IMPROVING ERYTHROPOIETIC STIMULATING AGENTS' RESPONSIVENESS WITH LESS BUT MORE FREQUENT IRON

OBSERVATIONAL STUDY

P. Carrilho[1], *A. R. Martins*[1], *M. Alves*[2], *A. Mateus*[1], *L. Gusmao*[1], *L. Parreira*[1], *J. Assuncao*[1], *I. Rodrigues*[1]

[1]NephroCare, Barreiro, Portugal
[2]Epidemiology and Statistics Research, Centro Hospitalar Lisboa Central, Lisboa, Portugal

INTRODUCTION

Many prevalent dialysis patients have functional iron deficiency[1], precluding adequate response to erythropoietic-stimulating agents (ESA), measured by ESA responsiveness index (ERI).
ERI is calculated as ESA dose (IU)/weight (kg)/week divided by a given value of hemoglobin (Hb) concentration (g/dl)[2].

Erythropoiesis is a continuous process and storage iron is less available for incorporation in erythrocyte percursors due to hepcidin blockade[3].
Frequent administration of a small dose of i.v. iron could improve erythropoiesis[4,5,7], although evidence is missing to recommend any different strategy of iron administration[8].

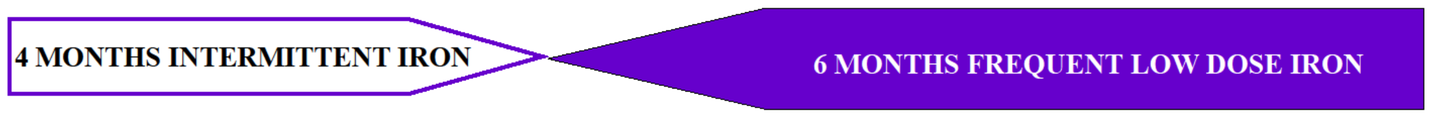
OBJECTIVES

Primary objective: to assess the impact on ERI of a frequent fixed low dose of iron sucrose in prevalent HD patients

Secondary objectives: to describe i.v. iron and ESA consumption and global anemia drug expenditure.

METHODS

The impact of **switching** from a variable, intermittent dose of iron sucrose to a **more frequent (thrice-weekly) fixed dose of 10 mg of iron** sucrose was assessed in a sequential single-center observational study comparing two periods of 4 months before and 6 months after, in stable HD patients receiving maintenance iron and ESA.



Patients were included if major blood losses were not evident, disregard of ferritin levels if they were between 150 and 600ng/mL. Iron supplementation during baseline period was determined by each nephrologist's practice. Medical management did not otherwise change during the period study.

ESA prescription was adjusted monthly according to target Hb of 10-13g/dL.
Exclusion criteria were hematological, active oncological disease or recent blood transfusion.
ESA (α-darbepoetin Aranesp®) was injected i.v. once weekly. Iron sucrose used was Venofer®.

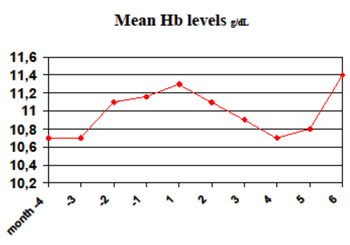
RESULTS

Of 219 patients at the centre, 57 patients were eligible and started a fixed dose of 10mg of i.v. iron sucrose thrice-weekly. 6 patients were excluded of final analysis because of death (1), transplant (1), oncological disease requiring radiotherapy (3) or prolonged absence to dialysis (1), leaving 51 patients.

Baseline demographic and clinical characteristics

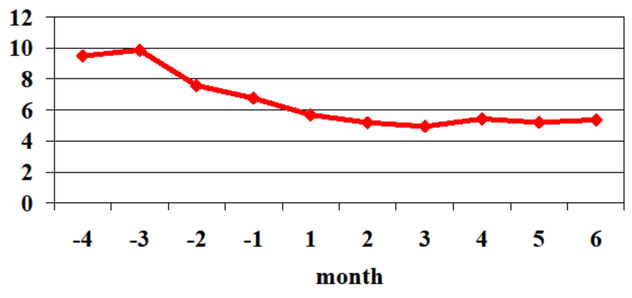
Age (years)	66,2 ± 13,8 (33-95)
Gender (male/female)	22 / 29 (43% male)
Ethnicity (black/white)	11 / 40 (21% black)
Dialysis vintage (months)	55,06 ± 58,4
PTHi (pg/mL)	472,7 ± 336,05
Charlson Index	6,58 ± 2,33
Primary Renal Disease	27 % Diabetes / 23% Hypertension / 21% Glomerulonephritis / 29% Other

Mean Hb levels g/dL



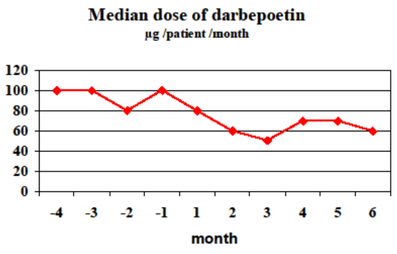
Mean **Hb levels** (g/dL) during baseline period (10,9 ± 0,70) **did not differ** from the study period (11,05 ± 0,59), p=0.061.

ESA Responsiveness Index (ERI)



ERI decreased from 6,169 (IQR 4,29-9,88) to 4,468 (IQR 3,01-6,03, p<0.001).

Median dose of darbepoetin
µg /patient /month



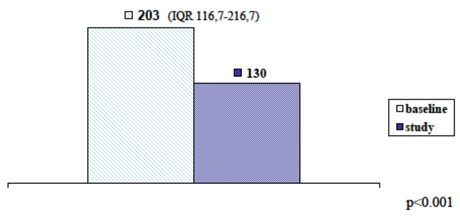
The median dose of **ESA** per patient per month **decreased** from 90 µg (IQR 65 - 142,5) to 70 µg (IQR 46,7 - 90, p<0.001).

Ferritin and TSAT at the beginning and at the end of the study

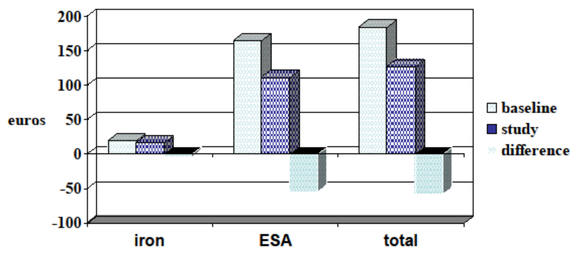
Mean ± SD	Baseline Period	Study Period	P-value
Serum ferritin (ng/dL)	389,3 ⊥ 120,6	385,3 ⊥ 192,2	P – 0,876
TSAT %	23,76 ± 8,48	29,38 ± 10,8	P < 0,001

Mean **ferritin levels did not differ**, but **TSAT** at the end was significantly **higher**, probably meaning a more efficient "transport" of iron.

Median iron dose / patient / month



Anemia drug expenditure / patient/ month



At the time of the study, the public cost of 100mg i.v. iron was 12.26 €/ampoule and darbepoetin was 1.344 €/µg. The mean total monthly cost of anemia treatment per patient decreased by 25%, from 146 € during baseline to 110 € during the period study.

CONCLUSIONS

Administration of less but more frequent iron allowed achieving target Hb, improving ESA response and reducing global costs.
Besides using 36% less iron than before, there was a significant 22% reduction in ESA's dose, suggesting an improvement in erythropoiesis.
Administration of a low dose of iron sucrose thrice weekly in HD patients should be addressed in prospective randomised trials.

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