Normocalcemic Hyperparathyroidism in Children

Dimitrios T. Papadimitriou1, Eleni Dermitzaki2, Kleanthis Kleanthous1,
Anastasios Papadimitriou2, George Mastorakos3

1. Pediatric Endocrine Clinics, Athens Medical Center, Greece
2. Attikon University Hospital, Haidari, Greece,
3. Areteio University Hospital, Athens, Greece.

No disclosures

Background

• Childhood and adolescence are the critical periods for the establishment of lifelong bone health.

• Normocalcemic primary hyperparathyroidism (NPHPT) has been recognized as a variant of primary hyperparathyroidism (PHPT) 15 years ago, characterized by elevated PTH level with persistently normal concentrations of albumin-adjusted total and ionized calcium, in the absence of secondary causes of hyperparathyroidism

• and related to increased risk in development of osteopenia or osteoporosis as well as development of parathyroid adenoma (15%) and hypercalcemia-hypercalciuria with renal consequences.

Aim

To identify and correct biochemical disorders of PTH in normocalcemic children

Methods

We performed in all patients that visited our pediatric endocrine unit for two years (1-Nov 2016 until 31-Oct 2018), a complete calcium metabolism evaluation (Ca, P, ALP, 25OHD, intact PTH).

Results & Interventions

• A total of 3060 patients - excluding those that consulted for vitamin D deficiency, Ca metabolism abnormalities or known renal pathology (i.e. Bartter syndrome)

• We identified 154 patients: 5.1% with hyperparathyroidism: PTH > 45 pg/ml, (Horn Res Paediatr 2015;84:124-129) and normal total serum calcium levels:

  51 % of them were vitamin D replete (25OHD3 >30 ng/ml, group 1)  
  49 % were vitamin D deficient (25OHD3 <30 ng/ml, group 2).

• All patients were treated with cholecalciferol (8000-16000 IU daily)+calcium supplementation 1000 mg/day.

• Evaluation of calcium metabolism (Ca, P, ALP, 25OHD, 1,25OHD, PTH) was performed every 3 months.

• In 6 patients (4 from group 1 and 2 from group 2) elevated PTH did not respond to 6 months of combined cholecalciferol/calcium therapy

• These patients were switched to the non-calcemic synthetic 1-25(OH)2-vitamin D analogue, paricalcitol, at the dose of 2 mcg x 1-3/day

• Evaluation of calcium metabolism (Ca, P, ALP, 25OHD, 1,25OHD, PTH, urine Ca/Cr) was performed every 3 months.

Parathormone levels normalized in 5 patients by 3 months of treatment and in 1 by 10 months of treatment, with calcium in serum and urine (Ca/Cr morning 2-hr sample) being within normal range for age during treatment in all patients.

Discussion and Conclusions

• The incidence of normocalcemic hyperparathyroidism in childhood is high

• In all normocalcemic children checked for vitamin D, concomitant measurement of PTH is required

• Most of the cases seem to be secondary hyperparathyroidism as they are resolved with administration of cholecalciferol and calcium

• Even in cases with vitamin D sufficiency, PTH fell to normal after administration of cholecalciferol and calcium

• This probably means that vitamin D sufficiency may not be for everybody a level > 30 ng/ml and that Calcium intake plays also a crucial role

• In the 6 cases that did not respond to therapy with cholecalciferol and calcium, hyperparathyroidism seems to be either primary or tertiary

• Even in primary hypercalcemic hyperparathyroidism, PTH is improved when Vitamin D levels are restored

• Vitamin D suppresses PTH gene expression and reduces parathyroid cell proliferation

• Subclinical hyperparathyroidism PTH<45 pg/ml should be treated with cholecalciferol (8000-16000 IU/day) + calcium supplementation (1000 mg/day), but since studies in primary hypercalcemic hyperparathyroidism have shown that high dose cholecalciferol may worsen calcioria,

• we propose to switch to paricalcitol 2-6 mcg/day, if PTH is unresponsive to cholecalciferol and calcium treatment after a minimum of 3 months

• Paricalcitol treatment normalizes PTH, protecting bone and general health

• Further studies are needed to standardize this approach.