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Response to "Paricalcitol for pre-dialysis stages of chronic kidney disease"

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To the Editor,

We were very interested by the comments submitted by Drs Almirall and Bolos from *Corporació Sanitària i Universitària Parc Taulí* at Hospital de Sabadell (Barcelona), regarding our article on the effectiveness of paricalcitol for controlling hyperparathyroidism in early stages of chronic kidney disease,[1] and first of all, we would like to thank them for their input.

They are completely correct in pointing out that we did not highlight the relevant fact that the level of 25-OH vitamin D was deficient in our patient population. We did not call attention to this fact because we are currently undertaking a larger study on vitamin D deficiency, including more than 300 patients with chronic kidney disease (CKD) in pre-dialysis stages, and given the scope and length of this article, we decided –perhaps erroneously– to leave it for a later occasion.

However, we would like to comment on some of the ideas expressed by these authors, with a particular view to compensate for the lack of information on vitamin D that they detected.

First of all, levels of both native vitamin D and calcitriol are low in CKD, and the complex relationships between them are still largely unclear. This is also reported by Dr Dusso in a recent article[2] regarding both the calcium-parathyroid hormone-bone axis and their so-called pleiotropic effects due to vitamin D receptors being widespread. It is interesting to note that CKD patients may have a vitamin D deficiency of up to 80%, even though the conversion to 25-OH vitamin D by 25-hydroxylase (CYP2R1) occurs in the liver and not the kidney.[3]

In addition, the cause of 25-OH D deficiency is unclear. Hypotheses include low exposure to sunlight, deficient intake of provitamin and many more. We know that calcidiol binds to DBP (vitamin D binding protein), is filtered by the glomerulus, and is later endocytosed via megalin into proximal tubule cells. It has been demonstrated that disease progression in renal patients is accompanied by a decrease in megalin. At the same time, there may be a loss of DBP and even 25-OH vitamin D in proteinuric kidney disease. Furthermore, 25-OH D deficiency is very common in nephrotic syndrome, even when renal function is normal. Similarly, in early stages of kidney disease, increased FGF 23 may inhibit activity by renal 1-alpha hydroxylase and increase catabolism of 1,25-D and 25-OH D, thereby activating production of the enzyme that breaks down both forms (24-hydroxylase). It has even been observed that calcium deficiency promotes depletion of 25-OH D. In addition, 1,25-D itself stimulates hepatic inactivation of 25-OH D.[4] We therefore completely agree with treating and maintaining proper 25-OH D levels from stage 1-2 kidney disease, as recommended by the S.E.N. 2011 guidelines.

However, a different issue is whether vitamin D supplements alone are sufficient to control hyperparathyroidism. It seems obvious that proper levels of 25-OH D, the substrate for calcitriol synthesis, must be reached in order to promote the synthesis process and prevent hyperparathyroidism. Nevertheless, it is unlikely that vitamin D supplements are enough to compensate for low VDR expression in tissues. It has been reported that using ergocalciferol as a supplement reduces PTH only in those patients with serum levels of 25 OH-D below 30ng/ml.[2] It has also been reported that only 50% of patients with stage 3 or 4 CKD who take vitamin D supplements see an increase in 25-OH D levels.[5]

In any case, we feel that the matter is open for debate. Preclinical and clinical trials with sufficient prospective power should be undertaken in order to determine the benefit in simultaneously providing vitamin D supplements and active metabolites of vitamin D. However, although Dr Dusso warns of the risk of toxicity associated with this combination and it does not seem recommendable at present.[2]

Lastly, regarding the economic savings associated with using a certain treatment or another (which is certainly a hot topic today), our attention was called to the last sentence in the letter, which reminds us that the most important consideration is the benefit to the patient. Public prices are established by the authorities which regulate and shape healthcare policy, and not by doctors. We believe that our role is to make efficient use of the resources which the Health System puts at our disposal and choose the best option for each patient and each specific situation. This will be the case as long as we are permitted to make choices, because given the current climate, it is likely that only one drug will be provided for treating a condition in the near future, and that it will be chosen by political

figures and not doctors. This will effectively put a stop to the debate.

Conflicts of interest

The authors affirm that they have no conflicts of interest related to the content of this article.

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Salicylate poisoning

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To the Editor,

Indications for renal and extra-renal clearance techniques as treatment for acute poisoning have decreased in recent years, given the increased efficiency of general support measures and the fact that a better understanding of toxin kinetics has shown such methods to be truly useful. With this in mind, we thought that readers of NEFROLOGÍA might be interested in our comments on a case published recently by Ruiz-Zorrilla et al on acetylsalicylic acid poisoning.[1]

Although the authors cited above state that the patient was treated with urinary acidification (Spanish version), we do not believe that this was really the case, since that treatment does not currently play any part in resolving cases of poisoning. The treatment which was in fact indicated was alkalisation of urine to reduce tubular reabsorption of acetylsalicylic acid.[2] On the other hand, the reported decrease in the serum concentrations of salicylates coinciding with haemodialysis should not be considered a result of the treatment's effectiveness. The fool proof way of demonstrating the results of these techniques is to measure the amount which is actually extracted. This is performed by using the system's clearance of the toxin and periodically measuring the afferent and efferent salicylate concentrations, which are then compared to the body's total toxin content. It is also necessary to point out that a patient with a serum salicylate concentration of 65.68mg/dl is not considered to absolutely require haemodialysis treatment due to poisoning, which most texts define as levels greater than 80-100mg/dl.[3,4]

Lastly, upon reviewing the treatment of this case of poisoning we were surprised to find no references to the use of activated charcoal. This treatment method, which cleanses the digestive tract, has nearly completely replaced gastric lavage and is fully indicated for cases of salicylate poisoning.[5]

We believe it necessary to stress that indications for renal and extrarenal clearance in acute poisoning depend on an evaluation of the toxin characteristics, patient's clinical situation, laboratory findings, serum toxin concentration, and the absence of other alternatives that are less costly and which may also be more effective. In the case at hand, it is very likely that the patient would also have responded well to alkaline diuresis, with early administration of activated charcoal and no haemodialysis.

Conflicts of interest

The authors affirm that they have no conflicts of interest related to the content of this article.

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