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 concentrations of OPG and total sRANKL were measured by ELISAs. Serum OPG levels were higher in CS patients than in controls ($p<0.001$); no significant difference was observed in serum sRANKL levels and sRANKL/OPG ratio. Serum OPG levels positively correlated with age in controls ($r=0.34$, $p<0.05$) but not in CS patients. Serum sRANKL levels and sRANKL/OPG ratio negatively correlated with age in controls ($r=-0.59$, $p<0.001$, and $r=-0.65$, $p<0.0001$, respectively); these correlations were weaker in CS patients ($r=-0.30$, $p=0.09$, and $r=-0.33$, $p=0.05$). In CS patients, OPG positively correlated with serum cortisol at 08:00 ($r=0.43$, $p<0.01$) and 24:00 ($r=0.31$, $p=0.08$), while sRANKL and sRANKL/OPG ratio negatively correlated with femur BMD, T- and Z-scores. Serum OPG levels were higher in CD than in AA patients. The two groups were comparable for age and serum and 24-h urinary cortisol levels, but expectedly differed for ACTH and DHEA-sulphate levels; consistently with previous results, lumbar and femur BMD values were higher in CD than in AA patients ($p<0.02$). In conlusion, OPG but not sRANKL levels were increased in CS patients: different tissues, including bone and endothelium, are likely to contribute to the observed increase. In CS patients OPG levels positively correlated with serum cortisol, and were higher in CD than in AA 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.