

Oral presentation

O323 High HIV viral load inhibits osteoblast function and signalling

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Purpose of the study

The prevalence of osteoporosis in a HIV-positive cohort is more than three times higher than in matched HIV-negative controls. While ART treatment has been associated with increased odds of reduced bone density compared with ART-naïve patients, the pathogenic mechanisms underlying the initiation and progression of osteoporosis in HIV patients remain to be elucidated. Recent studies have reported altered bone biology and function in response to ART exposure, including effects on osteoclasts and osteoblasts. However, the direct effect of HIV on bone cell biology has not been evaluated. We hypothesized that exposure to HIV alters human osteoblast function and activity and ultimately leads to osteopenia/osteoporosis.

Methods

Primary human osteoblasts (hOB) were cultured in growth medium in vitro. Growth medium was supplemented with serum from three distinct patient groups (HIV-negative, HIV-positive low [VL range 120; 4000] or high [VL range 100,000; 500,000]) viral load serum (5% conc., 72 hours, n = 5 per patient group, HIV serum obtained from ART-naïve patients). Cell proliferation (as a biological end-point) and calcium deposition (as a functional end-point) were determined using established methods. In addition, to identify the effect of HIV on transcriptional regulators of the bone phenotype, real-time PCR with gene-specific primers was used to quantify mRNA expression of RUNX-2, a pro-osteogenic transcription factor.

Summary of results

Exposure of hOB to control, low or high HIV viral load serum did not affect hOB cell proliferation, demonstrating that these exposures did not have a cytotoxic effect on osteoblasts in vitro. HOB calcium deposition reduced significantly ($p < 0.005$) after treatment with high VL serum compared to either low VL or HIV-negative control serum. Osteoblast RUNX-2 mRNA expression declined by 25% ($p < 0.05$) after exposure to high VL serum compared to HIV-negative controls.

Conclusion

These data demonstrate bioactivity of HIV in the setting of osteoblast cell culture. Serum obtained from HIV patients with high VL effected significant changes in the bone phenotype, as evidenced by reduced capacity for calcium deposition. Intriguingly, this functional effect was mirrored by changes in the expression of the osteogenic transcription factor RUNX-2. These findings support the hypothesis that HIV itself, in addition to the well described effect of ART, can modulate bone phenotype and at least in part, drive the osteopenia and osteoporosis which is increasingly seen in HIV patients.