levels remained high. Consequently, the level of potassium in his dialysis fluid was also lowered (from 2 to 1 mmol/l). After this, his potassium levels remained below 6 mEq/l.

A progressive decline in or maintenance of kidney function is associated with an increase in capacity for potassium secretion in the colon. The mechanism through which colon secretion of potassium is increased in these patients is complex and depends on several factors. On one hand, there is an increase in Na+/K+–ATPase pump activity in the basolateral membrane of the intestinal cell. This leads to an increase in intracellular potassium levels as well as an increase in potassium conductivity in apical cells. Colon secretion of potassium is also increased by aldosterone. Although its mechanism has not yet been fully reported, it appears to be related to an increase in expression of large-conductance potassium channels (BK channels) in the apical membrane of the intestinal cell.[3]

Konowa et al. published a case[4] in 2013 on a patient with end stage renal disease undergoing haemodialysis who underwent surgical resection of the ileocaecal junction and a temporary ileostomy. After this, the patient developed hyperkalaemia, which resolved following reanastomosis of the colon. Various *in vitro* and *in vivo* studies have used immunohistochemistry techniques to show that there is greater BK channel expression in patients with end stage renal disease than in those with normal kidney function, in whom small- or intermediate-conductance potassium channel expression predominates.

In summary, potassium secretion in the gastrointestinal tract is a complex and essential mechanism for maintaining its homeostasis in patients with terminal end stage renal disease. Our case demonstrated the importance of potassium secretion in the colon in patients with end stage renal disease.

REFERENCES

1. Mathialahan T, Maclennan KA, Sandle LN, Verbeke C, Sandle GI. Enhanced large intestinal potassium permeability in end-stage renal disease. J Pathol. 2005;206:46–51.
2. Hayes C, McLeod M, Robinson R. An extravenal mechanism for the maintenance of potassium balance in severe chronic renal failure. Trans Assoc Am Phys. 1967;80:207–16.
3. Sorensen M, Matos J, Sausbier M, Sausbier U, Ruth P, et al. Aldosterone increases KCa 1.1 (BK) channel-mediated colonic K+ secretion. J Physiol. 2008;586:4251–64.
4. Konowa N, Dickenman MJ, Jeong Kim M. Severe hyperkalemia following colon diversion surgery in a patient undergoing chronic hemodialysis: a case report. J Med Case Rep. 2013;7:1–4.

Paola Rodríguez*, Evangelina Mérida, Eduardo Hernández, Mónica Milla, Manuel Praga

Hospital Universitario 12 de Octubre, Madrid, Spain

* *Corresponding author.*
E-mail address: pao.rodriguezra@gmail.com (P. Rodríguez).

https://doi.org/10.1016/j.nefroe.2017.01.028

Denosumab and chronic kidney disease: Severe life-threatening hypocalcaemia☆

Denosumab y enfermedad renal crónica avanzada: hipocalcemia severa con riesgo vital

Dear Editor,

A few months ago, we published a case report of asymptomatic severe hypocalcaemia following a dose of denosumab in a patient with advanced chronic kidney disease.[1] We now report a new case, this time one that was life-threatening for the patient. We thought that it important to report this new case due to its severity and, to show that it does no longer seems to be so rare.

We present the case of a 62-year-old woman whose medical history included slight intellectual disability, diabetes mellitus, long-standing dyslipidaemia and hypertension; and colon neoplasm 3 years earlier. She had been diagnosed of chronic kidney disease likely related to nephroangiosclerosis secondary to hypertension, currently in stage 4. Her regular treatment consisted of olmesartan, repaglinide, insulin glargine, atorvastatin, escitalopram, bromazepam, quetiapine and pantoprazole. Six months earlier, she suffered a hip fracture following an accidental fall and underwent implantation of a total hip prosthesis. The Traumatologists started

DOI of original article:
http://dx.doi.org/10.1016/j.nefro.2017.01.004.
☆Please cite this article as: Monge Rafael P, Martin de Francisco ÁL, Fernández-Fresnedo G. Denosumab y enfermedad renal crónica avanzada: hipocalcemia severa con riesgo vital. Nefrologia. 2018;38:97–98.

Table 1 – Laboratory data at baseline and over time.

Laboratory parameters	Before treatment	Day 10	Day 13	Day 18	Day 30
Corrected calcium (mg/dl)	8.62	5.2	8.7	4.5	7.1
Phosphorus (mg/dl)	3.36	3.9	3.8	8.8	2.6
Magnesium (mg/dl)	1.5	1	1.4	0.9	1.2
iPTH (pmol/l)	–	–	–	–	317
25-OH Vitamin D (ng/ml)	–	–	–	–	7
Creatinine (mg/dl)	2.19	2.91	2.63	6.1	3.26
MDRD (ml/min)	17	17	19	7	15

treatment with denosumab 60 mg every 6 months and 1500 mg of calcium carbonate with 1000 IU of cholecalciferol daily to treat osteoporosis. After 10 days of administering denosumab, the patient visited the Emergency Department due to signs and symptoms of general malaise, as well as neck and leg muscle contracture. The testing performed revealed severe hypocalcaemia — 5.2 mg/dl. Following fluid and electrolyte replacement therapy, her laboratory parameters returned to normal and her signs and symptoms disappeared in 3 days. After a week, the patient visited the Emergency Department again due to new signs and symptoms of anorexia, watery diarrhoea, general malaise, muscle stiffness and hypotension. She had severe hypocalcaemia, hypomagnesaemia, metabolic acidosis and worsening of kidney function. She required admission to the Intensive Care Unit for intravenously managed fluid and electrolyte replacement therapy. She experienced clinical and laboratory improvement. When she was discharged from hospital, treatment was maintained with calcium carbonate, magnesium lactate and calcitriol (Table 1).

The patient was a woman with osteoporosis. However, in addition, she had advanced chronic kidney disease. In such a situation, osteomineral metabolism abnormality has some distinct, more complex features, with abnormalities in both remodelling and mineralisation rate, with different combinations of these, leading to different patterns of osteomineral abnormality (fibrous osteitis, adynamic bone disease, osteomalacia).[2,3] A few months ago, we published a similar case of severe hypocalcaemia, although that time it was asymptomatic. The use of a powerful antiresorptive agent such as denosumab[1] interferes with these mechanisms. This may lead to hungry bone syndrome by inhibiting osteoclast activity and causing severe hypocalcaemia. We believe that the use of denosumab in patients with advanced chronic kidney disease requires from clinicians to weigh up the risk/benefit ratio and, should they need to administer it, perform a tight follow-up of their patients' signs and symptoms as well as laboratory values.

[1] Denosumab is a human monoclonal antibody (IgG2) that binds with great affinity and specificity to RANKL and blocks activation of RANK, its receptor, on the surfaces of osteoclasts and their precursors. This reduces their activity and causes a decrease in bone resorption in trabecular and cortical bone. It is used to treat osteoporosis and administered every 6 months. It is not necessary to adjust the dose in renal failure, but there is an increased risk of hypocalcaemia.[4,5]

REFERENCES

1. Monge Rafael P, Arias M, Fernandez-Fresnedo G. Hipocalcemia severa tras la administración de una dosis de denosumab en un paciente con insuficiencia renal avanzada. Nefrologia. 2016;36:446–8.
2. Millar PD. Bone disease in CKD: a focus on osteoporosis diagnosis and management. Am J Kidney Dis. 2014;64:290–304.
3. Torregrosa JV, Bover J, Cannata Andía J, Lorenzo V, Francisco AL, Martínez I, et al. Recomendaciones de la Sociedad Española de Nefrología para el manejo de las alteraciones del metabolismo óseo-mineral en los pacientes con enfermedad renal crónica (S.E.N.-M.M.). Nefrologia. 2011;31 Suppl. 1:3–32.
4. Prolia (denosumab) solution for injection. Thousand Oaks, CA: Amgen, Inc.; 2016.
5. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in posmenopausal women with osteoporosis. N Engl J Med. 2009;361:756–65.

Pilar Monge Rafael[a], Ángel Luis Martin de Francisco[b], Gema Fernández-Fresnedo[b,*]

[a] *Servicio de Endocrinología, Hospital Universitario Marqués de Valdecilla, Santander (Cantabria), Spain*
[b] *Servicio de Nefrología, Hospital Universitario Marqués de Valdecilla, Santander (Cantabria), Spain*

[*] *Corresponding author.*
E-mail address: nefffg@humv.es (G. Fernández-Fresnedo).

https://doi.org/10.1016/j.nefroe.2017.11.014