Primary hyperparathyroidism (PHPT) is known as an endocrinopathy diagnosed by elevated serum calcium and inappropriately high normal or increased serum PTH. Disease complications vary from cases of asymptomatic disease to cases with classical symptoms as renal stones, loss of bone mass, neurocognitive symptoms and fractures.

The cure of PHPT is parathyroidectomy, but in case of contraindications of surgery, in patients who refuse surgery, or do not meet current operative guidelines and in the rare cases where parathyroidectomy fail to cure, medical treatment is an option (1).

The Calcium-sensing receptor (CaSR) is expressed on the parathyroid cell and seems to be the principal regulator of the PTH secretion (2). However CaSR is also expressed in the intestine and kidneys. The enhanced sensitivity towards extracellular calcium leads to decreased calcium reabsorption by the renal tubules. Calcimimetics has been developed by the pharmaceutical industry enables the clinicians to quickly and directly reduction of the patients elevated serum PTH levels by the compounds binding to CaSR and thereby leading to an increasing sensitivity to extracellular Calcium (3). Cinacalcet is approved for reduction of hypercalcemia in patients with PHPT for whom parathyroidectomy is indicated on the basis of calcium levels but in whom surgery is clinically inappropriate or is contraindicated.

Shoback et al have demonstrated that short-term (15 d) cinacalcet treatment reduced serum Calcium and serum PTH in patients with PHPT (4). The same research group showed in a later 1-year RCT in patients with mild to moderate PHPT that cinacalcet almost normalized serum Calcium and decreased, but did not normalise, serum the PTH levels. This could be due to the decreased renal reabsorption. (5).

In a newly published study by Peacock et al (6) they have assessed long-term tolerability, safety, and efficacy of cinacalcet evaluating serum Calcium, serum PTH and BMD in patients with mild to moderate PHPT who participated in the 1-year RCT (5) were followed in an open-label extension lasting an additional 4.5 years. The study confirms the observations from the 1-year study. Cinacalcet can almost normalize serum Calcium and decrease, but not normalise, serum the PTH levels for up to 5 years. However, BMD is not affected by the treatment (6).

One of the challenges in Cinacalcet treatment is the side effects. In the study of Peacock 99% had mild side effects, most commonly nausea (36%) (6). An American multicentre retrospective study has in seventy PHPT patients treated with Cinacalcet, found that the medical treatment were stopped in 26% (19 patients) due to side effects i.e. nausea and vomiting. Only 6% (3 patients) had relief of symptoms and none had gained BMD. All patients had a curative parathyroidectomy after medical treatment which in all cases lasted more than 1,5 years. These patients where followed prospectively after surgery and all had partial or complete resolution of symptoms within 3 months (7). However, the patients in this study were all referred to parathyroidectomy due to failed medical treatment.

Silverberg et al have shown that patients with intractable parathyroid carcinoma, Cinacalcet treatment reduces hypercalcemia in approximately two third of patients (8). Mayes et al have shown that cinacalcet treatment is effective in complex primary hyperparathyroidism patients like MEN-1. Both studies were open labelled (9).

**In conclusion,**
At the present time Cinacalcet is a secondary choice in managing PHPT where surgery remains the superior treatment option. In patients where surgery is not possible calcium levels and PTH levels can be reduced by cinacalcet and for some patients symptoms can be reduced. However, osteoporosis should be treated, as in osteoporosis patients in general as Cinacalcet have no positive effect on BMD.

In patients with parathyroid cancer Cinacalcet is effective in lowering serum calcium and is easier tolerated than in PHTP patients.

We need more randomizes controlled studies before we know when or if Cinacalcet has a beneficial effect on the long time risk factors for PHPT patients as well as how many patients can get symptom relief.
Figure 1.

**Predose serum Ca and plasma intact PTH levels over time in 5 years RCT (6)**

![Graph A: Serum calcium](image)

![Graph B: Plasma iPTH](image)

**References.**


