

Heterosexual and homosexual transmission of hepatitis C virus: relation with hepatitis B virus and human immunodeficiency virus type 1

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SUMMARY

A seroprevalence study was carried out on 1757 outpatients consecutively seen in a sexually transmitted disease (STD) clinic in order to evaluate the sexual transmission of hepatitis C virus (HCV). A total of 1442 consenting patients were tested for hepatitis C, hepatitis B and human immunodeficiency virus type 1 (HCV, HBV, HIV-1) antibodies. The relations between anti-HCV, anti-HBc and anti-HIV-1 were studied. Of 73 anti-HCV positive reactions, 45 (61·6%) were confirmed by the recombinant immunoblot assay (RIBA). The proportion of individuals with anti-HCV was higher in outpatients with a history of sexually transmitted disease than without. It was 2·8% in non drug user heterosexuals and 2·9% in non drug user homosexuals. Intravenous drug users (IDU) had higher anti-HCV prevalence when a history of STD was taken into account (42·3% in subjects with STD versus 36·7% in subjects without STD). Among non drug user heterosexuals an association was found between anti-HCV and anti-HBc. These data suggest that sexual transmission of HCV occurs, although it seems to be less efficient than other parenteral modes of transmission. When a more sensitive and specific marker of HCV infection become available, a more accurate estimate of the frequency and efficiency of the sexual transmission will be possible.

INTRODUCTION

A parenterally transmitted virus, associated with a non-A, non-B hepatitis and named hepatitis C virus (HCV), has been recently identified by molecular cloning [1]. A high proportion of patients with haemophilia, post-transfusion acute and chronic non-A, non-B hepatitis and intravenous drug users have antibodies against HCV related antigens (anti-HCV) [2]. In addition to blood exposure and intravenous drug use, other modes of transmission of hepatitis C virus are possible.

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Sexual exposure is a risk factor for heterosexual and homosexual transmission of hepatitis B [3, 4] and some evidence exists for sexual transmission of non-A, non-B hepatitis [5]. Patients with acute non-A, non-B hepatitis exposed to multiple sex partners had high rate of anti-HCV antibodies [5].

In order to evaluate the sexual transmission of HCV a seroprevalence study was carried out in a group of subjects at high risk of sexually transmitted infections recruited in a study on HIV-1 transmission (R. Corona and colleagues, unpublished data).

STUDY POPULATION AND METHODS

A total of 1757 outpatients seen consecutively between February and December 1989 in a sexually transmitted disease (STD) clinic in Rome were enrolled into the study without any selection.

After informed consent was obtained, a standard precoded anonymous questionnaire was administered by a trained interviewer to each study subject in order to obtain the following data: age, sex, place of birth, residence, education, family size, type of work, history of sexually transmitted diseases, use of intravenous drugs, history of transfusion with blood or blood products, sexual preference, number of sexual partners in the previous year. Patients were defined as having a history of STD if they reported a previous infection and/or had at the time of the interview a diagnosis of any of the following: genital infection with herpes virus type 2 (HSV2), gonorrhoea, syphilis, genital warts, chlamydia urethritis. Also included into the study were subjects without history of past or present STD who were referred to the clinic for minor inflammatory conditions of the uro-genital tract.

A total of 1442 consenting patients (82% of the total study population) had blood drawn. All were tested for HBV markers, 1435 for anti-HCV and 1439 for anti-HIV-1. Hepatitis C virus antibodies (anti-HCV) were detected by a commercially available enzyme-linked immunosorbent assay (ELISA) (Ortho Diagnostic Systems, USA). Positive tests were confirmed by recombinant immunoblot assay (RIBA) (Ortho Diagnostic Systems, USA).

Antibodies against hepatitis B core antigen (anti-HBc) were determined by an ELISA test (Abbott, USA). Anti-HIV-1 antibodies were determined by a commercially available ELISA test (Abbott, USA). Positive tests were confirmed by western blot analysis (Biotech/Du Pont, USA).

95% confidence intervals for prevalence rates were calculated by using the binomial probability distribution. Crude odds ratios and Mantel-Haenszel age-adjusted odds ratios ($O.R._{MH}$) were calculated to evaluate the association between presence of anti-HCV and positivity of HBV markers and anti-HIV-1.

RESULTS

The 1442 patients who provided specimens had a median age of 32 years (range 15-80); 1065 (74%) were male and 208 of these were homosexual or bisexual. Fifty-seven individuals (4%) reported the use of intravenous drugs and 671 (47%) had a history of sexually transmitted diseases.

Table 1. Prevalence of HCV and HBV markers by age in heterosexuals, homosexual-bisexual men and intravenous drug users

	Anti-HCV positive (%)	Total tested	Anti-HBc positive (%)	Total tested
Heterosexuals*				
15-24	1 (0.4)	225	17 (7.5)	226
25-34	4 (1.0)	413	83 (20.0)	416
35-44	8 (3.3)	243	87 (35.8)	243
45+	6 (2.4)	249	109 (43.4)	251
Total	19 (1.7)	1130	296 (26.1)	1136
(95% C.I.†)	(0.7-2.7)		(23.5-28.6)	
Homosexual-bisexual men*				
15-24	0 (—)	22	5 (22.7)	22
25-34	0 (—)	77	40 (51.9)	77
35-44	2 (4.1)	49	35 (71.4)	49
45+	2 (4.3)	47	36 (75.0)	48
Total	4 (2.1)	195	116 (59.2)	196
(95% C.I.†)	(0.05-6.1)		(52.5-66.3)	
Intravenous drug users				
15-24	4 (33.3)	12	7 (58.3)	12
25-34	16 (47.1)	34	23 (67.6)	34
35-44	1 (10.0)	10	9 (90.0)	10
45+	1 (100.0)	1	1 (100.0)	1
Total	22 (38.6)	57	40 (70.2)	57
(95% C.I.†)	(25.6-52.6)		(56.2-82.2)	

* Intravenous drug users are excluded.

† C.I. = Confidence Interval.

The 315 patients who refused the interview and/or the blood tests were similar to the consenting patients with regard to socio-demographic characteristics such as age, sex and education. Among these subjects 187 were heterosexuals, 115 had history of STD, and 14 were intravenous drug users.

The anti-HCV and anti-HBc seroprevalences by age among heterosexual males and females, homosexual-bisexual men and intravenous drug users are shown in Table 1. Of 73 anti-HCV positive results 45 (61.6%) were confirmed by the RIBA test. Among the heterosexual patients, but excluding the subjects who reported use of intravenous drugs, the overall prevalence of anti-HCV was 1.7%; the prevalence among non drug user homosexual-bisexual men was 2.1%, and 38.6% among intravenous drug users. No significant association was found between anti-HCV positivity and age and sex in any group. The prevalence of anti-HBc was 26.1% among non drug user heterosexuals, 59.2% among non drug user homosexual-bisexual men and 70.2% among intravenous drug users.

When only individuals with a history of past or present STD were considered, there were 477 heterosexuals, of whom 375 (79%) were males with a median age of 34 years (range 17-78). There were 142 homosexual-bisexual men in this category with a median age of 36 years (range 18-73). There were 27 intravenous drug users with STD of median age 30 years (range 21-80). Subjects with a history of STD had a higher number of sexual partners in the previous year than subjects without a history of STD: among the heterosexuals, 55% of those with STD had

Table 2. *HCV and HBV markers prevalence by history of sexually transmitted diseases in heterosexuals, homosexual-bisexual men and intravenous drug users*

	Anti-HCV positive (%)	Total tested	Anti-HBc positive (%)	Total tested
Heterosexuals*				
STD history	13 (2.8)	472	157 (32.9)	477
No STD history	6 (0.9)	656	139 (21.1)	659
OR _{M-H} † (95% C.I.)	3.07 (1.08-9.11)		1.84 (1.39-2.42)	
Homosexual-bisexual men*				
STD history	4 (2.9)	140	89 (62.7)	142
No STD history	0 (—)	54	27 (50.0)	54
OR _{M-H} (95% C.I.)	n.c.§		1.68 (0.85-3.32)	
Intravenous drug users				
STD history	11 (42.3)	26	24 (88.9)	27
No STD history	11 (36.7)	30	16 (53.3)	30
OR _{M-H}	n.c.		n.c.	

* Intravenous drug users are excluded.

† C.I., Confidence Interval.

§ n.c., not calculable.

† OR_{M-H}, Mantel-Haenszel age-adjusted odds ratio.

two or more sexual partners compared to 45% of those without STD ($P = 5.24 \times 10^{-7}$); among the homosexual-bisexual men, 88% of those with STD had two or more sexual partners compared with 77% of those without STD ($P = 0.076$); among the intravenous drug users, no difference existed in the number of sexual partners whether or not STD history was taken into account.

Among the 61 subjects who reported a history of transfusion with blood or blood products (49 heterosexuals, 6 homosexual-bisexual men and 6 intravenous drug users), 3 were anti-HCV positive: 1 was a heterosexual in the age group 35-44 with history of STD; 2 were intravenous drug users in the age group 25-34 without history of STD. As the prevalence of anti-HCV among subjects with a history of transfusion was not different from the group-specific prevalences found in subjects without this risk factor, these subjects were not excluded from the analysis.

Subjects with history of STD in any group had higher prevalences of anti-HCV and anti-HBc than subjects without history of STD, although statistically significant differences were found only in heterosexuals (Table 2). The anti-HIV-1 prevalence among subjects with a history of STD was 1.7% in heterosexuals, 17.1% in homosexual-bisexual men and 38.5% in intravenous drug users (R. Corona, unpublished data). Among non drug user heterosexuals an association was found between presence of anti-HCV and presence of anti-HBc antibodies (OR = 4.92, 95% C.I. = 1.36-19.32). There was no significant association between anti-HCV positivity and presence of anti-HIV-1 antibodies. Among homosexual-bisexual men and intravenous drug users no association was found between presence of anti-HCV positivity and anti-HBc or anti-HIV-1 (Table 3).

Table 3. Association between positivity of anti-HBc or anti-HIV-1 and positivity of anti-HCV in heterosexuals, homosexual-bisexual men and intravenous drug users with history of STD

	Anti-HCV positive (%)	Anti-HCV negative (%)	Odds ratio (95% C.I.†)
Heterosexuals*			
anti-HBc positive	9/13 (69.2)	144/459 (31.4)	4.92 (1.36-19.32)
anti-HIV-1 positive	1/13 (7.7)	7/448 (1.6)	5.25 (0.75-49.41)
Homosexual-bisexual men*			
anti-HBc positive	4/4 (100.0)	(84/136 (61.8)	n.c.‡
anti-HIV-1 positive	0/4 (—)	24/134 (17.9)	n.c.
Intravenous drug users			
anti-HBc positive	10/11 (90.9)	13/15 (86.7)	n.c.
anti-HIV-1 positive	4/11 (36.4)	6/14 (42.9)	n.c.

* Intravenous drug users are excluded.

† C.I., confidence interval.

‡ n.c., not calculable.

DISCUSSION

The results of our study are not entirely comparable with those of other studies. In fact, in our population the anti-HCV positive reactions have been confirmed by the newly developed RIBA test, which is more specific. Most of the subjects in this study ran a high risk of sexually transmitted infection and showed a prevalence of HBV and HIV-1 markers higher than that found in the general population. Data from other studies report an anti-HCV prevalence among the blood donors in Italy of 0.7% to 1.5% [2], using an ELISA test, and of 0.5% using the RIBA test in a sample of general population in the age range of 30-70 years (L. Capocaccia, unpublished data).

In our population the prevalence of anti-HCV was 1.7% in heterosexuals and 2.1% in homosexual-bisexual men. When subjects with a history of STD were considered, the prevalences of HCV and HBV markers increased in the heterosexuals as well as in the homosexual-bisexual men, although the small numbers did not allow to reach the statistical significance in the homosexual-bisexual group. The prevalences were higher also in intravenous drug users with STD when compared with those without STD, although they have a high baseline risk of HCV and HBV infection. Although a significant association was found between anti-HCV and anti-HBc positivity among the heterosexuals, no association was found with anti-HIV-1.

A study conducted in Barcelona among subjects attending an AIDS outpatient clinic between 1984 and 1988 found a prevalence of anti-HCV of 16% among 105 homosexual men and 11% among 143 heterosexual partners of intravenous drug users. This was higher than expected in the general population, but lower than prevalences of HBV and HIV-1 markers detected in the same groups (6). A cohort of homosexual men in Copenhagen, followed from 1981 to 1989 showed a

cumulative seroconversion rate of 4.1% for anti-HCV compared with 15.5% for anti-HBc and 12.9% for anti-HIV-1 [7].

The two studies concluded that sexual transmission of HCV occurs, but that it is not a frequent event. In our groups the prevalences of anti-HBc were higher than prevalences of anti-HCV. Anti-HBc is a sensitive marker of exposure to HBV and is present in the blood for many years after infection, but the same seems not to be true for the present marker of HCV infection. The currently used test for anti-HCV detects only antibodies against a recombinant non-structural viral protein that may disappear from the blood after an acute self-limiting infection [8].

Our data show a prevalence of anti-HCV higher in patients with a history of STD compared with those without a history of STD and an association between anti-HCV and anti-HBc in heterosexuals. This suggests that sexual transmission of HCV occurs, although it is probably less efficient than other parenteral modes of transmission. When a more sensitive and specific marker of HCV infection becomes available, a more accurate estimate of the frequency and importance of sexual transmission of HCV will be possible.

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