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Original article

Use of cinacalcet for the management of hyperparathyroidism in patients with different degrees of renal failure☆

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ABSTRACT

Background: The effects of cinacalcet in persistent and/or hypercalcaemia-associated secondary hyperparathyroidism (SHPT) have been described in patients on dialysis.
Objectives: To evaluate the efficacy and safety of cinacalcet in SHPT not on dialysis and its effects on bone turnover markers.
Methods: Non-randomised, longitudinal, observational, analytical study of patients with chronic kidney disease (CKD) and SHPT (PTH >80 pg/mL) as well as normo- or hypercalcaemia (≥8.5 mg/dL), treated with cinacalcet.
Results: Mean cinacalcet dose was 30 mg/day in 66.7%. We studied 15 patients (10 women), aged 66.0 ± 17.93 years. The aetiology was unknown in 20% of cases. Sociodemographic variables and renal function parameters were recorded. We compared values at baseline as well as after 6 and 12 months. Calcium (10.3 ± 0.55 vs. 9.4 ± 1.04) and iPTH (392.4 ± 317.65 vs. 141.8 ± 59.26) levels decreased. Increased levels of phosphorus (3.7 ± 1.06 vs. 3.9 ± 0.85) and β-CTX (884.2 ± 797.22 vs. 1053.6 ± 999.00) were detected, although there were no significant changes in GFR, urinary calcium or other bone markers. Two patients withdrew from the study (gastrointestinal intolerance and parathyroidectomy, respectively).
Conclusions: Cinacalcet at low doses is effective in the management of SHPT in CKD patients who are not on dialysis. Its use reduces iPTH and calcaemia, without causing serious side effects or significant changes in renal function.

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Uso de cinacalcet para el control del hiperparatiroidismo en pacientes con diferentes grados de insuficiencia renal

Palabras clave:
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Calcio
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RESUMEN

Antecedentes: Los efectos de cinacalcet en el hiperparatiroidismo secundario (HPTS), persistente o asociado a hipercalcemia han sido descritos en pacientes en diálisis.
Objetivos: Analizar la eficacia y seguridad de cinacalcet en HPTS no sometido a diálisis y sus efectos sobre marcadores de recambio óseo.
Métodos: Estudio analítico observacional, no aleatorizado, longitudinal, de pacientes con enfermedad renal crónica (ERC) e HPTS (PTH > 80 pg/mL); con normohipercalcemia (≥8,5 mg/dL), tratados con cinacalcet.
Resultados: La dosis media de cinacalcet fue de 30 mg/día en un 66,7%. Estudiamos 15 pacientes (10 mujeres), con edad de 66,0 ± 17,93 años. Etiología desconocida en 20% de los casos. Registramos variables sociodemográficas y parámetros de función renal. Comparamos valores basales, tras 6 y 12 meses. Descendieron los niveles de iPTH (392,4 ± 317,65 vs. 141,8 ± 59,26) y calcio (10,3 ± 0,55 vs. 9,4 ± 1,04). Aumentaron los valores de fósforo (3,7 ± 1,06 vs. 3,9 ± 0,85) y ß-CTX (884,2 ± 797,22 vs. 1.053,6 ± 999,00), sin variaciones significativas del FG, calciuria y demás marcadores óseos. Registrados 2 abandonos (intolerancia digestiva y paratiroidectomía, respectivamente).
Conclusiones: Cinacalcet a dosis bajas es eficaz en el manejo del HPTS del paciente con ERC no tratado mediante diálisis, al disminuir la iPTH y la calcemia, sin ocasionar efectos adversos graves ni variación significativa de la función renal.

Introduction

Cinacalcet (Mimpara®) is currently the only calcimimetic with an approved indication for the treatment of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) on dialysis,[1–3] as well as in primary hyperparathyroidism (PHPT) caused by parathyroid adenoma or carcinoma in patients who have not undergone a parathyroidectomy, or with persistence of the disease following parathyroidectomy.[2] Also, it has been used successfully in residual SHPT from a kidney transplant, although it does not a formal indication[4] in these patients.

The calcimimetics acts as a positive allosteric modulator of the calcium-sensor receptors expressed in multiple tissues such as the parathyroid glands, kidneys, bone (especially in osteoclasts) and blood vessels.[5] Its activation increases signal transduction, presumably inducing intracellular conformational changes and reducing the threshold for calcium sensitivity. At the glandular level, this translates to lower production and secretion of parathyroid hormone (PTH), which is essential in the management of resistant SHPT and SHPT associated with hypercalcaemia in patients in dialysis, in whom it has also shown modification of bone turnover markers.[6,7]

Less known are the effects of calcimimetics on patients with abnormal renal function not on dialysis, in whom mineral and bone disorder (MBD) associated with CKD is present.[5–7] The latter does not strictly include only abnormalities in calcium, phosphorus, PTH and vitamin D; it also comprises abnormalities in bone remodelling, volume and resistance; as well as vascular and soft-tissue calcifications.[7,8] In patients with CKD, the determination of collagen degradation products and classic bone turnover markers have greater utility than bone densitometry to predict the risk of fractures. Hence the importance of studying these parameters.[7]

This work aims to determine the efficacy and safety of cinacalcet in the treatment of SHPT in patients with CKD not treated with renal replacement therapy, in whom, owing to their serum calcium levels, the use of vitamin D and its derivatives is not safe, and in patients with severe hyperparathyroidism with a contraindication for surgery. It also aims to describe its effects on bone remodelling markers.

Patients and methods

We conducted an observational, longitudinal study in a cohort of patients followed in our outpatient clinics. Patients enrolled had a diagnosis of SHPT (iPTH level > 80 pg/ml), whether with hypercalcaemia (which limited the use of both calcium-chelating agents and vitamin D and its analogues) or with normocalcaemia (corrected calcium ≥8.5 mg/dl) resistant to these treatments. Patients were on stages 3–5 CKD (estimated glomerular filtration rate [eGFR] between 60 and <15 ml/min/1.73 m^2).

The sociodemographic variables of the sample were recorded.

In each patient the use of cinacalcet for compassionate use was requested and authorised.

The patients started treatment with cinacalcet at a dose of 30 mg in a single dose taken in the morning, and the dose was adjusted according to the evolution of the measured parameters.