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Reticulocyte hemoglobin content and iron therapy in CKD

Concentración de hemoglobina reticulocitaria y ferroterapia en la ERC

ARTICLE INFO

Dear Editor,

We read with great interest the review entitled, "*Iron therapy in the management of anaemia in non-dialysis chronic kidney disease: the perspective of the S.E.N. [Sociedad Española de Nefrología (Spanish Society of Nephrology)] anaemia group*"[1]. In this manuscript, the authors provide an update on the management of iron deficiency in patients with chronic kidney disease (CKD).

It is clearly shown that the diagnosis and treatment of absolute iron deficiency is simple and that there is a broad consensus on that matter[1–3]. The same does not apply to functional iron deficiency. In such clinical situation, caused in most cases by inflammation, there is an increase in hepcidin synthesis (due to IL-6) in the liver[4]. Hepcidin blocks ferroportin, the only cell channel that exists for exporting cellular iron into the bloodstream, thereby reducing suitable availability of iron in the bone marrow. This leads to deficient haemoglobin synthesis in the reticulocytes[5]. Unlike mean corpuscular haemoglobin, whose value diminishes after several weeks, bone marrow iron deficiency may be estimated in a few days based on reticulocyte haemoglobin content (CHr)[5]. Therefore, all the guidelines recommend the percentage of hypochromic red blood cells or CHr as the best laboratory parameters for the diagnosis of functional iron deficiency (1B)[6–8].

Inexplicably, the authors[1] state that we must continue to use the classic markers (serum ferritin and transferrin saturation - TSAT), suggesting that the *new markers are less accessible, more expensive and somewhat unreliable*. We cannot convey this concept, since following the widespread introduction of automated cell counters, most laboratories can now measure number, volume and CHr and thus detect iron deficiency at an early stage[6]. Moreover, not only are red blood cell markers not expensive, they are also the most rewarding option in comparison to the different tests that assess FID and response to treatment in patients with CKD on haemodialysis or not[8]. Finally, these markers are very reliable. Mast et al.[9] demonstrated, in patients undergoing a bone marrow examination for other reasons, that their predictive value for iron deficiency is higher than the classic parameters (serum ferritin or TSAT). We have also seen the excellent correlation between CHr and the classic markers[10], which is why we believe that at this point in time they are accessible, cost-effective and very reliable and that their use should be recommended in accordance with the guidelines[6–8].

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Hepatotoxicity induced by tolvaptan: A case report

Hepatitis tóxica inducida por tolvaptan: a propósito de un caso

ARTICLE INFO

Dear Editor,

Autosomal dominant polycystic kidney disease (ADPKD) is the most frequent hereditary kidney disease. Its estimated prevalence is highly debated and ranges from 1 in every 500 to 1 in every 2000 people.[1–4] Patients with ADPKD represent between 6% and 10% of the population on dialysis or kidney transplant, meaning that it is a disease with a major social impact.[5]

In 2015, the use of tolvaptan was approved in Europe for the treatment of patients over the age of 18 years with ADPKD and CKD stage 1-3 at the initiation of treatment and with signs of rapid progression in order to slow down the course of the disease.

The most frequent side effects of tolvaptan are aquaretic side effects (between 65%–95% of the patients have them).[6] For this reason, patients must have continuous access to water and maintain an adequate water intake in accordance with their diuresis.

However, the side effect requiring the greatest attention is idiosyncratic hepatotoxicity. In order to maintain a control this negative effect, liver function tests (LFT) must be monitored every month during the first 18 months of treatment and every three months thereafter as indicated by the autosomal dominant polycystic kidney disease consensus document published in 2020.[7]

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In the *Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and its Outcomes* (TEMPO) 3:4 study, the incidence of liver damage defined as an elevation of alanine aminotransferase (ALT) three times the upper limit of normal was 4.4%,[8] and we did not find liver damage indices as high as those of our own centre in the literature.[9,10]

In our experience, the incidence of liver toxicity is higher, since six of the 17 patients who received tolvaptan at our centre had altered LFT and the drug had to be definitively discontinued in two of them. Mean ALT was 192 U/L (54–544 U/L). These data increase the incidence to 35% in our series.

We present the case of one of the patients who required the discontinuation of the drug due to liver toxicity.

The patient is a 45-year-old man diagnosed with ADPKD in 2002 after an abdominal ultrasound. As complications of the disease, he presented recurrent urinary infections and was hypertensive and on treatment with olmesartan. In accordance with rapid progression criteria (Mayo Clinic 1D classification), treatment was initiated in March 2018 and liver function was monitored monthly. The dose of tolvaptan was 45 + 15 mg the first month, 60 + 30 mg the second month and reached the maximum dose (90 + 30 mg) in June 2018.

In the control of LFT in July 2018, it was observed an increase in ALT, with values of 211 U/L (4–41 U/L normal value), whereupon the dose was down-titrated to the inter-