

Hemoglobin levels and variability have increased over time in incident hemodialysis patients

Introduction

- Anemia management for incident hemodialysis (HD) patients has changed over the past decade. Increases in mean hemoglobin levels and attainment of threshold hemoglobin targets in the months after initiation have been documented.
- Time trends in patient hemoglobin level variability post-initiation have received little study.
- This study analyzed incident hemodialysis cohorts from two time periods to characterize hemoglobin dynamics and to assess change over time.

Methods

- The study population included all incident hemodialysis patients aged 65 years or older who:
 - initiated hemodialysis during two time periods: 7/1/1998 to 6/30/1999 or 7/1/2003 to 6/30/2004,
 - survived at least 6 months after initiation of dialysis,
 - had Medicare as primary payer and didn't change modality during the 6-month period, and
 - had EPO and hemoglobin data in each of the first 6 months of dialysis.

- Each patient was followed for 6 months from the month of initiation. Hemoglobin levels were obtained from the EPO claims, and three measures of hemoglobin variability were used:
 - Standard Deviation method: Standard Deviation of patient-level hemoglobin values across the 6 months was calculated.
 - Residual Standard Deviation method¹: A Simple Linear Regression was fitted to each patient's monthly average hemoglobin values across the 6-month period and standard deviation of residuals from the regression line was calculated to measure hemoglobin variability from the linear trend.
 - Hemoglobin Cycling method²: A hemoglobin excursion was defined as a series of decreasing or increasing monthly average hemoglobin values differing by at least 1.5 g/dL. A hemoglobin cycle was defined as two consecutive excursions in different directions.
 - Two Sample T-test was used to compare continuous variables such as Residual Standard Deviation or mean hemoglobin values for the two time periods (2003-2004 vs. 1998-1999).

- Chi-Square Test was used to compare categorical variables such as hemoglobin cycling between the two time periods.
- Multivariate regression was used to examine linear trend from month 1 to 4 after initiation and adjusted for age, gender, race.

Results

- This study included 11,643 patients in the 1998-1999 cohort and 15,896 patients in 2003-2004 cohort who met all the inclusion and exclusion criteria (Table 1).
- Patients in the later cohort had a higher mean hemoglobin value at month 1 (10.70 g/dL in 2003-2004 vs. 10.17 g/dL in 1998-1999; $P < 0.05$) and a steeper slope of increase at months 1 to 4 from initiation after adjusting for age, gender, and race ($P < 0.05$). Mean hemoglobins then flattened after month 4 for both cohorts (Figure 1 & Table 2).
- The mean Standard Deviation was higher in the later cohort (1.28 g/dL in 2003-2004, vs. 1.19 g/dL in 1998-1999; $P < 0.05$; Table 3).
- Mean intercept and slope from Residual Standard Deviation method also indicated that patients started with a higher intercept and a larger slope of increase in the later cohort (Table 4).

Table 1. Exclusions resulting in final cohort

Cohort	all ages ¹⁵ patients	death or payer changed	modality or EPO or Hb changed	missing EPO or Hb	Final number
1998-1999	47,883	20,097	4,480	377	11,286
2003-2004	59,451	24,425	5,953	418	12,759

Table 2. Mean and standard deviation of monthly hemoglobin values

Month	1998-1999		2003-2004	
	Mean	SD	Mean	SD
1	10.17	1.34	10.70	1.37
2	10.86	1.41	11.66	1.48
3	11.35	1.47	12.24	1.50
4	11.56	1.50	12.38	1.49
5	11.61	1.47	12.30	1.45
6	11.58	1.46	12.21	1.44

Figure 1. Mean monthly hemoglobin values for incident HD patients

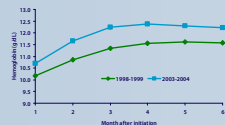


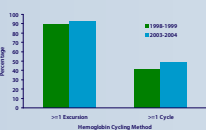
Table 3. Mean and standard deviation of individual Mean and Standard Deviation (Standard Deviation Method)

Cohort	Mean Mean(SD)	Std of Hb Mean(SD)
1998-1999	11.388 (0.951)	1.194 (0.557)
2003-2004	11.914 (0.917)	1.281 (0.561)

Table 4. Mean and standard deviation of intercept, slope, and Residual (Residual Standard Deviation Method)

Cohort	Intercept mean (SD)	Slope mean (SD)	ResStd mean (SD)
1998-1999	16.240 (1.585)	0.271 (0.394)	0.858 (0.449)
2003-2004	18.957 (1.632)	0.274 (0.406)	0.945 (0.472)

Figure 2. Percent of patients with at least one excursion or cycle (hemoglobin cycling method)



References:

- Rubeen K, Israni, Wei Yang, Marshall Joffe, Steve Fishbane, Harold L Feldman. A Novel Method of Measuring Hemoglobin Variability in Hemodialysis Patients. Presented at 2006 ASN.
- Fishbane S, Berns JS. Hemoglobin cycling in hemodialysis patients treated with recombinant human erythropoietin. Kidney Int. 2005;68:1337-1343.

- Mean Residual Standard Deviation, indicating hemoglobin variability from the regression line, was higher in the later cohort (0.95 g/dL in 2003-2004 vs. 0.86 g/dL in 1998-1999; $P < 0.05$; Table 4).
- A larger percentage of patients in the later cohort had at least one hemoglobin excursion or one full cycle of hemoglobin variation (Excursion: 92.6% in 2003-2004 vs. 89.5% in 1998-1999; $P < 0.05$; Cycle: 48.7% in 2003-2004 vs. 40.9% in 1998-1999; $P < 0.05$; Figure 2).

Conclusions

- In 2003-2004 vs. 1998-1999, patients initiated hemodialysis at higher mean hemoglobin levels, their levels rose more rapidly, and they demonstrated increased variability during the first 6 months.
- Further research suggested by these findings includes identifying the patient factors and treatment factors that are driving the observed changes in the rate of hemoglobin rise and hemoglobin variability, and analyzing the association of these changes with morbidity and mortality.