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EDITORIAL

Hypovitaminosis D in primary hyperparathyroidism: to treat or not to treat? That is the question

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A number of epidemiological studies have shown a high prevalence of hypovitaminosis D in the world, independent of the threshold used to define insufficiency or deficiency [1]. Somewhat counterintuitively, hypovitaminosis D appears to be more prevalent in patients with primary hyperparathyroidism [2–5]. The reasons for this finding may be multiple and not mutually exclusive. For example, parathyroid hormone (PTH) stimulates the renal 1α-hydroxylase causing an increased conversion of 25(OH)D to $1,25(OH)_2D$, leading to "conditional" vitamin D depletion [6]. The resulting increase in $1,25(OH)_2$ D has a negative feedback on PTH production and secretion, in addition to accelerated inactivation of 25(OH)D by 24-hydroxylase [7]. Other reasons for the common finding of low calcidiol levels may include an enhanced hepatic inactivation of 25(OH)D [8] or avoidance of vitamin D supplementation in a person with hypercalcemia for fear of further increasing serum calcium level. However, a number of investigations have shown that hypovitaminosis D in patients with primary hyperparathyroidism is associated with higher preoperative PTH levels, larger adenomas, more compromised skeletal health, and increased incidence of hungry bone syndrome after parathyroidectomy compared with vitamin D repleted or vitamin D sufficient patients [9–11].

Despite these rather convincing aspects on the prevalence and pathogenesis of hypovitaminosis D in patients with primary hyperparathyroidism, there is still a pervasive uncertainty whether we should treat or not to treat vitamin D depletion in patients with PHPT. There are now at least three papers favouring the correction of hypovitaminosis D [4, 12, 13]. First, in a meta-analysis of ten studies comprising of 340 patients, Shah et al. [4] concluded that vitamin D replacement in patients with primary hyperparathyroidism and coexistent vitamin D deficiency increases 25(OH)D levels and significantly reduces PTH values without causing hypercalcemia and hypercalciuria. Second, Rolighed et al. [12] have recently demonstrated that daily supplementation with 2800 IU of vitamin D safely improves vitamin D status and decreases PTH. Finally, Rathi et al. [13] in this issue of the Journal report on normalizing vitamin D nutritional status with significant reductions in serum PTH levels without any safety concerns.

In all the studies performed thus far, other aspects of vitamin D treatment have not been uniform; inconsistencies have been noted concerning, for example, the changes of bone numeral density and biochemical markers of bone turnover [14–16]. However, these discrepancies are clearly related to the site for bone mineral density assessment (lumbar vs proximal femur) or the biomarker employed. It is well known, for example, that changes of markers of bone formation lag behind those of bone resorption [17, 18]; therefore, the length of observation is another important parameter.

The conclusion of Rathi and co-workers [13] is that high oral doses of cholecalciferol normalise vitamin D levels without worsening underlying hypercalcemia in patients

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with primary hyperparathyroidism. Admittedly, further studies of longer duration are needed to better define the amount and modalities of refilling body stores with vitamin D. In the meantime, it seems prudent to suggest targeting vitamin D threshold (Endocrine Society, IOM), because this reduces the severity of the disease with no safety concerns. However, for those not undergoing surgery, further studies of longer duration are clearly required.

Conflict of interest The authors declare that they have no conflict of interest.

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