

Permanent hypoparathyroidism

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Permanent hypoparathyroidism is defined as the continuing need for calcium and/or vitamin D replacement at 1 year postoperatively. It is a rare complication when surgery is undertaken for PHPT (0.5%), but in secondary hyperparathyroidism it can range from 4% to 12%. Symptoms and signs relate to serum calcium levels. Symptoms include mild circumoral or digital numbness and paraesthesia, carpopedal or laryngeal spasms and cardiac arrhythmias. Chvostek's and Trousseau's signs may be elicited. Chvostek's sign refers to contraction of the ipsilateral facial muscles on percussion of the facial nerve below the zygoma. Trousseau's sign refers to the development of carpopedal spasm secondary to occlusion of the arm (usually with a blood pressure cuff). Biochemical investigations include total and ionised calcium levels as well as serum magnesium levels. An ECG may demonstrate a prolonged QT interval or QRS complex changes. Mild hypocalcaemia can be treated with oral calcium and vitamin D supplementation. Acute symptomatic hypocalcaemia is an emergency and should be corrected with intravenous as well as oral calcium and vitamin D replacement. Traditionally, 10 mL of 10% calcium gluconate is administered slowly intravenously. Supplemental magnesium may also be required, owing to the synergistic action of transporters for calcium and magnesium. Medical management is warranted in patients who are deemed unfit or who have contraindications to surgical intervention, in patients with failed surgical intervention or in the long-term management of parathyroid carcinoma. The aims are to prevent skeletal complications (improve bone mineral density and reduce fracture risk) and to stabilise biochemical parameters. There are only limited data on the long-term efficacy of such an approach as surgery is known to provide durable responses. Bisphosphonates/denosumab Bisphosphonates are pyrophosphate analogues that are concentrated in areas of high bone turnover. They inhibit osteoclast activity and apoptosis, thereby increasing bone mineralisation and reducing bone turnover. Studies looking at the management of PHPT utilising bisphosphonates are Frantisek Chvostek, 1835–1884, physician, The Jasefsacademie, Vienna, Austria. Armand Trousseau, 1801–1867, physician, Hôtel Dieu, Paris, France. does appear to stabilise bone mineral density without markedly altering the underlying serum biochemistry. Denosumab is a monoclonal antibody that works as a receptor activator of nuclear factor- κ B (RANK) ligand inhibitor. Data from the DENOCINA trial suggest that it may be a valid treatment option for patients in whom surgery is undesirable. Hormone replacement therapy and selective oestrogen receptor antagonists Hormone replacement therapy (HRT) has been shown to improve bone mineral density and reduce the associated fracture risk in postmenopausal women by reducing bone turnover. Two non-randomised controlled trials have shown a durable and similar response to surgery for PHPT at 4 years, with improvements in bone mineral density but without any improvement in the underlying serum biochemistry. The rationale for the use of selective oestrogen receptor antagonists (SERMs) is that they should confer the benefits of HRT but

without the potential adverse vascular and breast effects. The effect on the bone mineral, however, appears to be less significant than that of HRT. Calcimimetics The extracellular calcium-sensing receptor on the parathyroid cell surface negatively regulates secretion of PTH. Activation of the receptor decreases secretion of PTH, thereby decreasing bone turnover. Calcimimetics, such as cinacalcet, amplify the sensitivity of the calcium-sensing receptor to extracellular calcium, altering the set point and thereby decreasing PTH production. Cinacalcet was approved for use in PHPT by the European Medicines Agency in 2008 and subsequently by the US Food and Drug Administration in 2011 for the treatment of severe hypercalcaemia in patients with PHPT who were unfit for parathyroidectomy. Normalisation of serum calcium levels can be achieved with a similar reduction in the level of PTH, although not to within the normal range. Despite this, neither the urinary calcium nor the bone mineral density appear to change even after 3 years of treatment. Drug tolerance, especially gastrointestinal side effects, can be problematic and may limit the duration of usage. Permanent hypoparathyroidism

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