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Acute hepatitis C infection in HIV-negative men who have sex with men

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SUMMARY. Acute hepatitis C infection is recognized in HIV-infected men who have sex with men (MSM), but the risk in HIV-negative MSM remains unclear. We evaluated a population of MSM with acute hepatitis C. From January 2010 to May 2014, all cases of HCV antibody positive HIV-negative MSM were identified. European AIDS Network criteria were applied to determine acute infection, and 44 individuals fulfilled the criteria for acute hepatitis C. Ten were RNA negative at baseline and classed as prior spontaneous clearance. 15 (34.1%) had a previously negative HCV antibody within 1 year. 11 (25.0%) had significant elevation in ALT levels, and 18 (40.9%) were clinically diagnosed from risk exposure and history. Median age was 37 years (range 24–75). 41 (93.2%) individuals reported unprotected anal sex, 36 with (87.8%) both insertive and receptive intercourse, 4 (9.8%) with receptive intercourse, 1 (2.4%) with insertive intercourse, and no data were recorded for 3 (7.3%) patients. Individuals had an average of 7.3 reported (median 2, range 1–100) partners. 12 (27.3%) engaged in group sex, 11 (25.0%) practised fisting, 11 (25.0%) admitted using drugs during sexual activity, 16 (36.4%) reported nasal, and 9 (20.5%) reported injection drug use. 14 (31.8)% had unprotected sex whilst under the influence of recreational drugs. 29 individuals were aware of a partner's status. 2 (4.5%) individuals had sexual contact with a known HCV monoinfected partner, 13 (29.5%) with a HIV monoinfected partner and 6 (13.6%) with a HCV/HIV coinfected partner. 9 (20.5%) reported a partner/partners with no known infection. No data were available in 14 (31.8%) individuals. 13 (29.5%) individuals had a coexisting STI at the time of acute HCV diagnosis. 8 (18.2%) received HIV postexposure prophylaxis (PEP) within the 6 months prior to the HCV diagnosis (2 were participants in a HIV pre-exposure prophylaxis trial). 15 (34.1%) individuals achieved spontaneous clearance of HCV, and 11 patients received HCV treatment. Similar to the ongoing epidemic of acute HCV infection in HIV+ MSM, HIV-negative MSM remain at risk.

Keywords: acute, hepatitis C, HIV negative, men who have sex with men.

BACKGROUND

Injecting drug use and parenteral transmission are recognized as traditional routes of HCV transmission. Men who have sex with men (MSM) are now recognized as a risk group for HCV infection [1], particularly sexually active MSM with high numbers of sexual partners and those using intravenous drugs [2]. Other transmission factors include traumatic sexual activities and ulcerative sexually transmitted infections (STI) [3,4]. Acute hepatitis C (AHC) is well recognized in human immunodeficiency virus (HIV)-infected MSM [5], and incidence is increasing. HIV-negative MSM have lower observed rates of HCV infection compared with HIV-infected MSM [4]. We sought to identify the prevalence of acute hepatitis C in this population.

Abbreviations: AHC, acute hepatitis C; ALT, alanine aminotransferase; HIV, human immunodeficiency virus; NEAT, European AIDS Network; PEP, postexposure prophylaxis; STI, sexually transmitted infections; ULN, upper limit of normal.

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METHODS

We performed a retrospective review of hepatitis C testing in HIV-negative MSM attending a large urban sexual health service from January 2010 to May 2014. European AIDS Network (NEAT) criteria were applied to determine acute infection [6]. To be defined as AHC, a case required positive HCV antibody or HCV RNA, with (i)

previously documented negative HCV antibody or HCV RNA within the previous 12 months, or (ii) alanine aminotransferase (ALT) rise of greater than ten times the upper limit of normal (ULN), or five times ULN with a previously documented normal ALT within the last 12 months. Demographics, alcohol intake, recreational drug use, known HCV-infected partner(s), sexual behaviour including high-risk activities, number of recent partners, presence of co-infection with STI at diagnosis, hepatitis B immunity status, hepatitis C treatment and outcome were recorded. Data were collated and analysed using Microsoft Excel.

RESULTS

Forty-four individuals fulfilled diagnostic criteria for AHC. 10 were RNA negative at initial assessment and classed as spontaneous clearance. These 10 individuals had subsequent follow-up HCV RNA performed and remained negative. Data were collected from the 44 patients.

Fifteen (34.1%) had a previously negative HCV antibody (Abbott ARCHITECT anti-HCV assay; Abbott GmbH & Co. KG, Wiesbaden, Germany) within 1 year. 11 (25.0%) had significant elevation in ALT levels (as defined by NEAT criteria). 18 (40.9%) were clinically diagnosed with AHC from risk exposure and history.

Median age at diagnosis was 37 years (range 24–75). Ethnic origin was available for 41 patients: 25 (55.8%) identified as White British, 1 (2.3%) White Irish, 9 (20.5%) other White, 1 (2.3%) other/mixed, 2 (4.5%) Indian, 1 (2.3%) Chinese and 5 (11.4%) from other ethnic origins not specified.

Forty-one (93.2%) individuals reported unprotected anal sex. Of these, 36 (87.8%) reported both insertive and receptive intercourse, 4 (9.8%) exclusively receptive intercourse, 1 (2.4%) exclusively insertive intercourse, and no data were recorded for 3 (7.3%) patients.

There was an average of 7.3 reported partners per individual (median 2, range 1–100).

Twelve (27.3%) engaged in group sex, 21 (47.7%) did not engage in group sex, and no data were available for 11 (25.0%) individuals. 11 (25.0%) practised fisting, 24 (54.9%) did not practise fisting, and no data were available for 9 (20.5%) individuals. 11 (25.0%) admitted using drugs during sexual activity ('chem sex'), 25 (56.8%) denied sexual drug use, and no data were available for 8 (18.2%) individuals.

Twenty-two (50.0%) individuals reported any recreational drug use, 17 (38.6%) denied use, and no data were available for 5 (11.4%) patients. 16 (36.4%) reported nasal use and 9 (20.5%) reported injection drug use. Drugs used included cocaine, ketamine, gamma hydroxybutyrate, mephedrone and crystal methamphetamine. 14 (31.8%) had unprotected sex whilst under the influence of recreational drugs ('chem sex').

Individuals were asked about regular partner HIV and HCV status. 29 individuals were aware of a partner's status. 2 (4.5%) individuals had sexual contact with a known HCV monoinfected partner, 13 (29.5%) with a HIV monoinfected partner, 6 (13.6%) with a HCV/HIV coinfected partner. 9 (20.5%) reported a partner/partners with no known infection. No data were available in 14 (31.8%) individuals.

Thirteen (29.5%) individuals had a coexisting STI at the time of AHC diagnosis: 7 gonorrhoea (6 rectal infections, 1 not specified), 3 chlamydia (all rectal infections), 2 gonorrhoea with chlamydia co-infection (both rectal infections) and 3 syphilis.

Eight (18.2%) received HIV postexposure prophylaxis (PEP) within the 6 months prior to AHC diagnosis, and 2 (4.5%) were participants in a HIV pre-exposure prophylaxis trial (PROUD – PRe-exposure Option for reducing HIV in the UK: an open-label randomization to immediate or Deferred daily Truvada for HIV-negative gay men). 38 patients had follow-up data; none acquired HIV infection to date. 6 patients were lost to follow-up.

Median baseline HCV RNA at diagnosis was 5.47 $\log^{10}$ international units/mL (range 1.57–6.98 $\log^{10}$ iu/mL). Median alanine aminotransferase was 88 international units/L (range 16–2238 iu/L). Genotype was documented in 22 patients (19 genotype 1, 1 genotype 3, 2 genotype 4). Genotype information was not available for the remaining 22: 15 who achieved spontaneous clearance and genotype not captured; 7 with no genotype sent at diagnosis.

A total of 15 (34.1%) individuals achieved spontaneous clearance of HCV, none of whom had evidence of subsequent reinfection. 11 patients received treatment for HCV. 9 received pegylated interferon and weight-based ribavirin therapy. 6 were treated for 24 weeks, 2 treated for 48 weeks, 1 treated for 16 weeks, and treatment was ceased due to intolerability. 1 patient received pegylated interferon and ribavirin therapy with 12 weeks of NS34A serine protease inhibitor telaprevir (Vertex Pharmaceuticals, Boston, MA, USA and Johnson & Johnson, New Brunswick, NJ, USA). 1 patient received interferon monotherapy for 24 weeks. All patients but 1 achieved a sustained virological response.

We selected a typical month to review HCV screening in HIV-negative MSM. In November 2013, 3811 HIV-negative MSM attended this sexual health service. Only 14.8% (565/3810) had HCV testing with either HCV RNA or HCV antibody. To estimate testing frequency during the study period, we selected a month to review total HIV-negative MSM attendance for sexual health screening. In September 2013, 11 608 sexual health screens were performed: 41.9% (4861/11 608) in MSM, 4.3% (498/11 608) in HIV-positive MSM and 37.6% (4363/11 608) in HIV-negative MSM. We estimate during this study (January 2010 to May 2014) that there were 623 350 attendances for sexual health screening. Allowing similar attendance frequencies for

HIV-negative MSM during this time period, this equates to an estimated 261 036 attendances for HIV-negative MSM sexual health screening within this period. If our rate of screening for HCV is currently 14.8%, we may conclude 34 657 HIV-negative MSM were screened for HCV, and 199 618 were not screened.

CONCLUSIONS

We have identified a cohort of HIV-negative MSM with acute hepatitis C.

Half of these patients (50.0%) reported recreational drug use, but only 20.5% reported intravenous (IDU) use. This may be due to possible underreporting and identification of IDU. Contaminated drug sniffing equipment facilitates intranasal transmission of hepatitis C [7], and over one-third (36.4%) of this group report nasal drug use.

The majority of our patients engage in high-risk sexual practices: 93.2% in unprotected anal intercourse and 45.4% in group sex, 'chem' sex and fisting. 9 (20.5%) had a sexual partner with hepatitis C. 12 (27.3%) had a bacterial STI at diagnosis; 11 had rectal infections. These risks are similar to those for HCV acquisition in HIV-positive MSM and suggest sexual transmission may be relevant in MSM regardless of HIV status.

Fifteen (34.1%) spontaneously cleared hepatitis C infection; similar to the general population [8].

Two AHC patients were participants in a HIV pre-exposure prophylaxis trial. Current data from this study show 41% (160/393) individuals were tested for HCV [9].

Guidelines from the American Association for the Study of Liver Disease (AASLD), the European Association for the Study of the Liver (EASL) and the Infectious Diseases Society of America (IDSA) and the US Centres for Disease Control do not recommend HCV screening specifically in HIV-negative MSM [10–13]. Richardson *et al.* [14] suggest HCV testing be performed in all MSM, especially in areas of high HCV risk. Swedish data show a 0.2% prevalence of chronic and 0.3% prevalence of previously cleared HCV, the authors suggesting 'limited spread of HCV in MSM in Stockholm'. This may reflect differing sexual practices as opposed to lack of support for sexual transmission of HCV [15].

We have highlighted a low rate of HCV screening for at risk MSM, concerning for un-diagnosed HCV infection and onward transmission. HIV-negative MSM remain at risk of HCV infection, sharing similar risk behaviours as HIV-positive MSM. HCV testing should be part of routine sexual health screening in those with risk factors, particularly in environments with a high HCV prevalence. Accurate history taking, documentation of drug use and risk prevention strategies are crucial in this population. Larger, prospective cohort data are needed to further clarify the incidence and prevalence of hepatitis C in MSM without HIV infection.

REFERENCES

1 Osmond DH, Charlebois E, Sheppard HW *et al.* Comparison of risk factors for hepatitis C and hepatitis B virus infection in homosexual men. *J Infect Dis* 1993; 167(1): 66–71.

2 Buchbinder SP, Katz MH, Hessol NA, Liu J, O'Malley PM, Alter MJ. Hepatitis C virus infection in sexually active homosexual men. *J Infect* 1994; 29(3): 263–269.

3 Ndimbie OK, Kingsley LA, Nedjar S, Rinaldo CR. Hepatitis C virus infection in a male homosexual cohort: risk factor analysis. *Genitourin Med* 1996; 72(3): 213–216.

4 van de Laar TJ, van der Bij AK, Prins M *et al.* Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. *J Infect Dis* 2007; 196(2): 230–238.

5 Urbanus AT, van de Laar TJ, Stolte IG *et al.* Hepatitis C virus infections among HIV-infected men who have sex with men: an expanding epidemic. *Aids* 2009; 23(12): F1–F7.

6 The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel and Rockstroh JK. Acute hepatitis C in HIV-infected individuals–recommendations from the NEAT consensus conference. *AIDS* 25 2011: 399–409.

7 Aaron S, McMahon JM, Milano D *et al.* Intranasal transmission of hepatitis C virus: virological and clinical evidence. *Clin Infect Dis* 2008; 47 (7): 931–934.

8 Thomson EC, Fleming VM, Main J *et al.* Predicting spontaneous clearance of acute hepatitis C virus in a large cohort of HIV-1-infected men. *Gut* 2011; 60(6): 837–845.

9 Tiraboschi J BL, Michael B, Saunders J, Gabriel S, Roche N, Fox J, on and b.o.t.P. Study. Acute hepatitis C in the PROUD pilot study. in Third Joint Conference of the British HIV Association and the British Association for the Study of Sexual Health and HIV 2014. Arena and Convention Centre, Liverpool.

10 American Association for the Study of Liver Diseases. Viral hepatitis prevention, screening, and treatment. 2014. Available at: https://aasld.org/patients/Pages/ViralHepatitisPrevention.aspx#screening.

11 European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of chronic hepatitis B. *Journal of hepatology 50.2* 2009: 227–242.

12 American Association for the Study of Liver Diseases, and Infectious Diseases Society of America. Recommendations for testing, managing, and treating hepatitis C. January, 2014.

13 Centers for Disease Control. Testing recommendations for chronic hepatitis C virus infection. 2014. Avail-

able at: http://www.cdc.gov/hepatitis/hcv/guidelinesc.htm.
14 Richardson D, Fisher M, Sabin CA. Sexual transmission of hepatitis C in MSM may not be confined to those with HIV infection. *J Infect Dis* 2008; 197(8): 1213–1214, author reply 1214-5.
15 Blaxhult A, Samuelson A, Ask R, Hökeberg I. Limited spread of hepatitis C among HIV-negative men who have sex with men in Stockholm, Sweden. *Int J STD AIDS* 2013; 25(7): 493–495.