HYPOPARATHYROIDISM: CURRENT CONCEPTS AND APPROACHES TO THERAPY IN 2020

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In contrast to primary hyperparathyroidism, hypoparathyroidism (HPT) is a rare disease. Estimates have placed the incidence of HPT in the United States as fewer than 200,000 which places it in that category. In most other regions of the world, HPT is also rare. By far, the major etiology of HPT, about 75%, is after neck surgery. Another 'rule of 75' is that 75% of patients with HPT are postmenopausal women, explained by the preponderance of neck surgery being performed on women. Chronic HPT is defined by the coexistence of hypocalcemia and low or undetectable levels of parathyroid hormone (PTH) for at least 6 months following neck surgery. Seventy-five percent of post-surgical HPT is transient. The rest have chronic, 'permanent' HPT. It is important to note that HPT can occur years or even decades after neck surgery. There are other forms of chronic HPT with autoimmune and genetic etiologies forming most likely other causes. Signs of neuromuscular irritability, including Cvostek's and/or Trousseau's signs, paresthesias, and more life-threatening features such as laryngospasm and seizures are a function of the level of the serum calcium per se, its rate of decline, and individual variability. Common sites of extraskeletal calcifications include the brain and the kidneys. Reduced renal function is also seen often. A common feature of HPT is reduced quality of life (QOL) described by many as "brain fog". Conventional therapy consists of calcium, active vitamin D (1,25-dihydroxyvitamin D), parent vitamin D (chole- or ergocalciferol), and, if hypercalciuria is hard to control, thiazide diuretics. While these standard approaches may control the hypocalcemia, very high doses of oral calcium and active vitamin D may be necessary, raising further concerns about extraskeletal calcifications. Moreover, even if the serum calcium can be controlled, quality of life is generally not improved. Bone quality, which is not reflected by bone density but rather by microarchitectural abnormalities, is not improved either. Hormonal replacement therapy with recombinant human PTH(1-84) [rhPTH(1-84)] has become available. In placebo-controlled, double-blinded, major registration trials, rhPTH(1-84) was shown in daily amounts ranging from 25 to 100 mcg to permit dramatic reductions in the amounts of calcium and active vitamin D needed to maintain acceptable serum calcium levels. rhPTH(1-84) also has been demonstrated to improve QOL quickly and persistently. Recent long-term, observational studies of rhPTH(1-84) have confirmed its efficacy for as long as 8 years. rhPTH(1-84) is indicated for patients with HPT who cannot be well controlled on conventional therapy. The definition of 'poor control' relates obviously to recurrent signs and symptoms of hypocalcemia but also to those for whom large doses of calcium and active vitamin are needed, those who already demonstrate complications of the disease and compromised quality of life, as well as those who have syndromes that limit the absorption of calcium and vitamin D. With rhPTH(1-84), it is now possible to tailor patients' therapy to their needs with the goals being biochemical control without necessitating large replacement doses of calcium and vitamin D and the prevention of complications.

KEYWORDS: Hypoparathyroidism; hypocalcemia; treatment.