Risk Factors for HCV Acquisition Among HIV-Positive MSM in Belgium

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Objective: To better understand risk factors for the sexual transmission of hepatitis C viral (HCV) infection among men who have sex with men (MSM).

Design: Case–control study among HIV-infected MSM, attending AIDS Reference Centers in Belgium.

Methods: Cases were HIV-infected MSM who were diagnosed with HCV between January 2010 and December 2013. For each case, 2 controls were randomly selected among the HIV-positive MSM who tested negative for HCV around the same time as the cases were identified. Consenting participants were interviewed with a questionnaire on risk factors. Medical records were abstracted to document past episodes of sexually transmitted infections (STIs). Associations between HCV infection and risk factors were explored using bivariate analysis followed by multiple logistic regression analysis.

Results: A total of 52 cases and 90 controls were recruited. In multivariate analysis, douching before anal intercourse [adjusted odds ratio (AOR) = 9.84, 95% CI: 2.26 to 42.78], fisting (AOR = 3.54, 95% CI: 1.31 to 9.57), having intercourse with HIV-positive men (AOR = 5.51, 95% CI: 1.87 to 16.20), and a documented gonorrhoea or chlamydial infection in the year before inclusion in the study (AOR = 4.50, 95% CI: 1.11 to 18.31) were independently associated with incident HCV infection.

Conclusions: Our study confirmed fisting and suffering from other STIs as risk factors for HCV and suggested an increased risk of HCV associated with serosorting. Furthermore, we identified anal douching as being associated with HCV infection. The role that douching plays in the acquisition of HCV infection and other STIs requires further research, as well as the effect of serosorting on STI transmission.

Key Words: hepatitis C, HIV infection, risk factors, sexual transmission, MSM

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INTRODUCTION

Transmission of hepatitis C virus (HCV) through sexual activity has for long been a controversial issue, as drug use may be associated with higher risk sexual behavior and studies had to rely on self-reported use of drugs.[1] Up to 2000, sexual transmission of HCV was considered a rare event. Large studies among HCV-discordant heterosexual couples found low rates of HCV transmission suggesting that heterosexual transmission of HCV is inefficient.[2–4] In the 1990s, several studies were published that explored sexual transmission of HCV among men who have sex with men (MSM). These studies found intravenous drug use to be the most important risk factor for HCV infection, whereas there was little evidence for sexual transmission.[5,6] Nevertheless, a cross-sectional study within the Multicentre AIDS Cohort of HIV-infected MSM in the United States found an association between HCV infection and other sexually transmitted infections (STIs) and sexual practices, including insertive anal intercourse and douching or enema use before receptive anal intercourse.[7]

From 2000 onward, however, increases in prevalence and incidence of HCV infection among HIV-infected MSM have been reported from Western Europe.[8–12] In 12 European cohorts of HIV-infected MSM, the incidence of HCV infection rose from 0.9–2.2 per 1000 person-years in 1990 to 16.8–30.0 per 1000 person-years in 2002 and 23.4–51.1 per 1000 person-years in 2007.[11] These epidemics were attributed to sexual transmission[9] and occurred predominantly in HIV-infected MSM, whereas sexual transmission of HCV appeared to be very limited among HIV-uninfected MSM.[13,14] Also in the Multicentre AIDS Cohort the incidence of HCV infection was significantly higher in HIV-infected MSM than in HIV-uninfected men and sexual transmission of HCV appeared to have been going on since the early years of the HIV epidemic.[15]

The emergence of HCV as a sexually transmitted infection among HIV-infected MSM raises several questions.

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The first question is which sexual practices are associated with sexual transmission. Second, why does HCV infection affect disproportionally HIV infected MSM? A number of risk factors for the sexual transmission of HCV have been identified, including high numbers of sex partners; unprotected anal intercourse; sexual practices such as fisting, rimming, and the use of sex toys; a history and/or biological evidence of another STI; and the use of recreational drugs through the nose.[12,15–18] Schmidt et al found frequent bleeding during intercourse also to be associated with HCV infection, whereas a study from the United States found intimate partner violence, but not bleeding during intercourse, to be a risk factor for HCV infection.[17,19]

A better understanding of the risk factors for HCV infection, related to sexual behavior and practices and recreational drug use, is needed to develop strategies to prevent the (sexual) transmission of HCV. We designed a case–control study to explore risk factors for HCV acquisition among HIV-infected MSM in Belgium.

METHODS

The study was performed in 3 AIDS Reference Centers (ARCs) in Belgium, including the ARC of the Institute of Tropical Medicine (ITM) in Antwerp, the ARC of the University Hospital St-Pierre in Brussels, and the ARC of the University Hospital in Ghent. ARCs are specialized outpatient clinics that are staffed by multidisciplinary teams and provide high-quality care for HIV-infected persons. Most HIV-infected persons in Belgium are followed-up at an ARC. Patients who are stable are seen every 3–6 months. At each visit, CD4 count and HIV viral load are assessed. In 2006, after the rise in HCV infections in HIV-infected MSM, screening for HCV was added to the routine procedures at each clinic visit. In 2011, the ARC of Antwerp had 1105 HIV-infected MSM in active follow-up, the ARC of Brussels had 752, and the ARC of Ghent had 649. Being in active follow-up meant that these men were seen at least twice in 2011 for routine check-up and/or care.

The introduction of routine screening for HCV allowed for an unbiased estimate of the incidence of HCV infection in HIV-positive MSM in care and provided the opportunity to conduct a nested case–control study. In our study, cases were all HIV-infected MSM diagnosed with HCV infection between January 2010 and December 2013. Men whose last HCV negative test dated longer than a year before the current visit and men who had never been tested before for HCV, were excluded. In addition, patients newly diagnosed with HIV infection and concomitant HCV infection were not included in the study as in these men the temporal relationship between HCV and HIV infection could not be established. For each case, 2 controls were randomly selected among the HIV-positive MSM who tested negative for HCV around the same time as the cases (± 1 month).

For the estimation of the sample size, we used values for odds ratios and frequencies of known risk factors we found in the literature.[16,17] We estimated that a sample size of 70 cases and 140 controls would allow us to detect an association between HCV infection and the most important risk factors (unprotected anal intercourse, fisting, use of recreational drugs through the nose) at a significance level of 0.05 and with a power of 0.9. In 2009, a total of 27 new cases of HCV infection were diagnosed at the HIV clinic of ITM in Antwerp. By collaborating with the ARCs of Brussels and Ghent, we expected to limit the duration of the study to 2 years.

Cases and controls were asked by their treating physician for their informed consent to take part in the study. Consenting men were then contacted by an interviewer who made an appointment for a face-to-face structured interview. The questionnaire contained 56 items. Data were collected on socio-demographic characteristics; sexual behavior including numbers and characteristics of partners; sexual practices and condom use; recreational drug use; nonsexual risk factors for HCV infection (tattoos, surgical procedures, blood transfusion); history of another STI. The period covered by the questionnaire did not exceed 12 months, the maximum period of time in which the men with a new HCV infection could have acquired their infection.

The following data were extracted from the patients' records: syphilis serology, CD4 count and HIV viral load at the index visit; and any laboratory confirmed episodes of STIs within 1 year before the index visit. Testing for antibodies against Herpes simplex virus (HSV)-2 infection is not routinely done, but at the Antwerp ARC, serum samples from cases and controls taken at recruitment were tested a posteriori.

Laboratory Procedures

Screening for HCV infection was done using the Vitros ECI Immunodiagnostic System and as of May 2010 the Vitros 5600 (Integrated System) (Ortho Clinical Diagnostics, Rochester, NY). Confirmation of positive samples was done with the INNO-Line Immuno Assay HCV Score (Innogenetics, Gent Belgium). Qualitative determination of HCV RNA was performed in each patient with a positive confirmation test (COBAS Amplicor HCV test, version 2.0; Roche Diagnostics, Potters Bar, Hertfordshire England; limit of detection 50 IU/mL), and if this test was positive, HCV RNA was quantified by PCR (COBAS Amplicor HCV Monitor Test, version 2.0, Roche Diagnostics, Potters Bar, Hertsfordshire England; limit of detection 600 IU/mL). Since November 2006, HCV RNA was determined by the use of the Abbott RealTime HCV assay (Abbott Laboratories Abbott Park, IL). Testing for antibodies against HSV-2 was done with an HSV-2 type-specific IgG ELISA (Kalon Biological Ltd, Surrey, United Kingdom).

Data Analyses

First bivariate analyses were performed to explore associations between HCV infection and a variety of variables. The variables "lived with an HCV-infected person" and "had sex with an HCV-infected person" were not included in the analyses because they were particularly prone to information bias as cases were very likely to give a positive answer after counseling on HCV infection by their physician.

The variables that were associated with HCV infection at a significance level of 0.10 in bivariate analysis, as well as age, were entered in a multiple logistic regression model.

Variables were removed from the model by hand, one by one, starting with the variables with the highest *P* value. The final model included all variables that were associated with HCV infection at a significance level of 0.05 or below. Because of the colinearity between the variables "anal sex in the past 12 months" and "douching before anal sex," the analyses were repeated after excluding all patients who reported not having had anal intercourse in the 12 months before inclusion in the study. The data analyses were performed using IBM SPSS Statistics 21.

Ethical Considerations

The study was approved by the Institutional Review Board of the ITM in Antwerp and the Ethics Committees of the University Hospitals in Antwerp, Brussels, and Ghent.

RESULTS

Cases and controls were recruited between January 2010 and the end of December 2013. In the course of the study, the incidence of HCV infection declined, and we could not reach our estimated sample size of 70 cases within a reasonable time. At the end of December 2013, we therefore decided to stop recruiting patients by which time we had data on 52 cases and 90 controls.

The mean age of the cases was 44.9 and of the controls 43.6 years (Table 1). Most of the patients were of Belgian nationality. Nearly 3 in 4 cases were residing in Brussels or Antwerp, which was significantly more than among the controls. There was no difference in level of education between cases and controls. Of the cases, 82.7% were on antiretroviral treatment, and for the controls, this proportion was 75.3%. The difference was not statistically significant. Cases were diagnosed with HIV on average 6.0 years before inclusion (median 5 years), whereas controls were diagnosed on average 6.6 years (median 4 years) before inclusion.

In bivariate analysis, HCV infection was significantly associated with reporting of casual partners in the past 12 months and with higher numbers of nonsteady partners. Cases also reported more often intercourse with HIV-infected partners than controls. To explore differences in sexual networks between cases and controls, questions were asked about the venues where sex partners were found and where sex took place. There were no differences between cases and controls (data not shown).

Regarding sexual practices, anal intercourse in the past 12 months, unprotected anal intercourse (vs no anal intercourse or protected anal intercourse), group sex without a condom, douching before anal intercourse, fisting and rimming were all strong risk factors in bivariate analysis with odds ratios (ORs) exceeding 4. The use of sex toys was also associated, but this association was weaker.

Controls reported more often acupuncture or a piercing or tattoo in the past year than cases (OR = 0.26).Use of recreational drugs was very common among both cases and controls. The most commonly used drugs through the nasal route were poppers, speed, and cocaine. Methamphetamine use was reported by 14% of men. Altogether, 70% of controls and 83% of cases reported ever using drugs through the nasal route, and this difference was not statistically significant. However, cases reported significantly more use of drugs during sexual intercourse than controls.

Self-reports of another STI in the past year were risk factors for HCV infection in bivariate analysis, as was laboratory confirmed gonorrhoea or chlamydial infection. However, there was no significant association between HCV infection and laboratory confirmed ulcerative STIs [syphilis and lymphogranuloma venereum (LGV)]. A total of 33 cases and 46 controls, all from Antwerp, were tested for HSV-2 infection. In bivariate analysis, positive serology for HSV-2 was significantly associated with HCV infection (OR = 3.62, 95% CI: 1.39 to 9.47). This variable was not included in the multivariate analysis because data were missing for the study participants from Brussels and Ghent (19 cases and 44 controls).

In the multivariate analysis, the variable "anal sex in the past 12 months" was not included as only 1 case reported not having had anal sex in the past year. In the final multivariate model (Table 1), the following variables remained significantly associated with HCV infection: douching before anal intercourse (AOR = 9.84, 95% CI: 2.26 to 42.78), fisting (AOR = 3.54, 95% CI: 1.31 to 9.57), number of HIV-positive partners (AOR = 5.51, 95% CI: 1.87 to 16.20), and a documented gonorrhoea or chlamydial infection in the year preceding the inclusion (AOR = 4.50, 95% CI: 1.11 to 18.31). The association between age and HCV infection was of borderline significance (AOR = 1.05 per year, 95% CI: 0.99 to 1.10). None of the nonsexual risk factors for HCV infection were associated with HCV infection in multivariate analysis.

The analyses were repeated after excluding all patients who reported not having had anal intercourse in the 12 months before inclusion in the study. The same variables were independently associated with HCV infection as in the model with all men, including age, douching before anal intercourse, fisting, number of HIV-positive partners, and laboratory confirmed gonococcal or chlamydia infection (non-LGV) (Table 2).

We further examined whether the association between HCV infection and douching before anal intercourse could be confounded by frequency of unprotected receptive anal intercourse (URAI). Among the men who reported anal intercourse in the past 12 months, cases reported more frequent URAI than controls (61% vs 57%), but this difference was not statistically significant. After adjusting for frequency of URAI and condom use, the association between HCV infection and douching before anal intercourse remained statistically significant (AOR = 10.3, 95% CI: 2.4 to 43.7).

DISCUSSION

In our case–control study, we identified several sexual behavioral factors that are associated with an increased risk of HCV infection, some of which concur with findings from previous studies.

We found intercourse with HIV-infected sex partners to be strongly associated with an increased risk of HCV infection. Also, Schmidt et al[17] found HCV infection to be associated with reporting of intercourse with HIV infected

TABLE 1. Risk Factors for HCV Infection—All Men

Variable	Controls	Cases	*P*	OR Bivariate Analysis	OR Final Model Multivariate Analysis
Age, yrs, N = 141	43.62	44.90	0.41*	1.02 (0.98–1.06)	1.05† (0.99–1.10)
Nationality, N = 142			0.14		
Belgian	78, 86.7%	40, 76.9%		1.95 (0.80–4.73)	
Non-Belgian	12, 13.3%	12, 23.1%			
Residence, N = 142			0.105		—
Brussels	19, 21.1%	11, 21.2%		1.61 (0.62–4.22)	
Antwerp	32, 35.6%	27, 51.9%		2.35 (1.06–5.22)	
Elsewhere in Belgium	39, 43.3%	14, 26.9%		1	
Education, N = 142			0.51		
Primary/secondary	44, 48.9%	29, 55.8%		1.02 (0.42–2.48)	
High school	29, 32.2%	12, 23.1%		0.64 (0.23–1.76)	
University	17, 18.9%	11, 21.2%		1	
Sexual attraction, N = 142			0.19		
Men only	74, 82.2%	47, 90.4%		1	
Men and women	16, 17.8%	5, 9.6%		0.49 (0.17–1.43)	
Has a steady partner now, N = 140			0.84		
None	28, 31.8%	19, 36.5%		1	
Man	56, 63.6%	31, 59.6%		0.82 (0.39–1.69)	
Woman	4, 4.5%	2, 3.8%		0.74 (0.12–4.43)	
Type of partners in the past 12 mo, N = 142			0.002		—
None/steady partner only	25, 27.8%	2, 3.8%		1	
One or more sex buddies	21, 23.3%	13, 25.0%		7.74 (1.57–38.24)	
One or more casual partners	44, 48.9%	37, 71.2%		10.51 (2.33–47.35)	
No. nonsteady partners past yr, N = 142			0.001		—
None or <11	55, 61.1%	17, 32.7%		1	
>10	35, 38.9%	35, 67.3%		3.24 (1.58–6.63)	
No. HIV+ partners, N = 123			0.000		
No sex in past yr/no HIV+ partners/some HIV+ partners	47, 52.2%	9, 17.3%		1	1
Half/more than half/most	24, 26.7%	35, 67.3%		7.62 (3.15–18.40)	7.62 (3.15–18.40)
Do not know	19, 21.1%	8, 15.4%		2.20 (0.74–6.55)	2.20 (0.74–6.55)
Anal intercourse in the past 12 mo			0.000		
No	21, 23.3%	1, 1.9%		1	
Yes	69, 76.7%	51, 98.1%		15.52 (2.02–119.19)	
Unprotected anal intercourse past yr, N = 141			0.000		—
No	43, 48.3%	6, 11.5%		1	
Yes	46, 51.7%	46, 88.5%		7.17 (2.78–18.47)	
Group sex without a condom, N = 142			0.000		—
No	70, 77.8%	22, 42.3%		1	
Yes	20, 22.2%	30, 57.7%		4.77 (2.27–10.02)	
Douching before anal intercourse, N = 142			0.000		
No anal sex past yr/anal sex but no douching	38, 42.2%	4, 7.7%		1	1
Anal sex past yr with douching	52, 57.8%	48, 92.3%		8.77 (2.91–26.41)	9.84 (2.26–42.78)
Fisting (active and/or passive), N = 136			0.000		
Never/almost never	73, 84.9%	29, 58.0%		1	1
Occasionally to frequent	13, 15.1%	21, 42.0%		4.07 (1.80–9.18)	3.54 (1.31–9.57)
Rimming (active and/or passive), N = 134			0.107		
Never/almost never	35, 42.7%	15, 28.8%		1	—
Occasionally to frequent	47, 57.3%	37, 71.2%		1.84 (0.87–3.86)	
Use of sex toys, N = 134			0.101		—
Never/almost never	60, 73.2%	31, 59.6%		1	
Occasionally to frequent	22, 26.8%	21, 40.4%		1.85 (0.88–3.87)	

TABLE 1. (*Continued*) Risk Factors for HCV Infection—All Men

Variable	Controls	Cases	*P*	OR Bivariate Analysis	OR Final Model Multivariate Analysis
Blood at sexual intercourse, N = 126			0.23		
No	52, 64.2%	24, 53.3%		1	
Yes	29, 35.8%	21, 46.7%		1.57 (0.75–3.29)	
Blood transfusion, N = 140					
No	87, 98.9%	52, 100%			
Yes	1, 1.1%	0			
Endoscopy/surgery, N = 139			0.18		
No	60, 68.2%	29, 56.9%		1	
Yes	28, 31.8%	22, 43.1%		1.63 (0.80–3.32)	
Nonmedical procedures past yr, N = 137			0.068		—
No	75, 86.2%	48, 96.0%		1	
Acupuncture/tattoo/piercing	12, 13.8%	2, 4.0%		0.26 (0.06–1.22)	
Drug use ever, N = 139			0.22		
Never/oral drugs	20, 23.0%	6, 11.5%		1	
Drugs through nose	61, 70.1%	43, 82.7%		2.35 (0.87–6.34)	
IV	6, 6.9%	3, 5.8%		1.67 (0.32–8.76)	
Drug use during sex, N = 127			0.000		—
Never/oral drugs	24, 31.2%	1, 2.0%		1	
Drugs through nose	51, 66.2%	46, 92.0%		21.65 (2.82–166.43)	
IV	2, 2.6%	3, 6.0%		36.00 (2.46–527.06)	
Shared implements for sniffing, N = 64			0.15		
No	23, 60.5%	11, 42.3%		1	
Yes	15, 39.5%	15, 57.7%		2.09 (0.76–5.76)	
Has had IVDU partner, N = 115			0.005		—
No	64, 92.8%	34, 73.9%		1	
Yes	5, 7.2%	12, 26.1%		4.52 (1.47–13.89)	
STI in past yr (self- reported), N = 133			0.023		
None	57, 67.9%	23, 46.9%		1	
Non-GUD	12, 14.3%	7, 14.3%		1.45 (0.51–4.13)	
GUD	15, 17.9%	19, 38.8%		3.14 (1.37–7.22)	
Gono or chlamydia in past yr (from records), N = 140			0.004		
No	84, 94.4%	40, 78.4%		1	1
Yes	5, 5.6%	11, 21.6%		4.62 (1.50–14.19)	4.50 (1.11–18.31)
Syphilis or LGV in past yr (from records), N = 140			0.21		
No	77, 86.5%	40, 78.4%		1	
Yes	12, 13.5%	11, 21.6%		1.77 (0.72–4.35)	
CD4 count at inclusion, N = 140			0.53		
<350	7, 7.9%	7, 13.7%		0.5 (0.14–1.79)	
350–500	22, 24.7%	11, 21.6%		0.55 (0.18–1.70)	
>500	60, 67.4%	33, 64.7%		1	

*Comparison of means with analysis of variance.
†For each year of increase in age.
IVDU, intravenous drug using; GUD, genital ulcer disease.

nonsteady partners, but in their study, the association was only statistically significant in bivariate analysis. Reporting high numbers of HIV-infected partners may suggest that the study participant engaged in serosorting, a practice whereby men seek out sex partners of the same HIV serostatus to decrease the risk of HIV transmission while having unprotected anal intercourse. HIV serosorting may decrease the risk of HIV transmission, but studies have shown that it may increase the risk of transmission of other STIs.[20,21]

Serosorting could offer an explanation for the higher incidence of HCV infection in HIV-infected men compared with HIV-uninfected men. However, also biological factors could explain the predominance of HCV infection among HIV-infected men. Viral load of HCV has been found to be higher in HIV/HCV coinfected patients compared with monoinfected patients, and in heterosexual couples, higher viral load of HCV was associated with increased transmission of HCV from men to their female partners.[22] Furthermore, in the Multicentre AIDS Cohort Study, men with lower CD4

TABLE 2. Risk Factors for HCV Infection—Only Men Who Reported Anal Intercourse in the Past 12 Months

Variable	Controls	Cases	*P*	OR Bivariate Analysis	OR Final Model Multivariate Analysis
Age, yrs	42.26	45.12	0.084*	1.04 (0.99–1.08)	1.06† (1.002–1.12)
Nationality			0.43		
Belgian	58, 84.1%	40, 78.4%		1.45 (0.57–3.67)	
Non-Belgian	11, 15.9%	11, 21.6%		1	
Residence			0.17		—
Brussels	16, 23.2%	10, 19.6%		1.25 (0.45–3.46)	
Antwerp	25, 36.2%	27, 52.9%		2.16 (0.93–5.00)	
Elsewhere in Belgium	28, 40.6%	14, 27.5%		1	
Education			0.41		
Primary/secondary	32, 46.4%	28, 54.9%		1.03 (0.4–2.67)	
High school	24, 34.8%	12, 23.5%		0.59 (0.21–1.71)	
University	13, 18.8%	11, 21.6%		1	
Sexual attraction			0.56		
Men only	60, 87.0%	46, 90.2%		1	
Men and women	9, 13.0%	5, 9.8%		0.73 (0.23–2.31)	
Has a steady partner now			0.35		
None	19, 27.9%	19, 37.3%		1	
Man	48, 70.6%	30, 58.8%		0.62 (0.29–1.37)	
Woman	1, 1.5%	2, 3.9%		2.00 (0.17–23.96)	
Partners in the past 12 mo			0.075		—
None/steady partner only	11, 15.9%	2, 3.9%		1	
One or more sex buddies	20, 29.0%	13, 25.5%		3.58 (0.68–18.81)	
One or more casual partners	38, 55.1%	36, 70.6%		5.21 (1.08–25.15)	
No. nonsteady partners past yr			0.023		—
None or <11	36, 52.2%	16, 31.4%		1	
>10	33, 47.8%	35, 68.6%		2.39 (1.12–5.09)	
No. HIV+ partners			0.001		
No sex in past yr/no HIV+ partners/some HIV+ partners	27, 39.1%	8, 15.7%		1	1
Half/more than half/most	23, 33.3%	35, 68.6%		5.14 (1.99–13.26)	6.66 (2.09–21.21)
Do not know	19, 27.5%	8, 15.7%		1.42 (0.45–4.45)	2.42 (0.59–9.92)
Unprotected anal intercourse past yr			0.004		—
No	22, 32.4%	5, 9.8%		1	
Yes	46, 67.6%	46, 90.2%		4.4 (1.53–12.62)	
Group sex without a condom			0.001		—
No	49, 71.0%	21, 41.2%		1	
Yes	20, 29.0%	30, 58.8%		3.50 (1.63–7.50)	
Douching before anal intercourse			0.006		
No douching	17, 24.6%	3, 5.9%		1	1
Anal sex past yr with douching	52, 75.4%	48, 94.1%		5.23 (1.44–18.98)	13.54 (2.01–88.16)
Fisting (active and/or passive)			0.01		
Never/almost never	55, 80.9%	29, 59.2%		1	1
Occasionally to frequent	13, 19.1%	20, 40.8%		2.92 (1.27–6.70)	3.01 (1.07–8.44)
Rimming (active and/or passive)			0.35		—
Never/almost never	26, 37.7%	15, 29.4%		1	
Occasionally to frequent	43, 62.3%	36, 70.6%		1.45 (0.67–3.14)	
Use of sex toys			0.32		—
Never/almost never	46, 67.6%	30, 58.8%		1	
Occasionally to frequent	22, 32.4%	21, 41.2%		1.46 (0.69–3.11)	
Blood at sexual intercourse, N = 126			0.46		
No	41, 60.3%	24, 53.3%		1	
Yes	27, 39.7%	21, 46.7%		1.33 (0.62–2.84)	

TABLE 2. (*Continued*) Risk Factors for HCV Infection—Only Men Who Reported Anal Intercourse in the Past 12 Months

Variable	Controls	Cases	*P*	OR Bivariate Analysis	OR Final Model Multivariate Analysis
Blood transfusion, N = 140			0.39		
No	68, 98.6%	51, 100%			
Yes	1, 1.4%	0			
Endoscopy/surgery, N = 139			0.31		
No	45, 65.2%	28, 56.0%		1	
Yes	24, 34.8%	22, 44.0%		1.47 (0.70–3.11)	
Nonmedical procedures past yr			0.04		—
No	58, 84.1%	47, 95.9%		1	
Acupuncture/tattoo/piercing	11, 15.9%	2, 4.1%		0.22 (0.05–1.06)	
Drug use ever, N = 139			0.52		
Never/oral drugs	12, 17.6%	6, 11.8%		1	
Drugs through nose	50, 73.5%	42, 82.4%		1.68 (0.58–4.86)	
IV	6, 8.8%	3, 5.9%		1.00 (0.18–5.46)	
Drug use during sex			0.005		—
Never/oral drugs	15, 23.1%	1, 2.0%		1	
Drugs through nose	48, 73.8%	45, 91.8%		14.06 (1.78–110.85)	
IV	2, 3.1%	3, 6.1%		22.5 (1.51–335.34)	
Shared implements for sniffing, N = 64			0.25		
No	20, 57.1%	11, 42.3%		1	
Yes	15, 42.9%	15, 57.7%		1.82 (0.65–5.08)	
Has had IVDU partner			0.02		—
No	52, 91.2%	33, 73.3%		1	
Yes	5, 8.8%	12, 26.7%		3.78 (1.22–11.72)	
STI in past yr (self-reported)			0.14		
None	41, 61.2%	23, 47.9%		1	
Non-GUD	11, 16.4%	6, 12.5%		0.97 (0.32–2.10)	
GUD	15, 22.4%	19, 39.6%		2.26 (0.97–5.27)	
Gono or chlamydia in past yr (from records)			0.02		
No	63, 92.6%	39, 78.0%		1	1
Yes	5, 7.4%	11, 22.0%		3.55 (1.15–11.00)	5.19 (1.20–22.55)
Syphilis or LGV in past yr (from records), N = 140			0.42		
No	57, 83.8%	39, 78.0%		1	
Yes	11, 16.2%	11, 22.0%		1.46 (0.58–3.70)	
CD4 count at inclusion, N = 140			0.33		
<350	4, 5.9%	7, 14.0%		1	
350–500	16, 23.5%	11, 22.0%		0.39 (0.09–1.67)	
>500	48, 70.6%	32, 64.0%		0.38 (0.10–1.41)	

*Comparison of means with analysis of variance.
†For each year of increase in age.
IVDU, intravenous drug using; GUD, genital ulcer disease.

counts appeared to be more susceptible to HCV infection.[15] However, in our study, we did not find an association between risk of HCV infection and CD4 count.

As in studies from the United Kingdom, the Netherlands, and Germany, we found that fisting was associated with HCV risk.[16,17,23,24] Schmidt et al[17] found frequent bleeding during sexual intercourse to be associated with an increased risk of HCV infection, but we could not confirm this association. However, in our study, douching before anal intercourse was a strong risk factor for HCV infection. Two possible mechanisms could be put forward to explain this association. There is some evidence that enema's with soapsuds and tap water can damage the rectal epithelium, which could lead to increased susceptibility to HCV infection.[25] Douching has also been found to be associated with an increased risk of HIV infection and of LGV.[26,27] Another possible mechanism is the transmission of the virus through shared douching devices. Unlike HIV, HCV can survive for a long time outside the human body.[28] Furthermore, douching devices could be contaminated with infected blood.

In the Multicentre AIDS Cohort Study, syphilis increased the risk of HCV acquisition by more than 2-fold,[15] and Urbanus et al[24] found prevalent HCV infection to be associated with chlamydial infection. In bivariate analysis, we found self-reported STIs in the 12 months before recruitment into the study and documented gonorrhoea and/or

chlamydial infection to be associated with HCV infection, but in multivariate analysis, only documented gonorrhoea and/or chlamydial infection were associated with HCV infection. It is of note that 5 of 16 *Neisseria gonorrhoeae* and *Chlamydia trachomatis* non-LGV infections were diagnosed as proctitis.

Our study had a number of strengths and weaknesses. HIV-infected patients in the Belgian ARCs are routinely and regularly tested for HCV infection, which allowed us to conduct a case–control study with incident cases of HCV infection and controls matched for date of visit. Routine testing also made it possible to recruit an unbiased selection of cases of HCV infection. As our study was an observational study, we cannot exclude confounding of associations by factors we did not control for. A major weakness however was the lower than expected sample size and the resultant low power. We did not reach our sample size because the incidence of HCV infection in our study population was declining, as was also shown in other Western European settings. We can only speculate about the reasons for this decline in incidence, despite more intensive testing. There are indications that awareness of HCV has increased in the gay community, following campaigns by prevention organizations and reports in the gay press, and we cannot exclude that this had an influence on behavior while also increasing the likelihood of recall bias and social desirability bias in the responses to the questionnaire.

In conclusion, our study confirmed some factors that are associated with an increased risk of sexual transmission of HCV infection in HIV-positive MSM including intercourse with HIV-infected partners, fisting, and other STIs. In addition, we identified anal douching as a risk factor. Further studies are required to confirm this finding and to detail the mechanisms whereby douching is associated with the risk of HCV acquisition. More research is also needed to disentangle the role of biological factors and behavioral factors including networking and serosorting, in the recent HCV epidemics. Finally, we need more research on the effects of serosorting on STIs other than HIV infection.

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