Anemia Management: Using Epo and Iron

Ky Stoltzfus, MD
• University of Kansas Medical Center
• Assistant Professor Department of Internal Medicine

January 23, 2013
Regulation of red cell production

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Treatment of easily reversible causes of anemia may include:

- Iron
- Erythropoietin replacement
- Vitamin replacement (Vitamin B12, folate)
Iron replacement

- Oral
  - Patients tolerate some preparations more than others
- IV
  - INFeD (Iron Dextran)
  - Ferrlecit (Iron Glucose)
  - Venofer (Iron Sucrose)
  - Feraheme (Ferumoxytol)
What is the most common side affect of oral iron?

- 1) Constipation
- 2) Nausea
- 3) Red colored tongue
- 4) Shortness of breath
- 5) Singultus
What forms of IV iron have you seen given most often?

- 1) Infed (iron dextran)
- 2) Venofer (iron sucrose)
- 3) Ferrlicit (iron gluconate)
- 4) Ferumoxytol (iron polyglucose)
- 5) Dexferrum (high molec wt iron dextran)
## Preparations of IV iron

<table>
<thead>
<tr>
<th>Currently available intravenous iron preparations</th>
<th>Investigational agents (not FDA approved)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trade name</strong></td>
<td>DexFerrum</td>
</tr>
<tr>
<td><strong>Manufacturer</strong></td>
<td>American Regent</td>
</tr>
<tr>
<td><strong>Carbohydrate</strong></td>
<td>High-molecular-weight iron dextran</td>
</tr>
<tr>
<td><strong>Total-dose or &gt;500-mg infusion</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Test dose required</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Black box warning</strong></td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Infusion of IV iron

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Approved Dosing</th>
<th>Maximum Safe Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferric gluconate</td>
<td>125mg over 10 min</td>
<td>250mg over 1 hour&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Iron sucrose</td>
<td>100-400mg over 2-90 min</td>
<td>300mg over 2 hour&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Iron dextran</td>
<td>100mg over 2 min</td>
<td>TDI over 1-4 hours&lt;sup&gt;3-4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ferumoxytol (US only)</td>
<td>510mg over 17 seconds</td>
<td>510mg over 17 seconds&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ferric carboxymaltose (Europe only)</td>
<td>1000mg over 15 min</td>
<td>1000mg over 15 min&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Iron isomaltoside (Europe only)</td>
<td>20mg/kg over 15 min</td>
<td>20mg/kg over 15 min&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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IV Iron Supplementation

- Relatively expensive
- Requires an IV for infusion
- Avoids some unpleasant side effects
- Effective and replaces stores rapidly
- Should be used with caution in sepsis/infection and patients with chronic kidney disease
How much does IV iron cost?

- 1) $50-100 per treatment
- 2) $250-500 per treatment
- 3) $1000 per treatment
- 4) $10.99 with your Costco card
IV Iron

- Iron Dextran has the potential for anaphylactic reactions and rarely death.

- Iron gluconate is usually well tolerated as long as it is administered slowly at no more than 125 mgs per day.
IV iron

- Iron sucrose also well tolerated at doses up to 300 mgs over 90 minutes. May be given IV push 100 - 200mgs every other day. Can have hypotension with infusion.

- Ferumoxytol is new in the US
Erythropoietin

- Hormone produced in kidney and liver
- Stimulates red blood cell production
- Recombinant erythropoietin available
Epo continued

- Epoetin alfa (Procrit, Epogen)
  - Shorter acting, more frequent dosing
- Darbepoetin alfa (Aranesp)
  - Longer acting, less frequent dosing
Contraindications

- Contraindicated with uncontrolled hypertension.
- Instruct patient to report difficulty breathing, chest pain, seizures, severe headache.
- Necessary for transferrin saturation >20% for erythropoietin to be effective.
What potential side effect does Epo have?

- 1) DVT
- 2) Chest pain
- 3) Makes cancer worse
- 4) Death
New Safety Information - ESAs

- Chronic renal failure
  - Increased risk for death and serious CV events when administered to target higher vs lower Hb levels (13.5 vs 11.3 g/dL; 14 vs 10 g/dL) in 2 clinical studies
  - Individualize dosing to achieve Hb between 10 and 12 g/dL

ESA Safety

- **Cancer**
  - Shortened overall survival and/or time-to-tumor progression in clinical studies in patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers when dosed to target a Hb $\geq 12$ g/dL
    - Risks have not been excluded when dosed to a target Hb $<12$ g/dL
  - To minimize these risks, as well as the risk of serious cardio- and thrombovascular events, use lowest dose needed to avoid RBC transfusion
  - Use only for anemia due to concomitant myelosuppressive chemotherapy
  - Not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure
  - Discontinue following completion of CT course
ESA Safety

- **Perisurgery**
  - Increased rate of DVT in patients not receiving prophylactic anticoagulation
  - Use DVT prophylaxis
Pre-operative anemia management

- 35-75% of pre-operative patients are anemic
  - Depending on comorbidities
- Recommended that ALL pre-op patients be screened for anemia
- Unexplained anemia should be evaluated
- Surgery should be deferred until anemia is defined, and treated if possible

Strategies

- Use of pre-operative recombinant erythropoietin (with appropriate iron) is effective at increasing Hgb and decreasing allogeneic RBC transfusion
- Use of cell-saver intra-operative reduces RBC transfusion
- Acute normovolemic hemodilution and pre-operative autologous donation have mixed results
Pre-op Orthopedics

Multiple RTCs have shown:

- Dose-dependent increase in reticulocyte count with use of recombinant erythropoietin
- Decrease in risk of exposure to allogeneic blood in patients treated with erythropoietin (weekly vs daily makes no difference)
- Decrease in risk of exposure to allogeneic blood in patients treated with erythropoietin compared to cell saver
- All studies used iron at same time

Uhl L. JAMA, November 2, 2011—Vol 306, No. 17
Pre-op Cardiology

- Use of pre-operative recombinant erythropoietin reduces allogeneic RBC transfusion
- Use of IV iron alone has no significant impact in the absence of iron deficiency anemia

Use of single dose epo and IV iron one day prior to cardiac surgery reduced the risk of transfusion

Does your institution have a blood management (anemia management) program?

- 1) Yes
- 2) No
- 3) I’m not sure
Anemia Management Service

- Currently consultations are on an as-needed/as requested basis.
- Consults are answered by Anemia Management nurse with medical director oversight.
- Plan to start a routine outpatient consultation for all cardiothoracic surgery patients undergoing elective surgery.
Goals for the program

- Offer anemia management support to all surgical services for pre-operative treatment
- Offer inpatient anemia management consultation
KU transfusion order set

ADULT BLOOD TRANSFUSION

Indications for special product requirements: IRRADIATED: Bone Marrow, cord blood or peripheral blood progenitor cell transplants, intrauterine transfusion, neonates < 1200 grams or following intrauterine transfusions or when platelets are selected by HLA matching or crossmatching. CMV NEGATIVE - allogeneic bone marrow, cord blood or peripheral blood progenitor cell transplants where donor and recipient are CMV Seronegative WASHED - prevention of anaphylaxis in IgA deficiency or other patient with antibodies to plasma proteins. SICKLE CELL NEGATIVE - Sickle cell disease, neonatal RBC exchange and intrauterine transfusion.

ORDER SET NAME
ADULT BLOOD TRANSFUSION

BLOOD BANK

TYPE AND CROSSMATCH/HOLD

RBC BLOOD PRODUCTS
- Reminder: Make sure a Type & Crossmatch/hold is ordered and still valid before placing order for transfusion or hold for surgery.
  - Hold RBC's For Surgery/Procedure
    - Once
  - Transfuse RBC's Non-Bleeding Patient
    - Routine
  - Transfuse RBC's Bleeding Patient or Exchange Transfusion
    - Routine

NON-RBC PRODUCT ORDERS
- Reminder: Number of units to prepare must match the number of units to transfuse.
  - Reserve Apheresis Platelets for Surgery
    - Once, Routine
  - Prepare & Transfuse Apheresis Platelets
    - Once, Routine
  - Prepare & Transfuse Plasma (FFP)
  - Prepare & Transfuse Cryoprecipitate
PHYSICIAN'S ORDER FORM

Outpatient Anemia Management Order Set

(Date & Time) #

1. Service:
   Attending Physician: _______________ Pager # _______________
   Resident/PA/NP: _______________ Pager # _______________
   First Call for questions: _______________ Pager # _______________

2. Allergies: Weight in kg: _______________

Demographics:

Medications:

1. Iron Sucrose (Venofer®):
   □ 300 mgs elemental iron IV q week for 3 doses over 90 minutes
   □ 200 mgs elemental iron IV q week for 5 doses over 60 minutes
   □ _____ mgs elemental iron IV ______ for _____ doses over _______ minutes
   • Per American Regent Pharmaceutical, Inc. NO TEST DOSE required prior to the infusion.
   • DO NOT mix with any other medications.
   • GIVE iron if Ferritin is less than 100 or % saturation is less than 20%
   • HOLD iron if Ferritin is greater than 800 or Tsat >45%
   • HOLD iron if temp > 38.5 or HR > 100 with respirations >20
   • HOLD iron if patient has hemachromatosis - duplicate

2. Low-molecular weight iron dextran (Infed)
   □ 1000 mgs IV over 4 hours today
   • DO NOT mix with any other medications.
   • Give test dose 25mg IV over 25 minutes first. Monitor for signs of reaction (see above) for 2 hrs prior to giving full dose.
   • GIVE iron if Ferritin is less than 100 or % saturation is less than 20%
   • HOLD iron if Ferritin is greater than 800 or Tsat >45%
   • HOLD iron if temp > 38.5 or HR > 100 with respirations >20
   • HOLD iron if patient has hemachromatosis - duplicate
Questions or comments...