Curcumin intake in haemodialysis patients

Ingesta de curcumina en pacientes en hemodiálisis

Dear Editor,

For a long time, natural products have been used in the traditional medicines of different cultures. Many active substances used in current pharmacopoeia stem from research within this field. They are widely used, although their use is a source of controversy. A significant proportion of these products are normally contraindicated for patients on dialysis due to their possible deleterious effects.

We present the case of a 63-year-old woman from New Delhi, India, with chronic kidney disease of unknown cause who has been undergoing a chronic haemodialysis programme since March 2015 through a central venous catheter (CVC). She underwent a radiocephalic left arteriovenous fistula (RC lAVF) in September 2015. Following a maturation period, lAVF punctures were initiated, with haematomas developing at the puncture sites, and a lengthening of the haemostasis time of more than 2 h, with bleeding at home and a need for referral to the emergency department on multiple occasions, the dialysis parameters were adjusted to use a technique without heparin, antiplatelet therapy was suspended and heparin sealing of the CVC was minimised. However, the increased haemostasis times persisted, and there were also spontaneous bleeding episodes due to the lAVF at her home. A fistulogram was performed with normal results. In the laboratory tests, an altered prothrombin time (PT) of 63 s and an activated partial thromboplastin time (aPTT) > 140 s were observed. No underlying liver disease was revealed, and the patient was not taking oral anticoagulants. In light of this finding, the patient was questioned again. She reported taking turmeric infusions on a daily basis in quantities of 3–5 g. We decided to suspend these infusions after reviewing the literature which mentions a possible anticoagulant effect, as well as boosting the effects of antiplatelet therapy. After 2 weeks of not using the lAVF and of abstaining from the turmeric infusions, normal clotting times were displayed and the lAVF punctures were started again with no new haemorrhage incidences being presented until now.

Turmeric (*Curcuma longa*) is native to south-west India. It is a herbaceous perennial plant from the Zingiberaceae family. The most important chemical components of turmeric are a group of compounds called curcuminoids (curcumin or diferuloylmethane, demethoxycurcumin and bisdemethoxycurcumin).[1] It also contains volatile oils such as turmerone, atlantone and zingiberene, as well as sugars, proteins and resins. Curcumin is responsible for its yellow colouring. Turmeric is used routinely as a spice, especially in Indian cuisine, and as a food colouring. Turmeric is now also used as a textile dye, and it is used to dye wool, cotton, silk, leather, waxes, stains, etc.[2] A wide range of biological and pharmacological activities of turmeric has been researched. These include antioxidant, anti-inflammatory, antiviral, antifungal, hepatoprotective, anti-cancer, antimicrobial, cardiovascular, gastrointestinal, nephroprotective, anticoagulant and anti-diabetic effects.[2] Curcumin may bind to heavy metals such as cadmium and lead, reducing their toxicity. It also acts as an inhibitor of cyclooxygenase, 5-lipoxygenase and glutathione *S*-transferase, which converts it into an antioxidant, like vitamins C, E and beta-carotene.[2] The anti-inflammatory action of turmeric is probably due to a reduction in histamine production and also due to the fact that it increases and prolongs the action of cortisol. Turmeric acts by stimulating bile production, improving fat metabolism.[2] Pharmacokinetic studies in animals[3] have demonstrated that 40–85% of oral curcumin passes through the gastrointestinal tract without changes, the rest being absorbed by the intestinal mucosa and the liver. Due to its low rate of absorption, curcumin often combines with other compounds to increase absorption and boost the anti-inflammatory effect. It has rapid hepatic elimination following intravenous infusion, and it is a compound which is rapidly metabolised.[2] The anticoagulant effects of turmeric were analysed in an *in vitro/in vivo* study. It was demonstrated that turmeric inhibited the action of thrombin, factor Xa and increased the aPTT and PT.[4]

In the case that we present, the intake of high quantities of turmeric, with no other influencing factor, seems to be related to an increase in PT and aPTT, which were reversed after stopping the intake, with the altered parameters normalising.

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A light in the control of secondary hyperparathyroidism. Etelcalcetide IV in haemodialysis☆

Una luz en el control del hiperparatiroidismo secundario. Etelcalcetide intravenoso en hemodiálisis

Dear Editor,

Secondary hyperparathyroidism (HPT) is a very common complication that worsens and exacerbates chronic kidney disease (CKD). It is associated with the genesis of vascular calcifications and with increased cardiovascular morbidity and mortality.[1,2]

According to data from the Spanish Society of Nephrology, more than 23,000 patients in Spain undergo haemodialysis (HD), and approximately 35% of these patients have HPT.[3]

The treatment of HPT is based on the control of dietary phosphorus intake, the administration of phosphate binders and vitamin D supplements, the activation of vitamin D receptors, and the administration of calcimimetic agents that activate the calcium-sensing receptor (CaSR) of the parathyroid glands.[4,5] Most of these treatments are administered orally and are not entirely free from adverse effects; therapeutic outcomes depend to a large extent on patient adherence. Calcimimetic agents in particular are associated with gastrointestinal side effects.[1,4]

Recently, a new long-acting calcimimetic agent (etelcalcetide) was approved for intravenous use in HD patients with secondary hyperparathyroidism.[5] Etelcalcetide binds directly to CaSR, inhibiting the production and secretion of parathyroid hormone (PTH) by the parathyroid glands. One of the main advantages of the drug is its intravenous route of administration, which is likely to promote patient adherence to treatment.[5]

Since there are very few reports on its use in Spain, we believe that our experience in a patient with severe HPT and poor adherence to oral calcimimetics will be of interest.

This was a 57-year-old patient with CKD secondary to autosomal dominant polycystic kidney disease, who had been receiving HD since June 2011. She had undergone surgery for breast cancer in 2013, and presented difficult-to-control HPT despite treatment with lanthanum carbonate (2 g/8 h), calcium acetate (500 mg/day), sevelamer (1600 mg/8 h), cinacalcet (60 mg/day) and IV paricalcitol (1 μm after each HD session).

The patient had complained of gastrointestinal symptoms since the start of treatment with cinacalcet, which persisted despite antiemetics. The nausea and vomiting at times even prevented her from eating. Gastroscopy was performed, which was normal.

We requested authorisation to use etelcalcetide for compassionate use. Cinacalcet was discontinued, and after 10 days treatment was started at a dose of 2.5 mg after each HD session. Calcifediol was discontinued, but paricalcitol was maintained.

The results are shown in Table 1.

Table 1 – Changes in patient's serum level over time.

Date of test	PTH (pg/ml)	Calcium (mg/dl)	Phosphorus (mg/dl)
July 2017	1223	9.3	4.3
Start of treatment with etelcalcetide (07/08/2017)			
August 2017	912	9.8	5.3
September 2017	764	8.7	3.0
October 2017	686	7.8	5.6
November 2017	701	8.4	4.9
December 2017	486	8.4	4.8

PTH: parathyroid hormone.

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