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Seroprevalence of Herpes Simplex Virus Type 2 in Adult HIV-Infected Patients and Blood Donors in Croatia

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ABSTRACT

The present study estimates herpes simplex virus type 2 (HSV-2) seroprevalence and evaluates its association with age, sex, human herpesvirus type 8 (HHV-8) and human immunodeficiency virus (HIV) among adults in Croatia. A cross-sectional survey included 166 HIV-infected patients and 219 blood donors. Antibodies against HSV-2 were determined by enzyme immunoassays based on gG2 recombinant glycoprotein. HSV-2 seroprevalence was 45.8% in HIV-infected patients and 8.7% in blood donors ($p < 0.0001$; OR 8.8; 95% CI 5.05–15.49). Independent predictors of HSV-2 seropositivity were HIV infection (OR 11.0; 95% CI 5.93–20.41), female gender (OR 2.28; 95% CI 1.22–4.26), older age (OR 3.93; 95% CI 2.74–7.11), and HHV-8 seropositivity (OR 2.72; 95% CI 1.09–6.75). Understanding the epidemiology of HSV-2 is a critical first step in designing interventions to decrease HSV-2 and HIV transmission. The association of HSV-2 with HIV infection and HHV-8 antibodies suggests a similar transmission route.

Key words: HSV-2, Croatia, HIV, blood donors, HHV-8, seroprevalence

Introduction

Herpes simplex virus type 2 (HSV-2) is one of the most common causes of genital ulceration^{1–3}. Genital herpes is a lifelong incurable infection that causes medical, psychological and social concerns. There is a synergistic interaction between HSV-2 and HIV^{1–4}. HSV-2 increases risk of HIV acquisition and transmission while HIV increases clinical and subclinical HSV-2 reactivation⁴. Further, HSV-2 reactivation increases HIV viral load in secretions obtained from genital herpes lesions as well as in plasma^{1–4}. Accurate type specific HSV serological methods facilitate HSV diagnostics, and allow a better understanding of the burden of infection^{3,4}. The prevalence of HSV-2 varies in different populations^{5–10}. HSV-2 antibodies are found more frequently at older age, in females, in populations with risky sexual behaviour and in HIV-infected patients^{1–10}.

Human herpesvirus type 8 (HHV-8) seems to share similar transmission routes as HSV-2, and shows various prevalences in different populations^{11,12}. Low prevalence of HIV infection in Croatia has been reported so far^{13,14}.

The seroprevalence of herpes simplex virus type 2 (HSV-2) antibodies in adults in Croatia has as yet not been described. The aim of the present study is to report the HSV-2 antibody prevalence in adult HIV-infected patients compared to blood donors.

Methods

Study population

A cross-sectional study was conducted at the University Hospital for Infectious Diseases, Zagreb, Croatia between May 1999 and August 2001. The study included 385 participants: 166 HIV-infected patients and 219 blood donors. Age and gender was reported in all subjects as well as the risk groups in HIV-infected patients.

Serological testing

We analyzed serum samples for antibodies against HSV-2 and HHV-8. All sera were frozen and stored at

–20 °C till testing. Antibodies to HSV-2 were determined by enzyme-linked immunosorbent assays (ELISA) based on gG2 recombinant HSV-2 specific glycoprotein (ETI-HSVK-G 2, DiaSorin, Italy). Equivocal HSV-2 EIA results led to confirmatory immunoblot (HerpesSelect 1 and 2 Immunoblot IgG, Focus, USA). HHV-8 antibodies were analyzed with commercially available ELISA (HHV-8 IgG Antibody, ABI, Columbia, USA). All tests were performed and interpreted according to the manufacturer’s guidelines.

Statistical analysis

Bivariate associations were evaluated by odds ratio (OR) and corresponding 95% confidence intervals (CI). The association of gender, age (dichotomized at 40 years), and HIV and HHV-8 status with HSV-2 seropositivity was examined in a multivariable logistic regression model. Statistical analysis was performed with STATA software version 8.0.

Results

HSV-2 antibodies were analyzed in 166 HIV-infected patients (males, 74.1%) and 219 blood donors (males, 79.0%). The median age for both study groups was 39 years (ranges 19–74 for HIV-infected patients and 18–64 for blood donors). Seventy-three (44.0%) HIV-infected patients and 116 (53.0%) blood donors were older than 40 years.

The seroprevalence of HSV-2 was 45.8% in HIV-infected patients and 8.7% in blood donors ($p < 0.0001$; OR 8.84; 95% CI 5.05–15.49). Among HIV-infected patients and blood donors older than 40 years HSV-2 seroprevalence was 61.6% and 13.9% respectively ($p < 0.001$; OR 9.94; 95% CI 4.89–20.18). Among subjects younger than 40 years 33.3% HIV-infected patients and 2.9% blood donors had HSV-2 antibodies ($p < 0.001$; OR 16.67; 95% CI 4.89–56.83). We found HSV-2 antibodies in 43.9% male and 51.2% female HIV-infected patients ($p = 0.48$), and 7.5% male and 13.0% female blood donors ($p = 0.25$). Among HIV-infected men who had sex with men (MSM)

HSV-2 seroprevalence was similar to other risk groups (52.1% in MSM vs. 43.2% in non-MSM; $p = 0.31$). The data on HHV-8 has been previously reported (12). Briefly, the seroprevalence of HHV-8 was 13.3% (22 of 166 subjects) in HIV-infected patients and 4.1% (9 of 219 subjects) in blood donors¹².

In our analysis HSV-2-antibodies were associated with HIV-infection, female gender, older age and HHV-8 seropositivity (Table 1).

Discussion

We found that HSV-2 antibodies were more common in HIV-infected patients than in blood donors. HSV-2 seroprevalence of 45.8% in HIV-infected patients was similar to one found in Germany, but lower than in Coventry, United Kingdom^{8,9}. Higher HSV-2 seroprevalence rates in HIV-infected patients have been reported from Africa (up to 90%) or in clinics where many HIV patients of African origin are treated^{9,10}. HSV-2 seroprevalence in Croatian blood donors (8.7%) was similar to the 4 to 24% range reported by Peabody et al. in the general population of different European countries⁵. However, direct comparison of seroprevalence studies is difficult because study populations varied and different serological tests were used.

HSV-2 antibody status is stated as a surrogate marker of sexual behaviour. This could explain the higher seroprevalence rate in older age. Women generally had a higher HSV-2 seroprevalence compared to men^{1–10}. In our study females were 2.33 more likely to have HSV-2 antibodies than males on multivariable analysis. Peabody et al.^{3,5} reported that women were 1.26 to 1.64 more likely to have HSV-2 antibodies than men in different European countries.

There is epidemiological and biological evidence of an interaction between HSV-2 and HIV^{1–4}. The HIV infectiousness is increased in persons coinfecting with HSV-2. HSV-2 reactivation and shedding are more frequent among those with higher HIV plasma viral load and lower CD4⁺ T-cells count. HSV-2 increases HIV susceptibility by pro-

TABLE 1
FACTORS ASSOCIATED WITH THE PRESENCE OF HSV-2 ANTIBODIES AMONG 385 CROATIAN ADULTS:
166 HIV-INFECTED PATIENTS AND 219 BLOOD DONORS

| | Univariable (OR; 95% CI) | p value | Multivariable* (OR; 95% CI) | p value |
|----------------------------------|-----------------------------|---------|--------------------------------|---------|
| HIV infection (yes vs. no) | 8.84 (5.05–15.49) | <0.0001 | 11.00 (6.92–20.41) | <0.0001 |
| HHV-8 antibodies (yes vs. no) | 4.28 (2.02–9.07) | <0.0001 | 2.72 (1.09–6.75) | 0.031 |
| Gender (male vs. female) | 0.64 (0.38–1.08) | 0.09 | 0.43 (0.23–0.82) | 0.01 |
| Age (>40 vs. ≤40 years) | 2.29 (1.47–3.70) | 0.001 | 3.93 (2.17–7.11) | <0.0001 |

OR – odds ratio; CI – confidence interval

* The odds ratio for each variable was adjusted for all other variables in the table

viding a portal of entry, at which more activated CD4⁺ T-cells as the target for HIV can be found²⁻⁴. Recognition, diagnostics and treatment of genital herpes might prevent transmission of HIV¹⁻⁴.

HSV-2 is a well known sexually transmitted agent that is related with HHV-8, and vice versa¹¹. HSV-2 and HHV-8 might share similar acquisition modes, although the exact routes of HHV-8 transmission are still controversial^{11,12}. Mediterranean countries such as Croatia were labelled as areas with high HHV-8 prevalence¹¹, but we found that the seroprevalence of HHV-8 in our country was low (4.1% in blood donors and 13.3% in HIV-infected patients)¹².

Limitations of our study should be noted. We used a convenience sample; however, we studied 166 out of around 300 HIV-infected patients registered in Croatia from 1985 till 2001^{13,14}. Our subjects demographically resembled the HIV population in Croatia (13,14). Hence, our results might be generalized for the HIV-infected population in Croatia.

In conclusion, we found a relatively high HSV-2 seroprevalence in HIV-infected patients. HIV infection was the strongest predictor of HSV-2 seropositivity. Other factors associated with HSV-2 seroprevalence were age more than 40 years, female gender and HHV-8 seropositivity.

REFERENCES

1. WALD A, LINK K, *J Infect Dis*, 185 (2002) 45. — 2. PALU G, BENNETTI L, CALISTRI A, *Herpes*, 8 (2001) 50. — 3. WALD A, *Herpes*, 11 Suppl 3 (2004) 130A. — 4. CELUM C.L, *Herpes*, 11 Suppl 1 (2004) 36A. — 5. PEBODY RG, ANDREWS N, BROWN D, GOPAL R, DE MELKER H, FRANCOIS G, GATCHEVA N, HELLENBRAND W, JOKINEN S, KLAVS I, KOJOUHAROVA M, KORTBEEK T, KRIZ B, PROSENC K, ROUBALOVA K, TEOCHAROV P, THIERFELDER W, VALLE M, VAN DAMME P, VRANCKX R, *Sex Transm Infect*, 80 (2004) 185. — 6. SMITH SJ, ROBINSON J, *J Infect Dis*, 186 Suppl 1 (2002) S3. — 7. VAN BENTHEM BHB, SPAARGAREN J, VAN DEN HOEK JA R, MERKS J, COUTINHO RA, PRINS M, *Sex Transm Infect*, 77 (2001) 120. — 8. WUTZLER P, DOERR HW, FARBER I, EICHHORN U, HELBIG B, SAUERBREI A, BRANDSTADT A, RABENAU HF, *J Med Virol*, 61 (2000) 201. — 9. ALLAN PS, DAS S, *Sex Transm Infect*, 80 (2004) 77. — 10. WEISS H, *Herpes*, 11 Suppl 1 (2004) 24A. — 11. CATTANI P, CERIMELE F, PORTA D, GRAFFEO R, RANNO S, MARCHETTI S, RICCI R, CAPODICASA N, FUGA L, AMICO R, CHERCHI G, GAZZILLI M, ZANETTI S, FADDA G, *Clin Microbiol Infect*, 9 (2003) 274. — 12. RODE ĐAKOVIĆ O, LEPEJ ZIDOVEC S, BEGOVAC J, *Clin Infect Dis*, 40 (2005) 1208. — 13. BEGOVAC J, ZEKAN Š, SKOKO-POLJAK D, *Coll Antropol*, 30 Suppl 2 (2006) 17. — 14. MARGAN GJENERO I, KOLARIĆ B, *Coll Antropol*, 30 Suppl 2 (2006) 11.

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SEROPREVALENCIJA VIRUSA HERPES SIMPLEX TIP 2 U ODRASLIH OSOBA ZARAŽENIH HIV-OM I DOBROVOLJNIH DAROVATELJA KRV I U HRVATSKOJ

SAŽETAK

Prikazani su rezultati istraživanja seroprevalencije virusa herpes simplex tipa 2 (HSV-2) u odraslih osoba u Hrvatskoj te povezanost HSV-2 s dobi, spolom, humanim herpesvirusom tipa 8 (HHV-8) i virusom humane imunodeficijencije (HIV). U presječnu studiju je uključeno 166 HIV-inficiranih pacijenata i 219 dobrovoljnih darovatelja krvi. Protutijela na HSV-2 su određena imunoenzimskim testom koji se temeljio na gG2 rekombinantnim glikoproteinima. Seroprevalencija HSV-2 u HIV-inficiranih pacijenata bila je 45,8%, a u dobrovoljnih darovatelja krvi 8,7% (p<0.0001; OR 8,8; 95% CI 5,05–15,49). Nezavisni prediktori za HSV-2 bili su HIV-infekcija (OR 11,0; 95% CI 5,93–20,41), ženski spol (OR 2,28; 95% CI 1,22–4,26), starija dob (OR 3,93; 95% CI 2,74–7,11) i seropozitivnost HHV-8 (OR 2,72; 95% CI 1,09–6,75). Poznavanje epidemiologije HSV-2 je prvi korak u kreiranju mjera za smanjivanje prijenosa HSV-2 i HIV-a. Povezanost HSV-2 s HIV-infekcijom i protutijelima na HHV-8 upućuje na sličan put prijenosa.