Characteristics of Hepatitis C Infection in Injecting Drug Users in Zadar County, Croatia

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A B S T R A C T

The aim of the study was to determine additional risk factors that could increase the prevalence of hepatitis C (HCV) infection among injecting drug users (IDU). The study included 327 heroin addicts registered in Zadar County, Croatia. The participants were divided into two groups according to their HCV status. HCV-positive and HCV-negative study participants were compared. HCV-positive group started injecting heroin at earlier age (median 18.5 years) than HCV-negative group (median 20.0 years) (p=0.032) and had been injecting heroin for a significantly longer period (median 5 years vs. median 4 years, respectively; p<0.001). IDUs in HCV-positive group shared their injecting equipment significantly more often than IDUs in HCV-negative group (p<0.001; χ²=32.7). The main reasons for starting drugs were curiosity, psychological reasons (depression and/or neurosis), and peer or partner pressure in HCV-positive group, and fun, curiosity, and peer pressure in HCV-negative group (p=0.051; χ²=23.6). Earlier onset of heroin use, longer heroin use, sharing injection equipment, curiosity, and psychological problems as reasons for starting drugs were associated with higher prevalence of HCV infection among injecting heroin users in Zadar County.

Key words: heroin addiction, hepatitis C, injecting drug users, risk factors

Introduction

Shortly after it was discovered in 1989, hepatitis C virus (HCV) was recognized as the main cause of chronic liver disease. The World Health Organization (WHO) estimates that the prevalence of HCV infection is 2%, i.e. 123 million people in the world are infected with HCV[1]. Between 75% and 85% of population with acute HCV infection develops chronic hepatitis C with or without increase in alanine aminotransferase (ALT) blood levels[2,3]. Within 10–20 years, 8–25% of these patients develop liver cirrhosis[4] with a risk of liver damage, hepatocellular cancer, and death from liver disease[5,6].

In developed countries, HCV is primarily transmitted by injection drug use. The prevalence of HCV infection among injecting drug users (IDUs) who have injected drugs for six or more years is between 64% and 94%[7–10]. In Croatia, the number of opiate users is around 13,000 (2.7/1000 population). If we assume that 70–85% of IDUs in Croatia are positive to anti-HCV, then their number ranges between 9100 and 11,050[11].

Although drug use is more frequent in population of low socioeconomic status, a direct association between drug addiction and socioeconomic status has not been proven[12]. Many studies have shown that the increased incidence of HCV infection among IDUs is associated with higher frequency of drug injection[13–16]. The risk of exposure to HCV infection increases with the number of episodes of drug use[17]. Also, IDUs who share injection equipment are at greater risk of acquiring HCV infection[18,19]. Most IDUs come from a low socioeconomic background and live with their parents or family[20]. Although many risk factors for HCV infection in IDUs are known, there could be additional factors that have not yet been investigated. In the context of high prevalence and increasing incidence of injecting drug use, research into the characteristics of IDUs could contribute to early recognition of those at risk of HCV infection and improve the implementation of preventive and therapeutic measures.

The aim of our study was to determine additional risk factors associated with HCV infection in IDUs in Zadar County, Croatia.

Subjects and Methods

The questionnaire study was conducted among 421 current and former injecting drug users registered at the Center for Prevention and Outpatient Treatment of Addiction in Zadar, Croatia, between January 1, 2001 and January 1, 2005. The participation in the study was voluntary. IDUs who agreed to participate were asked to undergo testing for hepatitis C and B infection. Ninety-four registered IDUs were excluded from the study because they either refused testing or did not answer all the questions in the questionnaire. The final sample consisted of 327 IDUs with complete questionnaires and available HCV and HBV test results. There were 272 (83.2%) men and 55 (16.8%) women aged between 17 and 51 years (Table 1). Based on their HCV-serology results, they were divided into HCV-positive and HCV-negative group and compared by age, duration of heroin use, practice of injection equipment sharing, age of onset of drug use, and motives to start using drugs as key risk factors for HCV infection.

Questionnaire

IDUs were asked to complete the questionnaire during their regular visits to the Center. A physician or psychologists working at the Center helped them fill in the data. The questionnaire has been in standard use in Croatia since 1990. It is based on the Treatment Demand Indicator Protocol[21], a standard questionnaire developed by the European Center for Monitoring of Drugs and Drug Addiction and Pompidou group (*http://www.coe.int/T/dg3/pompidou/default_en.asp*). This questionnaire is used to collect uniform data on drug users in the treatment programs in over 35 European countries. The questionnaire consists of 11 sections covering the following areas: drug addiction treatment, sociodemographic background, drug abuse, risk behavior, other treatment, family data, legal issues, previous addiction history, health problems, causes of drug abuse, and confidential personal data (Appendix). The section on health problems includes information on the IDU's HCV and HBV status, which is provided by a physician after IDU's HCV and HBV testing results become available.

Testing for HCV infection

After IDUs completed the questionnaire, they were referred to the Department of Transfusion Medicine of Zadar General Hospital for blood sampling and HCV and HBV testing. Serum HCV and HBV antibodies were determined on the same day. Anti-HCV was determined with a highly sensitive microparticle enzyme immunoassay AxSYM HCV, version 3.0 (ABBOTT, Wiesbaden, Germany). The third generation of microparticle enzyme immunoassay (ABBOTT) AxSYM HBsAg(V2) was used to determine serum HBsAg.

Statistical analysis

Numerical data were tested for normal distribution by Kolmogorov-Smirnov test and presented as mean values with standard deviation ($\pm$ SD) or median with range.

TABLE 1
CHARACTERISTICS OF INJECTING DRUG USERS (IDUS) WITH AND WITHOUT HEPATITIS C VIRUS (HCV) INFECTION, REGISTERED AT ZADAR CENTER FOR PREVENTION AND OUTPATIENT TREATMENT OF ADDICTION

Characteristic	No. (%) of IDUs		p
	HCV positive (n=193)	HCV negative (n=134)	
Age (years; median, range)	28 (18–51)	26 (17–48)	0.004*
Sex (m/f)	164/29	108/26	0.298†
Education level:			N/A
elementary	23 (11.9)	10 (7.5)	
high school	164 (85.0)	112 (83.6)	
college or university	4 (2.1)	9 (6.7)	
unknown	2 (1.0)	3 (2.2)	
Socioeconomic level (EUR per month)			0.457†
low (<400)	74 (38.3)	41 (30.6)	
middle (400–800)	103 (53.4)	77 (57.5)	
high (>800)	16 (8.3)	12 (9.0)	
Unknown (missing data)	0	4 (3.0)	
Age of first-time heroin use (years; median, range)	18.5 (13.0–40.0)	20.0 (13.0–43.0)	0.032*
Age of first-time use of any drug (years; median, range)	16.0 (10.0–40.0)	16.0 (12.0–41.0)	0.628*
Total duration of heroin use (years; median, range)	5.0 (1.0–20.0)	4.0 (1.0–20.0)	0.001*

*Mann-Whitney test, †χ² test.

Variables that were not normally distributed or variables without homogeneous variance were compared using non-parametric Mann-Whitney test. Qualitative data were compared with either χ^2-test or Fisher's exact test, as appropriate. Logistic regression was used to assess multivariate prediction of HCV infection, which was presented as odds ratio (OR) with 95% confidence intervals (95% CI). All statistical analyses were performed with SAS System for Windows, release 8.02 (SAS Institute Inc., Cary, NC, USA) and $p < 0.05$ was considered statistically significant.

Results

The HCV-positive group consisted of 193 IDUs, and HCV-negative group consisted of 134 IDUs. Men-to-women ratio was 5:1 in both groups. The groups did not differ in education level and economic status of their families (Table 1). Although the median age of first use of any drug was 16 years in both groups, HCV-positive IDUs started using heroin at a significantly younger age than HCV-negative IDUs and had used it for a longer time. Also, HCV-positive IDUs were significantly older than HCV-negative IDUs at the time of the study (Table 1).

The median duration of heroin use in HCV-positive group was 5 years (range, 1–20), which was significantly longer than the 4-year median duration of heroin use in the HCV-negative group (range, 1–20) ($p < 0.001$; Mann-Whitney test).

HBV monoinfection was found in only 6 (4.5%) IDUs, whereas the serologic markers of HBV-HCV coinfection were detected in 55 (16.8%) of them.

In comparison with HCV-negative IDUs, HCV-positive IDUs shared their injecting drug equipment significantly more often (Table 2). They were also coinfected with HBV significantly more often than HCV-negative IDUs (Table 3).

IDUs were asked to choose the three most important reasons for starting experimenting with drugs from the following list: self-confirmation (showing off), influence of peers or partner, family problems, problems at school, psychological reasons (depression, neurosis, or adolescent insecurity), boredom, fun, curiosity, unawareness of any possible negative consequences, or unknown. Some of these motives were more frequent among HCV-positive IDUs, whereas others were more frequent among HCV-negative users (Table 4). In HCV-positive groups, curiosity was selected as the most common reason, fol-

TABLE 2
DISTRIBUTION OF INJECTING DRUG USERS (IDUS) INCLUDED IN THE STUDY WITH RESPECT TO INJECTION EQUIPMENT SHARING

Sharing injection equipment	No. (%) of IDUs*		
	HCV positive (n=193)	HCV negative (n=134)	total (n=327)
yes	183 (94.8)	72 (53.7)	255 (78.0)
no	10 (5.2)	62 (46.3)	72 (22.0)

*p<0.001; χ^2 test.

TABLE 3
DISTRIBUTION OF INJECTING DRUG USERS (IDUS) INCLUDED IN THE STUDY WITH RESPECT TO THE PRESENCE OF HEPATITIS B (HBV) AND HEPATITIS C (HCV) INFECTION

HBV infection	No. (%) of IDUs*		
	HCV positive (n=193)	HCV negative (n=134)	total (n=327)
yes	55 (28.5)	6 (4.5)	61 (18.6)
no	138 (71.5)	128 (95.5)	266 (81.4)

*p<0.001; χ^2t est.

TABLE 4
DISTRIBUTION OF INJECTING DRUG USERS (IDUS) INCLUDED IN THE STUDY WITH RESPECT TO THE ONSET OF EXPERIMENTING WITH DRUGS

Motive for experimenting	No (%) of IDUs		
	HCV positive	HCV negative	total
Wish for self-confirmation	19 (9.8)	9 (6.7)	28 (8.6)
Peer or partner pressure	34 (17.6)	21 (15.7)	55 (16.8)
Family problems	12 (6.2)	7 (5.2)	19 (5.8)
Problems at school	1 (0.5)	0	1 (0.3)
Psychological reasons	34 (17.6)	16 (11.9)	50 (15.3)
Boredom	23 (11.9)	12 (9.0)	35 (10.7)
Fun	15 (7.8)	30 (22.4)	45 (13.8)
Curiosity	50 (25.9)	29 (21.6)	79 (24.2)
Lack of knowledge about possible negative consequences	5 (2.6)	6 (4.5)	11 (3.4)
Unknown	0	4 (3.0)	4 (1.2)
Total	193 (100.0)	134 (100.0)	327 (100.0)

lowed by psychological reasons and peer- or partner-pressure. In HCV-negative groups, the top three reasons for starting experimenting with drugs in the order of frequency were fun, curiosity, and peer- or partner-pressure (Table 4).

The predictors of HCV infection included in the logistic regression model were age of onset of intravenous heroin use, duration of intravenous heroin use, sharing injecting equipment, and motives to start experimenting with drugs. The result showed that sharing injection equipment and duration of intravenous heroin use were the significant predictors of HCV infection (Table 5). Odds ratio point estimate for sharing injection equipment was 13.284 (95% CI = 4.957–35.601), showing that IDUs who shared their injecting equipment were over 13 times more likely to acquire HCV infection. The model was statistically significant (–2 log likelihood 280.803, $\chi^2_{12} = 65.466$, p<0.001), and its predictive accuracy was 74.9%.

Discussion

We found that IDUs positive to HCV infection had started injecting heroin at younger age, used it for a longer time, and shared their drug injection equipment more often than HCV-negative IDUs. The main finding was that they were significantly younger than HCV-negative IDUs. The combination of these factors could be the main risk for acquiring HCV infection. It has been found that early onset of heroin use increases the risk of both addiction and HCV infection[22]. In comparison with the experienced (registered) IDUs, young IDUs were found to be at higher risk of blood-borne infections because of their high-risk behavior pattern[18,23]. Young IDUs are usually less critical toward drugs, less cautious, and more easily influenced by others, therefore more exposed to HCV infection[13,24]. Also, young IDUs share their drug equipment more readily than older IDUs[25,26]. The possibility of HCV transmission via additional injection equipment, such as cotton swabs or water, is often underestimated, as well as the nature of social relationships among IDUs characterized by unlimited mutual trust. Young IDUs also know less about HCV infection and its transmission pattern. Furthermore, they have occasional or convenient sex more often, and are frequently involved in sex industry (prostitution), while at the same time they rarely use condoms[26–28] and easily agree to inject drugs[29]. This knowledge is valuable to the professionals working on the prevention of drug use among youth, as they can use it for the development of guidelines for timely health-care interventions, including dispensing sterile injection equipment[13].

The methods for prevention of HCV infection are the same as methods for prevention of HIV infection. A study among young HIV-positive drug users found that 88% of them had coinfection with HCV, showing that HCV-HIV coinfection is almost as frequent among drug users as HIV infection alone[13]. However, prevention is possible. It was shown that having a safe place for injecting drugs was successful in reducing the HIV and HCV infection incidence among young IDUs[22].

Age of diagnosis of HCV infection plays an important role in the guidelines for antiviral treatment and its outcome[2]. In young IDUs, HCV seroconversion occurs early, HCV mortality is high (even without cirrhosis), the infection is reversible after re-exposure despite successful antiviral treatment[30,31]. Therefore, it is important to identify IDUs and HCV infection as early as possible.

TABLE 5
LOGISTIC REGRESSION ANALYSIS OF PREDICTORS OF INJECTING DRUG USE*

Predictors	b (SE)	p	OR (95% CI)
Age of onset of drug use	0.009 (0.034)	0.786	1.009 (0.944–1.080)
Duration of drug use	0.130 (08.042)	0.002	1.138 (1.049–1.236)
Sharing injection equipment	2.587 (0503)	<0.001	13.284 (4.957–35.601)
Motives for experimenting with drugs		0.144	
self-confirmation	6.939 (22.247)	0.755	1031.529 (0.000–8.92E+21)
peer or partner pressure	7.386 (22.245)	0.740	1612.481 (0.000–1.39E+22)
family problems	6.886 (22.249)	0.757	978.890 (0.000–8.49E+21)
problems in school	11.122 (31.454)	0.724	67612.102 (0.000–4.02E+31)
psychological reasons	7.162 (22.244)	0.747	1289.306 (0.000–1.11E+22)
boredom	7.084 (22.244)	0.750	1192.441 (0.000–1.03E+22)
fun	5.648 (22.243)	0.800	283.727 (0.000–2.43E+21)
curiosity	6.690 (22.242)	0.764	804.070 (0.000–6.88E+21)
lack of knowledge about adverse consequences of drug use	6.157 (22.252)	0.782	472.043 (0.000–4.12E+21)
Constant	–9.204 (22.256)	0.679	

*Abbreviati: SE – standard error of β; OR – odds ratio; CI – confidence interval.ons

Most IDUs in our study were men. Men are more often in contact with drugs and more prone to experiment with drugs[22,32].

Lower socioeconomic background and lower education level are believed to be important factors for higher prevalence of HCV infection[33,34]. In our study, however, most IDUs had an average living standard, whereas those belonging to higher socioeconomic class were rare.

Our results showed that the longer the heroin use, the higher the risk of HCV infection. The risk of HCV infection doubles every 2 years of continuous heroin use; after 6 or more years of continuous use, it is 10-fold higher[13]. In our study, HCV positive IDUs were older than HCV-negative ones, which shows that age and the duration of drug use should be considered mutually associated factors influencing the occurrence of HCV infection[10,13,18,30,35–38].

Sharing injection equipment is one of the most important factors for HCV transmission[13–16]. HCV-positive group shared their equipment with other drug users significantly more often than HCV-negative group. HCV infection is not transmitted only by sharing needles, but also by sharing cotton swabs and other equipment[15,31,39,40]. In our study, we considered that drug injection equipment was shared if any of the equipment items were shared.

The incidence of HCV infection significantly decreased, especially among young IDUs, after the needle/ syringe exchange program has been introduced[41]. Reduced spread of HCV and other blood-borne diseases can also be achieved by better health education of population and implementation of law enforcement measures against drugs and drug use[42].

HCV infection is closely associated with HBV infection as the viruses share the same transmission route (blood and sexual intercourse)[43]. In our study, over a quarter of IDUs with HCV infection were HBsAg positive. This is important for the prognosis of HCV infection, as the risk of serious liver disease (cirrhosis or liver cancer) increases in patients with coinfection in comparison with those who have only HCV infection[44,45].

Motives to start experimenting with drugs differed between HCV-positive and HCV-negative IDUs in our study. Although family was selected as the most important reason, followed by school problems, peer pressure, media, and society in general[46], family problems were not high on the list of reasons. Parental acceptance or rejection was not an important reason either[12]. Fun and curiosity, followed by peer or partner pressure were the primary reasons to start using drugs in our sample of HCV negative IDUs. This showed that HCV-positive and HCV--negative IDUs had different attitudes toward drugs and drug use from the start. HCV-negative IDUs also seemed to be less open to the influence of microsocial environment, which could explain their lower risk of HCV infection.

Possible limitation of our study could be the fact that almost a quarter of IDUs registered at the Center refused testing or omitted to complete the questionnaire. Despite this possible exclusion bias, our results were similar to previous findings. Further research should look more thoroughly into risk factors for drug abuse and blood-borne infections among adolescents, when drug abuse usually starts[12]. Primary measures for drug abuse prevention should primarily target teenagers. Health education and injection equipment exchange programs are presently the only means of control of HCV infection spread among IDUs[19]. We should increase our understanding of HCV epidemiology within individual risk groups, predict the points of timely prevention, and choose the most effective time and manner to educate children and adolescents (senior elementary school) about the risks and consequences of drug use. Public health actions should target IDUs directly, especially the young ones, who are at highest risk of developing the addiction. The possibility to get in contact and start experimenting with drugs should be limited and use of hard drugs postponed as much as possible to older age, as it is known that the risk of HCV infection and addiction decreases with age and treatment is easier to implement and usually more successful. According to the evidence so far, the risk of HCV infection can certainly be reduced with the decrease in the number of IDUs.

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KARAKTERISTIKE HEPATITIS C INFEKCIJE IZMEĐU INTRAVENSKIH OVISNIKA U ZADARSKOJ ŽUPANIJI

S A Ž E T A K

Cilj ove studije je odrediti dodatne faktore rizika koji mogu povećati prevalenciju hepatitisa C (HCV) među intravenskim ovisnicima (IV ovisnici). Studija uključuje 327 heroinskih ovisnika u Zadarskoj županiji, Hrvatska. Sudionici su podijeljeni u dvije grupe prema HCV statusu. HCV-pozitivni i HCV-negativni sudionici su uspoređivani. HCV-pozitivni ovisnici ranije počinju koristiti heroin venskim putem (median 18,5 godina) u odnosu na HCV-negativne (median 20.0 godina) (p=0,032) i duže konzumiraju heroin (median 5 godina; median 4 godine, uzastopce; p<0,001). IV ovisnici HCV pozitivnoj grupi češće se dijele pribor za drogiranje od HCV-negativnih ovisnika (p<0,001: χ^2=32.7). Glavni razlozi za početak konzumiranja droga u HCV-pozitivnih ovisnika su znatiželja, psihološki razlozi (depresija, neuroza), te utjecaj partnera ili vršnjaka, dok su u HCV-negativnih ovisnika zabava, znatiželja, te utjecaj partnera ili vršnjaka (p=0,051; χ^2=23,6). Ranije uzimanje heroina, duže uzimanje heroina, dijeljenje zajedničkog pribora, znatiželja i psihološki problemi su razlozi povezani sa visokom prevalencijom HCV infekcije među intavenskim ovisnicima u Zadarskoj županiji.