Reticulocyte hemoglobin content and iron therapy in chronic kidney disease: Reply of the Anemia group of the Spanish Society of Nephrology

Concentración de hemoglobina reticulocitaria y ferroterapia en la enfermedad renal crónica: respuesta del grupo de Anemia de la Sociedad Española de Nefrología

Dear Editor,

We appreciate the comments by Deira et al.[1] to our article "Iron replacement therapy in the management of anaemia in non-dialysis chronic renal failure patients: Perspective of the Spanish Nephrology Society anaemia Group", as it allows us to clarify a little more the role of new ferrokinetic markers. One of the clinical-analytical circumstances that pose a challenge for the nephrologist is functional iron deficiency. This situation is very frequent in patients with chronic kidney disease (CKD) and it is mostly determined by an underlying inflammatory process that increases hepcidin levels. Hepcidin favors the sequestration of intracellular iron, rendering it unavailable for hemoglobin synthesis. We assume, therefore, that in these circumstances the patient will have a decrease in hemoglobin levels, an increase in ferritin levels (also an acute phase reactant) and a decrease in the transferrin saturation index, reflecting the inability to transport the sequestered iron to the bone marrow. It is a relatively complex situation with parameters that are not well defined in clinical guidelines, but which requires a clear therapeutic approach aimed at eliminating the source of the inflammation. It is also true that there is often a chronic process involving multiple comorbidities that do not always have a simple and agile solution (e.g., dialysis catheters, malnutrition, or hyperparathyroidism). In this sense, parameters such as the percentage of hypochromic red blood cells, reticulocyte hemoglobin content or the soluble transferrin receptor provide valuable information on iron metabolism.[2–4] Some studies have been published that combine these parameters with the more classical ones to identify patients who would respond better to parenteral iron supplementation, as a proxy of iron deficiency.[5]

As the authors of the letter rightly point out, reticulocyte hemoglobin content can provide guidance during therapy with iron and erythropoiesis-stimulating agents, as it reflects whether iron has been incorporated into red blood cells within 3 or 4 days of the start of iron therapy. In addition, the percentage of hypochromic red blood cells would be more representative of this incorporation in the preceding 2 or 3 months and, therefore, is a good marker of iron availability in the medium to long term. This parameter has a limitation worth considering, since it is not available in all hematology analyzers and because sample processing time affects it (it must be measured within less than 6 h of collection), among other factors.[6] However, despite providing valuable information, at present, the use of these parameters is limited by the absence of universally accepted clinical decision limits in Nephrology, as reflected in the latest KDIGO controversies.[7] Although the authors mention that all guidelines endorse the use of these two markers to assess functional iron deficiency, they mention only one British guideline not specific to nephrology, and two nephrology-specific versions of the British NICE guidelines. Other clinical guidelines in nephrology, such as the KDIGO or the European Renal Best Practice guidelines, do not include or recommend them for routine assessment of functional iron deficiency.[7–9] In fact, the latest KDIGO controversies on the subject, recently published,[7] state that the widespread clinical use of both parameters is limited by the absence of universal clinical decision limits. For this reason, the S.E.N. Anemia Group did not include them in its document.

We appreciate the commentary by Deira et al. because it may add knowledge and improve management of iron deficiency and anemia in CKD. However, it is a priority of this group to further study anemia in CKD, and to develop accessible, reliable, and widely validated diagnostic parameters that allow standardization of the diagnostic-therapeutic approach in this setting. However, more evidence is needed to enable the normalization and standardization of these parameters before they can be incorporated into routine clinical practice and be recognized in the guidelines in the future.

Conflict of interest

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BQ has received speaking fees or grants for attendance at conferences/courses from Vifor-Pharma, Astellas, Astellas, Amgen, Ferrer, Novartis, AstraZeneca, Sandoz, Laboratorios Bial, Esteve, Sanofi-Genzyme, Otsuka. He has also participated in Advisory Boards of AstraZeneca and Laboratorios Bial. He is currently the secretary of the Spanish Society of Nephrology (S.E.N.).

MJP has received speaking fees from Astellas, Vifor Pharma.

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