PRIMARY HYPERPARATHYROIDISM: UNSOLVED ISSUES AND TREATMENT

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Primary hyperparathyroidism (PHPT) is a common endocrine disorder characterized by elevated calcium and inappropriately high levels of serum PTH. Depending on severity, it may be accompanied by hypercalcemic symptoms, nephrolithiasis, hyperparathyroid bone disease, bone loss and neuromuscular weakness. Over the past 20 years a milder form of PHPT, characterized by the absence of the above clinical manifestations (asymptomatic PHPT) has increasingly been recognised as a clinical problem.

The primary aim of management is to normalize serum calcium and reduce PTH levels, leading to improvement in any associated symptoms. Parathyroidectomy (PTx) is the only curative treatment and in experienced hands it is successful in up to 95% of patients.

Surgery is an effective choice also in PHPT patients with asymptomatic PHPT who meet surgical criteria. In these patients, parathyroidectomy (PTx) has been shown to normalize parathyroid hormone [PTH] and serum calcium, and to increase bone mineral density (BMD). Parathyroidectomy has also been shown to normalize serum calcium and PTH and increase BMD in asymptomatic PHPT patients who do not met the surgical criteria. Further studies are needed to confirm whether surgery benefits neurocognitive and cardiovascular symptoms. Studies of the natural history of asymptomatic PHPT indicate that in the absence of surgery some patients show stability in biochemical measures (serum calcium and PTH levels) and BMD, however this is only temporary. Current guidelines therefore recommend that patients are regularly monitored and eventually appropriately managed by medical therapy. The guidelines define regular monitoring as annual monitoring of serum calcium and PTH, and bi-annual 3-site BMD.

However there are few alternative treatment options in patients who are ineligible for, or unwilling to undergo, surgery and those in whom PTx has failed. Medical therapy targets the compromised organ(s). Current options include the off-label use of bisphosphonates, selective estrogen receptor modulators and hormone replacement therapy, and the recently approved calcimimetics cinacalcet.

Bisphosphonates and hormone replacement therapy effectively increase BMD and decrease bone turnover, but have no significant impact on serum calcium or PTH levels. The calcimimetic cinacalcet reduces serum calcium and PTH and raises serum phosphorus in these patients, but has no effect on BMD. Medical management should be offered to patients with contraindication to surgery or unwilling to have PTx. It could also be considered in selected asymptomatic PHPT patients who meet the surgical criteria for PTx.