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Poster presentation

PI and OPG/RANKL levels in human osteoblast cells

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Purpose of the study

The association between loss of bone mineral density (BMD) and PI use is evidenced on several in vitro models and seems to have different etiology depending on specific molecule. Although an HAART regimen always contains one or more transcriptase inhibitors, there are no specific data available regarding specific PI action on BMD. However, some in vitro experiments showed that these compounds might induce the differentiation of osteoclast cells. In order to analyse the specific effect of each PI on human osteoblast we analysed OPG and RANKL levels after exposing the cells to each PI.

Methods

We performed two double-blind test and exposed for 24 hours a line of human osteoblast cells to suboptimal, therapeutic and toxic plasmatic levels of PI: indinavir 1 μg/mL, 5 μg/mL, 25 μg/mL, ritonavir 0.4 μg/mL, 2 μg/mL, 10 μg/mL, μg/mL, fosamprenavir 1.4 μg/mL, 7 μg/mL, 35 μg/mL, tipranavir 1 μg/mL, 5 μg/mL, 25 μg/mL, atazanavir 0.6 μg/mL, 3 μg/mL, 15 μg/mL, lopinavir/r 0.8 μg/mL, 4 μg/mL, 20 μg/mL, and darunavir 2 μg/mL, 6 μg/mL, 30 μg/mL, respectively. Tests with nelfinavir and saquinavir are ongoing. OPG and RANKL were quantified by ELISA kits purchased from Peprotech and R&D. Statistical analysis was performed using two-tailed Student's test.

Summary of results

We generally noticed in all cases a change in all the values from baseline, an extremely wide variability in the results of OPG and RANKL levels, not only between different PIs, but even between the three pre-determined concentrations for every single PI. Of note, at therapeutic concentration, FPV (OPG 5.36961 μg/mL, RANKL 0.301362 μg/mL) and ATV (OPG 5.477401 μg/mL, RANKL 0.464873 μg/mL) showed the best performance.

Conclusion

In a line of human osteoblast cells after exposition to different concentrations of PIs: 1) there is always a variation of OPG and RANKL levels from baseline; 2) there is an evident association between PI use and OPG and RANKL levels; 3) each single PI shows a specific different effect on OPG and RANKL levels; 4) the concentration of each single PI produces a different effect on OPG and RANKL levels; and 5) FPV and ATV shows the best performance. Not generally the class of PI, but each single PI, and its specific plasma level, by altering OPG and RANKL levels, may specifically act on HAART-related loss of BMD, suggesting an interesting mechanism and role of PI, and accounting for the different rates of osteoporosis/osteopenia described in the trials with different PIs.