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Hepatitis C in deceased drug addicts*

K. Trübner[1], S. Polywka[2], K. Püschel[1], and R. Laufs[2]

[1]Institut für Rechtsmedizin, Universität-Gesamthochschule-Essen, Hufelandstrasse 55, W-4300 Essen 1, Federal Republic of Germany
[2]Institut für Medizinische Mikrobiologie und Immunologie, Universitätskrankenhaus Eppendorf, Martinistrasse 52, W-2000 Hamburg 20, Federal Republic of Germany

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Summary. Needle sharing among drug addicts leads to the transmission of infectious diseases such as hepatitis B and AIDS. After development of a test system based on gene technology against the hepatitis C virus (HCV), drug addicts have been regarded as an important reservoir for hepatitis C. In our study 113 (40.1%) out of 282 addicts who died from drug abuse in Hamburg between 1988 and 1990 had antibodies against HCV (anti-HCV). The prevalence of anti-HCV differed in various age groups; the highest prevalence was found in addicts aged 30–34 years. Co-infections with hepatitis B and hepatitis C virus were found in 57 drug addicts (59.4%) out of 96 deceased with antibodies to hepatitis B (anti-HBc), whereas only 8 out of 23 HIV-infected were anti-HCV positive (34.8%).

Key words: Drug addicts – Drug deaths – Hepatitis B – Hepatitis C – HIV-infection

Zusammenfassung. Nachdem mit gentechnologischen Methoden ein Testsystem zum Nachweis eines Antikörpers gegen das Hepatitis C Virus entwickelt wurde, sind intravenös Drogenabhängige als ein bedeutendes Reservoir für die Hepatitis C bekannt. Unsere Untersuchungen an 282 Rauschgifttoten zwischen 1988 und 1990 in Hamburg zeigten, daß 131 Drogentote (40.1%) Antikörper gegen das HCV aufwiesen. Die Antikörperprävalenz variierte in den einzelnen Altersgruppen und war bei den 30–34jährigen am höchsten. 57 (59.4%) von 96 Drogentoten mit Hepatitis B Antikörper (anti-HBc) wiesen auch das anti-HCV auf, während nur bei 8 (34.8%) von 23 HIV-infizierten Drogentoten Antikörper gegen die Hepatitis C nachgewiesen werden konnten.

Schlüsselwörter: Intravenös Drogenabhängige – Drogentote – Hepatitis B – Hepatitis C – HIV-Infektion

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Offprint requests to: K. Trübner

Introduction

Choo et al. (1989) cloned the genome of a non-A, non-B hepatitis agent, designated the hepatitis C virus and Kuo et al. (1989) developed an assay to detect antibodies against a major gene product of that agent. It appears that HCV is a major cause of community-acquired sporadic non-A, non-B hepatitis as well as post-transfusion non-A, non-B hepatitis (Esteban et al. 1989) and could possibly play a pathogenetic role in autoimmune chronic active hepatitis (McFarlane et al. 1990). Furthermore the hepatitis C virus is associated with the development of hepatocellular carcinoma (Colombo et al. 1989). HCV is a single stranded encapsulated RNA virus probably belonging to the flaviviruses with a diameter of 50–60 nm (Grob and Joller-Jemelka 1990). However, until now only one HCV associated antigen was available for the detection of specific antibodies in infected patients. Seroconversion may take 3–6 months or more and may occur after the onset of clinical symptoms. Little knowledge is available about the persistence of HCV antibodies in cases of chronic or resolved non-A, non-B hepatitis. A negative antibody test therefore does not exclude HCV infection as the patient may have antibodies against other antigenic determinants of the virus. Confirmatory tests are necessary to give further information on the infectiousness and clinical outcome of patients with anti-HCV (Marwick and Skolnick 1990).

As HCV is obviously transmitted parenterally, groups at risk resemble those at risk for hepatitis B virus (HBV) or human immunodeficiency virus (HIV), i.e. intravenous drug addicts, hemophiliacs, homosexuals, and patients receiving blood transfusions (Laufs et al. 1989; Stremmel and Strohmeyer 1989; Mosley et al. 1990; Stevens et al. 1990). However, in approximately 40% seropositive patients the route of transmission remains unknown (Marwick and Skolnick 1990). To obtain further data on the frequency and association of parentally transmitted disease among high risk groups we tested sera from 287 drug addicts who died in Hamburg between 1988 and 1990 for antibodies against HBV, HCV, HIV 1 and HTLV I.

Materials and methods

Autopsies were carried out on 297 addicts (245 male, 52 female), who died from drug abuse in Hamburg between 1988 and 1990, in the Institute of Forensic Medicine at the University Hospital Hamburg-Eppendorf. Of these 74 died in 1988, 87 in 1989 and 136 in 1990; the ages varied from 15 to 47 years with a mean of 28.9 years. The blood samples were taken within 24 hours after admission to the Institute and centrifugated and stored at 4°C. A total of 282 blood samples were tested for anti-HCV, 284 for anti-HBc and 287 for anti-HIV. Sera were tested for anti-HBc using the commercially available test kit of Abbott Diagnostica (Chicago, Ill, CORZYME). Positively reacting sera were investigated for additional viral markers (AUSZYME Monoclonal for detection of HBsAg, AUSAB for detection of anti-HBs, and CORZYME M for detection of anti-HBc-IgM; Abbott Diagnostica).

Testing for HIV 1 was performed by ELISA (VIRONOSTIKA II, Organon Teknika, Eppelheim, FRG) as a screening method; samples with positive results were confirmed by an immunofluorescence test (self-production) and by Western blot (HIV-1 Biotech Western Blot Kit, DuPont, Wilmington, Del). For the detection of antibodies against HTLV I a commercial ELISA kit was used (Human T-Lymphotropic Virus Type I Abbott HTLV I-EIA, Abbott Diagnostika or DuPont HTLV I Elisa Kit, Dupont). Positive results were confirmed by Western Blot (HTLV I IgG Western Blot, Diagnostic Biotechnology (Pte.), Singapore).

Anti-HCV was detected with an ELISA system using recombinant HCV C 100-3 antigen on the solid phase (Ortho, Raritan, NJ).

Statistical methods used in this study included Chi-square-test and Fisher's exact test where appropriate. The hepatic histopathological investigations and their correlation with the serological data are reserved for a further study.

Results

In our study, we compared the occurrence of addicts showing seropositivity to HCV with those positive for HBV, HIV 1, or HTLV I. Out of 282 drug victims 113 showed antibodies against HCV (40.1%). Rates of anti-HCV positivity did not differ significantly between males and females (40.9% vs. 36%). Markers of an HBV infection (anti-HBc) were detected in 96 cases (33.8%) and 23 sera were positive for anti-HIV 1 (8.0%). Antibodies specific for HTLV I were found in only 2 cases (0.7%). From 1988–1990 the rates of positivity for HBV and HCV decreased continuously and the HIV-prevalence decreased in 1989 but increased in 1990 (Table 1).

Co-infections with HCV and HBV were seen in 57 cases (Table 2). In 8 cases we found evidence of infections with HCV and HIV 1 (Table 2); i.e. 59.4% of addicts infected with HBV showed markers of HCV infection, whereas only 8 out of 23 HIV infected drug deaths (34.8%) were positive for anti-HCV. These data show a statistically highly significant association between HBV and HCV ($P < 0.0001$), whereas no association could be shown between HCV and HIV 1 ($P > 0.1$). Hepatitis B and HIV-infections are not necessarily connected with hepatitis C and vice versa.

Table 1. Prevalence of HVC, HBV, HIV 1, and HTLV I antibodies in drug victims

	1988 $N=74$		1989 $N=87$		1990 $N=121$		Total $N=282$	
	n	%	*n*	%	*n*	%	*n*	%
HCV	32	43.2	36	41.4	45	37.2	113	40.1
HBV	33	44.6	29	33.3	34*	27.6	96	33.8
HIV 1	11	14.9	4	4.6	8**	6.3	23	8.0
HTLV I	1	1.4	1	1.1	–	–	2	0.7

* $n = 123$
** $n = 126$

Table 2. Association between anti-HCV and anti-HBc and HIV 1

	Anti-HBc		HIV 1	
	+	–	+	–
Anti-HCV +	57	56	8	105
Anti-HCV –	39	132	15	154

Table 3. Age and sex distribution of positive results for anti-HCV

Age	Total			Anti-HCV positive					
	n	*M*	*F*	*M*	%	*F*	%	Both sexes	%
<20	13	9	4	2	22.2	1	25	3	23.1
20–24	64	46	18	9	19.6	3	16.6	12	18.75
25–29	84	64	20	25	39.1	10	50	35	41.7
30–34	71	67	4	38	56.7	2	50.0	40	56.3
35–39	41	38	3	18	47.4	2	66.7	20	48.8
>40	9	8	1	3	37.5	–	–	3	33.3
	282	232	50	95	40.9	18	36	113	40.1

The rate of HCV infection among deceased drug addicts seems to rise with increasing age. Table 3 compares the age distribution of all addicts in our study with positive HCV results. The highest prevalence of HCV-positivity was found in the age group 30–34 years (56.4%). Drug addicts younger than 30 years old were less frequently positive than those older than 30 years (31.1% vs. 52.1%). The mean age of HCV negative individuals (27.3 years) was lower than that of HCV positive individuals (30.9 years).

The cause of death was mostly intoxication with heroin or other drugs (281 cases); 5 survived the intoxication several days and died of bronchopneumonia, 2 died of Aids, 4 from multiple trauma (3 suicidal falls from height, 1 traffic accident), 2 deaths were caused by asthma bronchiale, one by a bleeding gastric ulcer with a fatty liver and 2 from liver coma with liver cirrhosis.

Discussion

Intravenous drug addicts who share needles are at risk of acquiring hepatitis C as HCV is transmitted parenterally. The connection between intravenous drug abuse and the transmission of hepatitis could be shown by Pont

et al. (1991) inter alia who found anti-HCV in 73% of imprisoned intravenous drug abusers but only in 8% of the non-intravenous drug abusers. However, it has been suggested that transmission may also occur by the faecal-oral route. Polywka and Laufs (1991) observed double infection with HCV and hepatitis A virus (HAV) which supports this theory.

Currently serum samples from all drug victims are tested not only for HBV, HIV 1 and HTLV I (Püschel et al. 1987; Trübner et al. 1989) but also for anti-HCV. – In our 3-year-study, 40.1% of drug addicts, who died between 1988 and 1990 in Hamburg, showed antibodies against HCV. There is a slight decrease in the prevalence of anti-HBc, anti-HCV and anti-HIV from 1988 to 1990. The practice of more frequent usage of sterile needles, knowledge of risks, the shorter drug career of addicts because of cleaner and more lethal drugs could be the reasons for this decrease. In European countries the prevalence of anti-HCV in drug addicts varies between 48% and 92% (as reported on the 1st International Meeting on hepatitis C virus, Rome, 1989). Esteban et al. (1989) reported that 70% drug abusers were anti-HCV positive. Other groups at risk for hepatitis C are haemophiliacs with 65.4% positive (Polywka and Laufs 1991) and 82% reported by Rumi et al. (1990). Patients with multiple transfusions showed an anti-HCV prevalence of 38.5% (Polywka and Laufs 1991). Esteban et al. (1989) reported an anti-HCV prevalence of 85% in prospectively followed patients with post transfusion non-A, non-B hepatitis. Patients on haemodialysis have a lower anti-HCV prevalence; Polywka and Laufs (1991) reported 12.4% and Esteban et al. (1989) 20%. In addition to these studies a control study among healthy pregnant women showed an anti-HCV prevalence of only 2.8%. Polywka and Laufs (1991) reported an anti-HCV prevalence of 2.8% among the medical staff. As in our investigation, these studies comprised a mixture of different groups of addicts, such as long-term addicts or sporadic drug abusers. Compared to other groups of addicts which have been investigated our study showed a lower rate of HCV infections (40.1%). Interestingly, in our study antibodies to HBV (33.8%), HIV 1 (8%) or HTLV I (0.7%) were less frequent in addicts than HCV. Infections seem to play a subordinate role in mortality. Two drug addicts died of AIDS, only 2 deaths were caused by coma hepaticum with liver cirrhosis and one death was caused by bleeding from a gastric ulcer with a fatty liver.

The association between antibodies against HCV and markers for an HBV infection was highly significant, whereas no association could be detected between HIV 1 and HCV. Stevens et al. (1990) also found a correlation between both infections in voluntary blood donors. However, this strong association between HBV and HCV could not be demonstrated in other groups at risk, e.g. haemophiliacs or patients on haemodialysis.

Kuo et al. (1989) found a strong correlation between HCV and HBV. Out of 412 voluntary blood donors without anti-HBc only 0.5% showed anti-HCV but in 44% of the donors with anti-HBc and elevated ALT levels anti-HCV was also found.

It has been suggested that infectivity is highest in acute or chronic HBV infection followed by HIV 1, and lowest in HCV (Polywka and Laufs 1991). Therefore, the occurrence of HCV should also be lowest, however, mortality among persons who are already HIV 1 positive is highest followed by HBV and HCV and may account for the high prevalence of anti-HCV in surviving drug addicts.

There seems to be an increase of the anti-HCV prevalence with age although the deceased in age groups over 35 show a lower rate than the 30 to 34-year-old age group.

Stevens et al. (1990) observed an increase in prevalence of anti-HCV in blood donors younger than 40 years of age followed by a decrease in those older than 40 years. This may be due to a cohort effect, reflecting a lower exposure in older donors; it may also be due to a higher morbidity or mortality rate caused by HCV infection or a loss of detectable antibodies with increasing age. It is not certain if the anti-HCV persists throughout life. This could be a reason for the lack of correlation between anti-HCV and age as could be seen in the case of anti-HBc in drug deaths (Trübner et al. 1989).

Alter et al. (1989) observed that anti-HCV may disappear after a variable interval, particularly in patients who have rapid biochemical resolution of their hepatitis. Whether those who have lost anti-HCV are still infectious remains unclear. Although this tendency was also seen in this study, the number of drug victims over 39 years of age is too small to obtain statistically valid information. Further investigations are necessary to confirm this observation.

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