Natural control of HIV infection in a cohort of young women in South Africa: HPTN 068

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BACKGROUND

HIV controllers are able to suppress viral replication to low or undetectable levels without antiretroviral therapy (ART). Natural control of HIV infection is often characterized normally in younger women, with normal levels of immune activity, and slower progression to AIDS. The degree of viral suppression and duration of viremic control are often used to classify individuals as virologic or elite controllers. Differences in viral genetics, host genetics, hormonal, or adaptive immune responses have been associated with natural control of HIV infection.

The HPTN 068 Trial was conducted in a rural area in South Africa and evaluated the impact on HIV incidence of a cash transfer conditional on high school attendance. The study enrolled 81 HIV-infected and 2,448 HIV-uninfected young women who were followed annually until their expected graduation date; some women had a post-graduation follow-up visit 1-2 years later. We evaluated the frequency of HIV controllers in this cohort.

RESULTS

Figure 1. Identification of viremic controllers.

Figure 2. HIV viral load (Panel A) and CD4 cell count (Panel B) results for the 12 virologic controllers.

STATISTICAL ANALYSIS

HIV controllers were defined as:

- Viral load <40 copies/mL (elite controller) or <2,000 copies/mL (viremic controllers) at the first HIV-positive visit and at annual study visits (for at least 12 months)
- ARV drugs detected at the first visit

Statistical analysis was performed using SAS 9.4 software. Associations between viral control and participant characteristics were examined using Wilcoxon rank sum tests.

ETHICAL CONSIDERATIONS

Study participants and their parents/guardians provided written consent for participation in the HPTN 068 study. Written assent was obtained for participants younger than 18 years.

In HPTN 068, 245 women had HIV infection; 81 were HIV-infected at enrollment and 164 acquired HIV infection during the study (Figure 1). ARV drug testing was performed for 242 women. ARV drugs were detected at those visits in 20 (10.7%) women; those women were excluded from further analysis. Thirty-four (15.7%) of the remaining 216 women had a viral load <2,000 copies/mL at their first HIV-positive visit, including 3 with a viral load <40 copies/mL. The median viral load was 492 copies/mL (range: 40-1,479).

Fifteen (44.1%) of the 34 women who had an initial viral load <2,000 copies/mL were followed for at least 12 months (median follow-up period: 23 months; range: 13-51 months).

Twelve participants had sustained viral suppression (viral load <2,000 copies/mL for at least 12 months; median follow-up period: 20 months; range: 13-42; one woman had a single viral “blip” of 2,693 copies/mL during the study period; Figure 2).

None of the 12 women had a sustained viral load <40 copies/mL. ARV drugs were not detected in any samples collected during follow-up in these 12 women. These 12 women were classified as virologic controllers.

CONCLUSIONS

- Thirty-four (15.7%) of 216 young women in this cohort from rural South Africa were virologic controllers, including 5/12 virologic controllers. HIV subtyping was performed using pol region sequences; 200 women had subtype C infection, one had subtype A infection. All five virologic controllers had subtype C infection; the HIV drug resistance mutation, Y181C, was detected in HIV from one virologic controller.

HIV genotyping results were obtained for 201 (82%) of the 245 women at their HIV-positive visit, including 5/12 virologic controllers. HIV subtyping was performed using pol region sequences; 200 women had subtype C infection, one had subtype A infection. All five virologic controllers had subtype C infection; the HIV drug resistance mutation, Y181C, was detected in HIV from one virologic controller.

METHODS

STUDY COHORT

Samples were obtained from HIV-infected women aged 13-24 years who were enrolled HPTN 068 (2011-2015).

LABORATORY TESTING

The following tests were performed:
- HIV testing at enrollment and annual follow-up visits
- CD4 cell count and HIV viral load testing at the first HIV-positive visit and visit follow-ups (RealTime HIV-1 Viral Load assay; limit of detection: 40 copies/mL)
- ARV drug testing at the first HIV-positive visit and follow-up visits (using a qualitative assay that detects 20 ARV drugs in five drug classes)
- Genotyping at the first HIV-positive visit (ViroSeq HIV-1 Genotyping assay v2.8)

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