A) COMMENTS ON PUBLISHED ARTICLES

Comment on "Magnesium and chronic kidney disease"

Nefrologia 2013;33(6):849-50
doi:10.3265/Nefrologia.pre2013.Jul.12156

To the Editor:

We read with interest the abovementioned article and found little specific information on peritoneal dialysis (PD) patients.[1] There are several reports in the 1990s on the use of calcium acetate/magnesium carbonate (CAMG) as a phosphorus binder. In one particular series on 32 patients, phosphate binders were compared with calcium and metal binders.[2] However, this line of work was lost with the development of new binders (sevelamer and lanthanum). We have recently carried out studies that have renewed interest in CAMG in haemodialysis (HD), comparing its efficacy with that of other monotherapy binders. Nevertheless, we do not have similar clinical trials for PD. Studies that achieved the authorisation of CAMG included PD patients, but no specific subanalyses have been carried out on patients using this home technique. We already reported the need to carry out this type of study, since hyperparathyroidism (HPTH) management in PD is not identical to that of HD.[3]

As such, we wanted to contribute data on our preliminary experience with 10 patients on PD with moderate HPTH (mean baseline parathyroid hormone [PTH] 277pg/ml, range [150-606]), who we treated with CAMG (Osvaren®) for 6 months. Our main objective was to assess the tolerability and safety of the drug and obtain preliminary results on its efficacy in the control of serum phosphorus. The patients (54.8±9.4 years and 50% male) had a median time of 6.3 months on PD (7 on continuous ambulatory peritoneal dialysis, 3 on automated peritoneal dialysis) and achieved the dialysis efficacy objectives. The median treatment dose during follow-up was 2 pills per day (range 1-3). Treatment was well tolerated in all cases and it was not necessary to reduce the dose due to side effects. In two patients it was necessary to re-introduce another phosphorus binder at low doses (in one 750mg/24h of lanthanum carbonate and in another 1200mg/24h of sevelamer carbonate); 7 received Zemplar® and 3 Mimpara® from 3 months before the start of CAMG. At the start of treatment 7 patients displayed phosphorus within the range specified by the K/DOQI guidelines with the foregoing regimen and in just 4 months, all patients were well-controlled with CAMG. The number of patients who simultaneously achieved the objectives for phosphorus and PTH set by the K/DOQI guidelines increased from 4 to 8 in this time. Mean phosphorus had decreased from 4.8±0.6mg/dl to 4.6±1.0mg/dl at the end of the six-month follow-up.

We are aware of the limitations of our preliminary analysis, but we are interested in demonstrating the possibility of using CAMG in PD. It is striking that in the 30 laboratory tests we carried out during follow-up, we only found one high magnesium value (1.8mmol/l) and none for calcium above 10.5mg/dl. There was no clinical impact in any of these cases and it was easily corrected by adjusting the dialysate or diet. Four patients had cramp at the start and none at the end of follow-up. None of the patients displayed gastrointestinal intolerance and treatment allowed for a reduced use of laxatives.

The small amount of data available on the use of CAMG in PD may be due, on the one hand, to the fear of side effects (gastrointestinal intolerance and hypermagnesaemia), and on the other, to the difficulty of carrying out studies in PD units, which are still small in our country.

We have indirect evidence that hypomagnesaemia causes greater clinical problems than hypermagnesaemia in PD patients,[4] similarly to that reported by De Francisco for HD patients.[1] In fact, several observational studies have found that low magnesium is associated with worse control of HPTH, more calcifications, malnutrition and higher mortality.[5,6]

Furthermore, the laxative effect is interesting in PD, since the vast majority of patients require laxative drugs to achieve an adequate bowel pattern (one stool deposition per day). In conclusion, the cost of new non-calcium binders is 6 times the cost of CAMG, which is relevant for the sustainability of our health care system.[7]

Due to all of the above, we believe that CAMG may have a role to play as the first line of treatment in PD and that more PD-specific studies are necessary.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Response to the comment on "Magnesium and chronic kidney disease"

Nefrologia 2013;33(6):850-1
doi:10.3265/Nefrologia.pre2013.Jul.12207

To the Editor:

The authors reply to our publication on magnesium and chronic kidney disease[1] and provide data on their preliminary experience with 10 peritoneal dialysis patients who received calcium acetate/magnesium carbonate (Osvaren®). The median treatment dose during follow-up was 2 pills per day (range 1-3). In two patients, it was necessary to reintroduce another phosphate binder at low doses. During follow-up, they only found one high magnesium value (1.8mmol/l) and none for calcium higher than 10.5mg/dl.

Firstly, it is necessary to highlight that the most important factor in serum magnesium concentrations is the concentration in dialysate, which the authors did not report. In our experience in peritoneal dialysis the mean magnesium concentrations with dialysate of 0.25mmol/l and of 0.50mmo/l were 2.04±0.3mg/dl (n: 17 patients) and 2.35±0.3mg/dl (n: 56 patients), respectively.[2] We should bear in mind that, up to concentrations of <4.88mg/dl (<2.0mmol/l), hypermagnesaemia is clinically irrelevant and is associated with beneficial effects.[1] The question that we must answer is whether in peritoneal dialysis patients who receive calcium acetate/magnesium carbonate (Osvaren®) these serum magnesium values increase above these figures. In our experience with 12 peritoneal dialysis patients (11 with dialysate of 0.50mmol/l and one with 0.25mmol/l) treated exclusively with calcium acetate/magnesium carbonate (Osvaren®) for 6 months, the mean serum magnesium values increased from 2.38±0.33 to 2.63±0.64, with the highest value reached in a patient being 3.5mg/dl (Table 1).

In the Calmag study[3] on haemodialysis patients, the number of calcium acetate/magnesium carbonate pills (Osvaren®) required was 7.29±3.026/day, and as such, the dose the authors referred to in their letter (2 pills per day with a range from 1 to 3) is rather low, which may explain why in two patients, it was necessary to reintroduce another phosphate binder. In our haemodialysis studies over six months in real clinical practice (n: 52 patients), the mean CaMg dose required for the reduction of phosphorus (from 6.43±1.93 at baseline to 4.83±1.98mg/dl after six months) was 4.66±1.52 pills without the requirement for any other phosphate binder.[4]

Therefore, we agree with the authors of this letter that calcium acetate/magnesium carbonate (Osvaren®) has an important role as the first step of treatment in peritoneal dialysis and that it is important to carry out more comprehensive studies in peritoneal dialysis patients.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Table 1. Biochemical parameters in peritoneal dialysis patients treated with Ca-Mg

	Baseline	3M	6M
Mg	2.38±0.33	2.62±0.46	2.63±0.64
Ca	8.83±0.65	9.11±0.53	9.33±0.79
P	8.46±1.91	6.63±1.25	5.78±1.29
PTH	343±296	258±264	205±218

3M: 3 months; 6M: 6 months; Ca: calcium; Mg: magnesio; P: phosphorus; PTH: parathyroid hormone.