Associations between herpes simplex virus type-2 (HSV-2) and bacterial vaginosis (BV) in a cohort of HIV-1 infected women in Burkina Faso

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Background

•Bacterial vaginosis (BV) has been identified as a risk factor for both acquisition of herpes simplex virus type-2 (HSV-2) and increased genital shedding of HSV-2 DNA in HSV-2 seropositive women.[1,2] HSV-2 seropositivity has also been identified as a risk factor for BV acquisition.[3]

•The associations between BV and HSV-2 are important in light of the high prevalence of both of these infections in African women, and their observed associations with HIV-1.[4,5,6]

Objectives

• To examine the temporal associations between BV and HSV-2 DNA genital shedding among a cohort of HIV and HSV-2 seropositive women not taking antiretroviral therapy.

• To assess the effect of treatment for BV on HSV-2.

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Methods

• Data were acquired from a randomised placebo-controlled trial investigating the effect of HSV suppressive therapy on HIV-1 RNA levels in women dually infected with HIV-1 and HSV-2 in Bobo-Dioulasso, Burkina Faso.[7]

• Women attended 6 bi-weekly visits (baseline phase) before being randomised to receive either valaciclovir 500mg twice daily or matching placebo and then attending a further 6 follow-up visits (impact phase).

• At each study visit, genital samples were collected including swabs for the diagnosis of vaginal infections and an enriched cervico-vaginal lavage for the detection and quantitation of genital HIV-1 RNA and HSV-2 DNA.

• Temporal associations between BV and HSV-2 DNA genital shedding, and the effect of metronidazole (MTZ, prescribed as treatment for symptomatic BV) on HSV-2 were investigated among women randomised to the placebo arm of the trial only.

• The effect of valaciclovir (VCV) on BV was investigated among women randomised to both placebo and treatment arms.

Results

• 68 women were randomised to each arm of the trial. BV and genital HSV-2 DNA were detected among women in the placebo arm at 222/774 **(29.1%)** and 116/761 **(15.2%)** visits, respectively.

•Detectable HSV-2 DNA was associated with the presence of BV in both univariable (OR 1.58, 95% CI: 1.13-2.21) and multivariable analyses (OR 1.66, 95% CI: 1.18-2.34).

• BV was more likely to occur when genital HSV-2 DNA was detected at the previous study visit (OR 1.35, 95% CI: 0.88-2.07). Similarly, there was some evidence that genital HSV-2 DNA detection was associated with BV occurrence at the previous study visit (OR 1.40, 95% CI: 0.87-2.25).

Results (continued)

• There was no overall effect of treatment with MTZ on HSV-2 (placebo arm analysis; OR 1.03, 95% CI 0.65-1.62) nor of treatment with VCV on BV (treatment vs placebo arms analysis; OR 0.86, 95% CI 0.58-1.28).

• However, among women with detectable HSV-2 DNA during baseline, those receiving VCV were significantly less likely to have BV than those on placebo. In contrast, there was no significant effect of MTZ on HSV-2 among women who had detectable BV at previous study visit (Table).

Table: Effect of treatment for BV or HSV-2 on the alternate outcome

Detection of:	OR (95% CI)	p value for interaction
BV among women with genital HSV-2 at least once during baseline [*VCV vs placebo arms analysis*]	**0.46 (0.27 – 0.78)**	**0.005**
BV among women with no genital HSV-2 during baseline [*VCV vs placebo arms analysis*]	1.30 (0.79 - 2.16)	
HSV-2 among women with BV at previous study visit [*MTZ, placebo arm analysis*]	0.75 (0.34 - 1.66)	0.26
HSV-2 among women without BV at previous study visit [*MTZ, placebo arm analysis*]	1.19 (0.67 – 2.10)	

Summary of findings

• Previous studies have suggested that HSV-2 seropositivity is a risk factor for BV.[3, 8,9] We have found that HSV-2 DNA genital shedding was also associated with BV.

• Our results do not clearly demonstrate the nature of the temporal or causal association between BV and HSV-2. Both infections seemed to increase the detection of the other at the next study visit, although the results did not reach statistical significance, and we found no overall effects of treatment for one infection on the other.

•However, the significant impact of VCV in reducing BV occurrence among women who had detectable genital HSV-2 DNA at least once during the baseline phase may suggest a causal relationship. HSV-2 has been described as inducing profound immunological changes in the female genital tract[10] and it is plausible that this may disrupt the normal vaginal flora in some way.

Conclusion

Genital HSV-2 shedding may trigger changes in the vaginal flora leading to BV in HIV/HSV-2 co-infected women.

References
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The original trial was funded by the Agence Nationale de Recherches sur le SIDA (ANRS), France, with additional support from the UK's Department for International Development (DFID) funded Research Programme Consortium (RPC) on Sexual & Reproductive Health and HIV of the LSHTM. The views expressed do not necessarily represent those of DFID.

Programme for Research & Capacity Building on Sexual & Reproductive Health & HIV in Developing Countries