

result was slight alkalinisation of the blood at the end of the dialysis session. This modest change in blood pH suggested that this does not play a substantial role in vascular calcification. This was especially likely to be the case as this slight alkalinisation of the blood was lost after several hours.

Finally, without taking into account the fact that bicarbonate is responsible for the slight alkalinisation of the blood during dialysis, bicarbonate also plays a determinant role in the production of calcium crystals, including hydroxyapatite, as one of our studies has shown.<sup>4</sup>

Although it is a conceptual matter, it should be known that bicarbonate is responsible for the increase in the calcification process, whether directly by causing calcium crystals or indirectly by causing slight alkalinisation. Therefore, bicarbonate should be replaced with another buffering molecule or efforts should be made to reduce it during dialysis, like calcium, obviously within the available means.

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# Haemodialysis session: The perfect storm for vascular calcification<sup>☆</sup>

## Sesión de hemodiálisis: la tormenta perfecta para la calcificación vascular

Dear Editor:

We appreciate the interest shown and comments made by Villa-Bellosta et al. with respect to our recent publication.<sup>1</sup>

First, we agree that the dialysis bath should be personalised to generally achieve neutral calcium balances. As González-Parra et al.<sup>2</sup> effectively demonstrated in their article, the predialysis plasma calcium cut-off points that would allow one or another concentration of calcium in the dialysis bath to be decided on seem to be around 0.96 mmol/l and 1.01 mmol/l (8.75-9.15 mg/dl, respectively). However, the aim of our study

was not to determine these cut-off points, but to analyse changes in calcaemia with randomly assigned calcium baths, and their relationship with phosphorus and bicarbonate, in pursuit of a parallel with studies *in vitro* by Lomashvili et al.<sup>3</sup> and De Solis et al.<sup>4</sup> Hence patients were classified as hypo- or normocalcaemic based on 1.16 mM, the lower limit of normal determined by our laboratory. When we analysed changes in calcaemia in our sample, based on the bath used, we observed that the 1.25 mM calcium bath scarcely induced hypercalcaemia (>1.3 mM), while all patients dialysed with the 1.5 mM bath completed the session with hypercalcaemia (all

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independently of predialysis plasma calcium). Therefore, we understand that, while the 1.25 mM calcium bath could be considered to be “standard”, some situations require higher or lower concentrations in order to achieve balances that are as neutral as possible, as we initially remarked.

Second, we have little to add to the comments made about the calcium-phosphorus product and the role historically attributed to it in vascular calcification. As O’Neill said in his publication, this entrenched dogma represents a simplistic interpretation with little scientific basis,<sup>5</sup> since the key to this complex process lies in calcium more than phosphorus — to say nothing of the host of inductive and protective factors in vascular calcification proposed in recent years.

Finally, the question of whether it is the induction of alkalaemia or the addition of bicarbonate that induces vascular calcification in the patient in haemodialysis is difficult to answer. Indeed, when bicarbonate is infused, the increase in pH is lower than expected. This may be explained on the one hand by the isohydric principle (part of the bicarbonate is consumed thereby restoring other plasma buffers, including phosphate, thereby generating precursors of brushite and hydroxyapatite), and on the other hand by respiratory compensation.<sup>6</sup> The fact is that, although the increase in pH following a dialysis session might seem unimportant and even transient, this should not lead to underestimating the extent of underlying clinical-chemistry processes that are set in motion to buffer the alkalaemia induced in such a short space of time, and that probably play a role in vascular calcification associated with haemodialysis. In addition, as Villa-Bellosta et al. demonstrated in their article, bicarbonate in itself is able to form hydroxyapatite crystals when combined with infused calcium.<sup>7</sup> Based on the above-mentioned studies *in vitro*,<sup>3,4</sup> it seems that the critical moment in which the addition of bicarbonate would become more harmful coincides with the first hour of a session, when calcium increases in the presence of hyperphosphataemia. Although translating results *in vitro* to daily clinical practice would be hasty and reductionist, these findings should incite reflection on the potential alternatives. Despite all this, the use of bicarbonate has manifest benefits in bone and protein metabolism that in its day represented an advance with respect to acetate, which is now obsolete. This leads to considering other ways of administering bicarbonate, for example by delaying its infusion during a session so that it does not coincide with the adverse clinical-chemistry scenario described above. Research on new buffering

compounds would undoubtedly yield another opinion to be considered.

In any case, vascular calcification is extremely complex, and it seems that various factors — active or passive, within haemodialysis or outside of it — play one role or another in the process.

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