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## TOPIC: EVALUATION OF RENAL OSTEODYSTROPHY IN CHILDREN

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Our work over the last several years, have been focused on two main areas for the purpose of the workshop:

**1) Value of PTH assays as predictors of bone turnover in dialyzed children.** We have demonstrated that first-generation immunometric PTH assay (1<sup>st</sup> PTH-IMA) was a reasonably reliable predictor of the different subtypes of renal osteodystrophy in cross-sectional studies of dialyzed pediatric patients treated with calcium-based binders and either no active vitamin D sterols or low dose of daily oral calcitriol (KI 45:254, 1994). However, we have shown a discrepancy between final PTH levels and indices of bone turnover during intermittent calcitriol therapy (KI 54:907, 1998). Indeed PTH levels (1<sup>st</sup> PTH-IMA) between 400-600 pg/ml were associated with bone biopsy findings consistent with adynamic osteodystrophy. We have also demonstrated that second-generation immunometric PTH assay (2<sup>nd</sup> PTH-IMA, Immotopics, San Clemente CA) had a similar predictive value of bone turnover than 1<sup>st</sup> PTH-IMA, and both assays were found to be better predictors of bone formation than the ratio PTH(1-84) to amino N-terminally truncated PTH-derived fragments (ntPTH(1-84)) in cross sectional studies performed in dialyzed children (KI 63:1801, 2003).

**2) Effects of therapy for secondary hyperparathyroidism (2<sup>o</sup>HPT ) on biochemical parameters and bone histology in dialyzed children.** We have compared the effects of different active vitamin D analogues [calcitriol (1,25D) and doxercalciferol (1- $\alpha$ -D<sub>2</sub>)] in combination with calcium-based binders and sevelamer HCL on the control of the skeletal lesions of 2<sup>o</sup>HPT in pediatric patients treated with peritoneal dialysis. At present, a total of 40 pts on CCPD with bone biopsy (BBx) proven 2<sup>o</sup>HPT have completed the study with repeat BBx. Pts. were randomly assigned to 1 of 4 treatment groups using a 2x2 study design: Group 1 (1- $\alpha$ -D<sub>2</sub> + CaCO<sub>3</sub>), Group 2 (1- $\alpha$ -D<sub>2</sub> + sevelamer), Group 3 (1,25-D + CaCO<sub>3</sub>) and Group 4 (1,25-D + sevelamer) (Table). S-Ca, P, Alk.P'T'ase and PTH were measured monthly for 8 months when bone biopsies were repeated.

Overall there were no differences in S-P between groups, however S-Ca levels were higher in patients treated with CaCO<sub>3</sub>, while values remained unchanged from baseline in patients on sevelamer. Skeletal lesions of 2<sup>o</sup>HPT markedly improved in each of the groups. Baseline PTH (1<sup>st</sup> PTH-IMA, Nichols<sup>R</sup>) levels were 646±127 (SE), 684±123, 925±111 and

878±113 pg/ml in groups 1,2,3 and respectively (NS). S-PTH levels were determined also by 1<sup>st</sup> and 2<sup>nd</sup> PTH-IMAs, (Immutopics<sup>R</sup>). 1<sup>st</sup> PTH-IMAs values throughout the study period were highly correlated (r=0.93, p<0.01). Overall, 2<sup>nd</sup> PTH-IMA values were 40-50% lower as expected. PTH levels decreased by 40-55% from baseline (p<0.01) and final values did not differ between groups. Baseline ratio PTH(1-84)/ntPTH(1-84) did not differ and values remained unchanged throughout the course of the study despite differences in S-Ca. While acute changes in serum calcium levels appear to regulate the minute-to minute proportion of full-length PTH molecule to amino terminally truncated fragments, it appears that chronic alterations in calcium during therapy of 2<sup>o</sup>HPT do not result in sustained alterations on the proportion of ntPTH fragments in serum. Patients treated with sevelamer received higher doses of active vitamin D. Thus, therapy with sevelamer widens the margin of safety in treating 2<sup>o</sup>HPT with active vitamin D sterols.

Finally, serum PTH levels that corresponded to normal rates of bone formation at the conclusion of the study were higher than those recommended by KDOQI for stage 5 CKD. Indeed, patients who achieved normal rates of bone formation all maintained serum PTH between 400 and 600 pg/ml (1<sup>st</sup> PTH-IMAs) and PTH levels between 150 to 300 pg/ml (2<sup>nd</sup> PTH-IMA) correspond to normal rates of bone formation. Thus, optimal PTH levels remain to be defined during the treatment of 2<sup>o</sup>HPT in dialyzed patients to prevent complications of over-treatment.