Letter to the Editor

Experience of using haemodialysis with medium cut-off dialyser in cast nephropathy☆

Experiencia de hemodiálisis con dializador de mediano poro en la nefropatía por cilindros del mieloma

Dear Editor,

Multiple myeloma is a clonal proliferation of plasma cells that causes kidney involvement in 40% of cases, although only 12–15% of cases start with acute kidney failure, with cast nephropathy being the most common cause of this. When acute kidney failure occurs, it requires chemotherapy treatment as well as apheresis techniques in a high percentage of cases[1,2] aimed at reducing the concentration of free light chains (FLC) in plasma as early as possible, and thereby preventing their deposition in the kidney tubules.[3,4]

The emergence of high cut-off haemodialysis (HCO-HD) was postulated as a breakthrough compared to conventional high-flux haemodialysis (HF-HD) due to a faster withdrawal of circulating FLCs. However, preliminary results from two recent studies generate a certain level of controversy.[5,6]

Recently, medium cut-off (MCO) membranes have been developed, with an ability to eliminate molecules like the HCOs, but able to retain albumin,[7–9] which may be a more cost-effective alternative for the adjuvant treatment of acute kidney failure due to kappa myeloma.

We describe the cases of three patients who developed acute kidney failure secondary to kappa FLC tubular deposition (22.5 kDa). In all of them, chemotherapy treatment was started early with bortezomib and dexamethasone, according to the haematology protocol, as well as 6-h haemodialysis sessions with the MCO dialyser Theranova 500® by Baxter.

The weekly determination of pre-dialysis creatinine, of FLC kappa (Fig. 1) and of albumin before and after each haemodialysis session (Fig. 2) was carried out.

Case 1

A 46-year-old woman in whom hypercalcaemia was detected (15.6 mg/dl), kappa FLC levels of 48,900 mg/l and deterioration of kidney function (creatinine of 10.3 mg/dl). The diagnosis of multiple myeloma was confirmed by bone marrow biopsy (76% of plasma cells).

After 27 sessions of haemodialysis, kidney function remained stable without the need for dialysis and undetectable FLC levels.

Case 2

A 72-year-old male with acute kidney failure (creatinine 4.7 mg/dl) and elevated kappa FLC levels (1040 mg/l). The diagnosis of multiple myeloma was confirmed in a bone marrow biopsy with 14.37% of plasma cells.

The dialysis sessions were spaced out over time according to the analysis. After 32 sessions, the plasma creatinine levels stabilised around 3.4 mg/dl, without the need for dialysis.

Case 3

A 73-year-old male who presented with acute kidney failure (creatinine 4.6 mg/dl), hypercalcaemia (Ca 11.5 mg/dl), hyperproteinaemia (14.11 g/dl) and kappa FLC levels of 14,300 mg/l. The diagnosis of multiple myeloma was confirmed by bone marrow biopsy with 28.66% of plasma cells.

He received seven haemodialysis sessions after which the free light chain levels were reduced to 340 mg/l, and kidney function recovered to maintain creatinine levels of 1.4 mg/dl, without new dialysis sessions.

In the three cases described, a sustained decrease in kappa chain concentration pre- and post-dialysis was observed, with a mean reduction of 44.8 ± 19.5% in each session, without a significant reduction in the plasma albumin levels. All the patients recovered kidney function without the need for more dialysis sessions.

The development of new chemotherapy treatments and of apheresis, and their early administration has led to an

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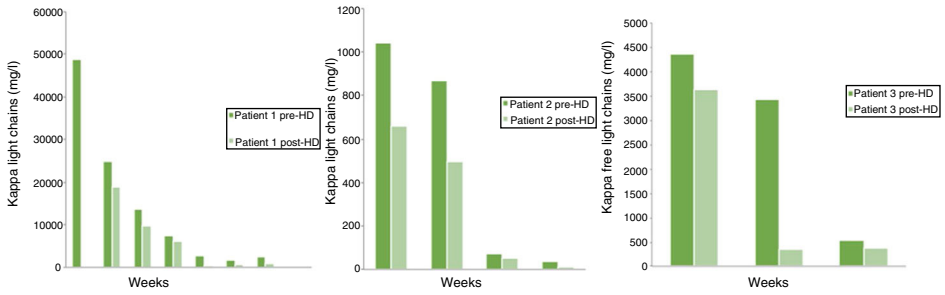

Fig. 1 – Weekly evolution of kappa light chain levels, pre- and post-dialysis.

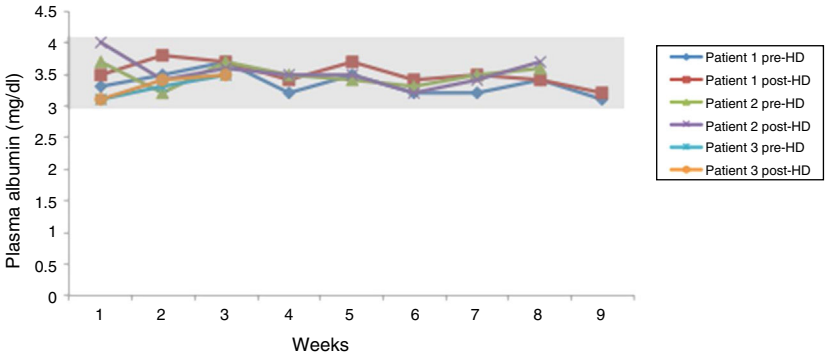

Fig. 2 – Weekly evolution of plasma albumin levels, pre- and post-dialysis.

improvement in survival and has increased the renal recovery rate in patients affected by acute kidney failure secondary to cast nephropathy. With the development of haemodialysis with new dialysers, firstly HCO-HD and subsequently MCO-HD, there has been an attempt to improve these results.

Preliminary results of two multicentre, randomised and controlled studies which compare chemotherapy treatment along with HF-HD or HCO-HD deliver contradictory results; while better renal outcomes for patients are shown in the MYRE study,[6] the EULITE study[5] does not provide statistically significant results. The study of the complete results will be necessary to understand the reason for these differences.

From our experience, the introduction of haemodialysis with medium cut-off dialysers has managed to reduce the loss of albumin which was produced with previous high cut-off dialysers, without this influencing the rapid and effective reduction of the plasma concentration of kappa light chains, obtaining good clinical outcomes and renal survival in treated patients.

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Letter to the Editor

New information on phosphate binder interactions with vitamin K☆

Nueva información sobre interacciones de captores de fósforo con la vitamina K

Dear Editor,

We recently published an editorial in the journal NEFROLOGÍA to draw attention to a little known aspect of phosphate binders, specifically their potential pharmacological interactions.[1] In this article, we underlined that sevelamer can reduce the absorption of fat-soluble vitamins D, E and K and folic acid (according to the summary of product characteristics), although with debatable clinical impact. These data from the summary of product characteristics were obtained from experimental pre-clinical studies in rats and dogs and *in vitro* studies.

In recent years, the distinction between vitamin K_1 (phylloquinone or phytomenadione) and vitamins K_2 (menaquinones) has been emphasised and, in the nephrology community, these vitamins have gained importance as it has been recognised that vitamin K deficiency is very common in kidney patients, in particular those on renal replacement therapy.[2] This vitamin K deficiency would limit the post-translational activation by carboxylation and phosphorylation of multiple proteins related to the inhibition of vascular calcification (**K**-alcification) (osteocalcin, Bone-Gla protein, Matrix-Gla protein [MGP], among other vitamin K-dependent proteins), in addition to their effects on the classic coagulation pathways (**K**-oagulation).[2] Therefore, as vitamin K is an important cofactor for the activation of these proteins, its deficiency produces an increase in inactive forms (dephosphorylated-uncarboxylated),[2] with vitamin K_2 being the preferred cofactor for the carboxylation of MGP (tissue inhibitor of vascular calcification).[3] In this way, very recent studies (included in Figure 1 of the publication) have underlined that sevelamer (just like sucroferric oxyhydroxide [SOH] and in contrast to lanthanum carbonate) did not seem to have interactions with vitamin K_2.[3] This information comes from the publication by Neradova et al.[3] in which it was reported that SOH and sevelamer did not bind to vitamin K_2 *in vitro*, both in the presence and in the absence of phosphate in the solution.

However, a subsequent study in patients with chronic kidney disease (CKD) (on haemodialysis, peritoneal dialysis and transplant patients)[4] has analysed the impact of phosphate binders on vitamin K status in humans for the first time. These authors measured dephosphorylated-uncarboxylated MGP (inactive MGP), with a validated and standardised technique that better reflects vitamin K status than "simple" measurement of uncarboxylated MGP.[5] This study demonstrated an association between monotherapy with sevelamer and higher levels of dephosphorylated-uncarboxylated MGP (inactive) after adjusting for age, gender and use of vitamin K, suggesting a possible worsening of vitamin K status with this phosphate binder, with the potential negative impact on vascular calcification progression in these patients.[6] However, as we have pointed out previously, these interactions with vitamins have a debatable clinical impact. For example, no significant interactions have been reported in any of the summary of product characteristics for sevelamer, lanthanum or SOH (in healthy volunteers at least) with warfarin (vitamin K antagonist, with acenocoumarol being our normal equiv-

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