Facility EPO Titration Practices, Hemoglobin Levels, and Transfusion Use

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Introduction

- Transfusion avoidance is a common goal of anemia treatment for patients on dialysis.
- Erythropoiesis stimulating agents (ESAs) are frequently used to treat anemia and are effective in increasing hemoglobin (Hb) levels and decreasing the need for red blood cell (RBC) transfusions.
- Safety concerns associated with targeting higher Hb levels with ESAs led to a label change in 2011 instructing providers to treat to lower Hb levels and use the lowest dose to avoid the need for transfusion.
- The clinical challenge is to determine how to optimally dose ESAs to minimize the risks associated with higher Hb levels and simultaneously reduce the need for transfusions.
- We studied ESA dose titration after implementation of the new dialysis payment system (Jan 2011) and FDA label (June 2011).
- The current EPO label advises initiating at Hb <10 g/dL and reducing or interrupting the dose at Hb ≥11 g/dL.

Objective

- To investigate facility-level EPO dosing practices in 2012 and effects on patient Hb levels and RBC transfusion event rates.

Methods

- Cohort: Adult (aged ≥18 years) patients with Medicare Parts A and B as primary payer undergoing hemodialysis in 2012.
- Jan-June 2012: Assessed facility EPO titration practice patterns
  - EPO dose titration was the % change in EPO dose between 2 consecutive months.
  - For each facility, the median EPO dose titration (month-to-month) when Hb <10 g/dL and >11 g/dL were calculated.
  - EPO dose titrations classified as
    - small (Hb<10 g/dL: <20%; Hb>11 g/dL: >-20%)
    - medium (Hb<10 g/dL: 20-30%; Hb>11 g/dL: -20% to -30%)
    - large (Hb<10 g/dL: >30%; Hb>11 g/dL: <-30%).
  - Facilities were then classified into 1 of 9 titration practice groups (T1-T9).

	EPO titration when Hb<10 g/dL			
		small ↑	medium ↑	large ↑
EPO titration when Hb>11 g/dL	small ↓	T1	T4	T7
	medium ↓	T2	T5	T8
	large ↓	T3	T6	T9

- July-Dec 2012: Assessed the effects of facility EPO titration practice (groups) on clinical outcomes:
  - Average Monthly Hb concentration
  - RBC transfusion rates
- Adjusted relative rate of RBC transfusions was determined using generalized estimating equations to fit Poisson regression models.
  - Covariates for patient and facility characteristics were included.

Results

- This study included 69,186 patients and 1,319 facilities in the 2012 study cohort.
- Patient case-mix did not differ across facility groups (not shown). However, we observed significant variation in facility characteristics across titration practices (see Table 1).
- Figure 1 shows percent patient-months with Hb<10, 10-11, and >11g/dL by titration practice groups. Large downward titrations when Hb>11 g/dL was associated with more patient-months with Hb < 10 g/dL, fewer with Hb>11 g/dL, and more with Hb within 10-11 g/dL (T3,T6,T9).
- Figure 2 presents unadjusted transfusion rate and mean (SD) Hb during follow-up. Whereas patient Hb levels differ across facilities, and in line with transfusion rate, the SDs are identical across facility groups.
- Figure 3 shows adjusted rate ratios for transfusion by EPO titration groups with T5 (medium ↑, medium ↓) as the reference group. Facilities with EPO titration patterns T6 (medium ↑ when Hb<10, large ↓ when Hb>11) or T7 (large ↑ when Hb<10, small ↓ when Hb>11) had significantly lower adjusted rates of transfusion events than the reference group (P values = 0.0005 and 0.0148).

Table 1. Number of patients and facilities and important facility characteristics, by facility EPO titration practice group.

Titration Group	T1	T2	T3	T4	T5	T6	T7	T8	T9
N of patients	11,085	4,689	3,304	9,591	10,069	5,041	7,279	10,421	7,707
N of facilities	193	96	72	180	185	98	139	200	156
Location type (%)									
Rural	13.4	21.1	25.4	17.2	19.3	18.6	18.4	18.9	19.4
Urban	86.6	79.0	74.7	82.8	80.7	81.4	81.6	81.1	80.7
Profit status (%)									
For-profit	68.7	76.8	87.3	88.5	80.7	92.8	91.2	90.8	92.3
Non-profit	31.3	22.1	12.7	11.5	19.3	5.2	8.8	9.2	7.7
LDO vs. other (%)									
Other	60.3	35.8	59.2	31.6	27.1	33.0	20.6	11.7	22.6
LDO	39.7	64.2	40.9	68.4	72.9	67.0	79.4	88.3	77.4

Figure 1. Overall percentage of patient-months with Hb below 10, within 10-11, and above11 g/dL, by facility EPO titration practice group.

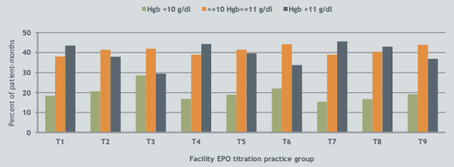


Figure 2. Patient transfusion rate (unadjusted) and mean (SD) hemoglobin during follow-up, by facility EPO titration practice group.

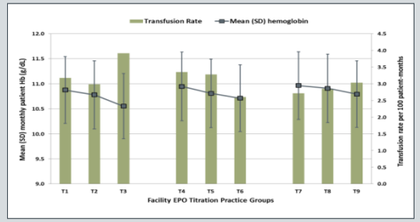
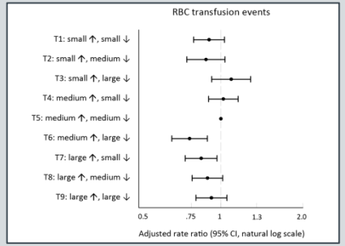


Figure 3. Adjusted rate ratios for RBC transfusion events by facility EPO titration practice groups with T5 (medium ↑, medium ↓) as the reference group. Rates were adjusted for patient and facility characteristics.



Discussion

- We observed significant variation in how facilities implemented the new EPO label.
- Despite this significant variation, the average Hb across facility titration groups was fairly similar and the standard deviation was nearly identical.
- Transfusion rates, on the other hand, did differ across facility titration groups, with the lowest rates observed in facilities with combinations of moderate escalation (when Hb < 10 g/dL) with large reductions (when Hb > 11), or large escalation with small reductions.
- These findings were not affected by patient case-mix or facility characteristics.

Conclusions

- Facility EPO titration practices that moderately increased dose when Hb <10 and implemented greater dose reductions when Hb >11 g/dL were associated with limiting RBC transfusions while maintaining the largest proportion of Hb levels between 10 and 11 g/dL.
- Understanding these practice patterns may help achieve a balance between maximizing benefits while minimizing risks, and help guide ESA therapy titration.

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