Iron Chef: Serving up high quality care in the setting of iron deficiency and iron overload

Donald Houston MD PhD FRCPC
Emily Rimmer MD MSc. FRCPC
May 1, 2020
Iron deficiency anemia (IDA): It’s easy as 1, 2, 3

Emily Rimmer MD MSc. FRCP-C
May 1, 2020
Presenter Disclosure

• Faculty / Speaker’s name: Emily Rimmer

• Relationships with commercial interests:
  – Grants/Research Support: none
  – Speakers Bureau/Honoraria: none
  – Consulting Fees: none
  – Other: none
Mitigating Potential Bias

• Not Applicable
Learning Objectives

1. Recognize the burden of iron deficiency
2. Understand investigations to diagnose iron deficiency
3. List the investigations required to identify cause of iron deficiency
4. Apply strategies to manage iron deficiency
Come on, come on, come on, let me tell you what it’s all about….

• I-D-A, its easy as 1-2-3…

• Step 1 – Identify iron deficiency
• Step 2 – Investigate cause of iron deficiency
• Step 3 – Iron repletion
Epidemiology of iron deficiency

• ~30% of the global population have anemia
• Iron deficiency is the predominant cause of anemia
  – Women and children are most at risk
  – Regardless of geography or SES
• Green represents iron deficiency anemia (IDA)

Iron deficiency (ID)

- Iron deficiency is highly prevalent: ~2 billion individuals
- Symptoms:
  - Fatigue, pica, depression, headache, restless legs syndrome
  - Anemia: dyspnea with exertion, lightheadedness, palpitations
- Many patients with ID are not anemic. Do they require treatment?
  - Will treatment improve their fatigue or quality of life?
  - Will it enhance physical performance?
The iron deficient but non-anemic patient...

- Meta-analysis of 18 randomized controlled trials
- Total n = 1162 individuals; mostly young healthy females
- Follow up duration: 90 days to 4 months
- Oral iron preparations studied in 14 trials
- Mean daily dose was 87 mg (elemental)

**Bottom line:** Iron supplementation reduced self reported fatigue, but didn’t really change measures of work capacity

1. Efficacy of iron replacement therapy on fatigue and work capacity in non-anemic adults with iron depletion: a systematic review of randomized trials. Houston et al BMJ Open. 2018
Step 1: Identify iron deficiency (ID)

• ID can occur in presence or absence of anemia (A)
• IDA is typically associated with microcytosis
  – All microcytic anemia are due to impairment of hemoglobin synthesis
• Serum ferritin is the single best test to identify ID/IDA
  – Drawback is ferritin is acute phase reactant
Although <15 historically used for diagnosis of IDA, <30 achieves a higher sensitivity (92%) while maintaining good specificity (98%).

<table>
<thead>
<tr>
<th>Test</th>
<th>Iron overload</th>
<th>Iron deficiency</th>
<th>Inflammation</th>
<th>Iron deficiency + inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>↔</td>
<td>↓</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td>MCV, MCHC</td>
<td>↔</td>
<td>↓</td>
<td>↓ or ↔</td>
<td>↓</td>
</tr>
<tr>
<td>Serum iron</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>TIBC</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>⇔</td>
</tr>
<tr>
<td>Tsat</td>
<td>↑**</td>
<td>↓**</td>
<td>↓ or ↔</td>
<td>↓</td>
</tr>
<tr>
<td>Ferritin</td>
<td>↑</td>
<td>↓**</td>
<td>↑</td>
<td>⇔</td>
</tr>
</tbody>
</table>
Step 2: Investigate cause of IDA

- NB: IDA is a symptom NOT a diagnosis
- To effectively manage IDA, the etiology MUST be identified and, if possible, corrected
Conditions associated with ID

Decreased iron availability

• Malabsorption
  – Gastric bypass, celiac, etc
• Inflammatory diseases
• CHF
• CKD
• (Diet)

Increased iron need

• Pregnancy, and breastfeeding
• Childhood

Iron loss in pregnancy/breastfeeding ~1000mg
Menstrual blood loss ~1mg/day
Iron loss in hemodialysis ~2000mg / year
Menstrual blood loss

• Most common cause in women of reproductive age
  – Detailed bleeding history is recommended
  – Use of a validated bleeding score recommended\(^1\)

• Strategies to reduce menstrual blood loss
  – Hormonal contraception (OCP, progesterone secreting IUD)
  – Anti-fibrinolytic agents (tranexamic acid)

1. www.letstalkperiod.ca
Iron Deficiency

Step 2: Investigate Cause of Iron Deficiency

Iron deficiency anemia

- In menstruating women
  - Menorrhagia?
    - Yes
      - Treat to control bleeding
    - No
      - All others
        - GI investigations and scope (see endoscopy referral form)

- Other cases
  - Lesion found?
    - Yes
      - Celiac serology
    - No
      - Go to Step 3: Replace iron

Legend:
- TSat = transferrin saturation (Iron / TIBC)
- TIBC = total iron binding capacity
- GIM = general internal medicine
- GI = gastroenterology
GI investigations

• Endoscopy referral for upper/lower scope
  – FOBT is NOT recommended when ID/IDA present

<table>
<thead>
<tr>
<th>SEMI-URGENT (4 WEEKS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Concerning/High risk rectal bleeding</td>
</tr>
<tr>
<td>NOTE: ONLY if symptoms have not been investigated recently AND one or more of: weight loss, new change in bowel habits, new anemia, or family history of colorectal cancer (Include: CBC)</td>
</tr>
<tr>
<td>□ Unexplained iron deficiency anemia (Include: CBC and ferritin, iron/TIBC and creatinine)</td>
</tr>
<tr>
<td>□ Bloody diarrhea/features suggestive of Inflammatory bowel disease (IBD) (Include: CBC, ferritin, albumin)</td>
</tr>
<tr>
<td>□ Severe/Progressive odynophagia/dysphagia (Include: CBC)</td>
</tr>
<tr>
<td>□ FOBT positive – (Include FOBT result) (NOTE: FOBT only in ages 40 - 75 years of age and not a single office-based FOBT from DRE)</td>
</tr>
<tr>
<td>□ Suspected stable upper GI bleed (Include CBC) Details:</td>
</tr>
</tbody>
</table>
Iron Deficiency

Step 2: Investigate Cause of Iron Deficiency

Iron deficiency anemia

In menstruating women

Menorrhagia?

Yes

Treat to control bleeding

No

All others

GI investigations and scope (see endoscopy referral form)

Lesion found?

Yes

Celiac serology

No

Go to Step 3: Replace iron

Additional tests to consider:
Urinalysis
Hemolysis screen: LDH, haptoglobin
Step 3: Iron replacement

• When to treat:
  – When ID confirmed AND causes considered
  – With anemia, but likely without anemia
• Oral iron supplementation
  – Preferred
• Intravenous iron
• Avoid RBC transfusion in IDA unless hemodynamic instability
Oral iron preparations (Full Replacement doses)

<table>
<thead>
<tr>
<th>Iron Preparation</th>
<th>Elemental Iron Content</th>
<th>Target Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous gluconate</td>
<td>~35 mg elemental iron /300 mg tab</td>
<td>(target dose: 4-6 tabs per day)</td>
</tr>
<tr>
<td>Ferrous sulphate</td>
<td>~60 mg elemental iron /300 mg tab</td>
<td>(target dose: 2-3 tabs per day)</td>
</tr>
<tr>
<td>Ferrous sulphate elixir</td>
<td>44 mg elemental iron / 5 mL</td>
<td>(target dose: 15-20 mL)</td>
</tr>
<tr>
<td>Polysaccharide iron complex (FeraMAX)</td>
<td>150 mg elemental iron per capsule</td>
<td>(dose is 1 capsule OD)</td>
</tr>
<tr>
<td>heme-iron polypeptide (Proferrin)</td>
<td>11 mg of elemental iron per tab</td>
<td></td>
</tr>
</tbody>
</table>

Recommended first line

Unproven claims of increased GI tolerability
Which oral supplement is preferred?

Which one is most efficacious?
• The one with the most iron

Which one is best tolerated?
• The one with the least iron

• There is no evidence that one preparation is more effective than another or has fewer side effects than another

# Oral vs. Parenteral Iron

<table>
<thead>
<tr>
<th></th>
<th>Oral</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pro</strong></td>
<td>Inexpensive ($5 – 25 /mo)</td>
<td>Fewest GI side effects</td>
</tr>
<tr>
<td></td>
<td>No risk of anaphylaxis</td>
<td>Certain compliance</td>
</tr>
<tr>
<td></td>
<td>Does not require clinic visit</td>
<td>Rapid correction of anemia</td>
</tr>
<tr>
<td></td>
<td>Lengthy Tx duration</td>
<td>Malabsorption? Still works</td>
</tr>
<tr>
<td><strong>Con</strong></td>
<td>Highest incidence of GI side effects</td>
<td>Iron dextran associated with anaphylaxis</td>
</tr>
<tr>
<td></td>
<td>May be insufficient in the face of substantial bleeding</td>
<td>Requires 3-4 hour infusion/trip to centre*</td>
</tr>
<tr>
<td></td>
<td>Requires consistent adherence of the patient</td>
<td>Patients can feel ill after large doses</td>
</tr>
</tbody>
</table>
When to consider IV iron?

- Intolerance to more than 1 oral regimen, even when ramping up slowly and taking with food and management of constipation
  - Try iron sulphate elixer EOD
- Malabsorption syndromes
- Inflammatory bowel disease
- Post gastric bypass surgery
- Chronic kidney disease – on dialysis (standard of care)

**In almost all instances, try oral replacement first**
Barriers to Practice Change

• Access to IV iron is challenging in Winnipeg
  – Community hematology (Dr. Harris) can provide some of this service to patients in Winnipeg
  – If patient followed by gastroenterologist, they should be able to provide this as well
  – Rural MD are encouraged to provide in local hospital
Take home message(s)

• Iron deficiency anemia is common
• Oral iron supplementation is preferred
• Forewarn patients about GI side effects
• Start low, go slow
Thank you
erimmer@cancercare.mb.ca