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Herpes simplex virus type 2 seroprevalence and incidence in acute and chronic HIV-1 infection

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Summary

Herpes simplex virus type 2 (HSV-2) HIV co-infection is common and associated with increased risk of HIV transmission. HSV-2 seroprevalence was assessed on stored samples from baseline and one year follow-up from 81 patients identified with acute HIV infection and 81 age-matched chronically infected men. HSV-2 seroprevalence at baseline was lower for those with acute rather than chronic HIV-infection, 51.9 versus 71.6% ($P = 0.01$); relative risk 0.72 (95% confidence interval [CI] 0.57–0.92). Since HSV-2 seroprevalence is lower in those newly HIV-infected, the diagnosis of early HIV infection may allow for counselling to reduce subsequent HSV-2 acquisition.

Keywords

herpes simplex virus type 2; HSV-2; seroprevalence; acute HIV infection; chronic HIV infection

INTRODUCTION

HSV-2 infection is often more common in those with HIV type 1 (HIV-1) infection (60–80%) than those HIV-1-uninfected, and is associated with HIV-1 transmission.^{1–4} It is not known whether the increased HSV-2 infection rate is present before or after HIV-1 seroconversion; thus, we compared the seroprevalence and incidence of HSV-2 in those with chronic and acute HIV-1 infection. This information could determine whether identification of those with early HIV-1 infection provides an opportunity for a behavioural intervention to reduce exposure to HSV-2.

METHODS

Chronically HIV-1-infected individuals were men who had sex with men (MSM) enrolled from two urban HIV clinics in Los Angeles and Long Beach, California, USA (2004–2006).⁵ Acutely HIV-1-infected patients were enrolled in Los Angeles (1997–2005), all of whom were MSM except for one woman with sexually acquired HIV-1.⁶ The current study

identified 81 patients from each cohort with at least one year of follow-up and pair-matched within two years of age at enrolment. The study was approved by local Institutional Review Boards and informed written consent obtained.

Sera from baseline and after one year of follow-up were tested for HSV-2 antibodies (HerpeSelect2 enzyme linked immunosorbent assay [ELISA] IgG, Focus Diagnostics, Cypress, CA, USA) with scoring of results as recommended by manufacturer. Acutely and chronically HIV-1-infected subjects were compared for baseline mean age, CD4 cell count and plasma HIV-1 RNA with paired *t*-test and for ethnic proportions with Mantel-Haenszel-matched acute-chronic pair stratified chi-square test. Potential predictors of HSV-2 seropositivity were assessed using generalized estimating equations to account for acute-chronic HIV pair matching. A log link function was used to express group differences with relative risks (RR) of HSV-2 seropositivity.

RESULTS

Mean age (standard deviation) at enrolment in both groups was 38 (7.2) years with the majority of acutely HIV-1-infected patients Caucasian (76.5%) and chronically infected Hispanic (67.9%). Baseline HSV-2 seroprevalence among the acutely and chronically HIV-1-infected patients was 51.9% and 71.6%, respectively ($P = 0.01$), a RR of 0.72, 95% confidence interval (CI) 0.57–0.92. Results were minimally changed when adjusting for age, baseline CD4 cell count or plasma HIV-1 RNA. When adjusting for ethnicity the RR was minimally changed (0.74) but CIs widened (0.52–1.07) and results were no longer significant ($P = 0.11$) (Table 1). In addition, HSV-2 antibodies were more common among those that were older in age ($P = 0.002$). Incident HSV-2 infection occurred in two acutely and three chronically HIV-1-infected patients for incidence rates of 5.2 and 12.6 per 100-person years of follow-up, respectively ($P = 0.34$).

DISCUSSION

HSV-2 seropositivity has been associated with significantly higher risk for acquiring HIV-1 infection.⁷ Previous studies have shown higher seroprevalence of HSV-2 in those with than without HIV-1 infection, but less is known about whether these shifts in HSV-2 prevalence occur before or after HIV-1 acquisition. The current study addressed this question by assessing HSV-2 seroprevalence as well as incidence among aged-matched patients with acute and chronic HIV-1 infection. We found that HSV-2 seroprevalence was significantly higher among those with chronic infection, independent of other covariates.

Although this is the first study to directly compare HSV-2 seroprevalence between acutely and chronically HIV-1-infected individuals, others have made this assessment in each of these groups in isolation. In fact, the HSV-2 seroprevalence in our acute HIV-1 infection cohort is concordant with the 41.5% seen in a cohort from San Diego.⁸ An Australian study of MSM attending inner city primary care clinics showed a HSV-2 seroprevalence of 60.9% in chronically HIV-1-infected compared with 27.8% of HIV-uninfected MSM.²

While cross study comparisons are limited, these studies along with ours suggest that the seroprevalence to HSV-2 in MSM is higher in those HIV-1-infected than uninfected. Our

data further show that HSV-2 infection is more common in those with chronic than acute HIV-1 infection. Not surprisingly, patient age has been shown to be an important predictor of HSV-2 infection and could in part account for these trends.^{1,9} We accounted for this covariate by age matching and adjusting for age in the models.

Incident cases of HSV-2 infection occurred in only five patients after one year of follow-up, a relatively low number that is consistent with another study of adults with newly diagnosed HIV-1 infection.¹ Together, these types of data could inform future recommendations regarding the potential role of serological screening for HSV-2 in HIV-1-infected patients.¹⁰

Limitations of the current study include the fact that the sample size was relatively small, a necessity when studying subjects with acute HIV-1 infection. In addition, the baseline characteristic between groups did differ, in particular, by ethnicity. While previous studies have noted higher HSV-2 seroprevalence in ethnic minorities,^{1,9} the RR was minimally changed after adjusting for this covariate, although results were no longer significant. It was also not possible to quantify level of past sexual activity in the groups and the results cannot necessarily be extrapolated to at-risk groups other than MSM. Finally, results were all derived from a highly sensitive and specific HSV-2 ELISA,¹¹ but without confirmation by other assays.

To our knowledge, this is the first study to directly compare seroprevalence and incidence of HSV-2 in newly and chronically HIV-1-infected individuals. Despite the limitations of this type of study, the finding that HSV-2 seroprevalence was significantly lower among those with newly acquired HIV-1 infection does provide preliminary insight into the dynamics of HSV-2 and HIV-1 infection. Moreover, these results support the potential importance of identifying those with early HIV-1 infection and counselling them about continued safe-sex practices.

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Table 1

RR for HSV-2 seroprevalence in those with acute versus chronic HIV infection

Adjusted for	RR (95% CI)	Pvalue
No adjustment	0.72 (0.57–0.92)	0.01
Age	0.74 (0.58–0.93)	0.01
Ethnicity	0.74 (0.52–1.07)	0.11
Baseline CD4 ⁺ T-cells	0.73 (0.57–0.94)	0.01
Baseline HIV RNA	0.70 (0.52–0.94)	0.02

RR, relative risk; HSV-2, Herpes simplex virus type 2; CI, confidence interval; HIV, human immunodeficiency virus