the univariate analyses. As presented in the methods section, we used multiple logistic regression to develop a theoretically informed model of statistically independent factors associated with HCV serostatus in this sample. Potential predictors were entered by the four classes noted above, and by the strength of their univariate associations within each class. If a factor added to the model was not significantly associated with HCV serostatus it was not retained. As years injecting is typically the strongest predictor of HCV serostatus among IDUs, we first entered years injecting (as a continuous variable) into the model. (As age was highly correlated with years injecting, we did not add it to the model to avoid multi-collinearity problems.) Race/ethnicity was significantly associated with HCV status in this sample, and might reflect engaging in HCV risk behaviors within a higher vs. lower prevalence racial/ethnic group, so that it was the second variable added to the model. Use of HIV prevention services may be associated with HCV serostatus through either a protective effect (protecting against HCV infection) or through a self-selection effect (highest risk persons self-selecting to use the services) and the services from Table 2 were added to the model in order of the strength of their associations with HCV serostatus. Finally, we added the drug use behaviors in the 6 months prior to the interview (Table 2), again in the order of the strength of their association with HCV serostatus. The final model is shown in Table 4. This model had the lowest Akaike Information Criterion value of all the models examined. For the variables that were retained in the multivariate model, the univariate ORs and the adjusted ORs were quite similar.

Figure 1 shows HCV seroprevalence by each years-of-injecting category and for subjects who did and did not report recent intranasal heroin use within each years of injecting

category. HCV prevalence is already high (33%) among subjects who had injected for 0–2 years and then rises modestly by increased years of injecting through 11–15 years. Finally, HCV prevalence is quite high among the subjects in the 16+ years of injecting category. For 4 of the 5 injecting-years categories, HCV prevalence is lower among subjects who reported recent intranasal heroin use. The difference in HCV prevalence by recent intranasal heroin use was significant in both univariate analyses (Table 2) and multivariate analysis (Table 4).

4. Discussion

4.1 Routes of administration

The data reported here should be considered in the context of other studies of route of drug administration and transmission of blood-borne viruses. There are reports of injecting drug users who ceased injecting but continued using drugs through non-injecting routes of administration in New York (Des Jarlais et al., 2007b), New Haven, CT (Schottenfeld et al., 1993), Baltimore (Highfield et al., 2007), Spain (de la Fuente et al., 1997), the Netherlands (Buster et al., 2009) and the United Kingdom (Gossop et al., 2004).

There have been a modest number of interventions that have attempted to prevent the transition from non-injecting drug use to injecting or to facilitate “reverse” transitions from injecting to non-injecting drug use. Des Jarlais, Casriel and colleagues (Des Jarlais et al., 1992) developed an intervention to reduce transitions from non-injecting to injecting drug use that was tested in a randomized controlled trial. The intervention consisted of four 2-hour group sessions over a 1-month period led by trained drug counselors. The intervention group did have a significantly lower rate of transition to injecting during the 9 month follow-up period (Des Jarlais et al., 1992). Dolan and colleagues (Dolan et al., 2004) conducted a pilot study of an intervention to encourage transitions from injecting to non-injecting drug use among persons who were exclusively injecting. The intervention consisted of five 1-hour sessions of individual therapy with a registered psychologist. At the 6 month follow-up, half of the subjects reported non-injecting drug use, but follow-up data were available for only 10 of the 30 subjects who began the program, and with services provided by a registered psychologist on a one-to-one basis, cost would clearly be an important factor. Hunt and colleagues developed the “Break the Cycle” program (Hunt et al., 1999; Hunt et al., 1998) in which current injecting drug users are trained not to initiate new people into injecting. An initial evaluation showed positive attitude changes, and the program has been replicated in several countries (USAID, 2007), but has not yet been rigorously evaluated. Based on these studies and others, Bridge (2010) recently concluded that the potential for interventions to assist individuals to change from injecting to non-injecting routes of drug administration is “largely unrealized.”

4.2 Current HIV and HCV prevention interventions

Recent use of syringe exchange, ever use of methadone maintenance, and ever having been tested for HIV and for HCV were all associated with being HCV seropositive rather than with remaining HCV seronegative. This is consistent with data from other areas showing that very high-risk injectors are particularly likely to self-select into HIV prevention services (Hagan et al., 2000; Wood et al., 2007). HCV seroprevalence in this sample was 71%,

substantially lower than the 91% HCV seroprevalence among IDUs entering the Beth Israel detoxification program in 1990–91 (Des Jarlais et al., 2005). Additional research is needed to examine how the group level seroprevalence is lower after implementation of various HIV/HCV prevention programs but participation in the programs is associated with a greater likelihood of being HCV seropositive.

4.3 Limitations and potential causal pathways

Several limitations of the present study should be noted. First, and perhaps most importantly, the design is cross-sectional, so that causal inferences between intranasal drug use and a lower likelihood of being HCV cannot be determined from these data. There are several potential causal explanations for the association observed here. At an event level, substituting an occasion of intranasal use for an occasion of injecting use would certainly reduce the chances of HCV transmission.

At an individual level, the ability to combine intranasal use and injecting use—as opposed to injecting only—may be a marker for a greater ability of a subject to manage his/her addiction to reduce at least some of the risks associated with injecting illicit drugs. (See Mateu-Gelabert et al. (2005) for a discussion of some strategies for avoiding blood borne infections.) A greater ability to manage one's addiction may be associated with both less injecting and less risk behavior when injecting. In this situation, the ability to (at least partially) manage one's addiction could be an underlying factor leading to both the continued non-injecting drug use and the lower likelihood of being HCV seropositive.

At a social network level, persons who use heroin through both injecting and intranasal use may preferentially associate with others who have the same combined drug use patterns. As HCV prevalence is generally lower among persons with the combined drug use pattern, this would lead to a smaller likelihood of exposure to HCV if drug injection equipment were shared within these social networks. Social networks that contained peers who used drugs both through injection and non-injecting routes of administration might also provide support to each other to avoid exclusively injecting. Thus, differential networks might also be a contributing cause to the association between non-injecting drug use and the lower likelihood of being HCV seropositive.

Longitudinal research would be needed to assess these different potential causal pathways. The different potential pathways are not mutually exclusive; indeed, they may be complementary. Randomized clinical trials of an intervention that effectively increased the frequency of intranasal drug use among already injecting drugs might be needed to rigorously evaluate the underlying causal pathways.

A second limitation is that some HCV seropositives and some HCV seronegatives may leave the active drug injecting population over time, so that interpretation of the relationships between years injecting and HCV seroprevalence must be made with caution. However, the positive association between years injecting and HCV seropositive status observed here is similar to that observed in many other studies (Hagan et al., 2007).

Third, intranasal drug use was assessed for the 6 months prior to the interview, and exposure to HCV undoubtedly occurred prior to the 6-month period for the great majority of HCV seropositive subjects. There may have been variation over time in intranasal drug use. Individual subjects may have had periods of injecting and intranasal drug use, periods of only injecting, periods of only intranasal use, as well as periods with no drug use. If individuals' routes of drug administration varied greatly over time, however, one would not expect to find an association between the most recent route of administration and a relatively permanent characteristic such as HCV serostatus. The observed relationships thus indicate the existence of some consistent, long-term factors that would link recent routes of drug administration with HCV serostatus.

Fourth, we did not ask why the subjects also used drugs through non-injecting routes of administration in addition to injecting. In a previous study of persons who had ceased injecting but continued to use drugs through non-injecting routes of administration (including intranasal heroin), we found a considerable variety of reasons for ceasing to inject, including concerns about AIDS, other health problems associated with injecting, the belief that it is easier to control drug use through non-injecting routes of administration, that non-injecting use is more socially acceptable, and the belief that it is easier to conceal non-injecting use from others (Des Jarlais et al., 2007b).

We would therefore assume that there would also be a considerable variety of reasons why the subjects in this study would have combined non-injecting drug use with injecting drug use.

Fifth, the research was conducted at a single site in a single city, so that replication in other locations is needed. Patterns of non-injecting drug use may vary greatly with local conditions, such as the availability and price of heroin and presence of social networks of intranasal users. These environmental factors may greatly influence the numbers of IDUs who are able to substitute non-injecting drug use for injecting drug use.

4.4 Conclusions

Despite these limitations, the present study makes several contributions to the possibility of non-injecting drug use as a viable strategy for reducing blood-borne viral infections among persons who inject drugs. First, the inverse association between non-injecting drug use and reduced likelihood of being HCV seropositive was substantial (AOR = .52, 95% CI .33 to .82 for intranasal heroin use, AOR = .41, 95% CI .31 to .80 for intranasal speedball use). Second, the inverse association was measured with a biological outcome (HCV prevalence) rather than simply with self-reported risk behaviors. Third, the inverse association was observed in persons who were currently injecting drugs, implying that it may not be necessary to completely cease injecting to reduce the likelihood of HCV infection. Finally, the inverse association was observed among persons with relatively long histories of injecting (16+ years since first injection) suggesting a durable inverse association.

Given the many difficulties in preventing HCV infection among persons who inject drugs and the high morbidity and mortality associated with HCV infection, these findings suggest much more attention should be paid to substituting intranasal drug use for injecting drug use.

Three possible interventions would be the implementation of “transitions to non-injecting” programs at syringe exchanges, at “low threshold” drug treatment programs (drug treatment programs that do not require abstinence for continued participation) and at “drop in centers” for drug users. Reaching injectors before they became infected with HCV would be most effective at preventing new HCV infections, though reducing HCV transmission behavior among persons who were chronically infected should also have an effect to reduce population-level transmission. New programs would most likely be effective in an environment of “combined” HCV prevention programming, in which the different programs might be synergistic (Hagan et al., in press). Implementation of “transitions to non-injecting use” programs would however, require that public health goals for addressing psychoactive drug use be broadened beyond the two currently dominant goals of abstinence or injecting with sterile needles and syringes.

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Figure 1.
HCV Prevalence by years of injecting and by intranasal heroin use among IDUs in New York City, 2005–2010, and among all IDUs

Table 1

HCV prevalence by demographics and drug use behaviors

	Total		HCV+		OR	LCL	UCL
	N		N	%			
Gender							
Male	604	427	70.7	1	-	-	
Female	122	89	72.95	1.1	0.7	1.7	
Race/Ethnicity							
White	188	115	61.17	1	-	-	
Black	131	91	69.47	1.4	0.9	2.2	
Hispanic	383	292	76.24	1.9	1.3	2.7	
Average age (STD)	39 (9)						
Median age	39						
IDUs at or below median age	368	223	61	1	-	-	
IDUs above median age	353	291	82	3.1	2.2	4.3	
Average years of injecting (sd)	15 (12)						
Median years injecting	13						
IDUs at or below median years injecting	376	213	57	1	-	-	
IDUs above median years injecting	345	301	87	5.2	3.6	7.6	
Drug Use							
Daily injecting							
No	167	103	62	1	-	-	
Yes	559	413	74	1.8	1.2	2.5	

HCV prevalence and participation in potential prevention services among IDUs in New York City, 2005–2010

Table 2

	Total	HCV+	
Injected Heroin			
No	69	56	81
Yes	657	460	70
Injected Cocaine			
No	396	271	68
Yes	330	245	74
Injected Speedball			
No	382	247	65
Yes	344	269	78
Intranasal Speedball			
No	647	469	73
Yes	79	47	60
Intranasal Heroin			
No	404	316	78
Yes	322	200	62
Intranasal Cocaine			
No	583	421	72
Yes	143	95	66
Smoking Crack Cocaine			
No	454	334	74
Yes	272	182	67

	Total	HCV+			
Ever HIV test		N	N	%	OR
No	16	7	44	1	-
Yes	710	509	72	3.3	1.2 – 8.9
Ever HCV test					

	Total		HCV+		%	OR	95% CI
Ever HIV test	N		N				
No	87		26		30	1	–
Yes	581		464		80	9.3	5.6 – 15.4
Ever in Methadone Maintenance Treatment Program							
No	266		166		62	1	–
Yes	460		350		76	1.9	1.4 – 2.7
Last 6 month use of Syringe Exchange							
No	457		298		65	1	–
Yes	269		218		81	2.3	1.6 – 3.3

Table 3

Factors independently associated (logistic regression) with HCV seropositivity among IDUs, New York City, 2005 – 2010

Factors associated with HCV serostatus	Odds Ratio	P	95% Confidence Interval
Black vs. White	0.94	0.86	0.50 – 1.78
Hispanic vs. White	1.71	0.02	1.07 – 2.73
Injecting Years/Year	1.10	0.00	1.08 – 1.13
Speedball Injection	1.79	0.01	1.15 – 2.79
Intranasal Heroin	0.52	0.01	0.33 – 0.82
Intranasal Speedball	0.41	0.01	0.21 – 0.80
HCV Test	9.16	0.00	5.10 – 16.45