Abstract

Plasma HIV-1 RNA set point is an important predictor of HIV-1 disease progression. We hypothesized that inoculum size and HIV-1 exposure prior to HIV-1 transmission may modulate set point. We evaluated predictors of set point among 141 African HIV-1 seroconverters and their HIV-1-infected study partners. We compared characteristics of seroconverters and their HIV-1-infected partners and HIV-1 set point. Data were from a clinical trial of genital HSV-2 suppression with acyclovir to reduce HIV-1 transmission in HIV-1 serodiscordant couples with HIV-1 transmission linkage assigned through virus sequencing. Our analysis includes data from all transmissions including those with transmission linkage to the HIV-1-infected "source partner" and those that were not linked to their HIV-1-infected study partner. In multivariable analysis, higher plasma HIV-1 in source partners was associated with higher seroconverter set point (+ 0.44 log10 copies/ml per log(10) source partner plasma HIV-1, $p < 0.001$). In addition, bacterial vaginosis (BV) among female source partners near the time of infection was associated with higher set point in their male seroconverters (+ 0.49 log(10), $p = 0.04$). Source partner characteristics associated with lower set point included male circumcision (- 0.63 log(10), $p = 0.03$) and assignment to acyclovir (- 0.44 log10, $p = 0.02$). The proportion of variation in set point explained by plasma HIV-1 RNA of the source partner, after controlling for other factors, was 0.06. Source partner plasma HIV-1 level is the most significant predictor of seroconverter set point, possibly reflecting characteristics of the transmitted virus. Acyclovir use, BV among women source partners, and circumcision among male source partners may alter the set point by affecting transmitted virus inoculum in the source partners' genital compartment.