Effects of risedronate on circulating osteoprotegerin and soluble RANK ligand serum levels in patients with rheumatoid arthritis
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Introduction: Osteoporosis in patients with rheumatoid arthritis (RA) is a serious problem. Osteoporosis is considered to reflect a relative enhancement of osteoclast activity and recent studies have identified three new members of TNF and TNF receptor families essential for osteoclast biology. RANKL stimulates osteoclast differentiation through its physiologic receptor RANK on osteoclast lineage cells, whereas secreted OPG acts as a decoy receptor and blocks RANKL, thus preventing RANK activation. This contact-dependent process links between the immune system and bone metabolism in RA. Risedronate has been described as a potent inhibitor of osteoclast activity and have been recently used for the treatment of osteoporosis in RA. The objective of the investigation reported here was to study the effect of risedronate on serum OPG and RANKL in patients with RA.

Materials and Methods: A total of 43 patients with RA, according to the ACR-criteria, were enrolled. The patients were received 2.5 mg of risedronate daily. At baseline and after 1, 3 and 6 months, serum OPG, RANKL, bone-specific alkaline phosphatase (BAP), N-telopeptide (NTX) and intact-PTH were measured. BMD of the lumbar spine (L1-L4) and the (total) hip was measured at baseline and after 6 and 12 months.

Results: Serum levels of OPG, RANKL, BAP, NTX and intact-PTH at baseline were found to be within normal range (86.3pg/ml, 104ng/ml, 32.4U/L, 17.5nmolBCE/L and 28.1pg/ml, respectively). Serum concentration of OPG at baseline was found to be increased with age (not significant). Serum OPG and RANKL levels were not related to biochemical markers of bone metabolism or BMD.

After 6 months of risedronate treatment, serum BAP had significantly decreased by 36.1% (p<0.0001), while NTX had significantly decreased by 31.0% (p<0.001), reflecting the efficacy of the anti-resorptive therapy. Serum concentration of OPG was found to be significantly decreased following therapy (p<0.05), while RANKL level was not significantly changed. This resulted in a 10.3% decrease of RANKL:OPG ratio, an index of osteoclastogenic stimulus.

Discussion: To our knowledge, this is the first time that an in vivo increase of serum OPG and RANKL after risedronate administration in RA has been demonstrated. We observed a favourable effect of risedronate on the BMD of the lumbar spine and on the markers of bone turnover in patients with RA. Although the OPG/RANKL system may have some clinical usefulness as a marker of bone turnover in RA, the role of bisphosphonates in the regulation of OPG and RANKL synthesis is still unclear. Further studies on these key molecules will elucidate the molecular mechanism of osteoporosis in RA.

4. Dobnig H, et al., Changes in the RANK ligand/osteoprotegerin system are correlated to changes in bone mineral density in bisphosphonate-treated osteoporotic patients. Osteoporos Int. 2006;17(5):693-703.