Tenofovir use is associated with an increase in serum alkaline phosphatase in the Swiss HIV Cohort Study

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BACKGROUND: Tenofovir (TDF) use has been associated with proximal renal tubulopathy, reduced calculated glomerular filtration rates (cGFR) and losses in bone mineral density. Bone resorption could result in a compensatory osteoblast activation indicated by an increase in serum alkaline phosphatase (sAP). A few small studies have reported a positive correlation between renal phosphate losses, increased bone turnover and sAP. METHODS: We analysed sAP dynamics in patients initiating (n = 657), reinitiating (n = 361) and discontinuing (n = 73) combined antiretroviral therapy with and without TDF and assessed correlations with clinical and epidemiological parameters. RESULTS: TDF use was associated with a significant increase of sAP from a median of 74 U/I (interquartile range 60-98) to a plateau of 99 U/I (82-123) after 6 months (P < 0.0001), with a prompt return to baseline upon TDF discontinuation. No change occurred in TDF-sparing regimes. Univariable and multivariable linear regression analyses revealed a positive correlation between sAP and TDF use (P < or = 0.003), but no correlation with baseline cGFR, TDF-related cGFR reduction, changes in serum alanine aminotransferase (sALT) or active hepatitis C. CONCLUSIONS: We document a highly significant association between TDF use and increased sAP in a large observational cohort. The lack of correlation between TDF use and sALT suggests that the increase in sAP is because of the bone isoenzyme and indicates stimulated bone turnover. This finding, together with published data on TDF-related renal phosphate losses, this finding raises concerns that TDF use could result in osteomalacia with a loss in bone mineral density at least in a subset of patients. This potentially severe long-term toxicity should be addressed in future studies.

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