

Cinacalcet Hydrochloride

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Secondary hyperparathyroidism (HPT) is a progressive and detrimental disease associated with chronic kidney disease (CKD). Although surgical parathyroidectomy (PTX) remains the gold standard therapy for severe secondary HPT, it is not without risk. PTX exposes patients to anaesthesia risks, potential surgical complications, and may result in a permanent state of hypoparathyroidism. On the other hand, current medical treatments, such as calcium salts and vitamin D derivatives, are limited by hypercalcaemia, hyperphosphataemia and an increase in serum calcium-phosphorus product ($\text{Ca} \times \text{P}$). Therefore, there was a need for a drug that efficiently, safely, and cyclically reduces parathyroid hormone (PTH) secretion. The discovery of the extracellular calcium-sensing receptor (CaR) and the recognition that its activation by changes in extracellular ionised calcium regulates PTH, led to the development of calcimimetics that act to amplify the sensitivity of the CaR to extracellular ionised calcium.

Cinacalcet hydrochloride (HCl) is a second-generation calcimimetic that reduces serum PTH levels by 60–70% 2 hours after its oral administration. Several worldwide, high quality clinical trials, carried out in more than 1000 patients receiving oral cinacalcet HCl 30–180 mg/day, have demonstrated its efficacy in reducing basal serum PTH levels during the first 12-week titration phase. Subsequently, a sustained reduction in PTH has been observed after 3 years of treatment without an increase in $\text{Ca} \times \text{P}$ product. Moreover, more patients receiving cinacalcet HCl achieved recommended US National Kidney Foundation Disease Outcome Quality Initiative (NKF-K/DOQI™) values for PTH, calcium, phosphorus and $\text{Ca} \times \text{P}$ than placebo-treated patients. No major side effects have been observed except transient hypocalcaemia and gastric discomfort.

Cinacalcet HCl is undoubtedly an important contribution to current medical therapies for the treatment of secondary HPT. However, further research is needed to document its efficacy compared with calcium salts and vitamin D derivatives, its long-term effects on bone remodelling and bone mineral density, and its potential beneficial effects on morbidity and mortality rates in CKD patients. ▲