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Effect of Endo/Exogenous Female Sex Hormones on HIV-1C Latent Reservoir Reactivation

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ABSTRACT

Background: Combination antiretroviral therapy (cART) effectively suppresses viremia but is not curative due to the latent viral reservoir found in long lived cells. A previous study identified ESR-1 as a key regulator of HIV-1 subtype B latency. However, its effects on other subtypes remain unknown. We therefore aimed to determine the effect of female sex hormone levels on the reservoir size and reactivation potential in women living with HIV (WLHIV) on suppressive cART in South Africa.

Methods: The study participants were divided into two groups, namely participants who started treatment during acute infection and participants who started treatment during chronic infection. RNA was extracted from CD4+ T cells, DNase treated and used to synthesize cDNA. Qualitative real-time PCR was performed to quantify ESR-1 mRNA expression levels. Plasma hormone levels were determined for E2, progesterone (P), follicle stimulating hormone (FSH), luteinizing hormone (LH) and testosterone (T) using Enzyme Linked Immunosorbent Assay (ELISA). The inducible viral reservoir was determined using Tat/rev Induced Limiting Dilution Assay (TILDA) by isolating CD4+ T cells, stimulating overnight and plating in a limiting dilution then performing reverse transcription qPCR.

Results: Slightly higher ESR-1 mRNA expression was observed at 1-year post infection compared to early infection and 2 years post successful cART. Hormone levels remained the same longitudinally, apart from LH and E2. The median LH levels were higher at seronegative than early infection (p=0.0035) and higher at 2 years post successful cART than in early infection and (p=0.0081). Median E2 levels were higher during early infection than at 1-year post infection (p=0.0434). LH levels correlated positively with CD4+ T cell counts during early infection for both early and late treated participants and were r=0.7151 p=0.0134 and r=0.7554 p=0.0302 respectively. The reservoir has been quantified in 19 individuals; our data shows that women have a higher inducible reservoir than men. However, these data cannot be shown because the manuscript is under review.

Conclusion: These data suggest that all studied hormones except for LH and E2 are unchanged over time and have no effect on the reservoir size.

Keywords: Combination antiretroviral therapy, ESR-1, mRNA, Reverse transcription, Tat/rev Induced Limiting Dilution Assay

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