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 ESA dose titration after large reductions in Hb levels are effective in increasing hemoglobin (Hb) levels and decreasing the need for red blood cell (RBC) transfusions. We studied ESA dose titration after large reductions in Hb levels. We observed significant variation in the dose at Hb <10 g/dL, and red cells or interrupting the dose at Hb <11 g/dL.

Objective
- To investigate facility-level ESA 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: Accessed facility EPO titration practice patterns
- EPO dose titration was the 9 change in EPO dose within 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%-30%)
  - large (Hb<10 g/dL: <30%; Hb<11 g/dL: <30%)
- Facilities were then classified into 1 of 9 titration practice groups (Table 1).

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 practice groups (see Table 1).
- Figure 1 shows percent-patient-months with Hb>10, 10-11, and >11 g/dL by titration practice groups. Large downward titrations when Hb<11 g/dL were associated with more patient-months with Hb>10 g/dL, fewer with Hb<10 g/dL, and more with Hb between 10-11 g/dL.
- Figure 2 presents unadjusted transfusion rate and mean (SD) Hb during follow-up. Whichever ESA 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 patterns with 7 studied (medium ↓, medium ↑) as the reference group. Facilities with EPO titration patterns T5 (medium ↓ when Hb>10, large ↓ when Hb<11), or T7 (large ↑ when Hb<11; small ↑ when Hb>11) had significantly lower adjusted rates of transfusion events in the reference group (P values = 0.0005 and 0.0148).

Discussion
- We observed significant variation in how facilities implemented the new ESA 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 >10 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.

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

<table>
<thead>
<tr>
<th>Facility EPO Titrator Practice Group</th>
<th>Number of Patients</th>
<th>Number of Facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (low)</td>
<td>11,085</td>
<td>96</td>
</tr>
<tr>
<td>T2 (medium)</td>
<td>3,304</td>
<td>193</td>
</tr>
<tr>
<td>T3 (high)</td>
<td>7,279</td>
<td>213</td>
</tr>
<tr>
<td>T4 (low)</td>
<td>5,041</td>
<td>98</td>
</tr>
<tr>
<td>T5 (medium ↓)</td>
<td>7,453</td>
<td>200</td>
</tr>
<tr>
<td>T6 (medium ↑)</td>
<td>5,842</td>
<td>205</td>
</tr>
<tr>
<td>T7 (high)</td>
<td>6,948</td>
<td>200</td>
</tr>
<tr>
<td>T8 (low)</td>
<td>5,041</td>
<td>98</td>
</tr>
<tr>
<td>T9 (high)</td>
<td>7,453</td>
<td>200</td>
</tr>
</tbody>
</table>

Note: Percentages were adjusted for patient and facility characteristics.