SHORT COMMUNICATION

Hepatitis B Virus Exposure in Human Immunodeficiency Virus Seropositive Cuban Patients

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In order to estimate the prevalence of serological markers of exposure to Hepatitis B Virus (HBV), 295 subjects were selected at random from the National Registry of human immunodeficiency virus positive subjects. Evidence of exposure to HBV was defined as: testing Hepatitis B surface antigen (HBsAg) and anti-Hepatitis B core antigen (anti-HBc) positive or anti-HBc positive only. Overall, 133 (45.5%) were positive for anti-HBc and 15 (5.1%) resulted positive to HBsAg. Significant statistical association was found between male sex and exposure to HBV ($p<0.01$). Homosexual or bisexual behavior was found to be strongly associated to HBV exposure ($p<0.001$). In conclusion, the prevalence of HBV serological markers is higher in Cuban HIV positive subjects compared to the Cuban general population.

Key words: Hepatitis B Virus (HBV) - Hepatitis B surface antigen (HBsAg) - anti-Hepatitis B core antigen (HBc)

The pathogenesis of human immunodeficiency virus (HIV) infection suggests that other cofactors are involved in the development of immunodeficiency (Hilleman 1994). Serological, biological and epidemiological evidence suggests that one of these cofactors could be the Hepatitis B virus (HBV) (Twu et al. 1993). The majority of HIV carriers show serological markers of previous exposure to HBV (Hilleman 1994). Also, both viruses affect individuals with similar risk behaviors (i.e. intravenous drug users and persons with many sexual partners). These viruses have similar routes of transmission and both infections induce a wide spectrum of disease in the affected host, from apparently healthy carriers to severe clinical pictures (Twu et al. 1993).

In Cuba, The National Program for HIV Control has detected 1,173 positive individuals (Pérez et al. 1996). Homosexual transmission accounted for 45.7% of all HIV-positive individuals (Pérez et al. 1996). On the other hand, prevalence of Hepatitis B surface antigens (HBsAg) in the Cuban general population has been estimated at 1% (Galban et al. 1992). However, epidemiological data on prevalence of serological markers of HBV exposure in HIV positive Cuban patients have not so far been published. To the author's knowledge these are the first research results covering this information.

In the context of a clinical trial of the Cuban Recombinant Vaccine against HBV in immunosupressed subjects, the sera of 295 positive HIV individuals were chosen at random before vaccination was started. The study sample (295 subjects) represents 25.1% of the National Registry of HIV positive subjects. The final sample included 214 (72.5%) males and 81 (27.5%) females aged 13 to 61 years (mean age, 30 years). Eighty seven patients (29.5%) were less than 26 years old and 208 (70.5%) were between 26 and 61 years of age. One hundred and seventy five (60%) were heterosexual and the remaining 120 (40%) were homosexuals or bisexuals (Table).

Clinical stages of HIV disease-infection were classified according to the Centers for Disease Control and Prevention revised classification of 1987. One hundred and forty three (48.5%) subjects were Stage II (asymptomatic), 44 (15.5%) were Stage III (persistent generalized adenopathies) and 108 (36.5%) were Stage IV (Aids cases, minor and major manifestations).

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TABLE

Prevalence of serologic markers and risk factors analysis of Hepatitis B virus (HBV) exposure in seropositive human immunodeficiency virus (HIV) Cuban patients (n=295)

	Anti-HBc		HBsAg		HBV exposure[a]	
Variable (n)	No. pos.	%	No. pos.	%	Odds Ratio	95% CI
Sex						
male	109	50.9	12	5.6	2.46	1.39-4.46[b]
female	24	29.6	3	3.7		
Age						
13-25 (87)	46	52.9	11	12.6	1.56	0.91-2.66
26-61 (208)	87	41.8	4	1.9		
Sexual behavior						
homo-bisexual (120)	81	67.5	10	8.3	4.88	2.89-8.37[c]
heterosexual (175)	52	29.7	5	2.9		
Clinical stage						
II (143)	70	49.0	4	2.8	0.64	0.45-1.20
III and IV (152)	63	41.4	11	7.2		

a: positive to both serologic markers, anti-HBc and HBsAg; *b*: p<0.01; *c*: p<0.001. HBV: Hepatitis B Virus; HBc: Hepatitis B core antigen; HBsAg: Hepatits B surface antigen.

The following serological methods were used: Vironostika HIV ELISA for the detection of antibodies to HIV in human serum (Organon Teknika); Western blot test (Pasteur Institute) for confirmation of HIV infection; ELISA for the detection of total antibodies to Hepatitis B core antigen (anti-HBc) (Organon Teknika); UltramicroELISA (10 µl UMELISA) for the detection of the HBsAg (Immunoassay Center, Havana, Cuba); Confirmatory UltramicroELISA (10 µl UMELISA) for the confirmation of HBsAg infection (Immunoassay Center, Havana). Serological evidence of exposure to HBV was defined as: testing HBsAg and anti-HBc positive or anti-HBc positive only. Prevalence of each serological marker was calculated as the proportion (percent) of those who tested positive within each group (sex, age group, sexual behavior and clinical stage of HIV infection). Univariate analysis was performed. Odds ratios (and 95% Confidence Intervals) were calculated as a measure of the effect of sexual orientation, sex and age on the likelihood of being infected with HBV. Data were analyzed using EPINFO version 6.03.

Overall, 133 (45.5%) were positive for anti-HBc and 15 (5.1%) resulted positive to HBsAg. All subjects positive to HBsAg were also positive to anti-HBc. Prevalence of both serological markers was found to be higher in men, in the younger group, and in subjects with homosexual or bisexual behavior respectively. Significant statistical association was found between male sex and exposure to HBV (p<0.01). Homosexual or bisexual behavior was found to be strongly associated to HBV exposure (p<0.001). There was not association found between age group (p=0.08), or HIV clinical stage (p=0.1) and HBV exposure.

Similar prevalence of HBV markers in HIV infected individuals has been reported in Poland (Radkowski et al. 1991). Other studies in Europe reported higher prevalence in these individuals (Ockenga et al. 1997, Denis et al. 1997). A recent study in men infected with HIV in Mexico City found a similar prevalence of HBV serological markers to that reported in this paper (Juarez-Figueroa et al. 1997).

It is of interest that the prevalence of HBsAg was higher in the studied sample (5.1%) than that reported in the Cuban general population (Galban 1992), indicating a high level of exposure to HBV in the subjects studied. This difference was accentuated in the group with homosexual or bisexual behavior (8.3%).

We believe that sexual behavior was likely to be a confounder for the association found between male sex and HBV exposure. Thus, the analysis was repeted with the exclusion of homosexual and bisexual subjects (all of them males). This way, no significant association was found (OR=1.01, 95% CI=0.50-2.04).

Male homosexuality has been reported amongst the main risk factors for the coexistence of HIV and HBV infections (Juarez-Figueroa 1997). In Cuba, homoxesuals men constitute 64.5% of all male individuals with HIV/Aids infection (Pérez et al. 1996).

Although no significant statistical association was found between age group and HBV exposure, the high prevalence in the younger group suggests a relatively early and increased exposure to HBV. This reinforces the need for early sexual education and vaccination against HBV. This will ensure that this population is protected before the onset of high risk behaviors and exposure to HBV and HIV infections (Wang et al. 1991). It also stresses the necessity of identifying patients who could benefit from the protection given by vaccination received while they are still immunocompetent. Currently, the Cuban population aged less than 20 years is being covered by a Nationwide Vaccination Program for HBV. According to Radkowski et al. (1991) people with HIV infection and symptoms associated with immunodeficiency have a high prevalence of HBV markers as compared with homologous, non-symptomatic carriers. Their study reasserted the possibility that HBV is a cofactor that influences the clinical development of the infection. By contrast, our results did not showed any difference in prevalence of HBV markers according to clinical stage of HIV infection.

There could be various reasons for the difference in our findings. Contact with HBV could have occurred prior to HIV infection, or the level of exposure does not varied according to HIV clinical stage. It might even be possible that T cell surveillance is sufficient to avoid HBV infection in symptomatic stages of immunodeficiency progression. Sunen et al. (1992) reported that HBV detection in peripheral mononuclear cells is more frequent in the HIV seropositive, but this is not related to the immunodeficiency state.

Another reason for the discrepancies could relate to the fact that some of the patients with advanced clinical stages of HIV/Aids may have died before this study was performed. Poor survival of patients with Aids coinfection with HBV or HCV has been reported (Ockenga et al. 1997).

In conclusion, our results indicate that prevalence of HBV serological markers is high in Cuban HIV positive patients in contrast with the Cuban general population. The study also shows that the relationship between HIV and HBV in the Cuban HIV positive population is similar to that reported worldwide. These data suggest that a personal history of homosexual or bisexual behavior markedly increases the likelihood for HBV infection in Cuban HIV positive patients.

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