Etelcalcetide in the Treatment of Secondary Hyperparathyroidism in Patients Uncontrolled with Cinacalcet: Results from a Prospective Study

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Introduction

1. Secondary hyperparathyroidism (SHPT) is associated with increased bone turnover, risk of fractures, vascular calcifications and cardiovascular all-cause mortality.1

2. Etelcalcetide is a new calcimimetic, recently approved for SHPT treatment, and has a pharmacokinetic profile that allows thrice weekly intravenous (IV) dosing after hemodialysis (HD).

3. There is limited clinical experience with this agent with respect to its efficacy in patients with SHPT that is uncontrolled with cinacalcet.

Methods

1. We conducted a prospective cohort study in prevalent HD patients treated at 3 DaVita clinics in Portugal who had SHPT that was uncontrolled with cinacalcet treatment for at least 3 months.

   - Inclusion criteria: intact PTH (iPTH) levels > 300 pg/ml and total calcium > 8.3 mg/dL in the previous 3 months.

   - After a 1-week cinacalcet washout period, etelcalcetide 5mg IV/HD treatment was initiated. PTH, serum calcium, and phosphorus were followed over 6 months; FGF-23 and sclerostin levels were analyzed before the start of etelcalcetide treatment and after 6 months.

   - Assays for FGF-23 (C-terminal) and sclerostin were performed by ELISA on the fully automated Gemini Stratec (Diatrom) equipment using Biomedica reagents and following the manufacturer’s protocols (Biomedica Medizinprodukte GmbH & Co KG).

   - Both assays were performed on plasma EDTA samples collected using BD Vacutainer K2E. Plasma separation was performed immediately by centrifugation (10 min at 1500g). Samples were stored at -25°C.

   - Results were considered as means, medians, interquartile ranges and percentages, respectively. P-values < 0.05 were considered significant. All statistical analyses were performed using SPSS IBM (v21, SPSS Inc, Chicago, IL, USA).

Results

1. Among the 34 patients included in the study:

   - Mean age was 60.7 (SD: 12.3) years
   - Median time on HD was 62.5 (7-294) months
   - Median iPTH dose at switch was 180 (90-840) mg/week
   - Median iPTH dose remained at 5mg/HD treatment at 3 months

2. Serum calcium, phosphorus, and iPTH were all lower at month 6 than at baseline (Figure 1).

   - Mean calcium decreased from 8.8 (8.1-9.1) mg/dL to 8.0 (7.4-8.6) mg/dL
   - Median phosphorus decreased from 4.0 (3.4-4.9) mg/dL to 3.4 (2.9-4.0) mg/dL
   - Median iPTH decreased from 1600 (1000-2000) pg/ml to 1000 (600-1600) pg/ml

3. Plasma sclerostin concentrations increased following the inhibitory effect of PTH on sclerostin expression.

   - plaque level: 37.2 (5.8-200.7) pmol/L to 71.7 (40.3-240.7) pmol/L

   - Serum FGF-23 decreased from 39.3 (23.0-43.3) pmol/L to 29.1 (11.5-115.6) pmol/L (P = 0.018).

   - Sclerostin increased from 37.2 (5.8-200.7) pmol/L to 71.7 (40.3-240.7) pmol/L (P < 0.0001).

Discussion

1. Etelcalcetide improved control of severe SHPT in patients undergoing cinacalcet treatment, with reductions in serum calcium and phosphorus levels and also in FGF-23 levels, compared to baseline values.

2. The observed increase in the sclerostin levels of patients already under cinacalcet treatment is an original observation and deserves further investigation:

   - This effect is not surprising because PTH down regulates sclerostin expression in osteocytes.2

   - It is possible that this effect of etelcalcetide on sclerostin levels may translate into a protective effect on vascular calcification, at the same time reducing osteoblast activity and bone remodeling in the setting of high-turnover bone disease.

Conclusions

1. Etelcalcetide was effective in improving SHPT control in this group of patients, previously uncontrolled with cinacalcet treatment.

2. Plasma sclerostin concentrations increased following the switch to etelcalcetide: this might be expected considering the inhibitory effect of PTH on sclerostin expression.2

   - To our knowledge, this is the first study describing the impact of etelcalcetide treatment on plasma sclerostin levels.

References


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