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CONCISE REVIEW

Cinacalcet HCl Treatment in Patients with Chronic Kidney Disease Stage 3–4

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Abstract: It has been clarified in patients with CKD stage 3–4, cinacalcet can reduce PTH levels without severe adverse events, however calcium levels significantly decrease and phosphorus levels increase. Increase of serum phosphorus level by cinacalcet in patients with CKD stage 3–4 is a problematic issue. Undesirable decreases in serum calcium and increases in serum phosphorus caused by cinacalcet require further investigation. For patients with CKD stage 3–4 who suffer from severely advanced 2HPT which cannot be controlled by the usual medical treatment or PTx, cinacalcet can be a useful medication for managing 2HPT.

Keywords: cinacalcet, chronic kidney disease, CKD, stage 3–4

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Secondary hyperparathyroidism (2HPT) is a common complication in patients with CKD (chronic kidney disease). It has been recommended that patients with CKD stage 3–4, maintain both serum phosphorus and calcium in the normal range to avoid progression of 2HPT and vascular calcification. In patients with CKD 3–4, usual progression of 2HPT can be controlled by dietary phosphate restrictions, phosphate binders, calcium supplementation and vitamin D sterols.

Cinacalcet HCl (cinacalcet) is a new allosteric modulator of the calcium sensing receptor (CaSR), which can reduce PTH secretion by binding to the CaSR in parathyroid cells.[1] Cinacalcet can dramatically reduce PTH levels, serum calcium and phosphorus levels and reduce requirement of PTx in patients with CKD stage 5D.

The use of cinacalcet in CKD stage 3–4 has yet to be approved and remains highly controversial. Only one long-term, randomized, double-blind, placebo controlled study of the efficacy and safety of cinacalcet in patients with CKD stage 3–4 has been published by Chonchol et al.[2] In this study 404 patients with CKD stage 3 or 4 were enrolled. Mean change of i-PTH level was significantly greater in the cinacalcet group than in the placebo group (43.1% vs. 1.1% $P < 0.001$). At week 32, serum calcium levels were 8.9 mg/dl vs. 9.9 mg/dL, and phosphate levels were 4.5 mg/dL vs. 4.0 mg/dL. This study, clarified that in patients with CKD stage 3–4, cinacalcet can reduce PTH levels without a severe adverse event, however calcium levels significantly decreased and phosphorus levels increased. The limitation of this study was the effect of vascular calcification, bone histomorphometry and other clinical outcomes which were not included in the design of this study.

Increase of serum phosphorus levels by cinacalcet in patients with CKD stage 3–4 is a problematic issue. The phenomena can be partly explained by the reduction of tubular re-absorption of phosphorus induced by decreased PTH action and the increase of phosphate absorption from the small intestine due to the additional intake of vitamin D sterols.

Fortunately in this study estimated glomerular filtration rate was not significantly changed by cinacalcet compared with the placebo.

Undesirable decreases in serum calcium and increases in serum phosphorus caused by cinacalcet requires further investigation.

Recently Foluslund et al reported efficacy of cinacalcet for severely advanced 2HPT in patients with CKD stage 3–4 who did not tolerate for PTx.[3] In patients with CKD stage 3–4 who suffer from severely advanced 2HPT which cannot be controlled by usual medical treatment or PTx, cinacalcet can be a useful candidate for managing 2HPT.

Disclosure

The author reports no conflicts of interest.

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