Influence of the Secondary Hyperparathyroidism in iron requirements in dialysis patients on erythropoiesis-stimulating agent therapy. A prospective controlled study.

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OBJECTIVES

To evaluate the influence of the intact parathyroid hormone (iPTH) level on the iron requirements and ferrokinetic parameters in hemodialysis patients under ESA (eritropoyesis stimulating agent) therapy.

METHODS

We conducted a prospective, clinically-controlled trial in a chronic dialysis unit from January 2010 to November 2011. Patients were stratified according to the iPTH level (Group A: iPTH 150pg/ml, Group B: 150-300pg/ml and Group C: > 300pg/ml). Follow-up period six months.
Main outcome measure To determine the difference in the iron requirements in each group from baseline to month 6 and the differences in the mean change between groups.
ESA dosage was administrated according to the following protocol: i) ESA dosages were increased by 25% for Hb decreases < 2 g/dl or Hb ≥ 9 and < 11 g/dl or by 50% when Hb decreases ≥ 2 g/dl or Hb < 9 g/d; ii) ESA dosages were decreased by 25% for Hb increases ≥ 1 g/dl or Hb ≥ 12 and ≤ 14 g/dl, or by 50% for Hb increases > 2 g/dl. If Hb was > 14 g/dl, we temporarily stopped ESA for a month. Then, we restarted ESA administration with a 25% reduction of the lower dose previously administered.
Intravenous iron supplementation (100 mg of iron sucrose, Venofer®) was prescribed in order to maintain TSI levels ≥ 20% during the study as needed.

	Group A n = 9	Group B n = 10	Group C n = 12	p-value
Age (years)	64 ± 11	55 ± 13	60 ± 22	0.47
Time on dialysis (months)	26 (19-38)	38 (17-53)	34 (24-41)	0.73
BMI (kg/m²)	22 (24-29)	24 (21-33)	29 (25-32)	0.16
Kt/V	1.62 ± 0.2	1.51 ± 0.2	1.54 ± 0.1	0.52
nPCR	0.79 (0.79-0.96)	1.01 (0.76-1.26)	0.96 (0.87-1.08)	0.42
Cholesterol (mg/dl)	132 ± 32	138 ± 48	153 ± 41	0.47
ESR mm	19 (9-29)	35 (21-55)	26 (18-39)	0.20
Albumin (g/l)	39 ± 3	38 ± 4	40 ± 3	0.24
Triglycerides (mg/dl)	98 (79-205)	135 (99-318)	233 (193-281)	0.05
Vitamin B12 (pg/ml)	572 ± 360	636 ± 253	405 ± 157	0.13
Folic Acid (ng/ml)	19 ± 3	18 ± 15	19 ± 13	0.98
Corrected calcium (mg/dl)	9.1 ± 0.3	8.7 ± 0.5	9.0 ± 0.6	0.21
Phosphorus (mg/dl)	3.8 ± 1.2	4.5 ± 1.1	4.5 ± 1.6	0.45
25 Vitamin D (ng/ml)	19 (15-31)	23 (11-33)	25 (14-27)	0.91
iPTH (pg/ml) log	1.97 ± 0.25	2.37 ± 0.07	2.64 ± 0.1	<0.01
ESA dose IU/week	8000 4500(10500)	4000 (3758-9750)	5000 (4000-8000)	0.55
ERI, IU/kg per week per g/dl	8.7 (4.8-17.1)	6.6 (3.3-11.2)	4.3 (3.2-10.7)	0.55
Comorbidities				
DM, Yes, n(%)	3 (33)	4 (40)	3 (25)	0.75
HTA; Yes, n(%)	8 (89)	9 (90)	11 (92)	0.97
DLP; Yes, n(%)	3 (33)	3 (30)	9 (75)	0.06
Treatments				
Venofer; Yes, n(%)	9 (100)	7 (70)	9 (75)	0.20
Iron, mg/month	100 (100-150)	100 (100-100)	100 (100-200)	0.66
Cinacalcet; Yes, n(%)	1 (11)	1 (10)	8 (67)	<0.01
Paricalcitol; Yes, n(%)	4 (44)	8 (80)	11 (91)	0.04

DM: diabetes mellitus, HT: hypertension, DLP: dyslipidemia; nPCR: normalized protein catabolic rate, TSI: transferrin saturation index, EBI: erythropoietin resistance index. EBI, (The erythropoietin resistance index (EBI) was determined as the weekly weight-adjusted dose of EPO (U/kg/week) divided by Hb concentration (g/dl). Media±SD, median (P25-P75).

RESULTS

31 patients completed the study (A: n = 9, B: n = 10 and C: n= 12). Baseline data in table 1. The hemoglobin levels and ESA doses were similar in all groups during the study. In Group A mean iron dose decreased 77 ± 66mg/month (P < 0.01), while increased in the groups B (20 ± 42mg/month, P = 0.16) and C (33 ± 115mg/month, P = 0.33).
There was statistical difference between the mean change in iron dose between groups A and C (P = 0.003). Transferrin saturation index (TSI) changes observed in Group A and C were significantly different (increased in Group A (median: 2.4%) and decreased in group C (median: 3.7%).

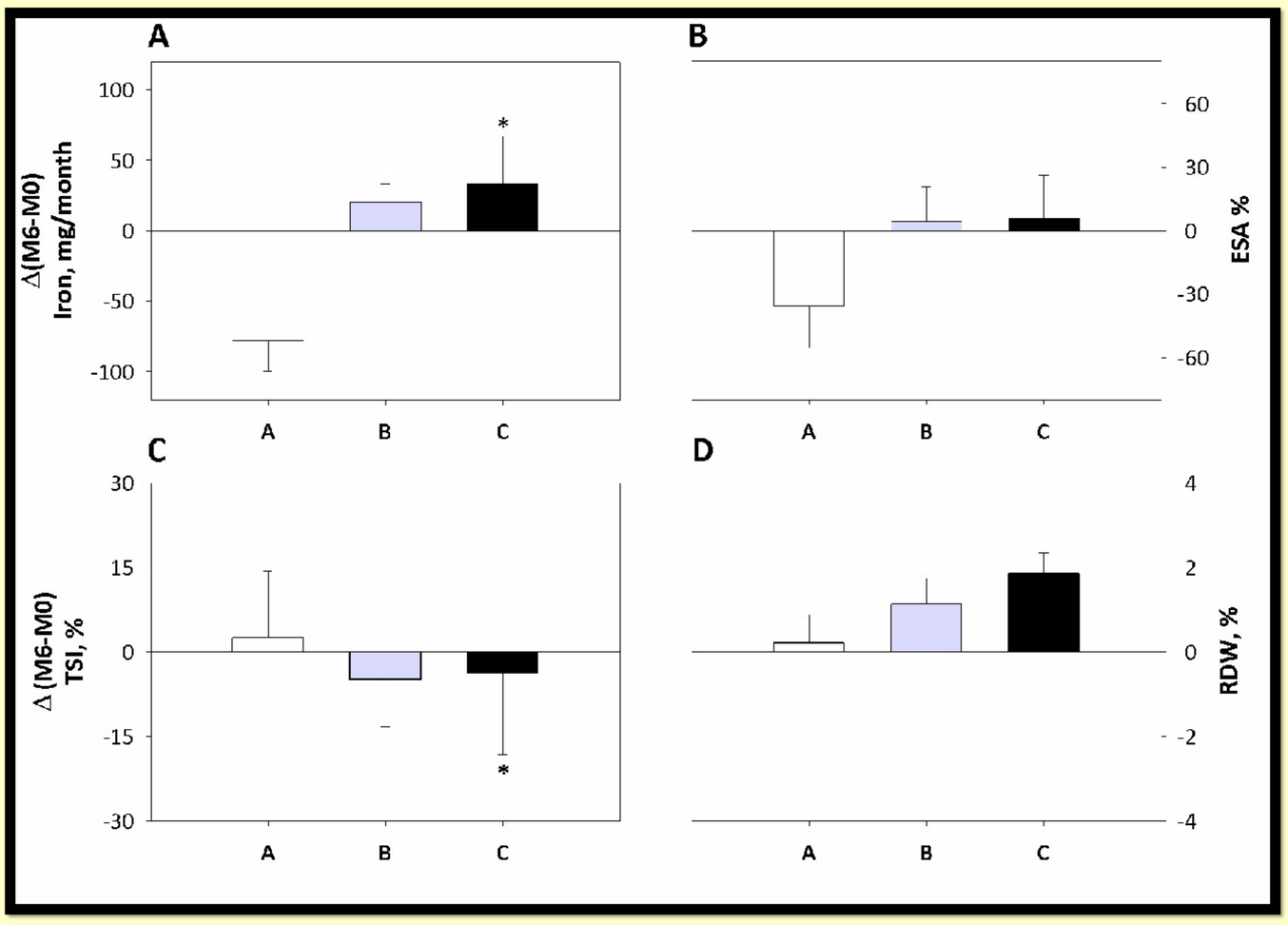

Figure 1. Variations from the beginning to the end of the study by groups according to PTHi. (A) Mean change iron dose, (B) Mean change in % of ESA, (C) Mean change in % of TSI, (D) Mean change in % of RDW. ESA: erithropoiesis stimulating agent, RDW: red cell distribution width, TSI: transferrin saturation index. * p<0.005 respect to group A

CONCLUSIONS

· Iron supplementation decreased in patients with the lower iPTH levels, and it was associated and with an increase in TSI, inversely than those with higher levels.
· These results suggest a possible relationship between iPTH levels and iron requirements.

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