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Editorial

Clinical administration of cinacalcet in parathyroid diseases

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Abstract

Cinacalcet has emerged as an effective therapeutic option for the management of secondary hyperparathyroidism (SHPT) and chronic kidney disease-mineral and bone disorder (CKD-MBD). Through its modulation of the calcium-sensing receptor (CaSR), cinacalcet demonstrates considerable clinical benefits in maintaining parathyroid hormone and serum calcium levels within target ranges. It offers a valuable addition to the available treatment options for patients with these conditions. Cinacalcet binds to the CaSR on parathyroid cells, increasing its sensitivity to extracellular calcium. This results in decreased parathyroid hormone (PTH; parathormone), release through inhibition of intracellular signaling pathways involved in PTH synthesis and secretion. Cinacalcet also indirectly reduces serum calcium and phosphorus levels by suppressing PTH-mediated bone resorption and enhancing renal phosphate excretion.

Keywords: Cinacalcet, Calcimimetic agent, Secondary hyperparathyroidism, Chronic kidney disease, Calcium-sensing receptor, Parathormone, Parathyroid hormone

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Introduction

Secondary hyperparathyroidism (SHPT) is a common complication in patients with chronic kidney disease (CKD) due to impaired renal function. Cinacalcet acts by modulating the calcium-sensing receptor (CaSR) on parathyroid cells, leading to a decrease in parathyroid hormone (PTH) secretion. By reducing parathormone levels, cinacalcet helps control mineral and bone disorders associated with CKD. This review article aims to provide an overview of the mechanism of action of cinacalcet, clinical efficacy, and safety profile (1,2).

Search strategy

For this study, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ), and Embase, using different keywords including cinacalcet, calcimimetic agent, secondary hyperparathyroidism, chronic kidney disease and calcium-sensing receptor.

Mechanism of action

Cinacalcet is a calcimimetic agent that targets the parathyroid gland's CaSR. The CaSR is a G-protein coupled receptor that is primarily expressed on the surface of parathyroid chief cells. When an increase in extracellular calcium levels activates the CaSR, it inhibits the release of parathyroid hormone (PTH). Conversely, when the CaSR is inhibited, such as by cinacalcet, it increases PTH secretion (3). Cinacalcet binds to the CaSR and acts as a positive allosteric modulator. It enhances the sensitivity of the CaSR to extracellular calcium, decreasing the set point at which the receptor responds to calcium levels. This means that even at lower calcium concentrations, the CaSR is activated and inhibits PTH secretion. By activating the CaSR, cinacalcet effectively suppresses PTH secretion, thereby reducing the overproduction of parathormone seen in hyperparathyroidism (4,5). This helps to normalize calcium and phosphorus levels in patients with SHPT associated with CKD. It is important to note that cinacalcet does not directly lower calcium levels. Instead, it indirectly reduces calcium levels by inhibiting PTH secretion and promoting the uptake of calcium into bone tissue. Overall, cinacalcet's molecular mechanism of action involves binding to and enhancing the sensitivity of the CaSR in the parathyroid gland, leading to decreased PTH secretion and improved management of hyperparathyroidism (6,7).

Primary hyperparathyroidism

In patients with primary hyperparathyroidism who are

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Implication for health policy/practice/research/medical education

Cinacalcet has demonstrated efficacy in managing secondary hyperparathyroidism (SHPT) and chronic kidney disease-mineral and bone disorder (CKD-MBD), leading to improved control of PTH (parathormone) and serum calcium levels. The overall safety profile of cinacalcet is favorable, although monitoring is necessary to prevent hypocalcemia. Further research is needed to explore its role in different clinical settings and patient populations.

unable to undergo surgery, cinacalcet may be used as an alternative treatment option. The initial recommended dose is 30 mg once daily, and the dose can be titrated up to a maximum of 180 mg per day based on the patient's serum calcium levels and PTH levels (8,9).

Secondary hyperparathyroidism in chronic kidney disease

Cinacalcet is commonly used in patients with SHPT associated with CKD. The initial recommended dose is usually 30 mg once daily, and the dose can be titrated up to a maximum of 180 mg/d based on the patient's serum calcium and PTH levels. The goal of treatment is to maintain serum calcium levels within the normal range and reduce PTH levels (10,11).

Efficacy in chronic kidney disease-mineral and bone disorder

Apart from SHPT, cinacalcet has also shown efficacy in managing chronic kidney disease-mineral and bone disorder (CKD-MBD) by improving bone mineral density and decreasing markers of bone turnover. In addition, it has resulted in a reduction in serum calcium-phosphorus product and decreased the need for parathyroidectomy in some cases (12).

Parathyroid carcinoma

Cinacalcet may also be used in the management of parathyroid carcinoma, a rare malignant tumor of the parathyroid glands. The dosage and frequency of administration are individualized based on the patient's response and tolerability (13).

Clinical efficacy

Numerous clinical trials have demonstrated the efficacy of cinacalcet in reducing PTH levels and improving mineral metabolism parameters in patients with SHPT. It has been shown to effectively lower serum calcium and phosphorus levels while maintaining appropriate bone turnover markers. Additionally, cinacalcet has demonstrated long-term benefits in reducing cardiovascular events and mortality rates among CKD patients. Cinacalcet is typically administered orally in the form of tablets. The dosage and frequency of administration depend on the specific condition being treated and the patient's individual response (14,15).

Safety profile

Cinacalcet is generally well-tolerated; however, some adverse effects have been reported. The most common side effects include gastrointestinal symptoms such as nausea, vomiting, and diarrhea. Hypocalcemia, which can be managed by adjusting calcium and vitamin D supplementation, is another potential complication. Cinacalcet use should be cautious in patients with hepatic impairment due to its metabolism primarily through the liver. It is important to closely monitor serum calcium levels and PTH levels during cinacalcet therapy. Regular laboratory tests are necessary to ensure that the medication effectively controls the levels of PTH and calcium within the desired range (16,17). Cinacalcet may be taken with or without food, and it is generally recommended to take it at the same time each day to maintain consistent blood levels of the medication. As with any medication, it is crucial to follow the prescribed regimen and consult with a healthcare professional regarding any questions or concerns about the clinical administration of cinacalcet (18).

Drug interactions

Cinacalcet is primarily metabolized by cytochrome P450 enzymes, particularly CYP3A4. Hence, caution should be exercised when co-administering cinacalcet with drugs that may affect these enzymes, potentially leading to altered cinacalcet concentrations (19).

Conclusion

Cinacalcet is an effective therapeutic option for managing SHPT in CKD patients on dialysis and hypercalcemia in parathyroid carcinoma. Its mechanism of action through CaSR modulation has been well-established, leading to significant reductions in PTH levels and improvements in mineral metabolism parameters. While generally safe, close monitoring for adverse effects such as gastrointestinal symptoms and hypocalcemia is necessary during cinacalcet therapy.

Authors' contribution

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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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