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Risk Factors Associated with Prescription Opioid Use and Hepatitis C Infection among Young Persons who Inject Drugs in Rural Wisconsin

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Abstract

Risk Factors Associated with Prescription Opioid Use and Hepatitis C Infection among Young Persons who Inject Drugs in Rural Wisconsin

By Farah Ahmed

Introduction: Recent research from the Centers for Disease Control suggest that the current increase of hepatitis C (HCV) cases in the United States is associated with the present opioid epidemic among young adults [1]. However, literature on the association between injecting prescription opioids (PO) and HCV infection is limited.
Methods: This cross-sectional study collected survey data between 2014 and 2015 from 280 injection drug users between the ages of 18 to 29 who visited one of three different syringe service programs in rural Wisconsin. Chi-square analyses were conducted to determine if there was a difference in the risk factors associated with injecting prescription opioids versus not. Logistic regression was conducted to examine the association between injecting prescription opioids and having a positive HCV test result after controlling for confounding variables.
Results: The majority of the study population were white (81.9%), had attained at least a high school diploma or GED (72.1%), and had a mean age of 23.4 years. Chi-square test results showed that race, sharing needles, number of lifetime injections, average number of injections for a single dose, and syringe barrel size significantly differed by use of POs at the p=.05 level. In bivariate analysis, using prescription opioids compared to not using prescription opioids, was found to be significantly associated with having a positive HCV test result at $p<0.05$ (OR=2.00, 95% CI: 1.20, 3.34) but was found to no longer be a significant predictor of HCV status when adjusted for other covariates (aOR=0.75, 95% CI: 0.37, 1.52). Age (aOR=2.26, 95% CI: 1.19, 4.30), number of lifetime injections (100-1000 lifetime injections, aOR=5.19, 95% CI: 1.34, 20.03) (1000+ injections, (aOR=9.46, 95% CI: 2.29, 39.05), and number of times a participant had shared needles in the past (aOR=6.48, 95% CI: 2.46, 17.01) were all significant predictors of HCV status in the final model.
Discussion: Although our analyses did not show that prescription opioid injection was associated with higher risk of HCV infection after adjusting for covariates, it is still important to understand the risk behaviors and characteristics of PO users in order to tailor HCV prevention strategies for this target population.

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Introduction

An estimated 3.5 million people in the United States suffer from chronic hepatitis C (HCV) [2] and approximately 19,600 deaths in 2015 were attributed to the disease as an underlying or contributing cause [3]. Hepatitis C is specifically prevalent among persons who inject drugs (PWID), with a recent systematic review estimating 53.1% of PWID in the United States are infected with the disease [4]. Individuals are at risk for HCV infection when coming into contact with infected blood, although PWID are at an especially high risk due to unsafe injection practices where infected blood can commonly be present [5]. These unsafe injection practices include sharing and reusing syringes; needles; and injection equipment such as filters, mix water, and cookers [5]. Those who develop chronic HCV are usually asymptomatic for decades and are often unaware of their diagnosis [6]. Due to this, infected PWID can unknowingly spread HCV when injecting drugs with others [6]. In a study analyzing the HCV epidemic specifically among PWID, once a PWID is infected, he/she is likely to infect approximately 20 others within three years of infection creating widespread transmission of the disease [7].

In the 2016, the National Survey on Drug Use and Health reported that the most frequently used illicit drugs other than marijuana were prescription drugs used for nonmedical purposes [8] and recent research from the Centers for Disease Control propose that the current increase of HCV cases may be associated with the present opioid epidemic among young adults [1]. Eighty to ninety percent of PWID have misused prescription opioids [9] and approximately 17,000 deaths in the United States

in 2016 resulted from overdosing on commonly prescribed prescription opioids [10]. The association between injecting POs and HCV infection isn't completely clear, but researchers have found in previous studies that PO users are often more likely to report unsafe and high-risk injection practices that increase their likelihood for infection, such as sharing of needles, syringes, and drug preparation equipment; daily injection; and longer lifetime duration of injecting drugs [9, 11-19].

There are also unique characteristics of PO injection that may be associated with a higher risk of HCV infection. To prepare for injection, PWID must use water to dissolve POs which contain excipients, a substance which binds with the active ingredient of POs [20]. The presence of these excipients in POs require more water than it typically does to dissolve heroin or methamphetamine [20]. This larger solution thus requires either larger syringes or a greater number of injections per dose, which in turn increases the likelihood of exposure to HCV [15]. Each additional injection increases the risk of HCV acquisition by 3-10% [21, 22] as well as increases the risk of contamination of the filters and needles used [22]. Using larger, "high dead space" needles and syringes are also associated with greater risk of HCV transmission [23, 24] as they can hold more blood and higher amounts of the HCV virus [25], compared to WHO recommended "low dead space" insulin syringes [26-29].

Another practice unique to prescription opioid injectors is "doing a wash [11]." Prescription opioids leave higher amounts of residue on injection equipment used during drug preparation than methamphetamine and cocaine [11]. PWID will commonly

save their filters containing this residue to use later in the day to achieve a slight high or to manage withdrawal symptoms. [11]. In one particular observational study from 2010, the main ethnographer reported commonly witnessing the practice of PWID gifting these "washes" to other drug users on the street as what he believed may have been a way to solidify relationships [11].

Few past studies have observed the relationship between hepatitis C and injecting prescription opioids (PO) compared to injecting other traditional street drugs such as heroin or methamphetamine. In two different cross-sectional studies conducted in rural Appalachian among PWID, those who injected POs were approximately twice as likely to be HCV infected compared to those who injected other drugs after controlling for other factors [30, 31]. In a different study analyzing PWID in New York, those who injected POs were 5 times more likely to be HCV positive than those who injected other drugs after controlling for other factors [26]. However, one cohort study in Vancouver found a strong association between PO injection and HCV infection compared to traditional street drugs in bivariate analysis (HR: 3.48, 95% CI: 1.7, 7.7), but found no higher risk of HCV for PO injection users than other drug users after controlling for other covariates [32].

Although numerous studies have reported the risk and risk factors of HCV among PWID, research and findings on the association between injecting prescription opioids and acquiring HCV infection are limited. Herein, we report the results of a cross-sectional study using survey data collected from young PWID at three different syringe

service programs. This analysis will assess the risk behaviors and characteristics of prescription opioid users as well as the association between injecting prescription opioids and HCV acquisition.

Methods

This cross-sectional study collected survey data between 2014 and 2015 from 280 injection drug users between the ages of 18 to 29 who visited one of three different syringe service programs in rural Wisconsin. The mission of syringe service programs is to provide sterile needles and syringes at no cost in order to prevent widespread transmission of infectious diseases such as HCV among injection drug users[33].

Visitors of the syringe service programs were asked to participate in the study. If they agreed, they were asked four questions to determine eligibility. To be eligible for the study, visitors of the syringe service program had to: 1) be between the ages of 18 and 29 years old; 2) report injecting drugs in the last 12 months; 3) be able to complete the survey in English; and 4) have a photo ID with them. After fulfilling eligibility requirements and giving consent, field staff at the syringe service program administered a hepatitis C test using the OraQuick rapid test, which involved a finger stick to acquire a blood sample. While the HCV test result developed, participants took an online survey that took approximately 40 minutes. The majority of the survey consisted of questions regarding lifestyle and drug use behaviors of the participant.

Since recruiting a rare and discrete population such as PWID can be difficult, respondent-driven sampling was used to collect data for this study [34]. Participants

who agreed to take the online survey at the site were considered “seeds” of the data population. Study subjects were provided a $20 visa debit card at the completion of the survey and after receipt of the rapid HCV test. They also received vouchers to refer other injection drug users they knew to come into the syringe service program and participate in the study. For each referral of an injection partner or peer that completed the study, an additional $5 incentive was added to the visa debit care of the referee. When participants completed the survey, they received their incentive as well as their rapid HCV test results. Patients who tested positive for HCV were referred for risk reduction education, clinical evaluation, and management services.

The survey included questions regarding demographics such as age, race, ethnicity, age, education level, and income. It mostly, however, consisted of questions concerning the use of syringes, cookers, filters, and mix water when injecting drugs as well as specific risk behaviors related to HCV infection. Other topics of interests covered in the survey included social network size, personality characteristics, and history of illicit drug use. The primary dependent variable in this study was HCV status which was determined by the HCV rapid test result. Prescription opioid use was the primary independent variable and was determined by participants marking prescription opioids as a drug they inject in the survey. HCV status and prescription opioid use were both categorized as binary variables. The demographic variables included in the analysis were age (18-23 years old/24-29 years old), sex (male/female), race (White; Black; American Indian; or Other), and education level (no high school diploma; high school diploma or GED; or Associate, Bachelor and/or graduate degree). Risk behaviors of

particular interest for this analysis were sharing of needles, sharing of filters, syringe barrel size typically used, average number of injections for a single dose, average number of daily injections, number of lifetime injections, the age of first injection and requiring more mix water for PO injection than for other drugs.

All data were analyzed using SAS version 9.4. Chi-square tests were used to determine which covariates were significantly different among the study population that used prescription opioids versus those who did not. Bivariate analyses were then conducted to determine if a relationship existed between independent variables and having a positive HCV test result.

Variables found to be statistically significant with the outcome, at a p-value <0.05, were included in the multivariate model. Plausible interaction terms between the independent variable and risk behaviors were also inserted into the full multivariate model. Logistic regression was then conducted to determine the association between prescription opioid use and HCV infection among the study population. After assessing for interaction and confounding through stratification, the final model was created and adjusted odds ratios (aOR) were calculated.

Results

Demographic Information and Behavioral Characteristics

Survey data and HCV OraQuick Rapid test results were collected from 280 individuals between the ages of 18 and 29. Table 1 displays the frequencies of demographics and risk behaviors of the total population as well as by prescription opioid

use. Of the 280 participants, 93 (33.2%) had a positive HCV test result. The majority were white (81.9%) and had attained at least a high school diploma or GED (72.1%). The mean age of participants were 23.4 years old. Two-thirds of the study participants reported sharing a needle at least once in their lifetime and 35% reported ever sharing filters. Over half the study population (55.3%) reported having injected drugs more than 100 times in their lifetime.

Forty-seven percent of the study population reported using prescription opioids. Chi-square test results showed that race, sharing needles, number of lifetime injections, average number of injections for a single dose, and syringe barrel size significantly differed by use of POs at the p=.05 level. Two-thirds of PO users (67%) reported sharing needles more than once in their lifetime compared to approximately one-third (38%) of non-PO users. PO-users also reported a significantly higher number of lifetime injections where 70.5% of PO-users reported 100+ injections compared to only 38.1% of non-PO users. PO-users were also more likely to inject more than one time (55.5%) per injection episode than non-PO users (36.7%). Lastly, a higher percentage of PO-users reported using a 1 cc or greater barrel syringe (72.5%) than non-PO users (52.7%).

Bivariate Analysis

Table 2 displays the results obtained from the bivariate analysis assessing factors associated with having a positive HCV test result. Using prescription opioids compared to using other drugs, was found to be a significant predictor of having a positive HCV test result (OR=2.00, 95% CI: 1.20, 3.34). Age, when categorized as a dichotomous

variable (18 to 23 years old or 24-29 years old), was found to be the only demographic variable that was a significant predictor of HCV status (OR=2.39, 95% CI=1.36, 4.20). Number of lifetime injections and sharing needles more than once in an individual's lifetime proved to be strong predictors of HCV status. Those who reported injecting between 100-1000 times in their lifetime were eight times more likely to be HCV positive (OR=8.31, 95% CI: 2.74, 25.18) and those who injected more than 1000 times were approximately 13 times more likely to be HCV positive (OR=12.72, 95% CI: 4.12, 39.28) than those who injected only 1 to 10 times in their lifetime. Other factors found to be significantly associated with having a positive HCV test result included sharing filters (OR=2.71, 95% CI: 1.46, 5.01), requiring more mix water for PO injection than for injection of other drugs (OR=2.98, 95% CI: 1.54, 5.78), and using syringe barrels greater than 1 cc (OR=6.42, 95% CI: 1.42, 28.91).

Multivariate Analysis

Table 3 summarizes the adjusted odds ratios (aOR) that were obtained from the final logistic regression model. No interaction terms were kept in the final model but the adjusted model controlled for age, number of lifetime injections, and the number of times an individual shared needles in the past. After controlling for these factors, prescription opioid use was no longer found to be a significant predictor of HCV status (aOR=0.75, 95% CI: 0.37, 1.52).

Among the study population of 18-29 years old individuals, being in the older half of the population (24 years or older) was statistically significantly associated with

having a positive HCV test result (aOR=2.26, 95% CI: 1.19, 4.30). Number of lifetime injections and sharing needles were also still found to be statistically significantly associated with being HCV positive in the adjusted model. Those who injected 100 to 1000 times were approximately 5 times (aOR=5.19, 95% CI: 1.34, 20.03) more likely to be HCV positive and those who injected more than 1000 times were more than 9 times (aOR=9.46, 95% CI: 2.29, 39.05) more likely to be HCV positive compared to PWID who injected drugs only 1 to 10 times in their life. Sharing needles was significantly associated with HCV infection especially when participants reported sharing needles more than five times in the past (aOR=6.48, 95% CI: 2.46, 17.01) compared to those who reported never having shared needles.

Overall, the Chi-square of the final model was significant ($p<0.001$) and the model was found to have a decent fit (Hosmer and Lemeshov test: $p=0.33$).

Discussion

In this study, we examined injection practices of prescription opioid users and whether these behaviors and PO use were associated with a higher risk of hepatitis C acquisition among young people who inject drugs in rural Wisconsin. Although our analyses did not show that prescription opioid injection use was associated with higher risk of HCV infection after adjusting for covariates, it is still imperative to understand the specific risk behaviors of prescription opioid users as approximately 65% of those who tested positive for HCV antibody in our study reported injecting POs. Our analyses did

find that certain injection behaviors were more prevalent among PO users than non-PO users. These risk factors included sharing needles, number of lifetime injections, and the average number of injections per injection episode, which have all been consistent risk factors of HCV acquisition [18, 20, 35].

Four previous studies [26, 30, 31, 36] have found prescription opioid use to be associated with HCV status, but one prospective cohort study that took place from 2005 to 2011 in Vancouver, British Columbia found similar results to our study [32]. In this study, prescription opioid use was also found to be a significant predictor of HCV status in bivariate analysis (HR=3.48; 95% CI: 1.57 to 7.70), but not a significant predictor in multivariate analysis after controlling for other covariates (aHR=0.94; 95% CI: 0.40 to 2.21). The study did indicate several limitations that potentially could have led to this null estimate, such as a small sample size of PO users and bias from self-reporting.

As with the study mentioned above, self-reported risk behaviors were also a limitation of this study as participants may have underreported certain behaviors, such as sharing of injection equipment, as it is often considered a stigmatized behavior [32]. Our sampling method was also not random and recruitment was conducted at a syringe service program. PWID that visit syringe service programs may not adequately represent PWID in rural Wisconsin, as they may be considered to be “safer” injectors than those who do not visit syringe service programs since they are already taking precautions to obtain a clean and new needle [37].

Information bias is an important potential limitation to note too. Some extent of non-differential misclassification of the independent variable in this analysis may be present due to the difficulty of classifying an exclusive group of long-term PO users. Firstly, the survey did not contain a question asking the duration an individual regularly injected prescription opioids, thus no difference was represented in the independent variable between PO users who had been injecting POs for years and PO users who had perhaps only been injecting POs for a few weeks. Secondly, most drug injectors do not solely use one type of drug, which creates challenges in analyzing the exact effect of PO injection when those who are injecting POs are simultaneously injecting other drugs as well. This potential differential misclassification of the independent variable among the study population could have created bias towards the null in our analyses. Future research should continue to assess risks for infectious diseases and risk behaviors among PWID by recruiting exclusively prescription opioid injecting young adults in order to improve estimates.

It is imperative to tailor prevention strategies based on a PWID's drug of choice. Injecting different drugs require altered preparation processes thus creating different risk behaviors among PWID. For example, when educating primarily PO users, it is important to discuss the use of WHO-recommended low dead space needles as PO users are more probable to use syringe barrels greater than ½ cc for their larger volume of injection substance [20]. Syringe service programs should be utilized for educating PWID of not only the dangers and health risks of injecting drugs but also of all injection

practice behaviors that increase their risk of infection, such as sharing “washes” and injecting multiple times for a single dose.

Despite our analysis suggesting that risk of HCV among PO users is not much different from that of all PWID, HCV is still a prevalent disease among the growing PO injecting population [1], and the denounced nature of injecting drugs has been found to decrease PWID’s inclination to get tested and seek care [38]. One of the strengths of this study is that it tested 280 high-risk individuals for hepatitis C for which 83 tested positive for HCV antibody. Awareness of one’s positive HCV diagnosis could lead to safer injection practices and decreased risk of transmission of the disease to others [38]. Critical steps to preventing HCV among PWID include providing more outreach and providing greater access to sites, such as syringe service programs, where they are more prone to get tested as well as seek care and services.

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List of Tables

Table 1. Demographics and risk behaviors by prescription opioid use

	Total, n (%) N=280	PO-users, n (%) N=131	Non-PO users, n (%) N=149	P-Value
Age				0.061
18-23 years old	122 (53.7)	58 (52.1)	64 (60.4)	
24-29 years old	105 (46.3)	63 (47.9)	42 (39.6)	
Sex				0.858
Male	163 (58.2)	86 (57.7)	77 (58.8)	
Race				0.002
White	231 (82.5)	134 (89.9)	97 (74.1)	
American Indian or Alaska Native	40(14.3)	14 (9.4)	26 (19.9)	
Black	7 (2.5)	0 (0.0)	7 (5.3)	
Other	2 (0.7)	1 (0.7)	1 (0.8)	
Education level				0.955
No high school diploma	64 (22.9)	34 (22.8)	30 (22.9)	
High school diploma or GED	202 (72.1)	107 (71.8)	95 (72.5)	
Associate, Bachelor or Graduate degree	14 (5.0)	8 (5.4)	6 (4.6)	
Age of first injection [Mean (SD)]	19.3 (3.8)	19.2 (3.7)	19.4 (4.0)	0.750
Sharing needles				<.001
Never	93 (33.2)	37 (24.8)	56 (42.8)	
1 time	37 (13.2)	12 (8.1)	25 (19.1)	
2-5 times	88 (31.4)	55 (36.9)	33 (25.2)	
More than 5 times	62 (22.1)	45 (30.2)	17 (13.0)	
Sharing filters				0.756
Yes	68 (35.0)	40 (34.2)	28 (36.4)	
No	126 (65.0)	77 (65.8)	49 (34.2)	
Number of lifetime injections				<.001
1 to 10 injections	48 (17.1)	15 (10.1)	33 (25.2)	
10 to 100 injections	76 (27.1)	29 (19.5)	47 (35.9)	
100 to 1000 injections	86 (30.7)	49 (32.9)	37 (28.2)	
1000+ injections	69 (24.6)	56 (37.6)	13 (9.9)	
Average number of injections in a day [Mean (SD)]	2.8 (1.9)	2.9 (1.8)	2.7 (1.7)	0.221
Average number of injections for a single dose				0.002
1 time	148 (52.9)	65 (43.6)	83 (63.4)	
2 times	74 (26.4)	43 (28.9)	31 (23.7)	
3-4 times	42 (15.0)	33 (22.2)	9 (6.9)	
5 or more times	16 (5.7)	8 (5.4)	8 (6.1)	

Table 1. Demographics and risk behaviors by prescription opioid use *(continued)*

	Total, n (%) N=280	PO-users, n (%) N=131	Non-PO users, n (%) N=149	P-Value
Barrel size used when injecting				0.006
1/2 cc	45 (16.1)	20 (13.4)	25 (19.1)	
1 cc	167 (59.6)	102 (68.5)	65 (49.6)	
>1 cc	10 (3.6)	6 (4.0)	4 (3.1)	
Unsure	58 (20.7)	21 (14.1)	37 (28.2)	

Table 2. Crude Odds ratios (OR) and 95% confidence intervals (CI) from bivariate analysis of being HCV positive

	Hep C Positive (%) N=93	n	crude OR	95% CI
PO use				
Non-prescription opioid user*	33 (35.5)	131	1.00	-
Prescription opioid user	60 (64.5)	149	2.00	(1.20, 3.34)
Age [Mean (SD)]				
18-23 years old*	30 (32.3)	122	1.00	-
24-29 years old	46 (49.4)	105	2.39	(1.36, 4.20)
Sex				
Female*	46 (49.5)	116	1.00	-
Male	47 (50.5)	163	0.63	(0.38, 1.03)
Race				
White*	78 (83.9)	231	1.00	-
American Indian or Alaska Native	15 (16.1)	40	1.18	(0.59, 2.36)
Black	0 (0.0)	7	-	-
Other	0 (0.0)	2	-	-
Education level				
Associate, Bachelor or Graduate degree*	2 (2.2)	14	1.00	-
High school diploma or GED	68 (73.1)	202	3.04	(0.66, 13.99)
No high school diploma	23 (24.7)	64	3.37	(0.69, 16.37)
Sharing needles				
Never*	13 (14.0)	93	1.00	
1 time	9 (9.7)	37	1.98	(0.76, 5.13)
2-5 times	35 (37.6)	88	4.06	(1.97, 8.39)
More than 5 times	36 (38.7)	62	8.52	(3.93, 18.46)
Sharing filters				
No*	34 (36.6)	126	1.00	-
Yes	34 (36.6)	68	2.71	(1.46, 5.01)
Number of lifetime injections				
1 to 10 injections*	4 (4.3)	48	1.00	-
10 to 100 injections	15 (16.1)	76	2.70	(0.84, 8.70)
100 to 1000 injections	37 (39.8)	86	8.31	(2.74, 25.18)
1000+ injections	37 (39.8)	69	12.72	(4.12, 39.28)

*Reference group

Table 2. Crude Odds ratios (OR) and 95% confidence intervals (CI) from bivariate analysis of being HCV positive *(continued)*

	Hep C Positive (%) N=93	n	crude OR	95% CI
Average number of injections for a single dose				
1 time*	41 (27.7)	148	1.00	-
2 times	29 (39.2)	74	1.68	(0.93, 3.03)
3-4 times	18 (42.9)	42	1.96	(0.96, 3.98)
5+ times	5 (31.25)	16	1.19	(0.39, 3.62)
Using more mix water for PO injection than other drugs				
Yes	80 (38.8)	206	2.98	(1.54, 5.78)
Barrel size used when injecting				
1/2 cc*	12 (26.7)	45	1.00	-
1 cc	62 (37.1)	167	1.62	(0.78, 3.38)
>1 cc	7 (70.0)	10	6.42	(1.42, 28.91)
Unsure	12 (20.7)	58	0.72	(0.29, 1.79)

*Reference group

Table 3. Adjusted odds ratio (aOR), 95% confidence intervals (CI), and p-values from multivariate regression

	aOR	95% CI	p-value
PO Use			
Non-prescription opioid user*	1.00	-	-
Prescription opioid user	0.75	(0.37, 1.52)	0.420
Age			
18-23 years old*	1.00	-	-
24-28 years old	2.26	(1.19, 4.30)	0.013
Sharing Needles			
Never*	1.00	-	-
1 time	1.90	(0.62,5.80)	0.260
2-5 times	2.72	(1.10, 6.72)	0.030
More than 5 times	6.48	(2.46, 17.01)	<0.001
Lifetime Injections			
1 to 10 injections*	1.00	-	-
10 to 100 injections	2.38	(0.60, 9.43)	0.216
100 to 1000 injections	5.19	(1.34, 20.03)	0.017
1000+ injections	9.46	(2.29, 39.05)	0.002

*Reference group