SERUM OSTEOPROTEGERIN LEVELS ARE INCREASED IN PATIENTS WITH CUSHING'S SYNDROME: A CASE-CONTROL STUDY

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RANKL/RANK/OPG system plays a key-role in bone, immune and vascular systems. In vitro, glucocorticoids inhibit OPG and stimulate RANKL expression in different cell types. Few data are available on serum OPG levels, and no data at all on serum sRANKL levels in Cushing's syndrome (CS). We studied 38 patients with CS (male/female 17/21, age (median, range) 55, 23-80 years). Twenty-seven of them had an ACTH-dependent syndrome (21 with Cushing's disease (CD), 6 with ectopic ACTH hypersecretion). Eleven had an adrenal-dependent syndrome (9 with adrenal adenoma (AA), 2 with adrenal carcinoma). 38 healthy subjects served as controls (male/female 16/22, age 55, 22-79 years). Serum concentiations of OPG and total sRANKL were measured by ELISAs. Serum OPG levels were highe in 23 pertients than in controls (p<0.001); no significant difference was observed in serum sRFNkL levels and sRANKL/OPG ratio. Serum OPG levels positively correlated with age in control. (r = 34, p<0.05) but not in CS patients. Serum sRANKL levels and SRANKL/DPG ratio negatively correlated with age in controls (r=-0.59, p<0.001, and r=-0.65, p<0.001, respectively); these surrelations were weaker in CS patients (r=-0.30, p=0.09, and r=-0.32, p=0.05) In Co patients, OFG positively correlated with serum cortisol at 08:00 (r=0.43, p<0.01) and 25:00 (r=0.31, p=0.08), while sky NKL and sRANKL/OPG ratio negatively correlated with form if PMD, T- and Z-scores. Salvin OPG levels were higher in CD than in AA patients. The two groups were comparable for ag and serum and 24-h urinary cortisol levels, but expectedly differed ior ACTH and DHEA-supriate levels; consistently with previous results, lumbar and femur BMD values were higher in CD than in A lipatients (p<0.02). In conlusion, OPG but not sRANKL levels were increased in CS be tients: different tissues, including bone and endothelium, are likely to contribute to the observed inc ease. In CS patients OPG levels positively correlated with serum cortisol, and were higher in CD than in A\ patients. Whether this difference is linked to the greater bone loss observed in AA with respect to CD patients remains to be elucidated. In CS patients sRANKL levels and sRANKL/OPG ratio were inversely correlated with femur, but not spine, BMD parameters. Such a correlation is consistent with the biological role of RANKL as a major pro-resorptive factor.