

Hepatitis A Prevalence among Injection Drug Users

REBECCA WELLS, DENNIS FISHER, ANDREA FENAUGHTY, HENRY CAGLE, ADI JAFFE

OBJECTIVE: The purpose of this study was to develop a descriptive model of the association between injection drug use and hepatitis A (HAV) in a sample of injection drug users (IDUs).

DESIGN: From May 1997 to July 1999, 493 subjects were administered the NIDA Risk Behavior Assessment (RBA). Participants had blood drawn; sera were tested for antibodies to HAV, hepatitis B core (HBcAB), and hepatitis C. The principal method of analysis was logistic regression.

SETTING: The study took place in a community-based field station in Anchorage, Alaska.

PARTICIPANTS: Eligibility was determined using the following criteria: a) age greater than 17 years, b) possession of picture identification, c) positive urinalysis for cocaine metabolites, morphine, and/or amphetamines using the ONTRAK® system (Roche Diagnostics), and d) injection drug use in the last six months as confirmed by presentation of track marks.

MAIN OUTCOME MEASURE: Presence of antibodies to HAV infection.

RESULTS: The prevalence of total HAV antibody in our sample was 33% (161/493). The final multivariate logistic model, using positive HAV serostatus as the outcome, included positive HBcAB serostatus ($OR = 3.43$; 95% CI, 2.22-5.30), less than high school education (vs. high school or greater education) ($OR = 2.05$; 95% CI, 1.33-3.17), age ($OR = 1.06$ (each year); 95% CI, 1.03-1.09), number of days

injected heroin in the last 30 days ($OR = 1.05$ (each day), 95% CI, 1.01-1.08), and race (White vs. all other race/ethnicities) ($OR = 0.49$; 95% CI, 0.32-0.75).

CONCLUSIONS: A model including both demographic and drug use variables best describes HAV prevalence in this sample. Findings suggest that IDUs are targets for interventions focusing on hepatitis vaccinations and hygiene practices. Further research is needed to understand the association of HAV with hepatitis B infection.

ABBREVIATIONS USED: CI = confidence interval; HAV = hepatitis A; HBV = hepatitis B; HCV = hepatitis C; HIV = human immunodeficiency virus; IDUs = injection drug users; M = mean; OR = odds ratio; RBA = risk behavior assessment.

INDEX TERMS: hepatitis A; hepatitis B; injection drug users; risk behavior assessment.

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Injection drug users (IDUs) are known to engage in injection behaviors that put them at risk for human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV).¹⁻⁴ Further, IDUs have also been shown to be at high risk of hepatitis A (HAV) infection; anti-HAV antibody prevalence rates among IDUs are four to eight times what is expected in the general population.⁵

Hepatitis A infection causes acute disease with symptoms including fever, loss of appetite, nausea, abdominal pain, and jaundice.⁶⁻⁸ Infection does not persist beyond the acute stage and results in lifelong immunity.⁷ The mode of transmission is generally person-to-person through the fecal-oral route.^{6,8} Persons at high risk of hepatitis infection include daycare workers, travelers to areas where HAV is endemic, men who have sex with men, and injection and other drug users.⁶⁻⁹

Pathways for transmission of HAV to IDUs include parenteral routes.^{6,9-11} Drugs could be contaminated while being transported in a condom carried in the rectum or while being prepared for injection by contaminated hands.¹¹⁻¹⁶ However, an attempt to identify the virus in drug samples during an outbreak among drug users in Finland was not successful.¹⁴ In addition, an ill person may directly infect others through blood-to-blood contact when sharing injection equipment, although the short viremic phase of hepatitis A infection makes this somewhat unlikely.^{10,12,14}

The purpose of the current study was to describe characteristics of injection drug users associated with positive HAV serostatus, and to ascertain the contribution of drug injection. Knowledge of characteristics associated with being anti-HAV positive may help tailor preventive efforts and vaccination programs to IDUs who may be at high risk of infection.

MATERIALS AND METHODS

Participants

Potential participants were recruited from Anchorage, Alaska using targeted sampling and respondent-driven sampling methods.^{17,18} Targeted sampling was employed using census tracts as the geographical boundaries while respondent-driven sampling, a refinement of snowball sampling, was utilized by providing initial participants with incentive bearing referral coupons. The recruitment period ran from May 1997 to July 1999. Eligibility was determined using the following criteria: a) age greater than 17 years, b) possession of picture identification, c) positive urinalysis for cocaine metabolites, morphine, and/or amphetamines using the ONTRAK[®]

system (Roche Diagnostics), and d) injection drug use in the last six months as confirmed by presentation of track marks.¹⁹ Informed consent was obtained from eligible IDUs ($N = 493$) and documented on a form approved by the University of Alaska Anchorage Institutional Review Board.

Baseline procedures

At session I (baseline) data were collected using the NIDA Risk Behavior Assessment (RBA; National Institute on Drug Abuse 1991) and a supplemental hepatitis questionnaire. The RBA is a structured interview that assesses high-risk drug and sexual behaviors and has good test-retest reliability and validity for self-report.^{3,20-24} After the interview, a pretest counseling session was completed. Finally, blood was drawn and sera were tested for hepatitis A, B, and C antibodies by Quest Diagnostics. Participants were paid for their time. Approximately one week later, participants returned for session II during which posttest counseling and appropriate referral were provided.

OUTCOME MEASURES

HAV Prevalence

HAV serostatus was determined by a blood test for total antibody to HAV. This test does not distinguish between current infection, past infection, and vaccination.²⁵ For prevalence calculations, participants were considered HAV positive if they tested positive for anti-HAV at baseline.

Statistical analyses

Chi-square tests of association for categorical data and t tests for continuous data were conducted examining associations between HAV serostatus and variables from the RBA including demographic, drug use, and sexual behaviors variables. When cell sizes had expected values less than five on the chi-square tests, Fisher's exact test was used. Variables with $p \leq 0.10$ were then used to construct a logistic regression model (PROC LOGISTIC) with HAV serostatus as the outcome using backward elimination. All statistical analyses were performed using SAS software version 6.12 (SAS Institute, Cary NC). Prevalence rates with confidence intervals were performed using methods from Daly.^{26,27}

RESULTS

The study sample ($N = 493$) had a mean age of 38 years ($SD = 8.2$) and consisted of 77.7% (383/493) men. The participants were 18.7% (92/493) Black, 56.6% (279/493) White, 19.1% (94/493) Native American, and 5.6% (28/493) Hispanic, Asian, or other. 55.4% (273/493) had less than a high school education and 44.6% (220/493) graduated from high school

or had a greater than a high school education. Forty-six percent (227/493) of participants earned less than \$500 in the 30 days prior to interview. Participants had a mean of 14.2 years of injection ($SD = 9.7$). Years of injection were defined as number of years from first injection to most recent injection.

The prevalence of total HAV antibody in this sample was 32.7% (161/493; 95% CI, 28.5% to 37.0%). Of those who also had a hepatitis B test, 41.5% (202/487; 95% CI, 37.1% to 46.0%) were core antibody (HBcAB) positive, and of those who also had a hepatitis C test, 54.7% (269/492; 95% CI, 50.2% to 59.1%) were antibody positive. Due to the fact that we could not distinguish HAV vaccination from HAV infection, we examined the baseline supplemental hepatitis questionnaire which revealed that 5% (22/493) of the participants reported that they had ever accepted a hepatitis A vaccine.

Candidate variables with $p \leq 0.05$ on bivariate analyses are shown in Table 1. Other variables considered for the logistic regression model included proportion of times used a previously used needle or syringe in the last 30 days, number of days had sex in the last 30, sexual orientation, and having used drugs with sex in the last 30 days.

The final multivariate logistic model, using positive HAV serostatus as the outcome, included positive HBcAB serostatus ($OR = 3.43$; 95% CI, 2.22 to 5.30), less than high school education (vs. high school or greater education) ($OR = 2.05$; 95% CI, 1.33 to 3.17), age ($OR = 1.06$ (each year); 95% CI, 1.03 to 1.09), number of days injected heroin in the last 30 days ($OR = 1.05$ (each day), 95% CI, 1.01 to 1.08), and race (White vs. all other race/ethnicities) ($OR = 0.49$; 95% CI, 0.32 to 0.75). Model fit was good; Hosmer and Lemeshow goodness-of-fit χ^2_8 ($N = 487$) = 5.74, $p = 0.68$). This model was rerun excluding participants who reported they had ever accepted a hepatitis A vaccine at baseline; there were no substantial changes.

There was also a significant relationship between HAV serostatus and years of injection. Those who were HAV positive had significantly more years of injection ($M = 16.7$, $SD = 10.7$) than those who were HAV negative ($M = 13.1$, $SD = 9.4$) ($t = 3.86$, $p = 0.0001$).

DISCUSSION

A model that includes both demographic and drug use variables best describes hepatitis A prevalence in this sample of injection drug users. These data support the notion that

the association between hepatitis A and injection drug use may be due to many factors, both social and drug-use related.^{15,16,28-31}

The strongest association found in the current study was between hepatitis B serostatus and hepatitis A serostatus. Lange was the first to report this association and they suggest that, among drug users, similar risk factors may exist for both viruses, and that these risk factors may be sexual or otherwise.³² It should be noted that, in the current study, a significant association was also found between HAV serostatus and HCV serostatus by chi-square test. This association, however, did not persist in multivariate analyses. Villano in the study of total HAV antibody among IDUs did not find any association between HAV serostatus and hepatitis B or C serostatus.³³

In addition to participants with positive hepatitis B serostatus, participants with less than a high school education were more likely than those who graduated high school to be anti-HAV positive. A comparable finding was reported by Hutin in the case control study of a methamphetamine-associated hepatitis A outbreak in Iowa.¹⁶ The authors found that case patients were more likely than controls to have fewer than 12 years of schooling, and note that less education may be indicative of lower socioeconomic status. Low socioeconomic status may be related to situations or behaviors that contribute to HAV transmission.³⁴

In the current study non-Whites were twice as likely as Whites to be anti-HAV positive. The two largest groups of non-Whites in this sample of IDUs were Native American/Alaska Natives and Blacks. Native Americans have been reported to have the highest rates of infection with HAV of all racial/ethnic groups.^{35,36} Further, Native Alaskans in particular are at risk due to inadequate sewage and waste disposal; approximately half of the households in rural Alaska Native villages do not have adequate running water and sewer services and most communities have active open dumps (Rural Alaska Sanitation Coalition www.anhb.org/sub/rasc/sanifacts.html). Lange found that Black drug users were HAV seropositive more often than White drug users.³² As with level of education, the CDC notes that the association with race may reflect variation in HAV infection risk due to factors associated with lower socioeconomic status, such as crowding.³⁵

In general, as hygienic standards have improved over time, HAV prevalence has declined.⁹ In accordance with this, older age groups tend to have a higher prevalence of HAV;

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Table 1. Candidate variables for logistic regression model

Variable	Hepatitis A Serostatus				p
	Positive		Negative		
	M	SD	M	SD	
Age	41.0	8.2	36.7	7.9	0.0001
Days used crack*	12.2	10.5	10.0	9.8	0.03
Days used heroin*	3.0	7.1	1.7	5.9	0.03
Days used speedball*†	0.5	3.3	0.1	0.6	0.03
Days used amphetamines*	0.1	0.7	0.5	2.3	0.05
Days injected heroin*	3.0	7.1	1.6	5.6	0.02
Days injected speedball*†	0.5	3.3	0.1	0.5	0.02
Years of injection	16.7	10.7	13.1	9.4	0.0001
	Positive		Negative		p
	#	%	#	%	
Race					
White	79	28.3	200	71.7	0.02
Non-white	82	38.3	132	61.7	
Education					
Less than high school	76	27.8	197	72.2	0.01
High school or greater	85	38.6	135	61.4	
Living with a partner of the opposite sex‡					
Yes	30	42.9	40	57.1	0.05
No	130	30.8	292	69.2	
Ever used marijuana					
Yes	157	32.2	331	67.8	0.04§
No	4	80.0	1	20.0	
Ever used heroin					
Yes	111	36.8	191	63.2	0.02
No	50	26.2	141	73.8	
Ever used speedball†					
Yes	88	38.9	138	61.1	0.006
No	73	27.3	194	72.7	
Any alcohol use*					
Yes	136	31.0	303	69.0	0.02
No	25	46.3	29	53.7	
Any amphetamine use*					
Yes	6	16.2	31	83.8	0.03
No	155	34.0	301	66.0	
Ever told had an STD					
Yes	101	39.2	157	60.8	0.001
No	60	25.5	175	74.5	
Hepatitis B core antibody positive					
Yes	104	51.5	98	48.5	0.001
No	55	19.3	230	80.7	
Hepatitis C antibody positive					
Yes	113	42.0	156	58.0	0.001
No	48	21.5	175	78.5	

* Last 30 days.

† Heroin and cocaine mixed together

‡ N = 492

§ 2-tailed Fisher's exact test.

this pattern has been noted in both the general US population and drug users. For example, The National Health and Nutrition Examination Survey II (NHANES) seroprevalence data, which used a representative sample of the U.S. population (1976–1980), found that prevalence of anti-HAV was lowest in those less than five years of age and increased with age; this same pattern was repeated in the NHANES III (1988-1994) data.^{35,36} Not surprisingly, older age was also associated with positive HAV serostatus in this group of IDUs.

Of relevance specifically to drug users, outbreaks of hepatitis A have been associated with heroin use, and parenteral transmission of HAV has been documented.^{31,37} One injection-related variable was associated with HAV serostatus in the current study: the number of days injected heroin in the last 30 days. The number of days in the last 30 days may be a proxy for severity of recent addiction. It is possible that continued injection over time is related to greater addiction and a longer history of injection. In addition, HAV serostatus was associated with more years of injection. HAV may have been acquired early in a drug user's injection career through one of several possible means of transmission, i.e., contaminated drugs, person-to-person.³⁸

The current study had some limitations, the most important of these being the use of a test for total antibody (IgM and IgG) to HAV to determine HAV serostatus. This test does not distinguish between acute infection, past exposure, and vaccination.²⁵ Although lifetime prevalence was clear, there was no means to determine the timing of infection in relation to data collected from the RBA, especially those

questions with a 30-day reference period. Although behavior in the last 30 days is likely not causally related to HAV infection, it is assumed to be representative of past behaviors that were related to HAV infection.

We considered whether the inability to distinguish vaccination from infection was problematic. In order to determine the effect vaccination may have had on the analyses, the supplemental questionnaire was used to determine whether participants had ever accepted a hepatitis A vaccine. Only 28 (5%) of the 491 participants reported vaccination. Moreover, the logistic regression was rerun excluding those participants who said they had accepted vaccination with no substantial changes in the results of the model.

A second limitation was the use of self-report data. Self-report data, especially those that pertain to risk behaviors, can have measurement error resulting from factors including a willingness of the participant to provide socially acceptable answers, underreporting, and recall problems.³⁹ The problems associated with using self-report data may be less of a concern in our study because, as previously indicated, our data collection instruments have been shown to have acceptable reliability and validity. In addition, injection was confirmed with track mark examination and drug use with urine tests.

Our data suggest that IDUs are targets for interventions focusing on vaccination and hygienic practices. Injection drug use may affect immune status, which in turn could impact the risk of clinical illness if exposed to hepatitis A.⁴⁰ Lange found that 14% of drug users, most of whom were IDUs, had abnormal leukocyte counts.³² Laskin and Black report a case of fulminant hepatitis A in an IDU and suggest that the patient's injection drug use may have affected her immune status, leaving this person more vulnerable to fulminant disease when infected with HAV.⁴⁰ Indeed, a hepatitis A outbreak in Australia led to higher hospitalization rates among IDUs than non-IDUs, which suggests IDUs had more severe disease.⁴¹

An important subset of IDUs who should be targets for HAV vaccination and prevention activities are those with chronic hepatitis B or C or both.^{29,42,43} Data from the current study revealed an independent association between HAV and HBV infection, and suggest an association between HAV and HCV infection although this association was only marginally significant. Recent studies suggest that individuals with chronic liver disease, including those with chronic HBV or HCV, are at risk for more severe HAV

infection than those without underlying liver disease.^{42,43} Vaccination may serve as a method to avoid severe disease in these groups.³³

The Advisory Committee on Immunization Practices has recommended HAV vaccination for all IDUs.³⁵ Injection drug users have been difficult to target due to factors such as transience and a poor response to preventive programs.³¹ Vaccination programs implemented in places such as drug treatment facilities, jails, and emergency rooms may be able to reach a larger proportion of IDUs.⁴⁴ Research programs that enroll IDUs are another possible access point for vaccination.⁴⁵ In addition, education programs that focus on the risk of HIV and hepatitis to IDUs should include information on hepatitis A transmission and prevention.¹⁶ Further research is needed to clarify the associations between injection drug use and hepatitis A infection. The associations of HAV with HBV and HCV are particularly important considering that previous research has revealed increased risk of severe HAV disease in those with chronic liver disease, including chronic HBV and HCV.

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