Health-Related Quality of Life in Active Injecting Drug Users With and Without Chronic Hepatitis C Virus Infection

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This study assessed the effect of chronic hepatitis C virus (HCV) infection on the health-related quality of life (HRQOL) of injecting drug users, comparing the HRQOL of injecting drug users with and without chronic HCV infection. The study included 199 injecting drug users of more than 18 years of age who participated in a needle exchange program. Blood samples were tested for the presence of HCV RNA in serum with a polymerase chain reaction method. HRQOL was measured using the questionnaire SF-36, measuring HRQOL over the last 4 wk. The HCV RNA test was positive in 102 (51%) and negative in 97 (49%) subjects. The HRQOL scores of actively injecting drug users were markedly reduced compared to the population norm. However, we did not find poorer HRQOL in injecting drug users with chronic HCV infection than in injecting drug users without HCV infection. HCV RNA positive injecting drug users who were aware of the infection had lower HRQOL scores than those unaware of the infection in 4 of the 8 SF-36 dimensions (general health, physical functioning, physical role, and vitality). HCV RNA negative subjects, who believed they were infected, scored worse in one dimension (general health) compared to those who did not believe they were infected. In conclusion, chronic HCV infection *per se* did not negatively affect the HRQOL of active injecting drug users. Those who thought they were infected had a lower HRQOL scores than those who believed they were not infected. (HEPATOLOGY 2004;39:74–80.)

The majority of persons infected with hepatitis C virus (HCV) develop chronic infection.[1,2] Whether chronic HCV infection without liver cirrhosis has a negative impact on patients' health-related quality of life (HRQOL) is still under debate.[3–5] It has repeatedly been shown that patients with HCV infection have a poorer HRQOL than published population norms.[6–8] However, in the Western world, most HCV transmission has occurred through injecting drug use or transfusion of blood products. Consequently, physical and mental comorbidities are common in HCV patients.[9,10] These comorbidities are likely to confound the assessment of the HRQOL.[3,4]

The psychologic impact of knowing about the infection may contribute to the low HRQOL in HCV patients, as recently reported in an Australian study.[11] However, the study was small and additional studies are necessary to confirm the results.

The aim of this study was to compare the HRQOL in injecting drug users with and without chronic HCV infection, and to compare the HRQOL in injecting drug users who believed they were HCV infected with those who did not.

Patients and Methods

The needle exchange program in Oslo was initiated in 1988 and is believed to serve 90% of approximately 5,000 active injecting drug users in Oslo by providing sterile needles and syringes.[12] The equipment is free of charge and is delivered from one mobile unit that serves all users in Oslo. The unit, which is available every evening 365 days a year, moves between 2 locations in the city center. Injecting drug users younger than 18 years of age are not allowed to participate in the program.

In this cross-sectional study, all users of the needle exchange program within an 11-d period in the autumn of 2002 were eligible for inclusion. Subjects were approached by 1 of 2 trained staff members after they had used the service of the needle exchange program. Subjects

Abbreviations: HCV, hepatitis C virus; HRQOL, health-related quality of life.

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Table 1. Subject Characteristics According to HCV RNA Result Among 199 Injecting Drug Users in Oslo

	All Subjects (n = 199) (%)	HCV RNA Positive (n = 102)	HCV RNA Negative (n = 97)	*P*-Value
Age—mean yr (range)	34 (18-54)	36	33	0.01
Sex				0.12
Female	71 (36)	32	39	
Male	128 (63)	70	58	
Anti-HCV				0.001
Positive	158 (79)	99	59	
Negative	41 (21)	3	38	
Reports being HCV infected				0.001
Yes	116 (58)	77	39	
No	80 (42)	24	56	
HbsAg positive				
Yes	7 (4)	2	5	
No	192 (96)	100	92	
HIV positive				
Yes	2 (1)	2	0	
No	197 (99)	100	97	
Married or cohabitant				0.35
Yes	25 (13)	15	10	
No	174 (87)	87	87	
More than 9 years of education*				0.51
Yes	104 (52)	51	53	
No	95 (48)	51	44	
Homeless				0.17
Yes	32 (16)	20	12	
No	167 (84)	82	85	
Frequency of injecting				0.31
Daily	144 (72)	77	67	
Less than daily	55 (28)	25	30	
Drug most often injected				0.61
Heroin	113 (57)	55	58	
Amphetamine	39 (20)	23	16	
Heroin and amphetamine	26 (13)	13	13	
Other	19 (10)	11	8	
Duration of injecting drug use—mean yr (range)	14 (0-36)	16	12	0.01
Alcohol consumption				0.46
<60 g/day	186 (93)	96	90	
>60 g/day	13 (7)	6	7	

*Obligatory duration of schooling in Norway is 9 years.

influenced by drugs were also included. No systematic record was kept of reason for non-participation.

Within the study period, 3,697 visits at the program were recorded; however, identities of the users were not recorded. Some persons visited the program more than once during the study period. The exact number of persons visiting the program is therefore not known. Within the study period, 410 persons consented to have a venepuncture and an x-ray taken. This was done inside a mobile unit parked by the needle exchange program. Thereafter, the subjects were asked to move to another location to be interviewed by 1 of 10 persons trained for this. Altogether, 340 injecting drug users were interviewed. At the end of the interview, the subjects were asked to fill out the self-administered short-form 36 (SF-36) questionnaire on HRQOL and 199 (57%) responded. One trained person was available to aid in the filling out of the questionnaire. The respondents' mean age was 34 years (range 18–54), 128 (64%) were men, and 144 (72%) had injected daily during the last 4 wk (Table 1).

All responders provided written consent. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was presented to the regional Ethics Committee and the Norwegian Data Inspectorate.

Blood Tests

All sera were frozen within 4 h and stored at –60°C for later analyses. The sera were only thawed once and were then screened for anti-HCV with an EIA-3 assay (Orto-Clinical Diagnostics, Raritan, NJ) and tested for HCV RNA with an "in-house" polymerase chain reaction amplification of viral RNA (detection limit approximately 100 IU/ml). Sera were also tested for hepatitis B core

Table 2. Internal Consistency Reliability by SF-36 Dimension

	Internal Consistency (n = 199) Cronbach's α
Physical functioning	0.79
Role, physical	0.75
Bodily pain	0.83
General health	0.77
Vitality	0.78
Social functioning	0.75
Role, emotional	0.80
Mental health	0.80

antibodies (anti-HBc), hepatitis B surface antigen, and HIV antibodies (anti-HIV). Unfrozen sera were not available; hence, alanine aminotransferase measurements were not possible.

Interview

A structured interview was performed by 1 of 10 trained interviewers. Juice and a sandwich, but no money, was offered. The interview focused on history of drug use and possible risk factors for HCV transmission. Subjects were asked whether they believed they were infected with HCV, believed that they were not infected, or did not know. In the data analyses, replies to this question have been dichotomized. Those who responded "yes" to the question are categorized as "believed they were infected," and those who answered "no" or "do not know" are categorized as "did not believe they were infected."

HRQOL

HRQOL was assessed using the SF-36 questionnaire, which is self-administered and contains 36 items. From answers to these items, a score is derived on 8 dimensions presumed to be important for the HRQOL (physical function, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health). Within each dimension, 0 is the worst and 100 is the best possible score. In addition, the physical and mental component summary were scored using standard algorithms.[13] The SF-36 was developed in the U.S. It is a generic instrument that has been used in various patient groups and general populations. It has been extensively validated, is accepted well by patients,[13–17] and has showed satisfactory psychometric properties across diverse population groups. Floor effects were negligible except for the 2 role disability scales.[18] We used the Norwegian standard SF-36 version 1.2, assessing HRQOL the last 4 wk.

Statistical Analysis

Descriptive statistics was presented using means or medians (range) where appropriate. The *t*-test was used for comparisons of SF-36 scores between 2 groups. Univariate analyses using linear regression were performed with the physical and mental component summary scores as dependent variables. Independent variables included in multiple regression are HCV RNA result, assumed HCV diagnosis, sex, age, and drug of choice.

Chi-square tests were used for categorical data. A two-tailed *P*-value less than .05 was considered significant. Internal consistency was assessed using Cronbach's α.[19] SF-36 scores of the subjects were compared with published Norwegian population norms adjusted for age and sex. Data analyses were performed using the Statistical Package for Social Sciences (SPSS 9.0, Chicago, IL).

Results

Anti-HCV was detectable in 158 (79%) and HCV RNA in 102 (51%) of the 199 participating injecting drug users (Table 1).

The internal consistency reliability was good for all dimensions of the SF-36 (α = 0.75–0.83) (Table 2).

The HRQOL scores were reduced in all 8 dimensions of the SF-36 in HCV RNA positive subjects compared to the Norwegian population norms adjusted for age and sex[1] (Fig. 1). There was no difference between the scores

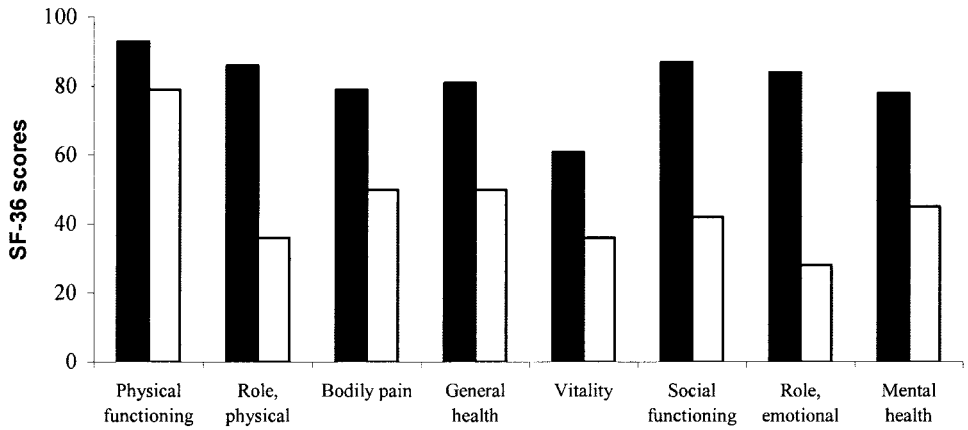

Fig. 1. SF-36 scores for injecting drug use (open columns, n = 199) and the Norwegian population norm adjusted for age and sex (black columns).

Table 3. Mean SF-36 (SD) Scores in HCV RNA Positive and Negative Injecting Drug Users

	HCV RNA Positive (n = 102)	HCV RNA Negative (n = 97)	*P*-Value
Physical functioning	78 (24)	80 (20)	0.47
Role, physical	35 (37)	36 (37)	0.84
Bodily pain	51 (30)	49 (30)	0.65
General health	50 (27)	50 (22)	0.95
Vitality	38 (20)	34 (21)	0.23
Social functioning	42 (31)	42 (31)	0.98
Role, emotional	26 (32)	29 (39)	0.46
Mental health	48 (22)	41 (20)	0.02
Physical component summary	42 (12)	42 (10)	0.80
Mental component summary	32 (11)	29 (12)	0.10

of HCV RNA positive and negative subjects in 7 of the 8 SF-36 scales (Table 3). HCV RNA positive subjects scored higher than HCV RNA negative subjects in the mental health dimension ($P = .02$).

Among the 199 injecting drug users, 116 believed they were infected with HCV. However, only 77 (66%) of these were HCV RNA positive. Among the 80 subjects who believed they were not infected, 24 (30%) were HCV RNA positive.

Among 57 anti-HCV positive and HCV RNA negative subjects, 37 (65%) falsely believed they were infected as opposed to 2 (5%) of 38 anti-HCV and HCV RNA negative subjects ($P = .01$).

HCV RNA positive subjects who were aware of the infection scored lower than those unaware of the infection in 4 of the 8 dimensions (general health, physical functioning, physical role, and vitality; $P = .01$, $P = .03$, $P = .01$, and $P = .03$, respectively) (Fig. 2).

HCV RNA negative subjects who believed they were infected scored lower on the general health dimension than those who believed they were not infected ($P = .04$ for both scores) (Fig. 3).

In multiple regression models, answering "yes" to the question "do you believe you are infected with HCV" was independently associated with low physical component summary score, while female sex and heroin as drug of choice were associated with a low mental component summary score (Tables 4 and 5).

Discussion

In this study, we did not find poorer HRQOL in injecting drug users with chronic HCV infection than in injecting drug users without HCV infection. We also showed that the HRQOL of injecting drug users was lower than the reported Norwegian population norm.[20] Previous HRQOL of life studies done on participants in an HCV treatment trial by Bonkovsky et al.[8] and on consecutive patients at an outpatient clinic by Foster et al.[7] have found reduced HRQOL in HCV patients compared to population norms. Active injecting drug use was probably an exclusion criterion in the treatment trial by Bonkovsky et al.[8] However, 43% of the patients were infected through injecting drug use, and making, in our view, comparison with a population norm difficult.[21] Foster et al.[7] stratified for drug use and found that HCV patients who did not report drug use had a much better HRQOL than those who had been infected through drug use, although it was still significantly poorer than the British population norm. However, HCV infection in non-injecting drug users is also associated with comorbidity and low socio-economic status, which again are associated with poor HRQOL.[9,10,22] Comparison between these and the present study should be drawn with care. The former were treatment trials and it is to be anticipated that one of the motivations for seeking HCV treatment was poor HRQOL. Furthermore, treatment trials tend to exclude active drug users.

The strongest support for the assumption that HCV infection causes reduced HRQOL comes from studies that have shown improved HRQOL in HCV patients 6 months after successful treatment of the infection.[8,23–25] Patients who were non-responders did not have any im-

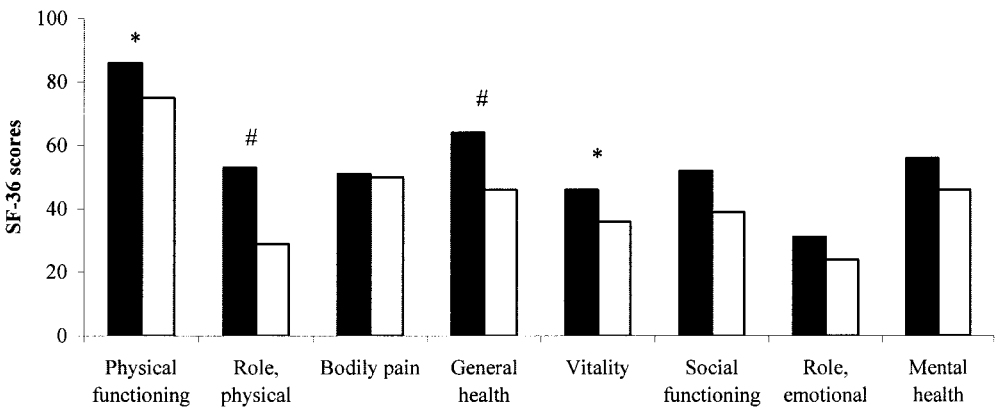

Fig. 2. SF-36 scores for HCV RNA positive injecting drug users who were (open columns, $n = 74$) or were not aware (black columns, $n = 24$) of the HCV infection. Comparisons are adjusted for age and sex. *$P = .04$; #$P = .01$.

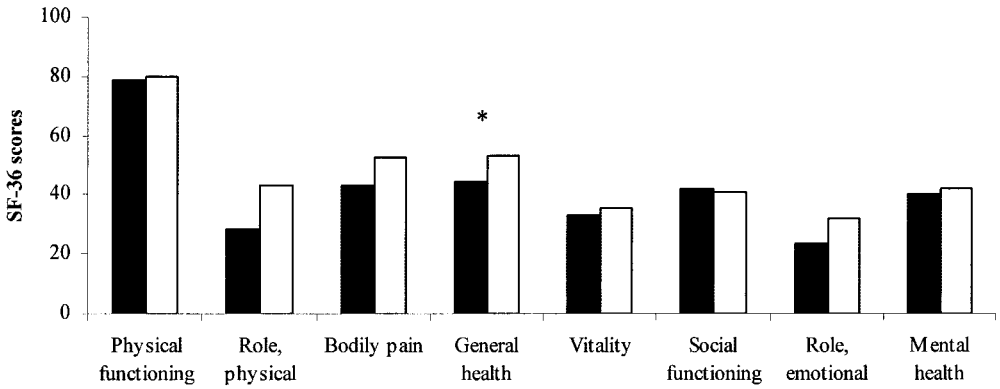

Fig. 3. SF-36 scores for HCV RNA negative injecting drug users who believed(black columns, $n = 77$) or did not believe (open columns, $n = 24$) they were HCV infected. Comparisons are adjusted for age and sex. *$P = .04$.

provement of HRQOL. Although the patients in those studies were blinded for the HCV RNA results during follow-up, they could not be blinded for the alanine aminotransferase results. Thus, a positive psychologic effect of knowing the treatment result could not be ruled out.

Interestingly, in our study, those who believed they were infected with HCV had a poorer HRQOL than those who did not believe or did not know if they were infected. It should be noted that people who stated they "did not believe they were infected" or "did not know if they were infected" have been combined in one group and that this is not accurate. Persons who responded they did not know could have assumed they were or were not HCV infected. However, results of our analyses are in line with the findings of an Australian group that reported HCV RNA positive injecting drug users unaware of the infection to have a better HRQOL than those aware of the infection.[11] It is possible that those aware of the infection are those with most symptoms and therefore most likely to seek medical consultation and testing. It may also be that the negative psychologic effect of a positive HCV test worsens an already poor HRQOL in injecting drug users. Such effects have been noted in other populations after positive test results from other diseases.[26] Hence, it is disturbing to note that as many as 65% of those with anti-HCV but undetectable HCV RNA falsely believed they were HCV infected. HCV testing of injecting drug users should, in our opinion, include testing not only for anti-HCV but also for HCV RNA, along with concise and adequate information.

Our study showed that actively injecting drug users have extremely poor HRQOL. The SF-36 profiles seen was similar to that reported from injecting drug users entering a methadone maintenance program.[27] The overall profile was more in line with that of patients with psychiatric diseases than patients suffering from predominantly physical symptoms.[28]

The multiple regression analyses showed that, in addition to beliefs about HCV infection, female sex and her-

Table 4. Univariate Analyses Exploring Selected Variables' Correlations With Low Scores on the SF-36 Summary Measures for Physical and Mental Health Among 199 Actively Injecting Drug Users in Oslo

	Physical Component Summary		Mental Component Summary	
	β*	*P*-Value	β*	*P*-Value
Answering yes to the question: "Do you believe you are infected with HCV?" (1:Yes, 2:No)	5.1	0.01	1.4	0.42
HCV RNA result (1:Positive, 2:Negative)	0.5	0.75	−2.9	0.10
Age	−0.6	0.59	0.2	0.05
Sex (1:Female, 2:Male)	2.0	0.24	6.8	0.01
Drug of choice (1:Heroin, 2: Amfetamin)	4.2	0.03	7.4	0.01
Injecting daily (Yes, 2:No)	1.6	0.42	2.1	0.31

*β: Regression coefficient.

Table 5. Results of Multiple Regression Models Identifying Variables Independently Related With Low Scores of the Eight SF-36 Scales Among 199 Actively Injecting Drug Users in Oslo

	Physical Component Summary*		Mental Component Summary†	
	β‡	*P*-Value	β‡	*P*-Value
Answering yes to the question: "Do you believe you are infected with HCV?" (1:Yes, 2:No)	4.8	<0.01	2.4	0.19
HCV RNA result (1:Positive, 2:Negative)	−1.5	0.41	−3.2	0.07
Age	−0.3	0.79	0.1	0.28
Sex (1:Female, 2:Male)	1.4	0.41	6.3	<0.01
Drug of choice (1:Heroin, 2: Amfetamin)	1.5	0.47	7.5	<0.01
Injecting daily (1:Yes, 2:No)	0.3	0.89	−1.0	0.62

*$R^2 = 6\%$.
†$R^2 = 21\%$.
‡β: regression coefficient.

oin as drug of choice were predictors of poor HRQOL. Further research addressing this important issue is warranted.

A weakness of the present study is that the validity and reliability of the SF-36 questionnaire has not been determined for this very special group of patients. The subjects were active injecting drug users and some were under drug influence at the time of filling out the questionnaire. The HRQOL of life scores were extremely low, and it is reasonable to ask whether changes in HRQOL due to chronic hepatitis C are detectable at this low level. However, a difference in HRQOL was detected between those who believed and those who did not believe they were HCV infected. In line with this, McHorney et al.[18] found that SF-36 discriminated well at low scores.

Subjects influenced by drugs were not excluded from participation. It was not feasible to check urine for drug metabolites; thus, we do not know to what extent persons influenced by drugs were included. It is possible that intoxicated subjects have a higher risk of being HCV RNA positive than those not intoxicated, thus introducing a bias. It is also possible that the reliability of the answers of intoxicated persons is low and thereby increases the possibility of overlooking a true difference between two groups. However, the internal consistency reliability measured with the Cronbach α test was good (α 0.75–0.83) and comparable to what has been reported from selected groups and in the general population.[28] It has been suggested that health status measures can be used for comparisons at group level if reliability is above 0.70.[29]

The majority of the HCV RNA negative group had anti-HCV. A false negative HCV RNA test in some of these subjects cannot be ruled out, and the mean difference in SF-36 scores between those with and without chronic HCV infection may therefore have been underestimated.

We did not measure alanine aminotransferase activity; thus, a significant number of the patients may have had mild hepatitis with normal alanine aminotransferase levels. However, several studies have not found any relationship between HRQOL in HCV patients and liver disease parameters such as liver histology and serum ALT.[6,7,30,31]

It should also be noted that only 57% of the 350 participants in the screening program filled out the SF-36 questionnaire. Some did not participate because they were too intoxicated and some did not find time to participate. A selection bias is therefore possible.

In conclusion, active injecting drug users with chronic HCV infection did not have lower HRQOL scores than injecting drug users without HCV infection. Those who thought they were infected had poorer scores than those who did not believe they were infected.

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