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Impact of acyclovir on ulcer healing and HIV-1 lesional and genital shedding among patients with genital ulcer disease in Malawi: a randomized controlled trial

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Background: Herpes simplex virus type-2 (HSV-2) is the predominant cause of genital ulcer disease (GUD) worldwide, and has synergistic relationships with HIV-1. HSV-2 control strategies for HIV prevention are urgently required.

Methods: A randomised double-blind placebo-controlled trial of acyclovir 800mg BID for five days was conducted at Kamuzu Central Hospital STI clinic in Lilongwe, Malawi. Patients presenting with GUD received syndromic management plus either acyclovir or placebo. At enrolment, we determined serostatus of HIV-1, HSV-2, and syphilis, and HIV-1 plasma viral load and CD4 count in HIV-1 seropositive patients. GUD aetiology was determined from lesional swabs by real-time multiplex PCR. Ulcer characteristics were recorded at days 0, 7, 14 and 28. Ulcer and cervical swabs or semen were collected from HIV-1 positive participants to detect HIV-1 RNA. Regression models were used to assess the impact of acyclovir on genital ulcer healing, the presence and quantity of lesions and plasma HIV-1 RNA. Primary endpoint was Day 14.

Results: 422 GUD consenting patients (74% male) were enrolled. Overall, 60.9%, 71.7% and 5.0% had antibodies to HIV-1, HSV-2 and T. pallidum respectively. The median CD4+ count was 233 cells/µL, and mean plasma HIV-1 RNA was 4.80 log10copies/mL. Most ulcers were due to HSV-2 (67.1%). Overall 85% of ulcers were healed at Day 14 and this was similar among those on acyclovir or placebo RR=1.02, 95%CI 0.93-1.15. Among HIV-1/HSV-2 dually seropositive patients, acyclovir was associated with reduced detection of lesional and seminal HIV-1 RNA (lesional: adjusted RR=0.60, 95%CI 0.34-1.03; seminal: RR=0.58, 95%CI 0.39-0.89). There was no impact of acyclovir on detection of cervical HIV-1, nor on plasma HIV-1 RNA at Day 28.

Conclusions: Adding acyclovir to syndromic management had little impact on ulcer healing rates, but reduced detection of lesional and seminal HIV-1 RNA. This suggests that herpes therapy may reduce genital HIV-1 transmission.

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