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Anemia Management Practice in French Hemodialysis Centers

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Authors' contributions

This work was carried out in collaboration between all authors. Author JR designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors PUT, HLMDS and KS managed the literature searches, analyses of the study and author CE managed the statistical analysis and authors LZ, LM and JW corrected the protocol. All authors read and approved the final manuscript.

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ABSTRACT

Objective: Evaluate the hemoglobin (Hb) target values in hemodialysis (HD) patients treated with erythropoiesis-stimulating agents (ESA).
Methods: Records of anemia parameters of HD patients treated during year 2012 in 5 French dialysis centers were retrospectively analyzed. Patients were stratified into "annual Hb categories" according to their monthly mean Hb: Low Hb (< 10 g/dL), Ideal Hb (from 10 to ≤ 12 g/dL), High Hb (> 12 g/dL) if they spent ≥ 75% of time in the respective category; otherwise patients were

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classified as Fluctuating Hb.
Results: Out of 636 evaluable patients (mean age 66.6 [SD 14.9] years; male 59.4%), 91.4% received ESA treatment and 74.2% received intravenous iron. Most patients (68.9%) belonged to the Fluctuating Hb category (Ideal 18.7%; High 9.6%; Low 2.8%). Patients in the Fluctuating category experienced more frequently ESA dose changes, transfusions, hospitalizations and co-morbidities compared with patients in other Hb categories. Multinomial logistic regression identified presence of at least one comorbidity (odds-ratio [OR]=7.6), hospitalization (OR=2.2), transfusion (OR=2.9), male gender (OR=0.6) and serum ferritin ≥500 vs. <200 µg/L (OR = 0.4) as predictors of Fluctuating vs. Ideal annual Hb category.
Conclusions: Only 18.7% of patients had stable Hb levels within the target range according to French and international guidelines; most had fluctuating Hb levels and few patients had a consistently low annual Hb. These findings suggest that development and implementation of improved hematologic assessment and anemia treatment strategies are needed to minimize fluctuating Hb values in HD patients.

Keywords: Anemia; hemodialysis; erythropoiesis-stimulating agents; intravenous iron complexes; end-stage renal disease.

1. INTRODUCTION

Anemia is common in hemodialysis (HD) patients and hemoglobin (Hb) levels <11 g/dL are associated with higher morbidity, higher mortality, impaired quality of life and increased treatment costs [1-3], even if the diagnosis criteria for anemia are slightly different [4,5]. Low endogenous levels of erythropoietin and insufficient available iron (absolute or functional iron deficiency) are the most important factors affecting erythropoiesis in HD patients [4].

Currently, treatment of anemia in HD patients includes in most cases iron supplementation and an erythropoiesis-stimulating agent (ESA) [5]. However, there is some controversy about the optimal and upper limit of Hb levels based on three large studies in patients with chronic kidney disease, not on dialysis, comparing ESA treatment with high Hb target levels (≥ 13 g/dL) vs. low Hb targets (~11 g/dL) or placebo. Although these trials have some limitations [6], it should be considered that only one showed a significant benefit of high Hb target levels. In CREATE, general health and physical function improved significantly better in the high Hb target group and there was no significant difference in the likelihood of a first cardiovascular event [7]. In CHOIR, high Hb target levels (13.5 vs. 11.3 g/dL) did not result in better improvement of quality of life but were associated with increased risk of a composite endpoint of death, myocardial infarction, hospitalization for congestive heart failure and stroke [8]. TREAT, comparing ESA treatment (target Hb 13 g/dL) vs. placebo, showed only a modest improvement in patient who reported fatigue, but showed also an increased risk of stroke and an increase of composite endpoint including death and cardiovascular events in the ESA group [6].

Previously, only one trial was related to hemodialysis patients, the Normal Hematocrit Cardiac Trial (NHCT) [9]. The NHCT study randomized hemodialyzed patients with congestive heart failure or ischemic heart disease who had been receiving ESA to achieve hematocrit target of 42% versus 30%. The study was halted early because of a trend towards increased risk of the composite endpoint of death or first non fatal myocardial infarction associated with the normal hematocrit target, with more thrombosis of the vascular access, but less transfusion rate in this group [9].

Accordingly, European and US guidelines for ESA-treated dialysis and non-dialysis patients recommend Hb target levels in the range of 10–12 g/dL [10-11]. Very recently, the guidelines provided by KDIGO recommended Hb target from 9.5 to 11.5 g/dL [5]. Hb levels should not exceed 12 g/dL, particularly in patients with severe cardiovascular disease or diabetes and concurrent peripheral vascular disease [11,12].

However, a lower and narrow Hb target range may result in more and/or prolonged periods with insufficient anemia correction before achieving the designated Hb target. As a consequence there is a growing interest for the recurrent cyclic fluctuations of Hb levels frequently observed in patients with end-stage renal disease [13-16]. Awareness of Hb cycling and its consequences is important to maintain Hb levels in a stable range and enhance the quality of anemia

management [17]. The aim of this study was to describe the current therapeutic management of anemia in French hemodialysis centers in comparison to national and international guidelines and assess the evolution of Hb levels (Hb fluctuations) in HD patients.

2. PATIENTS AND METHODS

2.1 Study Design and Patients

This retrospective observational study was conducted in five French hemodialysis centers using Hemodial® software (PHP Développement, Roubaix, France) for follow-up of patient records. Records of patients who were included in the Hemodial database and underwent hemodialysis between January 1st and December 31st, 2012 were analyzed if they had at least one Hb value per month over a period of at least four months available or either died or received a kidney transplant in 2012 and had at least one post-baseline Hb value available. Medical treatment and diagnostic monitoring were left to the centers' discretion following their routine practice (mostly 3 dialysis sessions per week for four hours each). As required by law, no formal approval was necessary by the independent ethic committee.

The main objective of the study was the description of the therapeutic anemia management in HD patients in France. Secondary objectives included a quantitative description of the used treatment strategies in comparison to national and international guidelines and fluctuations in actual compared to target Hb levels.

2.2 Data Collection

Anonymized data on sex, height, weight, underlying disease causing renal failure, glomerular filtration rate, co-morbidities (diabetes, hypertension, cancer, chronic infectious disease such as hepatitis B and C or HIV infection), dates of dialysis sessions in 2012, vascular access and change during the period, blood pressure, laboratory tests for anemia (complete blood count, Hb, serum ferritin, serum iron, transferrin saturation [TSAT]), C-reactive protein, serum albumin, protein electrophoresis, serum creatinine, urea, uric acid, potassium, alkaline reserve, evaluation of phospho-calcic metabolism (calcium, phosphorus, parathyroid hormone, aluminum), Kt/V for each dialysis session, treatments of anemia (transfusions, ESA, iron) and significant events such as hospitalizations, surgical procedures, kidney transplant and death were extracted from the Hemodial database of each center.

2.3 Statistical Analysis

No formal statistical hypothesis was tested and the statistical analysis was essentially descriptive (percentages, mean and standard deviation [SD], median and interquartile range [IQR]). Groups were compared using Student's t-test or Wilcoxon's test for quantitative variables and Fisher's exact test or Chi-2 test for qualitative variables. All tests were bilateral at the level 0.05.

"Annual Hb values" were categorized according to the patient's monthly mean Hb as Low (Hb <10 g/dL), Ideal (Hb 10 – ≤12 g/dL) or High (Hb >12 g/dL) if the Hb levels remained >75% of the observation period in the respective category; otherwise the annual Hb was categorized as Fluctuating. This classification was derived from the Hb level fluctuation classifications of Ebben et al. [17] and Kalantar-Zadeh et al. [18].

Predictive factors of the annual Hb category were assessed by multivariate analyses (multinomial logistic regression) using the Ideal category as reference category.

Data management and statistical analysis were performed using SAS version 9.1 (SAS Institute, Inc., Cary, North Carolina, USA).

3. RESULTS

3.1 Patient Characteristics

Among 830 patients who were hemodialyzed in 2012, 636 patients (77%) were evaluable (117 in Center 1, 218 in Center 2, 81 in Center 3, 124 in Center 4 and 96 in Center 5). Mean age was 66.6 (SD 14.9) years, 59.4% of evaluable patients were male (Table 1) and 83.2% had their first hemodialysis before November 2011. Median of hemodialysis sessions per patient during year 2012 was 143.5 (IQR 100–155). Eighty-eight patients (13.8%) died and 22 (3.5%) received a kidney transplant in 2012 (recorded in two centers only).

Table 1. Characteristics of the hemodialysis patients analyzed in the study

	Annual Hb category, n (%)				
	Low N=18	**Ideal N=119**	**High N=61**	**Fluctuating N=438**	**Total N=636**
Age, years, mean (SD)	64.1 (14.6)	66.3 (16.3)	63.0 (13.9)	67.3 (14.5)	66.6 (14.9)
Male gender, n (%)	14 (77.8)	70 (58.8)	44 (72.1)	250 (57.1)	378 (59.4)
Death*	10 (55.6)	20 (16.8)	8 (13.1)	50 (11.4)	88 (13.8)
Kidney transplantation*	0	7 (5.9)	7 (11.5)	8 (1.8)	22 (3.5)
Comorbidities, n (%) †					
Diabetes	3 (21.4)	30 (31.6)	13 (21.7)	112 (30.2)	158 (29.3)
Cardiovascular diseases	0	4 (4.2)	6 (10.0)	43 (11.6)	53 (9.8)
Cancer	2 (14.3)	2 (2.1)	5 (8.3)	33 (8.9)	42 (7.8)
Other	6 (42.9)	52 (54.7)	32 (53.3)	197 (53.1)	287 (53.1)

** During year 2012 (transplantation probably recorded in only 2 centers), † n=540, no data reported in one center*

3.2 Assessment of Hematological Parameters and Evolution of Hb Levels

On average, Hb levels were assessed 15.7 (7.6) times per patient and year, serum ferritin and TSAT were assessed 6.4 (3.5) and 5.7 (4.8) times per patient. The mean annual Hb level was 11.5 (1.0) g/dL (Table 2) and was ≤ 11.0 g/dL in 25% of patients. Mean annual serum ferritin was < 200 µg/L in 14.6% and TSAT was < 20% in 13.3%.

Mean monthly Hb levels remained in the Ideal range in 18.7% of patients and fluctuated between Low, Ideal and High levels in 68.9%. Continuously low Hb levels were recorded for 2.8% and high Hb levels for 9.6%. Patients who had started with dialysis in or after November 2011 had significantly lower mean Hb levels than patients with a longer history of dialysis (11.1 vs. 11.6 g/dL; $p < 0.0001$). These 'new' dialysis patients were more frequently in the Low and Fluctuating Hb category (7.5 and 77.6% vs. 1.9 and 67.1%, respectively; $p = 0.0002$).

3.3 Anemia Treatments

96.5% of patients were treated for anemia and 59.9% received ESA supplemented only with i.v. iron and this was the most frequently used anemia treatment option (Table 3). Overall, 91.4% received an ESA (darbepoetin alfa, 61.6%; epoetin alfa, 21.2%; epoetin beta, 11.8%) and 74.2% received i.v. iron. Epoetin doses were converted from IU to µg using European (200: 1) product label guidelines. Transfusions, either alone or in addition to another treatment, were given to 14.9% of patients.

Patients in the Low Hb category received the highest mean weekly ESA dose per patient (65.7 µg; $p<0.0001$ for overall comparison) (Table 3, Fig. 1) and the lowest i.v. iron dose (13.6 mg $p=0.012$). Furthermore, the transfusion rate was highest in the low Hb category (66.7%). Patients in the Fluctuating category experienced more frequently ESA dose changes than patients in the Ideal category: 73.9% vs. 58.8%, respectively (Table 3).

3.4 Predictive Factors for Annual Hb Category

Multinomial logistic regression showed that the presence of comorbidities, hospitalization and transfusion were associated with increased risk of Fluctuating vs. Ideal Hb levels (odds-ratio [OR] = 7.6, 2.2 and 2.9, respectively) (Table 4). Conversely, male patients and those with high serum ferritin levels (≥ 500 µg/L vs. < 200 µg/L) had a lower risk of Fluctuating Hb levels (OR = 0.6 and 0.4, respectively). Hospitalization was associated with High Hb category (OR = 2.5 vs. Ideal category) while higher ESA dose consumption (40–80 µg/week vs. < 40 µg/week) was negatively associated with High Hb category (OR = 0.2). Low Hb category was associated with blood transfusions (OR = 67.9) and high ESA dose consumption (OR = 138.7 for consumption ≥ 80 vs. < 40 µg/week); however the number of patients in this category was rather low (n=18).

Table 2. Biological anemia parameters of the cohort of hemodialysis patients in 2012

	Annual Hb category, n (%)				
	Low N=18	**Ideal N=119**	**High N=61**	**Fluctuating N=438**	**Total N=636**
Hemoglobin, n	18	119	61	438	636
Mean (SD), g/dL	8.9 (0.6)	11.1 (0.4)	13.1 (0.7)	11.5 (0.8)	11.5 (1.0) [a]
Interquartile range, g/dL	8.6 –9.1	10.8–11.5	12.6–13.4	11.0–12.0	11.0–12.1
Number of assessments/patient, mean (SD)	11.2 (10.9)	14.9 (7.0)	14.4 (8.2)	16.3 (7.4)	15.7 (7.6) [b]
Serum ferritin, n	14	115	56	433	618
Mean (SD), µg/L	771.2 (856.8)	453.8 (225.0)	547.1 (546.7)	487.9 (324.6)	493.3 (357.1)
Category, n (%)					
< 200	3 (21.4)	11 (9.6)	12 (21.4)	64 (14.8)	90 (14.6)
200 – < 500	5 (35.7)	65 (56.5)	21 (37.5)	211 (48.7)	302 (48.9)
≥ 500	6 (42.9)	39 (33.9)	23 (41.1)	158 (36.5)	226 (36.6)
Transferrin saturation (TSAT), n	12	106	51	378	547
Mean (SD), %	25.9 (10.4)	31.5 (10.3)	33.4 (14.2)	30.5 (11.0)	30.8 (11.2)
Category, n (%)					
< 20%	3 (25.0)	11 (10.4)	7 (13.7)	52 (13.8)	73 (13.3)
20 – <40%	8 (66.7)	78 (73.6)	30 (58.8)	257 (68.0)	373 (68.2)
≥ 40%	1 (8.3)	17 (16.0)	14 (27.5)	69 (18.3)	101 (18.5)

[a] $p < 0.0001$; [b] $p = 0.0062$ (p-values for overall comparisons)

Table 3. Anemia treatment of the cohort of hemodialysis patients according to the annual Hb category

	Annual Hb category, n (%)				
	Low N=18	**Ideal N=119**	**High N=61**	**Fluctuating N=438**	**Total N=636**
Patients treated with ESA, n (%)	13 (72.2)	110 (92.4)	44 (72.1)	414 (94.5)	581 (91.4) [a]
Dose (µg) by week, mean (SD)	65.7 (67.8)	34.6 (27.7)	13.7 (16.1)	31.1 (27.0)	31.1 (29,3) [a]
Dose (µg) by kg, mean (SD)	0.6 (0.9)	0.5 (0.5)	0.2 (0.2)	0.4 (0.5)	0.4 (0.5) [a]
Number of dose changes, mean (SD)	1.5 (2.0)	1.2 (4.4)	1.1 (1.5)	2.2 (3.6)	2.0 (3.2) [a]
No dose change, n (%)	6 (46.2)	46 (41.8)	22 (50)	108 (26.1)	182 (31.3) [b]
Patients treated with i.v. iron, n (%)	6 (33.3)	87 (73.1)	38 (62.3)	341 (77.9)	472 (74.2) [a]
Dose of i.v. iron, mg/week, mean (SD)	13.6 (26.9)	34.7 (32.9)	30.8 (38.2)	38.3 (34.7)	36.2 (34.7) [c]
Patients treated with oral iron, n (%)	2 (11.1)	5 (4.2)	2 (3.3)	7 (1.6)	16 (2.5) [d]
Patients transfused, n (%)	12 (66.7)	7 (5.9)	2 (3.3)	74 (16.9)	95 (14.9) [a]
Anemia treatment options, n (%)*					
ESA + i.v. iron	2 (11.1)	76 (63.9)	29 (47.5)	274 (62.6)	381 (59.9)
ESA only	1 (5.6)	24 (20.2)	12 (19.7)	64 (14.6)	101 (15.9)
ESA + i.v. iron + transfusion	4 (22.2)	3 (2.5)	2 (3.3)	52 (11.9)	61 (9.6)
ESA + transfusion	4 (22.2)	2 (1.7)	0	18 (4.1)	24 (3.8)
i.v. iron only	0	4 (3.4)	7 (11.5)	12 (2.7)	23 (3.6)
No treatment	3 (16.7)	3 (2.5)	9 (14.8)	7 (1.6)	22 (3.5)
Transfusion only	2 (11.1)	2 (1.7)	0	3 (0.7)	7 (1.1)

*i.v.: intravenous; * Treatments or combinations of treatment in ≥ 1% of total study population, [a] p < 0.0001; [b] p = 0.0003; [c] p = 0.012; [d] p = 0.04 (p-values for overall comparisons)*

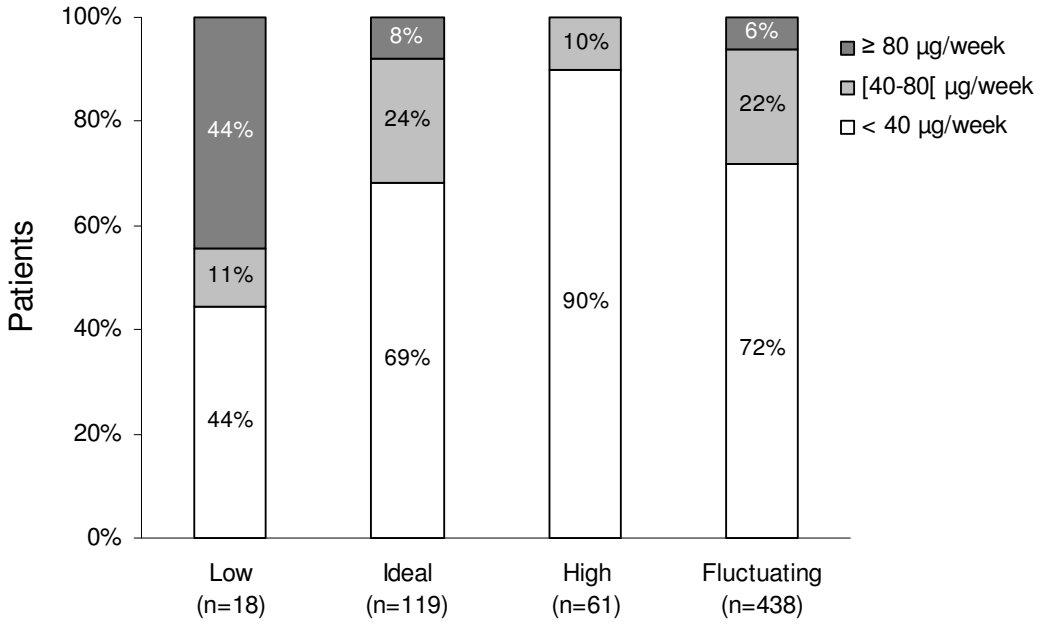

Fig. 1. ESA dosage according to annual Hb category

Table 4. Multivariate analysis for adjusted predictive factors of annual Hb category

	Annual Hb category		
	Low	**High**	**Fluctuating**
Age, years			
< 55	1	1	1
55 – <65	1.7 (0.1–18)	0.9 (0.3–2.5)	0.9 (0.5–1.9)
65 – <75	0.1 (0.05–3.1)	0.7 (0.2–2.1)	1.2 (0.6–2.7)
≥ 75	0.3 (0.02–5.1)	0.7 (0.3–1.9)	1.2 (0.6–2.3)
Male gender	1.5 (0.2–13)	1.1 (0.5–2.3)	0.6 (0.3–0.9)
At least one comorbidity	NE	2.7 (0.2–32)	7.6 (1.2–48)
At least one hospitalization	1.9 (0.2–16)	2.5 (1.1–6)	2.2 (1.2–4.2)
Transfusion	67.9 (7.6–610)	0.6 (0.1–3.2)	2.9 (1.1–8.1)
Weekly consumption of ESA, µg			
< 40	1	1	1
40 – <80	0.9 (0.06–12.4)	0.2 (0.04–0.9)	0.6 (0.3–1.1)
≥ 80	138.7 (2.5–7737)	NE	2.3 (0.3–19.4)
Weekly consumption of i.v. iron, mg/week			
< 50	1	1	1
50 – <100	0.05 (0.0–2.1)	0.9 (0.4–2.3)	1.1 (0.6–1.9)
≥ 100	NE	1.5 (0.08–28.6)	1.2 (0.1–11.5)
Ferritin, mean, µg/L			
< 200	1	1	1
200 – <500	0.3 (0.0–6.7)	0.3 (0.08–1.1)	0.5 (0.2–1.2)
≥ 500	0.2 (0.0–3.9)	0.4 (0.1–1.3)	0.4 (0.1–0.9)
Albumin, g/L			
< 35	3.6 (0.6–23.7)	0.2 (0.02–1.4)	0.6 (0.3–1.3)
≥ 35	1	1	1

Results are given as odds-ratio vs. the Ideal category and 95% confidence interval (n=496)
NE: no estimation (low statistical power)

4. DISCUSSION

This study in a cohort of HD patients showed that only 18.7% of patients maintained Hb levels in the Hb target range of 10–12 g/dL (Ideal category) although the annual mean Hb (11.5 [SD 1.0] g/dL) was within the acceptable target range according to European guidelines. The majority of patients (68.9%) had monthly mean Hb values that fluctuated between the predefined Hb categories (Low, Ideal and High) throughout the year. In the study of Ebben et al. [17], only 6.5% of the 152,846 patients were in the target range (11–12.5 g/dL) and 47.4% of patients during a three-month period in the USRDS system [19].

As expected, most patients of our study were treated with an ESA and/or i.v. iron to control anemia, yet patients with fluctuating Hb levels had the highest rate of ESA dose changes and received more frequently blood transfusions than patients in the Ideal or High Hb category. Notably, the highest mean ESA dose and transfusion frequency was reported for patients in the Low Hb category who also comprised the population that received the lowest i.v. iron doses.

The large percentage of patients with fluctuating Hb levels in our study and the observation that these patients had more ESA dose changes than patients in the other categories is in line with previous studies showing the challenge to maintain Hb target levels in ESA-treated HD patients [17,20-22]. Ebben et al. [17] reported that 39.5% of end-stage renal disease patients had high-amplitude fluctuations, 21.3% low-amplitude fluctuations in low Hb levels and 28.9% low-amplitude fluctuations in high Hb levels. Portolès et al. [20] reported that only 3.8% maintained Hb values within their target Hb range of 11-13 g/dL over one year and that ESA dose changes were a risk factor of Hb variations. Also Fishbane and Berns showed that frequent ESA dose adjustments were the most important driver of Hb fluctuations with 84% of Hb rises being associated to an increase in ESA dose and 62% of Hb decreases related to an ESA dose reduction [13]. The importance of ESA dose changes in Hb fluctuations was further confirmed by a recent French study [16].

A narrow Hb target range might perpetuate Hb fluctuations since off-target Hb values are immediately followed by ESA dose adjustment to change the trajectory of Hb variation [23,24]. This could be exacerbated with rigid protocols for ESA dose adjustment not accounting for individual patient responsiveness [13,23]. Indeed, patients who were frequent cyclers appeared to be significantly more responsive to ESA [13].

Fishbane and Berns also observed that Hb fluctuations are associated with changes in serum ferritin levels [13] and it is well known that HD-associated blood loss results in higher iron requirements [25,26], that could be compensated with i.v. iron maintenance treatment (total dose 2.5 g iron/year) [27]. Intravenous iron can rapidly replenish iron stores and compensate for the rapid increase of iron needs associated with rapidly increased erythropoiesis after ESA treatment. Accordingly, i.v. iron supplementation with 25-150 mg/week is recommended for ESA-treated HD patients even in the absence of iron deficiency to achieve serum ferritin target levels of 200–500 µg/L and a TSAT of 30–40% [10,28,29]. Replenishment of iron stores with weekly maintenance iron treatment rather than intermittent iron treatment may be more adequate considering the physiology of Hb synthesis and its complex relationship with iron storage and homeostasis in HD patients [13].

Since, the combined effects of ESA and i.v. iron treatment might partly complicate Hb maintenance and result in additional, i.v. iron-related, Hb fluctuations [13], regular monitoring of Hb and iron status parameters is an important aspect of HD patient management. In our study, we observed that HD patients were approximately two to three-fold more often assessed for their Hb levels than for their iron status (serum ferritin, TSAT). This means that a complete hematological status is only assessed by every second laboratory evaluation or, even worse, in every second patient. This underestimation of a balanced iron status in our cohort is also reflected by the observation that 19.7% of ESA-treated patients did not receive i.v. iron. Moreover, 14.6% had serum ferritin levels < 200 µg/L and 13.3% had a TSAT < 20%. The very high mean serum ferritin levels in patients of the Low Hb category combined with the lowest mean TSAT levels across the different categories suggest that these patients suffered from iron-restricted erythropoiesis due to chronic inflammation and might have particularly benefited from i.v. iron; in fact these were the patients that were least frequently treated with i.v. iron.

Other risk factors of fluctuating Hb levels in the presented patient cohort were at least one hospitalization and at least one comorbidity (the Low Hb category was too small to evaluate the comorbidity risk). Hospitalization was also reported as risk factor of low or fluctuating Hb levels by Ebben et al [17] and Portolès et al [20]. Overall, our data suggest that patients in the Fluctuating category appear to be more heavily treated in a context of higher morbidity compared with patients in other Hb categories and confirm previous studies showing that disease severity was associated with fluctuating Hb levels [30]. Particularly blood transfusions provide only a transient increase in Hb levels and can contribute to Hb fluctuations [31] in addition to the other negative outcomes reported for blood transfusions [31].

Although the evaluated cohort was representative of the 2012 HD patient population in France [32], the Low Hb category was too small to allow for analyses with sufficient statistical power. Some data such as deaths or kidney transplantation were not systematically recorded by some centers (e.g. 8.2% of French hemodialyzed patients have been transplanted in 2012 vs. only 3.5% in our study). However, data on Hb and anemia were consistent with national data (mean Hb level 11.3±1.4 g/dL in the entire 2012 HD population) assuring the validity of the cohort data on the hematological aspects [32]. From the retrieved patient record data, it was not always possible 1) to identify which i.v. iron preparation had been used and 2) whether the used i.v. iron had been changed during the observation period. Such a change in i.v. iron formulation can result in significant Hb fluctuations and ESA-dose adjustments as recently reported [33].

5. CONCLUSION

Only 18.7% of patients were kept within the acceptable target range according to French and international guidelines due to frequent Hb fluctuations. Only few patients had consistently low annual Hb levels. These findings suggest that an average Hb level may not be the optimal assessment of anemia. Implementation of more frequent hematological assessments, particularly of iron status parameters, and optimized/individualized treatment strategies may minimize Hb fluctuations and improve anemia management in hemodialysis patients.

DECLARATION OF FUNDING

Vifor Pharma.

DECLARATION OF FINANCIAL/OTHER RELATIONSHIPS

LZ, JW and LM are employees of Vifor Pharma.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. No formal approval was necessary by the independent ethic committee.

COMPETING INTERESTS

J. Rottembourg has received lecturing fees from Amgen, Vifor, Fresenius, D. Pablo Urena Torres has received fees for research from Amgen, Shire, Genzyme and Fresenius, and lecturing fees from Amgen, Abbot and Shire. HLM, KS, CE declared they had no competing interests

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