RAPID REFERRAL ANEMIA CLINICS

REDUCING INAPPROPRIATE TRANSFUSION AND OPTIMIZING PATIENT CARE

ALAN TINMOUTH

ORBCON

APRIL 11, 2018
1. Review rationale for rapid referral anemia clinics
2. Understand the potential causes of anemia presenting to Emergency Department
3. Review the role of intravenous iron to reduce unneeded transfusions and improve patient satisfaction.
ANEMIA AND TRANSFUSIONS IN THE EMERGENCY DEPARTMENT

- Referrals from GP
- Symptomatic patients

- ANEMIA IS A COMMON PROBLEM IN THE EMERGENCY DEPARTMENT

Symptoms of Anemia

Low Hemoglobin Levels

Bleeding
PATIENT PERSPECTIVE

1. Long waits in Emergency Department
2. Many patients do not meet criteria for transfusion
3. Underlying etiology of anemia not addressed if chronic anemia
4. Most appropriate therapy not given in Emergency Department
1. GP have limited resources / options for acute treatment of severe anemia
2. Many patients in ED do not meet criteria for transfusion
   - Transfused inappropriately
   - Sent back to GP with no treatment
3. Prolonged stay for transfusion in ED taxes over burdened area
4. ED has limited capacity for follow-up
5. Referrals to specialty clinic for urgent assessment
COMMON OUTCOMES

- Patients transfused inappropriately
  - Not symptomatic
  - Receive more RBCs than needed
- Underlying cause for anemia not treated
  - Sent back to GP with no transfusion
  - Return to ED for additional transfusion
- Referred to hematology
  - No investigations
  - No treatment
RAPID REFERRAL ANEMIA CLINIC

Hematology clinic to see patients with moderate - severe clinics
  • Referrals from ED and GPs

▶ Reduce transfusions in ED
▶ Receive most appropriate therapy for anemia in ED
▶ Alternative to ED for assessment and management of anemia
EMERGENCY DEPARTMENT

- Algorithm for management of anemia
  - Appropriate workup
  - Appropriate therapy

- Criteria for referral to Rapid Referral Anemia clinic
  - Appropriate patients

- Assurance of rapid follow-up
  - Timely
  - Appropriate therapy
ALGORITHM FOR MANAGEMENT ANEMIA IN ED

- Guidelines for RBC transfusion
  - Thresholds
  - Number of units
- Administration of iron
  - IV
  - PO
The AABB recommends a restrictive RBC transfusion threshold which the transfusion is not indicated until the hemoglobin level is

- 70 g/L for hospitalized adult patients who are hemodynamically stable, including critically ill patients (strong recommendation, moderate quality evidence).
- 80 g/L for patients undergoing orthopedic surgery or cardiac surgery and those with preexisting cardiovascular disease, (strong recommendation, moderate quality evidence).
<table>
<thead>
<tr>
<th>HEMOGLOBIN</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90 g/L</td>
<td>Likely inappropriate except in exceptional circumstances.</td>
</tr>
<tr>
<td>70-90 g/L</td>
<td>Likely to be appropriate if there are signs or symptoms of impaired oxygen delivery (e.g., tachycardia, hypotension, cardiac ischemia, syncope, pre-syncope).</td>
</tr>
<tr>
<td>&lt;70 g/L</td>
<td>Likely to be appropriate.</td>
</tr>
</tbody>
</table>
| <60 g/L   | **Transfusion recommended**<sup>38</sup>  
- Young patients with low risk of ischemic cardiovascular disease can sometimes tolerate greater degrees of anemia.  
- Patients with chronic iron deficiency may often be better managed with IV or PO iron alone. (PO iron works very well in children with iron deficiency anemia and Hgb level as low as 30 g/L in the absence of concerning symptoms of anemia and assurance of reliable follow-up.) |
IRON THERAPY

**Oral**
- **Advantages**: inexpensive (over the counter), available
- **Disadvantages**: absorption only 10% of elemental Fe, takes a long time to correct anemia and replenish iron stores
- **Adverse effects**: GI side effects -> non-compliance

**IV**
- **Advantages**: rapidly effective
- **Disadvantages**: cost, availability, need for a hospital visit
- **Adverse effects**: Allergic reaction, hypotension, metallic taste, headache, nausea, vomiting, diarrhea, abdo pain, back pain, muscle cramps, arthralgias, infusion site reactions

<table>
<thead>
<tr>
<th>Oral iron supplement</th>
<th>Dose, mg</th>
<th>Elemental mg</th>
<th>Cost, $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous sulfate</td>
<td>300</td>
<td>60</td>
<td>0.06</td>
</tr>
<tr>
<td>Ferrous fumarate</td>
<td>300</td>
<td>100</td>
<td>0.12-0.21</td>
</tr>
<tr>
<td>Iron Polysaccharide (Feramax)</td>
<td>150</td>
<td>150</td>
<td>0.46</td>
</tr>
<tr>
<td>Heme Iron (Proferrin, Optifer)</td>
<td>398</td>
<td>11</td>
<td>0.50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IV Iron Supplement</th>
<th>Iron sucrose (Venofer)</th>
<th>Iron gluconate (Ferrlecit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MW (kDa)</td>
<td>43</td>
<td>289-440</td>
</tr>
<tr>
<td>Plasma ½ life</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Dose</td>
<td>200-300 mg</td>
<td>62.5 - 125 mg</td>
</tr>
<tr>
<td>Administration</td>
<td>30 -120 min</td>
<td>30-60 min</td>
</tr>
<tr>
<td>Cost</td>
<td>$37.50 (100mg)</td>
<td></td>
</tr>
<tr>
<td>Life threatening ADE</td>
<td>0.6 per 10^6</td>
<td>1.1 per 10^6</td>
</tr>
</tbody>
</table>
ALGORITHM FOR MANAGEMENT OF ANEMIA IN THE EMERGENCY DEPARTMENT

Inclusion Criteria:
- Patients with hemoglobin below lower limit of reference range
- No evidence of hemodynamic instability
- No evidence of active bleeding

Exclusion Criteria:
- Patient is hemodynamically unstable
- Patient has active bleeding
- Patient has known sickle cell disease
- Patient has myelodysplastic syndrome

**URGENT SYMPTOMS**

- Transection 1 unit of red blood cells (RBC) then reassess
- Administer Furosemide before transfusion if required
- Start volume expansion and factor replacement
- Refer patient to Hematology Rapid Referral Clinic (RRC)
- Advise patient to return if they experience urgent symptoms

**Significant complications**
- e.g. coronary artery disease, respiratory distress, pulmonary hypertension

**Hemoglobin 50g/L**

**Hemoglobin 50-70g/L**

- Iron IV
- Advise patient to return if they experience urgent symptoms
- Oral iron
- Refer patient to Hematology RRC

**Hemoglobin 71-100g/L**

**MCV less than 80 or low feritin**

**MCV less than 80**

**DISCHARGE:** (If patient stable)
- Refer patient to Hematology Rapid Referral Clinic for consultation
- Advise patient to seek emergency care if experiencing chest pain or shortness of breath not relieved by rest
- Recommendations for oral iron given to patient if appropriate
- If history of system-specific bleeding (i.e. heavy menstrual bleeding, melena stool, hematuria), make appropriate outpatient referral

ORAL IRON
ONE UNIT RBC TRANSFUSION

- Recent RCTs evaluating RBC thresholds in inpatients mandated 1 unit
- Increased no. of units associated with TACO
- 1 unit transfusions decrease overall exposure
- Increases time to next transfusion

http://www.transfusion.ca/CSTM/media/images/
Recent RCTs of inpatients evaluating RBC thresholds mandated 1 unit transfusions decrease overall exposure and reduces time to next transfusion.

**OUR GOAL for ED**

Transfuse minimum number of units to avoid adverse events related to anemia.

http://www.transfusion.ca/CSTM/media/images/
**PRE-PRINTED ORDERS**

- Start work-up for anemia
- Treatment of anemia and iron deficiency

---

**MANAGEMENT OF ANEMIA IN THE EMERGENCY DEPARTMENT**

**Instructions to Physician**

1. Determine if patient has symptoms of anemia requiring immediate management
2. Check hemoglobin, hematocrit, and MCV
3. Check for co-existing conditions such as renal or cardiac disease
4. Check for hematological disorders such as sickle cell disease or thalassemia
5. Check for malignancies
6. Check for bleeding diathesis
7. Check for gastrointestinal bleeding
8. Check for liver disease
9. Check for infections
10. Check for drugs and medications

**Production**

- Hemolysis
- Iron / B12

**Transfusion orders**

- Transfusion

**Iron orders**

- Iron
- B12

---

**Symptoms**

- Fatigue
- Palpitations
- Shortness of breath
- Headache
- Dizziness
- Chest pain
- Weakness
- Nausea
- Vomiting
- Diarrhea

**Initial Laboratory Investigations**

- CBC
- Blood smear
- Reticulocyte count
- Ferritin
- B12
- Iron
- ECG
- Thyroid function tests
- Liver function tests
- Coagulation studies

**Diagnosis**

- Anemia
- Iron deficiency
- Hemolysis
- Malignancy
- Infection
- Drug-induced
- Nutritional

**Discharge**

- Ensure patient receives all discharge recommendations and has been referred to Hematology/Rapid Referral Clinic
RAPID REFERAL ANEMIA CLINIC

- Stable, non-bleeding patients with Hemoglobin <100 g/L
  - Not already followed by TOH physician for anemia or related conditions
- Seen in clinic within 2 weeks
  - Stable patients only
  - First dose of IV iron in ED
- Referals to other specialists initiated in ED

**HEMATOLOGY RAPID REFERAL CLINIC**
**ED Anemia Referral Form**

*Patients referred will be seen in 3-2 weeks*
*If patient requires more urgent consultation, call staff on call for benign hematology*

The following patients SHOULD NOT be referred (please see ANEMIA ED algorithm):
- Patients with active bleeding
- Patients who are hemodynamically unstable
- Patients with ongoing urgent acute symptoms of anemia
- Patients with Sickle Cell Disease
- Patients followed by TOH physician for anemia

**Patient Demographics:**

**Relevant Patient History (please complete all boxes):**

- Hemoglobin <110 g/L: □ Yes □ No
  - Hgb __________ g/L
  - MCV __________

- ED Treatment Provided:
  - RBCs transfused: □ Yes □ No
  - __________ units
  - Venose: □ Yes □ No

- Referrals to other specialties from ED (please make all appropriate referrals and check boxes):
  - Gynecology □
  - GI □
  - General surgery □
  - Urology □
  - Other: __________

- The following tests must be performed in the ED:
  - CBC □
  - Blood film □
  - Reticulocyte count □
  - Ferritin □
  - B12 □
  - LDH □

- Referring physician name (PRINT): __________
RAPID REFERRAL ANEMIA CLINIC - PILOT

- 6 month pilot program
- 84 patients
  - Referrals from ED
  - Regular Hematology referrals
- Patients with Hgb < 100

<table>
<thead>
<tr>
<th>Referral</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED Physician</td>
<td>36</td>
</tr>
<tr>
<td>GI</td>
<td>1</td>
</tr>
<tr>
<td>Family doctor</td>
<td>35</td>
</tr>
<tr>
<td>Oncologist</td>
<td>1</td>
</tr>
<tr>
<td>OBS/GYN</td>
<td>8</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>84</td>
</tr>
</tbody>
</table>
RAPID REFERRAL ANEMIA CLINIC - PILOT

- Mean Hgb 76 g/dl (45-101)
- Median MCV 71 fl (53-106)
- Median ferritin = 5 umol/l (0-2269)
ED REFERRALS

84 patients

- 36 patients from ED
  - 18 patients transfused
  - 19 received IV iron
# Referrals to Other Specialists from ED

<table>
<thead>
<tr>
<th>Referral BEFORE RRAC</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>39</td>
</tr>
<tr>
<td>Gynecology</td>
<td>9</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>31</td>
</tr>
<tr>
<td>General Surgery</td>
<td>1</td>
</tr>
<tr>
<td>Urology</td>
<td>1</td>
</tr>
<tr>
<td>Neurology</td>
<td>1</td>
</tr>
<tr>
<td>Thoracic Surgery</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
</tr>
</tbody>
</table>

![Specialist referrals before visit to RRAC](image-url)
## Etiology of Anemia

<table>
<thead>
<tr>
<th>Etiology of Anemia</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron Deficiency</td>
<td>65</td>
</tr>
<tr>
<td>Acute Bleed</td>
<td>13</td>
</tr>
<tr>
<td>Diet</td>
<td>2</td>
</tr>
<tr>
<td>B12</td>
<td>1</td>
</tr>
<tr>
<td>Malabsorption from gastric bypass</td>
<td>1</td>
</tr>
<tr>
<td>Anemia of Chronic Disease</td>
<td>1</td>
</tr>
<tr>
<td>Chronic Renal Failure</td>
<td>3</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>0</td>
</tr>
<tr>
<td>Bone Marrow Disease</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
</tr>
</tbody>
</table>

### Source of Iron Deficiency Anemia

- GI
- Gynecological
- Urological
- Unknown

### Etiology of Anemia

- Iron Deficiency
- Acute Bleed
- Diet
- B12
- Malabsorption from gastric bypass
- Anemia of Chronic Disease
- Chronic Renal Failure
- Bone Marrow Disease
- Other
TREATMENT INITIATED BY RRAC

<table>
<thead>
<tr>
<th>Therapies ordered by RCC physician</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO Iron</td>
<td>15</td>
</tr>
<tr>
<td>IV Iron</td>
<td>35</td>
</tr>
<tr>
<td>Both PO and IV Iron</td>
<td>17</td>
</tr>
<tr>
<td>B12</td>
<td>7</td>
</tr>
<tr>
<td>RBC Transfusion</td>
<td>6</td>
</tr>
<tr>
<td>OCP</td>
<td>1</td>
</tr>
<tr>
<td>Cyclokapron</td>
<td>1</td>
</tr>
<tr>
<td>Iron therapy alone</td>
<td>57</td>
</tr>
<tr>
<td>No therapies ordered</td>
<td>13</td>
</tr>
</tbody>
</table>

Total number of iron therapy ordered: 68
**IV IRON THERAPY**

- 10-14 days to see reticulocyte response
- Increased hgb by 10 g/L per week
- Either to to kickstart hematopoiesis
  - 1-3 doses of IV iron then oral iron
- “Full course” of IV iron
  - 1 gm over 5-8 treatments q1-2 weeks

**Venofer** (Iron sucrose)
- Limited supply in Canada. (resolved?)
- Larger dose - 200 mg over 30 min
- Fewer reactions
- Large experience in pregnant women
- 1 gm dose
  - $375, 5 visits

**Ferrlecit** (sodium ferric gluconate)
- Lower dose - 125 mg
- ? Need for test dose
- ? Increase minor reactions
- Not given to pregnant woman
- 1 gm dose
  - $268, 8-9 visits
Validated survey of ambulatory care patient experience was modified to reflect the nature of the RRAC clinic

- 23% had worsening symptoms while waiting for RRAC appointment
  - 13/84 sought further help from primary care MD or ED
- Only 84% of patients reported that RRAC doctor knew the important information about their medical history.
- > 90% felt information about their problem and treatment were clearly explained.
- 100% felt appointment was useful or somewhat useful in helping with health problems.
- 27% felt that time between identification of health problem and clinic visit was too long
- 91% of patients rated experience with RRAC as 8 or higher on scale of 0-10 where 10 is the best experience possible
• 78% patients required at least 1 follow-up up in RRAC.

  • Assess response to iron therapy.
  • Follow-up on additional investigations / consults
IRON DEFICIENCY ANEMIA IN THE EMERGENCY DEPARTMENT

- 3 month retrospective study at Sunnybrook
  - 14,394 patients
  - 49 patients with Iron Deficiency Anemia
- 27 patients with IDA treated and discharged
  - 17 (63%) referred by primary care physician

*Transfusions*
- 8 (30%) transfused
- 1 treated with IV iron
- 6 prescribed oral iron

*Diagnose IDA:*
Hb < 130 in men or
Hb < 120 in women
AND one of:
1) ferritin < 30 ug/L
2) MCV < 75 fL when previously normal

<table>
<thead>
<tr>
<th>Hemoglobin (g/L)</th>
<th>Total (n)</th>
<th>Admitted (n)</th>
<th>Discharged (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>2</td>
<td>2 (100)</td>
<td>0</td>
</tr>
<tr>
<td>50-59</td>
<td>6</td>
<td>4 (67)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>60-69</td>
<td>12</td>
<td>9 (75)</td>
<td>7 (57)</td>
</tr>
<tr>
<td>70-79</td>
<td>8</td>
<td>2 (25)</td>
<td>4 (25)</td>
</tr>
<tr>
<td>≥80</td>
<td>21</td>
<td>2 (10)</td>
<td>14 (7)</td>
</tr>
</tbody>
</table>

Spradbrow et al.  CJEM 2017: 19: 167
NEXT STEPS

1. Assess the effect of RRAC on transfusions in ED
   • Focus on patients discharged home from ED
2. Further reduce time between referral and clinic visit
   • Embed program into regular hematology clinics
3. Expand program to primary care MDs outside of ED
4. Reduce wait times for IV iron as outpatient
5. Expand program to surgical and medical specialists
ACKNOWLEDGEMENT

- Dr. Elianna Saidenberg
- Dr. Abhi Iyengar
- Dr. Guy Hebert
- Dr. James Worral
- Dr. Magdalena Kisilewicz
- Janice Lennerton
- Elizabeth Chatelain
- Kendall Saravanmuttoo