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ARTICLE

Hepatitis C virus infection among transmission-prone medical personnel

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Abstract Hepatitis C virus (HCV)-infected physicians have been reported to infect some of their patients during exposure-prone procedures (EPPs). There is no European consensus on the policy for the prevention of this transmission. To help define an appropriate preventive policy, we determined the prevalence of HCV infection among EPP-performing medical personnel in the Academic Medical Center in Amsterdam, the Netherlands. The prevalence of HCV infection was studied among 729 EPP-performing health care workers. Serum samples, stored after post-hepatitis B virus (HBV) vaccination testing in the years 2000–2009, were tested for HCV antibodies. Repeat reactive samples were confirmed by immunoblot assay and the detection of HCV RNA. The average age of the 729 health care workers was 39 years (range 18–66), suggesting a considerable cumulative occupational exposure to the blood. Nevertheless, only one of the 729 workers (0.14%; 95% confidence interval [CI]: <0.01% to 0.85%) was tested and confirmed to be positive for anti-HCV and positive for HCV RNA, which is comparable to the prevalence of HCV among Amsterdam citizens. Against this background, for the protection of personnel and patients, careful follow-up after needlestick injuries may be sufficient. If a zero-risk approach is desirable and costs are less relevant, the recurrent screening of EPP-performing personnel for HCV is superior to the follow-up of reported occupational exposures.

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Introduction

When an infected surgeon cuts him- or herself during an operation, the transmission of a blood-borne virus to the patient may occur. Over 45 reports document the transmission of hepatitis B virus (HBV) from health care workers to patients [1]. Only four cases of HIV transmission from personnel to one or more patients are known, all before 2003, of which two cases are poorly understood [2–5].

Compared to HBV, the iatrogenic transmission of hepatitis C virus (HCV) occurs less frequently, but several reports document transmission from personnel to patients, including reports on seven HCV-infected British surgeons infecting at least 15 patients [6]. In Spain, Israel and the USA, two anaesthesiologists and a nurse transmitted HCV to many patients; they were addicted and injected themselves during work [7–9].

Consensus has been reached on how to prevent the transmission of HBV from personnel to patients [1, 6]. Most HBV transmissions occur during ‘exposure-prone procedures’ (EPPs). EPPs are invasive procedures with the potential for contact between the skin of the health care worker and sharp surgical instruments, needles or sharp tissues, in body cavities or poorly visualised/confined body sites [1]. The prevention of HBV transmission to and from EPP-performers is based on the vaccination of personnel, on the screening for HBV infection of non-immune EPP-

performers and on the restriction of HBV-infected EPP-performers if their HBV-DNA load exceeds a certain level. No European consensus has been reached for the management of HCV- or HIV-infected personnel. Regarding HCV, guidelines for the management of infected health care workers vary widely. For example, in the United Kingdom, since 2007, health care workers are excluded from EPPs if they test positive for HCV RNA. Testing for HCV is performed if the worker him- or herself decides that there may have been exposure to HCV. In Ireland, since 2005, one must undergo polymerase chain reaction (PCR) testing if one performs EPPs. In the Netherlands, no HCV policy has been defined. This study aims to gain insight into the prevalence of HCV infection among Dutch medical personnel performing EPPs in a large academic hospital in Amsterdam, by screening anonymous serum samples of employees.

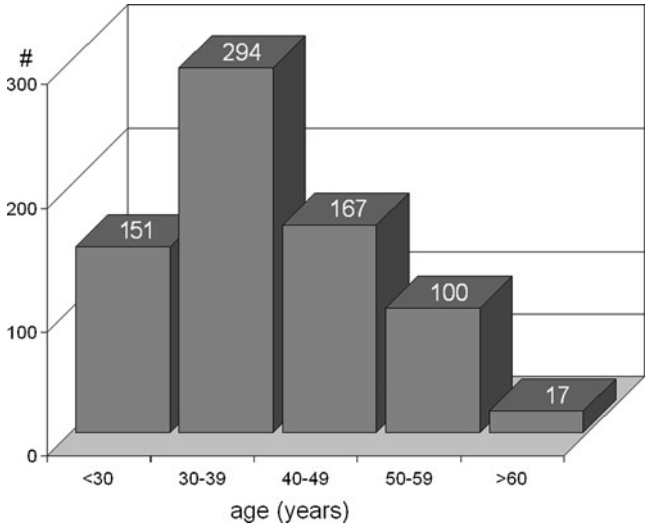

Fig. 1 Distribution of the age of 729 health care workers performing exposure-prone procedures (EPPs) and tested for hepatitis C virus (HCV) infection

Materials and methods

Samples

At the Academic Medical Center (AMC) in Amsterdam, for the monitoring of the HBV immune status of personnel, distinction is made between persons who only run the risk of acquiring infection and persons such as thoracocardiac, orthopedic and gynaecological surgeons, who, in addition, may transmit HBV to patients during EPPs. This enabled the computer-aided selection of samples from EPP-performing personnel. The sample collection at AMC—Laboratory of Clinical Virology includes all submitted sera over the last 10 years. Samples are stored at −20°C. During 2000–2009, sera from 5,190 different persons were submitted by the Occupational Health and Safety Department for post-vaccination anti-HBs testing. Of these, 734 (14%) were encoded as EPP-performing personnel. The exact nature of the profession was not available. Five samples contained no or insufficient serum. Thus, sera from 729 EPP-performing persons were available for anti-HCV testing.

At the time of sampling, the age of the medical personnel was, on average, 38.6 years (range 17.5–66.0); the cumulative age was 28,147 years (Fig. 1). If it is assumed that significant occupational exposure to blood, and a risk of transmitting infection, occur after medical training has been completed at an age of 25 years, this study represents $28,147-(25*729)=9,922$ person-years of occupational exposure to and potential transmission of blood-borne viruses. For comparison, the prevalence of HCV infection among patients at the AMC was assessed as follows. In the years 2005 to 2010, 1,248 needlestick accidents and other occupational exposures were recorded by the Occupational Health and Safety Department. In 526/1,248 cases (42%), the HCV status of the source patient was known or tested; 8% of the patients (44/526) were HCV-infected.

Testing for HCV

Before testing, the 729 samples were renumbered with no relation to the original identification. The anonymous sera were tested for antibodies to HCV using the automated AxSYM HCV chemiluminescent antibody assay (Abbott Laboratories, Abbott Park, IL, USA). Initially reactive samples, showing a sample to cut-off ratio (S/CO) ≥ 1, were considered to be positive if they again showed reactivity in repeated testing. Repeat reactive samples were subjected to confirmatory testing using an immunoblot assay for the detection of HCV antibodies (RIBA HCV 3.0 Strip Immunoblot Assay, Chiron Corporation, Emeryville, CA, USA) and a PCR for the detection of HCV RNA (Roche Cobas AmpliPrep/Cobas TaqMan HCV assay, Roche Molecular Systems Inc., Pleasanton, CA, USA). The 95% confidence interval (CI) of the HCV-positive proportion of the tested samples was calculated using the adjusted Wald method.

Effects of long-term storage on HCV testing

Prolonged storage may cause increased non-specific serological reactivity in the samples, while HCV RNA and HCV antibodies may deteriorate. To assess increasing non-specific reactivity, the anti-HCV signal distribution of the 729 archived samples was compared to the signals in 4,786 fresh samples, routinely tested for anti-HCV in 2010 on the

same system. A limited assessment of degradation was performed as follows. Serum samples from three hepatitis C patients (patients A–C) were retrieved, which were kept in the same freezer together with the oldest samples of this study since 2000. Anti-HCV testing was repeated in 2011, and the signals were compared to the original signals of 2000. On three serum samples from 2001 (patients D–F), kept in the same freezer as the study samples, quantitative HCV RNA was determined in 2011, and compared to the level of HCV RNA as determined on plasma samples in 2001, using the HCV RNA bDNA assay (Siemens, Deerfield, IL, USA).

Ethical considerations

The Medical Ethical Committee (MEC) of the AMC, the judicial department of the AMC and the Dutch National Health Council approved this study. The HCV testing was performed anonymously, based on several considerations. The samples in this study were drawn for anti-HBs testing. Obtaining retrospective permission for non-anonymous HCV testing was not feasible. In addition, it had to be avoided that HCV-positive persons could have been excluded from work, in an unregulated situation, for example, without insurance for the loss of income, while at the same time in other hospitals, HCV-infected personnel remains undetected. On the other hand, knowing one's HCV infection status enables the timely treatment of HCV infection. Therefore, if significant prevalences of HCV were to be detected in this study (to be judged by the MEC), HCV testing is planned to be advised to all EPP-performing personnel. In addition, independent of this study, the confidential testing and treatment of blood-borne infections has been available for all EPP-performing personnel at the AMC for many years.

Results

Ten of the 729 (1.4%) serum samples were positive for anti-HCV after repeated testing in the anti-HCV screening assay. One sample was strongly reactive and nine samples showed marginal anti-HCV signals (Table 1). Confirmatory testing demonstrated the presence of HCV RNA (37,300 IU/mL) and a complete immunoblot pattern only in the strongly reactive sample, hence, the prevalence of HCV infection among the health care workers was 1/729 or 0.14% (95% CI: <0.01% to 0.85%).

In the nine weakly reactive, PCR-negative samples, the anti-HCV immunoblot tested negative in six samples, invalid in one, positive in one and indeterminate in one sample (Table 1). The invalid immunoblot pattern concerned isolated anti-NS5 reactivity together with reactivity against the fusion protein, which indicates non-specific reactivity [10]. Possibly, the weak reactivity in the positive and indeterminate immunoblot pattern concerned waning antibodies after cleared or cured HCV infection in the past. The weak anti-HCV reactivity in the nine samples may very well be non-specific. Weak signals (S/CO<3) in a chemiluminescent anti-HCV immunoassay are associated with false-positive reactivity [11]. In addition, comparing the signals in the stored and fresh samples, the archived samples show elevated background reactivity, below and around the cut-off value (Fig. 2). It is unlikely that the weakly reactive samples represent an early stage of HCV infection. In that case, peak levels of HCV-RNA would have been present, detectable by PCR, despite the degradation of HCV-RNA during storage (see below).

The anti-HCV signal in the stored sera of three patients was still strongly positive upon retesting in 2011. The S/CO ratio in 2000 and in 2011 was, respectively, in patient A 78.67 and 63.78, in patient B 81.64 and 68.75, and in patient C 111.77 and 91.77. The HCV RNA levels in the three patient sera from 2001 seem to be reduced upon retesting in 2011, with test results in 2001 and in 2011 as follows: in patient D 462,000 and 186,000 IU/mL, in patient E 362,000 and 112,000, and in patient F 11,700 and 110 IU/mL.

Discussion

Based on look-back studies, the transmission rate of HCV from infected surgeons to their operated patients was 0.26% in the United Kingdom and 0.13% in Germany [6]. In Norway, a cardiac surgeon transmitted HCV during open heart surgery to 3.7% (n=10) of operated patients [12]. Should surgeons be screened for HCV to protect their patients against iatrogenic infection? To define appropriate preventive measures, the prevalence of HCV among medical personnel must be known. This survey was undertaken in order to estimate the prevalence of HCV among transmission-prone medical personnel.

The screening of anonymous samples of 729 persons who perform EPPs at the Academic Medical Center in Amsterdam revealed only one HCV infected health care worker (0.14%, 95% CI: <0.01% to 0.85%). After the sampling of Amsterdam citizens, Baaten et al. calculated a similar overall prevalence of HCV infection in Amsterdam of 0.62% (95% CI: 0.1–1.1%). The large majority of the HCV-positive citizens in the sampling concerned immigrants with risk factors such as intravenous drug abuse and blood transfusion before 1991 [13].

The low prevalence of HCV among EPP-performing health care workers in Amsterdam is reassuring, considering that the large majority of the personnel was over

Table 1 Confirmatory test results in ten anti-hepatitis C virus (HCV) reactive health care workers

Sample no.	Anti-HCV EIA		Anti-HCV immunoblot	Immunoblot pattern (c100, c33, c22, NS5, SOD)	HCV-RNA PCR
	Initial S/CO	Repeat S/CO			
1	59.80	51.32	Positive	4+, 4+, 4+, 4+, 0	Positive, 37,300 IU/mL
2	2.21	2.29	Invalid	0, 0, 0, 4+, 2+	Negative
3	2.65	2.28	Positive	0, 1+, 2+, 0, 0	Negative
4	1.39	1.47	Negative	0, 0, 0, 0, 0	Negative
5	1.11	1.12	Indeterminate	0, 1+, 0, 0, 0	Negative
6	1.24	1.09	Negative	0, 0, 0, 0, 0	Negative
7	2.95	1.04	Negative	0, 0, 0, 0, 0	Negative
8	1.21	1.02	Negative	0, 0, 0, 0, 0	Negative
9	1.18	1.02	Negative	0, 0, 0, 0, 0	Negative
10	1.37	1.01	Negative	0, 0, 0, 0, 0	Negative

C100, c33, c22 and NS5=artificial HCV antigens

SOD = superoxide dismutase, fusion protein

S/CO = sample to cut-off ratio; positive if ≥1

30 years of age, representing significant occupational exposure to blood in the past. Failure to detect HCV infection in the archived samples, due to deterioration during prolonged storage, seems unlikely. In addition, our results are in line with the early findings of Beltrami et al., who reviewed seroprevalence studies among hospital-based personnel in the 1990s, and also found HCV seroprevalence rates comparable to or lower than in the general population in several Western countries [14]. More recently, Marconi et al. found no HCV infection following 390 Italian health care workers from 1999 to 2009 [15].

Unrelated to this anonymous study, two physicians at the AMC acquired HCV infection after a needlestick injury, respectively, in 2000 [16] and in 2009. At first sight, these incidents seem inconsistent with the low prevalence of HCV infection as reported in this study. However, in both incidents, the physician was aware of HCV infection in the patient. Apparently, effective self-referral took place. Obviously, both infections occurred after the sampling for anti-HBs testing of the surgeons took place. This illustrates that our study does not provide a cumulative measurement of all HCV transmissions to EPP-performing personnel at the AMC up till now; it provides a cross-sectional overview of the HCV status of 729 workers, with careers covering nearly 10,000 person-years of occupational exposure to blood at the time of sampling. Nevertheless, it cannot be ruled out that increased exposure to HCV occurred after the sampling of the personnel for this study took place, which would cause an underestimation of the prevalence of HCV in this report.

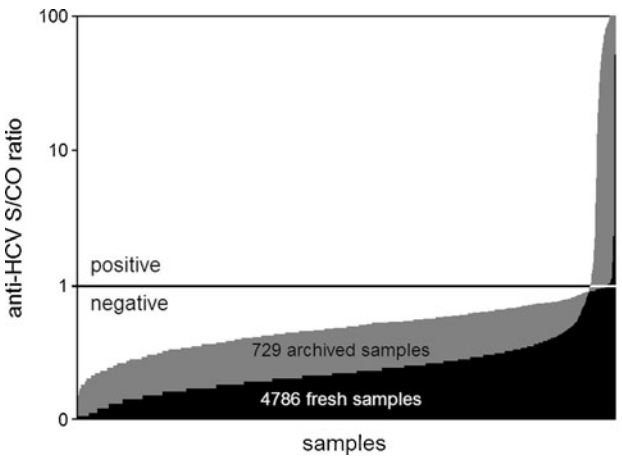

Fig. 2 Distribution of the anti-HCV signal in 729 archived samples of health care workers and in 4,786 fresh samples routinely tested for anti-HCV (S/CO = sample to cut-off ratio; positive if ≥1)

Among Amsterdam citizens, HCV infection can be attributed to risk factors such as intravenous drug abuse, blood transfusion before 1991 and unprotected sex between HIV-infected men [13, 17]. HCV infection among local surgeons can be attributed to occupational exposure to the blood of HCV-infected patients or to personal non-occupational risk behaviour. From an occupational health care perspective, HCV infection among hospital-based personnel can be an occupational disease for which simple screening and rapidly improving antiviral therapy is available [18, 19]. The recurrent screening of personnel for HCV may reveal HCV infections caused by unreported needlestick injuries and non-occupational sources. However, in this study, only one of 729 health care workers was found to be HCV-infected. Against this background, for the protection of personnel and patients, the follow-up of physicians after occupational exposures may be sufficient, without recurrent screening of personnel for HCV infection.

Recurrent screening is less productive if the incidence of HCV is low and a careful follow-up of occupational exposures takes place, but it is superior to the follow-up of reported needlestick injuries if a zero-risk approach is desirable and costs are less relevant.

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