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A cross-sectional comparison of serum bone markers in patients on stable abacavir (ABC) or tenofovir (TDF) containing therapy

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Purpose of study

Reductions in bone mineral density may occur secondary to HIV per se or antiretroviral therapy; bone toxicity may differ by NRTI backbone. We analysed makers of bone turnover in patients stable on ABC or TDF containing regimens.

Methods

Prospective, cross-sectional, single-centre study of individuals stable for >6 months on ABC- or TDF-based regimens (naïve to TDF and ABC respectively) and <50 cps/ml. The study was designed to measure marker of renal and bone function. The serum bone markers were quantified: alkaline phosphatase (ALP; specific and therefore total ALP are useful markers of bone turnover, specifically resorption), beta crosslaps (measure of type I collagen degradation fragments, a marker of osteoclast activity or bone resorption) and osteocalcin (a polypeptide secreted by osteoblasts, a marker of bone formation). Parameters independently, significantly associated with changes in these markers by univariate analysis ($p < 0.15$) were entered into a multivariable regression model.

Summary of results

391 subjects (145 on ABC, 246 on TDF) were recruited to. Most were male (95% on ABC, 92% on TDF); median age (48 vs. 46 years; $p = 0.021$) and CD4 count (552 vs. 475; $p = 0.007$) were higher in ABC recipients. Regarding markers of bone turnover 3 patients (2%) on ABC and 12 (5%) on TDF had elevated ALP (≤162.5); OR for elevated ALP was 0.41 on ABC but – this was not statistically significant ($p = 0.167$), only elevated creatinine (>104 vs. <84; $p = 0.048$) was significantly associated with elevated ALP by univariable analysis. There was a trend to more frequent ALP elevation in females (OR 3.34; $p = 0.075$) and patients in the lowest quartile for beta crosslaps were less likely to experience an elevated ALP (OR 0.12 for ≤0.22 vs. >0/56; $p = 0.047$). 9 subjects on ABC and 38 on TDF (6% & 15% respectively) has elevated osteocalcin (>34.5). By multivariable modelling, factors associated with elevated osteocalcin were: TDF use (OR on ABC 0.01; $p = 0.039$), elevated cystatin c (OR for 0.68 vs. >0.86 0.03; $p = 0.005$), higher beta crosslaps (<0.34 vs. >0.56; $p < 0.002$) and low LDL-cholesterol (OR for ≤2.40 vs. >3.57 0.02; $p = 0.003$). No significant differences were observed in frequency of hypophosphataemia.

Conclusion

Abnormalities in markers of bone turnover were infrequent but more common on TDF than ABC. There was no association between altered bone markers and duration of TDF use but the clinical impact of these changes should be assessed longitudinally.