Bone Mineral Density in a Cohort of Young Adult Women Using Depo-Provera and Tenofovir, Kampala, Uganda

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PhD Thesis Abstract

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Antiretroviral therapy (ART) initiation with tenofovir disoproxil fumarate (TDF) leads to bone loss with greatest declines occurring within the first two years of use. Among women of reproductive age, the three-monthly contraceptive, intra-muscular depot medroxyprogesterone acetate (DMPA-IM, Depo Provera) also negatively impacts bone mineral density (BMD). To date, no studies have examined the combined impact of both in women living with HIV (WLWH). To address this gap, we evaluated the combined effect of DMPA-IM and TDF on BMD in a two-year follow-up study among young Ugandan women aged 18 to 35 years. Women were recruited from health facilities around Kampala, Uganda between March 2015 and October 2017. They were classified into four groups based on their combination of HIV status, TDF use, and DMPA-IM use: i) WLWH using DMPA-IM and initiating TDF-containing ART (HIV+/IM-DMPA+/TDF+), ii) WLWH initiating TDF without DMPA-IM (HIV+/IM-DMPA-/TDF+), iii) WLWH using DMPA-IM not eligible for ART per local guidelines at the time of enrollment (HIV+/IM-DMPA+/TDF-), and iv) controls not using DMPA-IM (HIV-/IM-DMPA-/TDF-). BMD of lumbar spine (LS), total hip (TH) and femoral neck (FN) were measured using DXA at enrollment and at 6-monthly intervals thereafter. The primary outcome was percent (%) change from baseline in lumbar spine (LS), total hip (TH), and femoral neck (FN) BMD. BMD was measured at baseline, 6, 12, 18 and 24 months using dual energy x-ray absorptiometry. In addition, we conducted a review of published data synthesizing the current state of knowledge on bone health and HIV in resource limited settings (RLS) paying special attention to young women of reproductive age group. The review revealed important gaps in knowledge in bone health in RLS. There were very few studies of bone health in WLWH in RLS, the majority of which were cross-sectional in nature. No studies were found on the effect of TDF-containing ART initiation on BMD, nor on BMD among WLWH on DMPA-IM for contraception. In the prospective cohort, we enrolled 265 WLWH initiating ART (159 DMPA-IM users, 106 non-hormonal contraceptive users), 187 WLWH using DMPA-IM but not eligible for ART, and 69 controls without HIV. We assessed the association between HIV and/or baseline DMPA-IM and baseline BMD for this cohort. The mean age was 26.1 years (SD, 4.2) with a median duration of DMPA-IM use among current users of 24.0 months (12, 48). A higher proportion of previous (12.7%) or current DMPA-IM users (20.3%) and non-hormonal users living with HIV (15.0%) had low BMD (Z-score ≤ −2 at any of the three sites) compared with age-

matched control without HIV (2.9%). From the longitudinal analysis, there were significant declines in BMD from baseline in WLWH on TDF with or without DMPA-IM at the LS (-3.4% vs. -1.1%), TH (-3.9% vs. -1.7%), and FN (-4.4% vs -2.0%), p<0.001, while significant gains (1.5% at LS) and non-significant declines (-0.1% at TH and FN) were observed among controls. Concurrent use of TDF and DMPA-IM resulted in significantly greater % BMD declines (p<0.001) than TDF alone (LS (-2.7% (-3.7, -1.6)), TH (-2.5% (-3.6, -1.5)) and FN (-2.9% (-4.1, -1.7)) or controls (LS (-5.0% (-6.4, -3.6)), TH (-4.2% (-5.6, -2.7)), and FN% (-4.8 (-6.4, -3.1)). In summary, HIV-infection and DMPA-IM use were independently associated with significantly lower mean BMD Z-scores at all sites, with the greatest difference being among current DMPA-IM users living with HIV (5.6%-8.0%) versus non-hormonal controls without HIV. Concomitant DMPA-IM use was associated with a doubling of bone loss in WLWH initiating TDF-containing ART. Identification and use of safer contraceptive and bone-sparing ART options should be prioritized for the optimal care of WLWH.