Hepatitis B and C in Heterosexual Patients with Various Sexually Transmitted Diseases

**Summary:** The seroprevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections were prospectively assessed in 356 heterosexuals with STDs (sexually transmitted diseases) and compared to a control group of 381 healthy first-time blood donors. Eighty-one of 356 STD patients were anti-HBc positive (22.8%) compared to 14/381 blood donors (3.8%; p<0.001). In addition, 18 of the 81 anti-HBc positive STD patients, but none of the controls, were positive for HBsAg (p = 0.06). The prevalence for anti-HCV was also significantly higher in the STD group than in the controls (5.3% vs. 0.5%; p<0.001). Among the various STDs syphilis (anti-HBc: 67.5%; anti-HCV: 12.5%) and *Chlamydia trachomatis* infections (anti-HBc: 20.2%, anti-HCV: 8.1%) had the highest prevalence for both infections. This study provides strong evidence of heterosexual transmission of hepatitis B and C virus infections. Thus, heterosexuals with STDs or multiple partners should be actively vaccinated against hepatitis B.

**Zusammenfassung:** Hepatitis B und C bei heterosexuellen Patienten mit verschiedenen sexuell übertragenen Krankheiten. Bei 356 heterosexuellen Patienten mit sexuell übertragbaren Infektionen (STD) wurde die Seroprävalenz für Hepatitis B-Virus- und Hepatitis C-Virus-Infektionen untersucht. Als Vergleich diente eine Kontrollgruppe von 381 gesunden Erstblutspendern. 81 der 356 STD-Patienten waren anti-HBc-positiv (22.8%), dagegen nur 14 der 381 Blutspendern (3.8%; p<0.001). Bei 18 der 81 anti-HBc-positiven Patienten konnte zusätzlich HBsAg nachgewiesen werden, dagegen bei keinem der Blutspender (p = 0.06). Die Durchseuchung mit Hepatitis C war ebenfalls bei den Patienten mit STD signifikant höher als in der Kontrollgruppe (5.3% vs 0.5%, p<0.001). Unter den verschiedenen Infektionen waren die Syphilis (anti-HBc: 67.5%, anti-HCV: 12.5%) und eine Infektion mit *Chlamydia trachomatis* (anti-HBc: 20.2%, anti-HCV: 8.1%) mit der höchsten Seroprävalenz für beide Hepatitisinfektionen assoziiert. Die Untersuchung belegt die Bedeutung der heterosexuellen Übertragung sowohl des Hepatitis B- wie auch des Hepatitis C-Virus. Promiskuitive Patienten und Patienten mit STD gehören zur Risikogruppe und sollten daher aktiv gegen Hepatitis B geimpft werden.

**Introduction**

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are major causes of chronic hepatitis, cirrhosis, and primary hepatocellular carcinoma [1]. Five percent of the world's population, equivalent to approximately 300 million individuals, are said to be chronic HBV carriers. Chronic hepatitis B is considered to be the most important human chronic viral infection [2]. In countries with low endemicity sexual activity, both homosexual and heterosexual, is the greatest risk factor for HBV infection and spread of the disease. The prevalence of HBV in heterosexuals varies strongly depending on promiscuous behaviour and other STDs and is less well documented in European countries than in the US.

Recently, the HCV responsible for the majority of parenterally transmitted cases of non A-, non B-hepatitis has been identified and partially characterized, thus allowing for a test system to detect antibodies to HCV [3,4]. However, anti-HCV has been found to be frequently positive in chronic hepatitis C patients without previous parenteral exposure [5,6], suggesting additional modes of transmission. Since hepatitis B and hepatitis C are epidemiologically similar, sexual transmission was considered a potential way of HCV infection.

In the present study we screened heterosexual patients with various STDs for HBV and HCV seromarkers to establish the prevalence of HBV and HCV infections in this risk group compared to a control group not at risk.

**Patients and Methods**

**Design:** The study was designed as an open, comparative seroprevalence study, approved by the ethical review committee of the main investigator and performed according to the EC Good Clinical Practice Guidelines (GCP).

**Subjects:** Included in the trial were male and female heterosexual patients presenting with an acute sexually transmitted disease at the outpatient STD clinic of one of the participating referral university hospitals. There was no age limit for inclusion into the study. Patients with other risk factors for HBV or HCV were excluded.

Received: 5 February 1992/Revision accepted: 20 April 1992

Prof. Dr. med. E. E. Petersen, Universitätskrankenhaus Freiburg, Hugstetter Straße 55, W-7800 Freiburg; Dr. med. R. Clemens, Dr. med. H. L. Bock, Medizinische Abt., SmithKline Beecham Pharma, Sapporobogen 6-8, W-8000 München 40; Dr. med. K. Friese, Universitätsfrauenklinik, Theodor-Kutzer-Ufer, W-6800 Mannheim 1; Prof. Dr. med. G. Hess, Medizinische Universitätsklinik, Langenbeckstraße 1, W-6500 Mainz, Germany.
transmission such as drug addiction, homosexuality, previous blood/plasma transfusion or organ transplantation, household contacts with HBV carriers or health-care work were excluded from the seroprevalence survey as well as those vaccinated against hepatitis B. Consecutive first-time blood donors without any known risk factors for hepatitis transmission served as control group. Blood donors who were vaccinated and those with a history or serological evidence of STD during routine screening were excluded.

Methods: Serum samples were taken from each subject on admission to the STD clinic or the blood donation centre and kept at −20°C until analyzed. Sera were tested for antibodies to hepatitis B core antigen (anti-HBc). Those positive for anti-HBc were also analyzed for the hepatitis B surface antigen (HBsAg) and antibodies to HBsAg (anti-HBs) by commercial tests (Abbott Laboratories). Antibodies to HCV (anti-HCV) were tested by first generation ELISA (Abbott Laboratories). All tests were done in duplicate. In case of discrepancies, sera were reanalyzed a third time (in addition, each patient was asked to fill in a questionnaire on sexual activity and behaviour).

Statistics: The main outcome measure in this trial was the prevalence of HBV and HCV infections in various STDs compared to healthy blood donors. Demographics of the STD patients and the blood donors were compared by the Wilcoxon-test or Chi-square tests, as appropriate. For comparing the prevalence of HBV and HCV among STD patients and blood donors, the Chi-square test or Fisher’s exact test were applied, depending on the sample size in the STD groups. Levels of significance were adjusted for multiple testing according to Bonferroni Holm.

Results

In all, 396 STD patients and 390 blood donors were included in the study (Table 1). Forty out of the 396 STD patients had to be excluded from the seroprevalence analysis because of other risk factors for HBV or HCV transmission. Nine out of the 390 blood donors were not included in the control group because of evidence of previous STDs. Reasons for exclusion and the HBV- and HCV-seroprevalence of the excluded subjects are given in Table 2. Thus, 356 patients with STDs and 381 blood donors were evaluable for HBV and HCV seroprevalence. Both groups were comparable with respect to age and but not as to sex ratio.

The most common presenting condition in the STD patients was herpes genitalis, followed by Chlamydia trachomatis infections and condylomata acuminata (Table 3). The questionnaire on number of lifelong sexual partners or partners within the last six months was only filled in by a subset of STD patients. Thus, the data in Table 4 only gives an estimate of sexual activity in the study population.

The seroprevalence for both HBV and HCV infection was significantly higher in the STD patients compared to the control group of blood donors (Table 5). Eighteen of 81 STD patients positive for anti-HBc were also found positive for HBsAg (22.2%) indicating acute infection or carrier status, whereas none of the 14 anti-HBc-positive blood donors was HBsAg positive (p = 0.06).

HBV and HCV seroconversion was not age or sex related in either of the two groups. Thus, the imbalance in sex distribution between the two groups did not interfere with the main study criteria. HBV and HCV seroprevalence specified for the various sexually transmitted diseases are given in Table 6. The highest prevalence of HBV markers was found in patients with syphilis. Of the syphilis-positive patients 67.5% were also positive for HBV compared with 17% (54/316) in the syphilis-negative ones (p<0.001).