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SERUM OSTEOPROTEGERIN (OPG) IN CHILDREN WITH CHRONIC KIDNEY DISEASE AND IN HEALTHY CHILDREN.

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Repetitive transiliac bone biopsy is not a practical clinical tool to determine bone disease or its therapy. Non-invasive assessment of bone cell activity, a major determinant of histomorphometric classification of metabolic bone disease, would be preferable for these purposes. To date, levels of bone-associated proteins (osteocalcin, etc) or markers of collagen metabolism (type I procollagen propeptide; C- or N-terminal NTX, etc.) have provided little information about the osteodystrophy of CKD. Recently, the signaling system for control of osteoclast function that involves soluble TNF-receptor (sRANKL) and its several cognate ligands (OPG, RANK) has been of interest, since blood levels of two of the components of the system are available. This has direct interest to osteodystrophy of CKD, since the level of osteoclast function determined by histomorphometry has defined the varieties of the disorder. We have established normative data for levels of serum osteoprotegerin and RANKL in children, and have shown a relationship of the [OPG/sRANKL] ratio to serum levels of IGF-1 in children. We have examined the [OPG/sRANKL] ratio in a group of children with normal GFR but diminished bone density (cystic fibrosis), and have shown that there was a decrease in the [OPG/sRANKL] because of a decrease in OPG and increase in sRANKL. Further, the decrease in IGF-1 was inversely correlated with an increased ratio. The purpose of this exploratory study was to define the levels of OPG, PTH, growth, and CKD stage in children. Methods: OPG levels were measured in 50 children with CKD stages 1-5 and after kidney transplantation. Additionally, OPG levels were measured in patients with idiopathic hypercalciuria and diminished bone density, and in several other disorders of mineral metabolism. We used our normative data in 89 healthy children of both genders for comparison. OPG was determined using a modification of an enzyme immunoassay (ALPCO Diagnostics, Windham, NH). All assays were performed in duplicate and reported in pg/mL. Results: Compared to normal children ($\bar{x} \pm s = 67 \pm 20$), children with CKD, regardless of stage, had similar OPG levels to each other that were no different than normals ($p = NS$), while for comparison, children with idiopathic hypercalciuria had reduced OPG ($p < 10^{-3}$). In CKD, PTH levels ranged from normal to above normal, as expected. There was a positive correlation between OPG and iPTH levels that disappeared when iPTH levels were log-adjusted. There was no relationship between OPG and statural-growth parameters. Data on IGF-1 and OPG are being evaluated. Conclusion: In this exploratory study in children with CKD, measurement of OPG has not shown clinical utility that surpasses measurement of PTH. The ratio of [OPG/sRANKL] may yet be of benefit, and especially if indexed to IGF-1 levels, in children with CKD. However, it is unlikely to be the case, since in other populations that we have studied, both OPG and sRANKL levels were different from normal children, as was the [OPG/sRANKL] ratio. The search for an ideal biomarker of osteodystrophy in children that supplants bone biopsy remains elusive.