HEMOGLOBIN VARIABILITY DURING TREATMENT WITH DIFFERENT ERYTHROPOIESIS STIMULATING AGENTS - MULTICENTER STUDY

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INTRODUCTION AND OBJECTIVES

Erythropoiesis-stimulating agents (ESA) treatment is the optimal therapy for anemia in hemodialysis (HD) patients. However, the ability to maintain hemoglobin (Hgb) within narrow targets remains a significant clinical problem as during ESA treatment the level of Hgb usually fluctuates widely; this phenomenon is known as "hemoglobin cycling". In addition, it is uncertain whether different types of ESAs affect such cycling and whether is it associated with higher mortality. Objective of our study was to estimate the prevalence of hemoglobin cycling by patient-year in Serbian HD patients treated with four different ESAs, to analyze risk factors and one-year mortality.

METHODS

A retrospective multricentic study was conducted on 603 chronic HD patients who were treated with epoetin alpha, beta, zeta or darbepoetin alpha between during one year period. Hemoglobin cycling was defined as Hgb variability over a period of at least 8 weeks and amplitude of more than 1.5 g/dl.

RESULTS

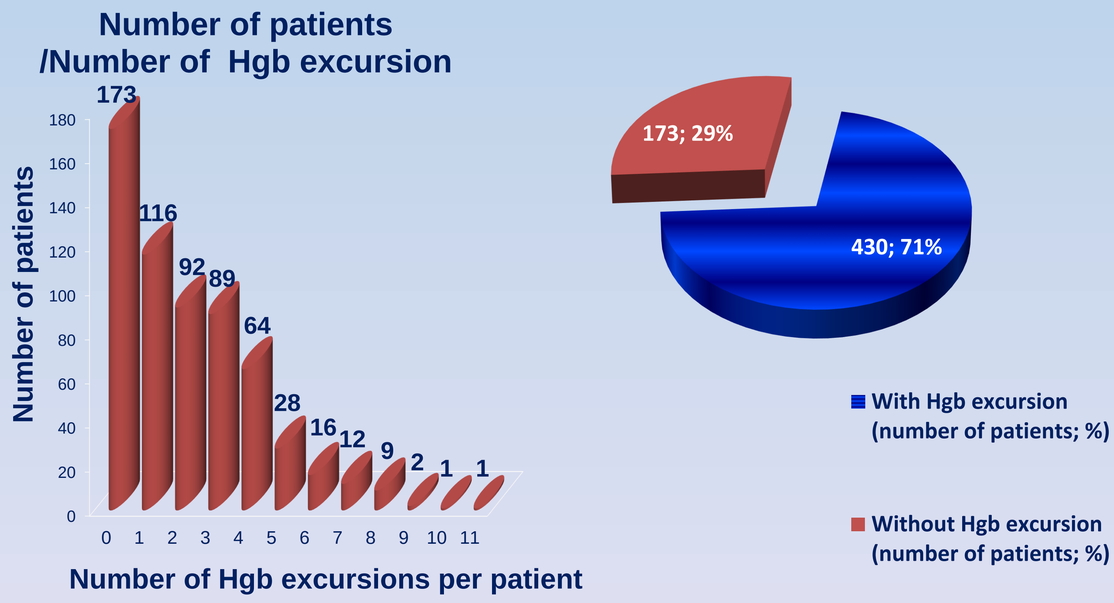
Of 603 patients included, 84.6% were on hemodialysis (HD) and 15.4% on hemodiafiltation (HDF). Darbepoetin received 16.1% and EPOs 83.9% of the patients. During the observation period, the majority of patients (95.02%) had at least one dose modification, the median number of dose adjustments per patient was 4.3 (range 0-9).

Table 1. Factors associated with Hgb fluctuation

	Patients with Hgb variation	Patients without Hgb variation	p
Number of patients	430	173	
Sex (females%)	39,31	38,25	0,593
Age (years)	62,39±12,36	63,96±12,64	0,604
AVF (%)	78,74	91,57	0,002
Duration of HD(months)	59,76±62,27	58,04±55,13	0,05
DM (%)	19,5	21,4	0,248
HTA (%)	65,72	69,19	0,068
Number of ESA dose changes	4,25±2,41	2,96±2,62	<0,001
ESA dose IU/kgTT/week	70,08±47,37	63,37±55,52	0,996
Hgb (g/L)	101,73±10,46	104,70±4,60	0,004
Ferritin (ng/ml)	648,55±493,33	525,6±325,82	0,003
TSAT (%)	30,93±15,40	35,54±36,25	0,784
CRP (mg/L)	13,58±2,26	7,31±2,1	<0,001
Kt/V	1,3±0,3	1,35±0,3	0,159
PTH (pg/ml)	563,8±550,2	236,7±314	0,002
ERI (U/kg/Hgb)	8,10±4,96	6,13±5,32	0,021

RESULTS

Neither the magnitude nor the directions of ESA dose adjustment were affected by the ESA type. Hemoglobin cycling was experienced by 71 % of patients. The mean amplitude was 2.24 ± 0.89 g/dL and mean duration of hemoglobin cycling was 8.3 ± 5.3 weeks. Most patients (19.23%) experienced one episode. On logistic regression, the factors associated with Hgb cycling were central vein catheters (p=0,002), C reactive protein (p<0.001) and erythropoietin resistance index (p=0.021). The overall 1-year mortality was 16.92%. Cardiovascular disease was the most common cause of death, occurring in 33 patients (32.03%), followed by cerebrovascular disease (20.38%), malignancy (14.70%) and infections (14.0%). There was no difference in mortality as assessed by Kaplan-Meier analysis neither with different ESA agents nor with Hgb cycling. CRP (odds ratio [OR] = 1.02, 95% confidence interval [CI] = 1.00-1.04; *P* = 0.02), male gender (OR = 1.51, 95% CI = 1.01-2.31; *P* = 0.04), catheter vascular access (OR = 2.89, 95% CI = 1.30-6.49; *P* =0 .01), and ferritin levels (OR = 2.12, 95% CI = 1.31-3.48; *P* = 0.002) were predictive of 1-year mortality.



CONCLUSION

Hemoglobin cycling was commonly found in Serbian ESRD patients treated with HD and ESA. Despite the study limitations of retrospectivity, the influence of different ESA types on Hgb cycling and mortality rates could not be demonstrated. Factor influencig Hgb cycling are probably of higher influence on patients' survival than Hgb cycling per se.

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