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Hepatitis C virus infection among short-term intravenous drug users in southern Taiwan

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Abstract. The purpose of this study was to determine the correlation between the prevalence of hepatitis C virus (HCV) infection with duration of drug use and other risk factors among drug users. This survey covered 899 male drug users from Kaohsiung Narcotic Abstention Institute and Kaohsiung prison. The prevalence of positive anti-HCV was 67.2% among intravenous drug users (IVDU) and 14.7% among non-intravenous drug users (non-IVDU). Among intravenous (IV) drug users, age and duration of drug use were independently related to HCV seropositivity. Seroprevalence rate for HCV in the IVDU group increased with increasing duration of injection use within the first seven years of drug use. However, the steepest trajectory in seroprevalence of HCV infection occurred within the first four months. Due to the high rate of HCV infection among drug users, investigation of risk behaviors should be routine in such a group. A high frequency of HCV infection was also found among short-term injectors, which indicated that early risk reduction intervention was an important measure in moderating HCV infection.

Key words: Hepatitis C virus infection, Intravenous drug users, Risk factors, Sexual behavior

Introduction

In developed countries, intravenous drug users (IVDU) are the only individuals exposed to blood that has not been screened for preventing transmission of viral infections. They constitute, therefore, the largest group at risk of viral hepatitis [1–3]. Transmission is primarily parenteral through sharing contaminated hypodermic syringes [4–6].

An important variable to consider when differentiating the risk of HCV infection among drug users is the duration of hypodermic syringe use. A high rate of HCV infection is likely among short-term injectors [7–9]. To be effective, it is important to target preventive intervention at beginners, who are exposed to increased risks. Further studies are required to understand why injectors in certain stages of their drug use are at greater risk of being infected with HCV than in others.

Although very high values of HCV prevalence were reported among Taiwanese drug users [10, 11], so far, few investigations have focused on the association between duration of drug use and HCV infection. The purpose of the present study was to investigate seroprevalence rate in relation to duration of drug use in order to (a) identify the time periods when infection rates were increased and (b) evaluate the differences in risk factors among IVDU and non-intravenous (non-IVDU) drug users in Taiwan.

Materials and methods

During the period from October 1994 to February 1996, a total of 899 male drug users, aged 14–59 years (mean age: 31.5 years), were examined at the Kaohsiung Narcotic Abstention Institute and Kaohsiung prison. Of these, 247 (27%) had a history of injecting pentazocine and heroin. In this study, an intravenous drug user is defined as a person who had ever been an intravenous user of illicit drugs, regardless of whether or not he is an illicit intravenous drug user currently.

Anti-HCV testing was done by enzyme immunoassay (Abbott HCV EIA 2nd generation, Abbott Laboratories, Abbott Park, IL), using a recombinant antigen of viral genome including putative structural and non-structural proteins. All samples had been stored frozen at −70 °C; they were thawed at room temperature and tested according to the manufacturer's instructions. Specimens with absorbance values greater than the cutoff value were considered reactive. The reactive samples were retested and considered positive if both tests were reactive. All

serum samples were tested for HBsAg, anti-HBs and anti-HBc by radioimmunoassay (RIA) using commercially available reagents (Abbott Laboratories, Abbott Park, IL). HBV seropositivity was defined as a positive finding from any of the HBsAg, anti-HBs, or anti-HBc tests.

On the day of blood sampling, copies of a structured questionnaire were distributed among the respondents, and all 899 volunteers answered them. The questionnaires included information about demographic data, education, occupation, history of hepatitis and blood transfusion, tattoos, age of starting drug use, duration of drug use, average number of injections per day, and occurrence of syringe sharing. Duration of drug use among IVDU subjects is defined as the period of time from a participant's reported first injection to his last injection of illicit drugs. Although some IVDU subjects used illicit drugs by intravenous method intermittently, the duration of drug use was calculated by summing up the time periods of injections. In order to reduce the underreported risk factors, the participants underwent confidential, face-to-face interviews with a trained family physician in a quiet, private room.

Data were analyzed by SAS 6.04 software package. A χ^2-test was used for categorical variables to examine the difference between groups. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to estimate the risks of acquiring HCV infection in relation to the risk factors identified by our questionnaire. Those showing significant OR were subsequently examined in a multiple logistic regression model to obtain adjusted OR.

Results

Of the 899 respondents tested, 262 (29.1%) were found positive for anti-HCV (Table 1), and increased with increasing age. The prevalence rate was present in 67.2% of the IVDU group and 14.7% of the non-IVDU group. The results of univariate analyses for postulated risk factors are shown in Table 2. Age was found to be a significant risk factor of HCV infection in the IVDU group. In all, 76% of >30 year old IVDU individuals were found HCV seropositive compared with 47% of $\leqslant 30$ year old IV drug users. Histories of blood transfusion, tattooing, and marital status were not risk factors of HCV infection in the IVDU group.

The number of lifetime IVDU sex partners and frequency of condom use were found to be significantly associated with HCV infection among IVDU, with OR ranging between 3.56 and 4.35 (Table 2). Intravenous drug users with $\geqslant 5$ lifetime sex partners were exposed to the same risk as those with <5 lifetime sex partners. A history of gonorrhea or HBV infection was not significantly related to HCV infection in the IVDU group.

Table 1. Prevalence of anti-hepatitis C virus by type of drug use and age among drug users

Characteristics	No. tested	No. (%) positive	*p*
Overall	899	262 (29)	
Type of drug use			
Intravenous	247	166 (67)	<0.001
Other	652	96 (15)	
Age, years			
<20	29	4 (14)	<0.001
20–24	121	29 (24)	
25–29	248	44 (18)	
30–34	228	63 (28)	
35–39	142	65 (46)	
40–44	92	40 (43)	
$\geqslant 45$	39	17 (44)	

HCV infection was found to be significantly associated with duration of drug use (Table 2), but not with frequency of drug use or history of needle sharing among IV drug users. The prevalence of HCV infection in IVDU men with >1 month of drug use was significantly greater than in those with $\leqslant 1$ month. In the non-IVDU group, these variables (i.e. age, marital status, history of blood transfusion, tattooing, sexual behavior, sexually transmitted disease, duration and frequency of drug use) were not significantly associated with HCV infection (data not shown).

The prevalence of HCV infection in serial cohorts with increasing duration of drug use is depicted in Figure 1, demonstrating a dramatic rise in the prevalence of HCV infection within the first four months of intravenous drug use, followed by a relatively modest increase in the next seven years. The same prevalence in the non-IVDU group during this period remained essentially unchanged.

We performed logistic regression analysis to determine which factors were independently associated with HCV infection in the IVDU group. The significant risk factors of anti-HCV (i.e. age, lifetime IVDU sex partners, frequency of condom use, and duration of drug use) revealed in univariate analysis were included into the logistic regression analysis (Table 2). Age and duration of IV drug use were statistically significantly and independently associated with HCV infection. HCV seropositivity was found to be significantly associated with IVDU men older than 30 years old, who injected drugs for longer than one month (odds ratio, 2.96 and 5.14). The number of IVDU sex partners and frequency of condom use were not found associated with HCV infection according to logistic regression modeling.

Table 2. Analysis of risk factors associated with HCV among IVDU subjects

Variable	N	N (%) Positive	OR (95% CI)	aOR (a95% CI)
Age, years				
>30	169	129 (76.3)	3.57 (2.04–6.20)	2.96 (1.64–5.36)
⩽30	78	37 (47.4)	1.00	1.00
Marital status				
Single	169	116 (68.6)	1.23 (0.69–2.19)	–
Married	78	50 (64.1)	1.00	
Blood transfusion				
Yes	37	29 (78.4)	1.93 (0.85–4.39)	–
No	210	137 (65.2)	1.00	
Tattooing				
Yes	161	113 (70.2)	1.47 (0.84–2.56)	–
No	86	53 (61.6)	1.00	
Lifetime sex partners				
⩾5	52	35 (67.3)	1.00	–
<5	195	131 (67.2)	1.00	
Lifetime IVDU sex partners				
⩾2	23	20 (87.0)	3.56 (1.09–11.60)	2.62 (0.73–9.35)
<2	224	146 (65.2)	1.00	1.00
Condom use				
Never/seldom	238	163 (68.5)	4.35 (1.18–16.10)	2.97 (0.66–13.27)
Always	9	3 (33.3)	1.00	1.00
Gonorrhea				
Yes	62	36 (58.1)	0.59 (0.32–1.06)	–
No	185	130 (70.3)	1.00	
HBV				
Positive	239	163 (68.2)	3.57 (0.90–14.11)	–
Negative	8	3 (37.5)	1.00	
Drug use frequency				
⩾4 times daily	106	76 (71.7)	1.44 (0.83–2.48)	–
<4 times daily	141	90 (63.8)	1.00	
Duration of drug use, months				
>1	231	162 (70.1)	7.04 (2.51–19.77)	5.14 (1.53–17.27)
⩽1	16	4 (25.0)	1.00	1.00
Needle sharing				
Yes	73	52 (71.2)	1.30 (0.72–2.35)	–
No	174	114 (65.5)	1.00	

Anti-HCV indicates antibody to hepatitis C virus; IVDU, intravenous drug user; OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; a95% CI, adjusted 95% confidence interval.

Discussion

The data presented here showed that HCV infection was common among drug users. The prevalence of positive anti-HCV was 67.2% in the IVDU group and 14.7% in the non-IVDU group. The seroprevalence in the IVDU men in southern Taiwan (67%) was somewhat lower than in similar groups of people in Spain (73%), Amsterdam (74%), Baltimore (85%), and comparable to those in Rome (67%) and New Zealand (67%) [4, 5, 7, 12, 13].

A major finding of this study was the dramatic rise of HCV infection observed within the first 7 years of intravenous drug use. Seroprevalence of HCV (86.7%) in the cohort embracing men with a history of 49 to 72 months of injection was slightly higher than that observed in the ALIVE study (85.0%) [9]. We also found that the seroprevalence rate increased in these seven years with increasing duration of injection use. The steep trajectory in seroprevalence within the first four months of injection use suggested that most new HCV infections occurred soon after beginning intravenous drug use. Prevalence of HCV infection in the 2 to 4 month cohort was significantly higher than that in the ⩽1 month group. There are several obvious explanations for this result. In the first month of IV drug use, injections are relatively infrequent and this reduces the risk of infection.

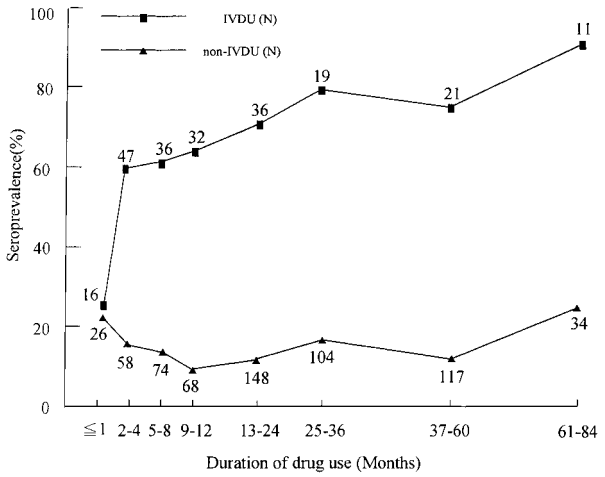

Figure 1. The prevalence of hepatitis C virus infection in serial cohorts with increasing duration of drug use among IVDU and non-IVDU, not including the cases with more than 7 years of drug use.

Furthermore, a number of factors typical of drug addiction may contribute to HCV infection, such as polydrug abuse, tattooing, and iatrogenic injections.

Univariate analyses indicated that age, duration of drug use, number of lifetime IVDU sex partners, and frequency of condom use were all significantly associated with HCV infection among the IV drug users. However, age and duration of drug use were independently related to the rate of seropositive HCV infection, suggesting that HCV was readily transmitted parenterally. This finding is comparable to other studies [4–8]. Giradi et al. [4] found that anti-HCV presence was associated with duration of IV drug use. Donahue et al. [5] documented a significant association between duration of IV drug use and hepatitis C seropositivity. History of needle sharing was not significantly associated with HCV infection among the IVDU group. The reason for this may be explained by the fact that most of our subjects might have underreported their risk behaviors in the prison environment.

Although the prevalence of HCV infection in the non-IVDU group was much lower than that in IV drug users, it was still 10 times higher than that (1.5%) observed among 20,768 healthy blood donors in Taiwan [14]. This difference could not be explained by age distribution, marital status, tattooing, history of blood transfusion, sexual behavior, or sexually transmitted diseases. However, a high frequency of non-needle sharing subjects with HCV infection in the IVDU group was found in our study (66%), and age was an independent risk factor for HCV infection. It indicated other routes of transmission which we had not investigated, such as that reported by Chang et al. [15]. In their study, they found that iatrogenic injections, frequently given at illegal medical service stations, played an important role in HCV infection in a Taiwanese aboriginal community.

In contrast with our present findings, several studies have found that HCV may be sexually transmitted [6, 16–18]. As age is a cumulative factor related significantly to sexual behavior, it may decrease any association between sexual behavior and HCV infection. According to univariate analysis in our study, however, age was an independent risk factor of HCV infection, which was significantly associated with sexual behavior among the IV drug users. This would suggest that sexual transmission may still occur, albeit infrequently.

Respondents may have inaccurately answered or underreported certain risk behaviors, such as intravenous drug use, sexual habits, syringe sharing, etc., and this may have limited the value of the present findings. In addition, we may have underestimated the seroprevalence of HCV in our population sample, due to seroconversion and the fact that the second-generation assay used here may have failed to identify patients either with low titers of anti-HCV or with antibodies to other antigens of HCV [19]. The small number of each age group (Figure 1) may also have limited the power of our study in identifying the changeable prevalence of HCV infection.

These findings suggest that intravenous drug use is the predominant risk factor of HCV infection. These data also strongly suggest that the interval soon after beginning injections is a particularly dangerous period for infection with the hepatitis C virus. Due to the high levels of infection within the first four months of drug use, our data provide an additional rationale to reemphasize the need for primary substance abuse prevention. The prevalence of HCV infection among drug users is very much higher than among blood donors in Taiwan. However, it would be worthwhile to carry out further studies into this serious public health problem.

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