A) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

Is there difficulty for maintaining target levels of haemoglobin in pre-dialysis patients treated with erythopoeisis-stimulating agents?

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To the Editor,

Different scientific societies have frequently revised the recommendations for the treatment of anaemia in patients with pre-dialysis (no-D) chronic kidney disease (CKD), which include target values of haemoglobin (Hb), ferritin and transferrin saturation rate (TSAT). In 2005, the Agence Française de Sécurité Sanitaire des Produits de Santé recommended target Hb values between 110-130g/l[1]. The KDOQI2006 guidelines (Kidney Disease Outcomes Quality Initiative) recommend not intentionally maintaining Hb>130g/l and in 2007, recommended a range of 110-120g/l[2]. In 2007, the European Medicine Agency recommended an Hb range of 100-120g/l and in 2009, the ERBP guidelines (European Renal Best Practice) recommended 110-120g/l, not exceeding the value of 130g/l[3,4]. The latest update to the KDOQI2012 guidelines recommends maintaining an Hb level between 100-115 g/l[5].

A retrospective observational study of the degree of compliance of the established target values according to the different guidelines, we carried out a retrospective observational study of all the patients with no-D CKD and non-transplant patients treated with an erythopoiesis-stimulating agent (ESA) on 1 September 2012; with no dosage modifications during the last 6 months, was performed to evaluate the degree of compliance of the different guidelines. Data were obtained from the outpatient pharmacy programme and the hospital clinical workstation. The following variables were recorded: age, sex, Hb, ferritin and TSAT, CKD stage, type of ESA and monthly dose, treatment with angiotensin-converting-enzyme inhibitors (ACE inhibitors), angiotensin II receptor antagonists (ARBs), iron supplements and treatment for secondary hyperparathyroidism (SHPT); and diabetes mellitus (DM) as underlying comorbidity.

The study included a total of 305 patients (141 male) with stage 3 CKD (65 patients), stage 4 CKD (140 patients) or no-D stage 5 CKD (100 patients). The mean age was 68 years (range: 22-95 years). The administered average monthly dose of ESA (expressed in micrograms of darbepoetin) was 90μg. 17% of the patients were being treated with ARBs and 14 % with ACE inhibitors. 40 % took iron supplements and 60 % received treatment for SHPT. 25% of patients presented DM.

Mean Hb was 112g/l, mean ferritin 195μg/l and mean TSAT 20% (Table 1). No statistically significant differences were observed between the parameters studied (mean Hb, mean ferritin, mean TSAT, Hb<100g/l, Hb>130g/l, ferritin <100μg/l and TSAT<20%) according to CKD stage, type and dose of ESA, iron supplement, concomitant medication for anaemia (ACE inhibitors, ARBs), SHPT treatment. A higher percentage of patients with Hb<100g/l was observed in advanced stages of CKD.

Compliance of the established objectives according to different guidelines is shown in Figure 1. The percentage of patients within the suitable range is less than 60%. Only 40.7% of the patients presented an Hb level within the range recommended by the KDOQI2012 guidelines, and 54.7 % according to the objectives of the ERBP. The results of this study coincide

Table 1. Values of haemoglobin, ferritin and the rate of transferrin saturation according to the stage of renal function and the type of erythropoiesis-stimulating agent.

		Total	CKD stage (%)			ESA	
			CKD 3	CKD 4	CKD 5 no-D	Darbepoetin	Methoxy polyethylene glycol-epoetin beta
Hb (g/dl)	Mean (range)	111.6 (68-160)	112.6 (81-138)	110.6 (78-160)	111.3 (68-158)	111.8 (68-158)	110.8 (79-160)
	100 g/l.	21.70 %	18.50 %	21.90 %	24.30 %	22.10 %	19.80 %
	130 g/l.	10.70 %	9.30 %	8 %	10 %	11.10 %	8 %
Ferritin (µg/l)	Mean (range)	195 (6-923)	174 (6-898)	207 (9-874)	170.5 (10-665)	197 (6-923)	193.4 (9-898)
	< 100 µg/l	35 %	39 %	34 %	32 %	33.90 %	38.50 %
TSAT (%)	Mean (range)	20.10	22.70	18.80	20.00	19.30	21.90
		60.00 %	61.10 %	60 %	60 %	62 %	57.20 %

ESA: Erythropoiesis-stimulating agents; CKD: Chronic kidney disease; Hb: Haemoglobin; No-D: Non-dialysis; TSAT: Transferrin saturation rate.

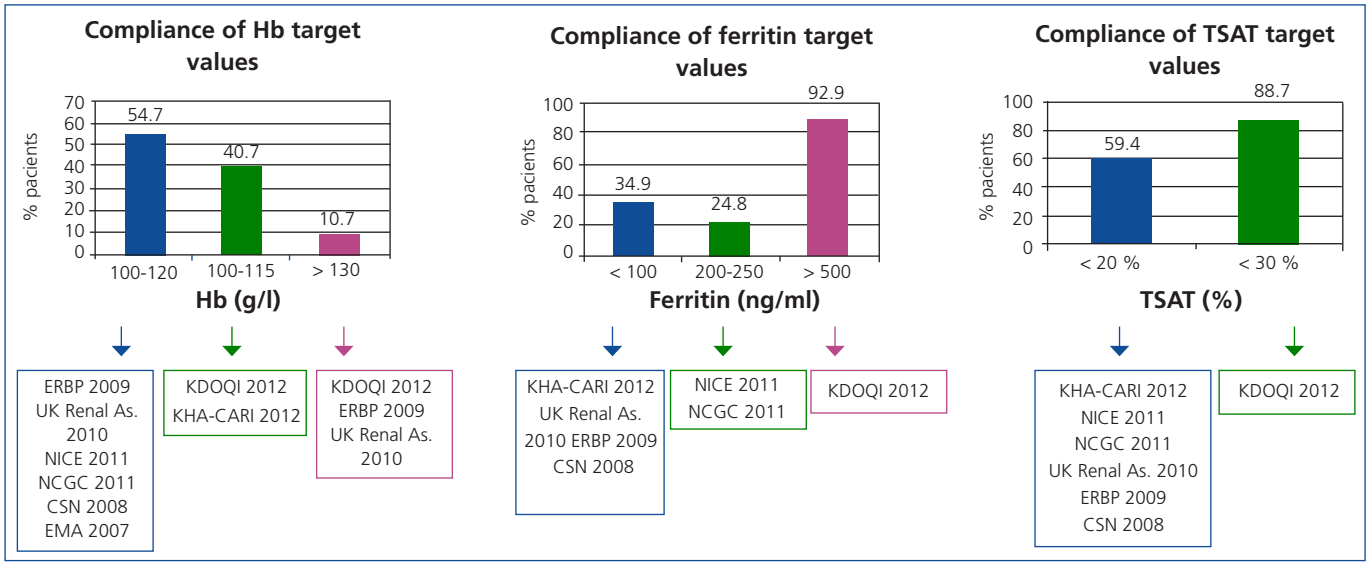

Figure 1. Degree of compliance of the established objectives according to the different clinical guidelines.
CSN: Canadian Society of Nephrology; EMA: European Medicine Agency; ERBP: European Renal Best Practice; Hb: haemoglobin; KHA-CARI: Kidney Health Australia-Caring for Australasians with Renal Impairment; KDOQI: Kidney Disease Outcomes Quality Initiative; NCGC: National Clinical Guideline Center; NICE: National Institute Health and Care Excellence; TSAT: transferring saturation rate; UK Renal As: United Kingdom Renal Association.

with those obtained in OCEANE[6] study, where only 50% of the patients met the objective values of Hb (100-120g/l). In another previous study[7], the percentage of patients compliant with the objective Hb values (100-120g/l) was 38.4%. According to Valderrabano et al.[8], 96% of the patients had levels of Hb>100g/l. In our study this percentage was 78.3%. These results reflect the difficulty in maintaining Hb within the recommended margins, due to a narrow objective range, the variability of Hb values and the complexity of patients (age and cardiovascular comorbidities).

Conflicts of interest

Dr A. Martinez-Castelao has collaborated with Novartis, Boëhringer, Abbvie, Shire, Amgen and Roche laboratories and has participated in advisory boards from Abbvie and Amgen laboratories.

1. Afssaps. Traitement de l'anémie au cours de l'insuffisance rénale chronique de l'adulte: recommandations de l'Afssaps. Nephrol Ther 2005;1 Suppl 1:S1-48.
2. National Kidney Foundation. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for anemia in chronic kidney disease: 2007 update of hemoglobina target. Am J Kidney Dis 2007;50:471-530.
3. European Medicines Agency (EMA). Public Statement. Epoetins and the risk of tumour growth progression and thromboembolic events in cancer patients and cardiovascular risks in patients with chronic kidney disesase. 23 october 2007. EMEA/496188/2007. Available at: http://www.emea.europa.eu (accessed 01/09/2013).
4. Locatelli F, Aljama P, Canaud B, Covic A, De Francisco A, Macdougall IC, et al.; on behalf of the Anaemia Working Group of European Renal Best Practice (ERBP). Target haemoglobin to aim for with erythropoiesis-stimulating agents: a position statement by ERBP following publication of the Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) study. Nephrol Dial Transplant 2010;25:2846-50.
5. Kidney Disease: Improving Global Outcomes (KDIGO). Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int Suppl 2012;2:279-335.
6. Frimat L, Mariat C, Landais P, Koné S, Commenges B, Choukroun G. Anaemia management with CERA in routine clinical practice: OCEANE (Cohorte Mircera patients non-dialyses), a national, multicenter, longitudinal, observational prospective study, in patients with chronic kidney disease not on dialysis. BMJ Open 2013;3(3):e001888.
7. Lacson E, Ofsthun N, Lazarus JM. Effect of variability in anemia management on hemoglobina outcomes in ESRD. Am J Kidney Dis 2003;41:111-24.
8. Valderrábano F, Hörl WH, Macdougall IC, Rossert J, Rutkowski B, Wauters JP. PRE-dialysis survey on anaemia management. Nephrol Dial Transplant 2003;18:89-100.

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