Patient Blood Management (PBM) in Obstetrics & Gynaecology

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● Importance of PBM in O&G

● Background on PBM in O&G patients

● HA Guideline on the Management of Iron Deficiency & Iron-deficiency Anaemia in the Obstetrics & Gynaecology Unit (March 2019)

● A retrospective review on the use of intravenous iron infusion among menorrhagic patients with severe anaemia

● Recommendations & future directions to consider
Why is PBM important in O&G?

We are a “Bloody” Specialty!
Causes of severe iron-deficiency anaemia in O&G patients

- **Chronic periodic blood loss - menorrhagia from various causes**
  - Intolerance to / unwillingness to take oral iron supplement
  - Inadequate or failed medical treatment to reduce menstrual flow
  - Unwillingness to take medication to reduce menstrual flow due to patient’s misconception
  - Decline surgery as definitive treatment
  - Long waiting time to OT

- **Acute massive blood loss**
  - Gyn emergencies e.g. ruptured ectopic pregnancy
  - Complicated, extensive Gyn OTs
  - Obstetric - antepartum haemorrhage (APH), primary postpartum haemorrhage (PPH)

BLOOD TRANSFUSION(S) !!
Our Challenges

- How to reduce the need for repeated blood transfusions in O&amp;G patients?
- How to raise the Hb level safely, cost-effectively and with sustained efficacy?
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Recommendations & future directions to consider
1 ml blood = 0.5 mg elemental iron
Hb ↓ by 1g/dL ≈ loss of 200mg elemental iron

Menorrhagia (> 80ml blood loss / cycle) for 1 yr

Loss of > 500mg elemental iron / yr
i.e. > 2.5 g/dL ↓ in Hb in one year !
Majority of red cell transfusion for Gyn patients were non-operation related i.e. mainly MENORRHAGIA!!
What are the alternatives to blood transfusion(s)?

- IV iron therapy has been shown to be an effective and safe alternative to blood transfusion in both Gynaecology and Obstetric patients
Case 1: Menorrhagia
A 20 y/o female university student had exertional dyspnea from anemia caused by chronic menstrual blood loss.
P/E: Resting heart rate was 126
Ix: Hb 7.0 g/dL, MCV 55 fL, ferritin 2 µg/L
Treatment: Received 1 g IV iron dextran over 4 hours in preference to red cells.
Response: Within 24 days, her Hb was 11.7 g/dL, MCV 71 fL, ferritin 28 µg /L
RESULTS
Significantly more pregnant women achieved anemia correction with FCM vs. FS [Hb 11.0 g/dL; 84% vs. 70%; odds ratio (OR): 2.06, 95% confidence interval (CI): 1.07, 3.97; P=0.031] and within a shorter time frame (median 3.4 vs. 4.3 weeks). FCM treatment significantly improved vitality (P=0.025) and social functioning (P=0.049) prior to delivery. Treatment-related adverse events were experienced by 14 (FCM; 11%) and 19 (FS; 15%) women, with markedly higher rates of gastrointestinal disorders reported with FS (16 women) than with FCM (3 women). Newborn characteristics were similar across treatments.

CONCLUSIONS
During late-stage pregnancy, FCM may be a more appropriate option than first-line oral iron for rapid and effective anemia correction, with additional benefits for vitality and social functioning.
Postpartum and early postoperative anemia after gynecological surgery: treatment with intravenous iron

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Servicio de Anestesiologia y Reanimación. Hospital Universitario Maternal La Paz (Madrid)

Inclusion: 200mg 200mg 200mg
Hb<10g/dL

RESULTS:
Hb rose by 3.2g/dL in postpartum group, n=250, median age 31, range 18-42
Hb rose by 2.7g/dL in post gynecological surgery group, n=52, median age 41, range 28-76
The incidence of side effects was low (12 obstetric patients and 1 gynecological surgery patient). Most side effects were related to pain at the injection site (in 12 of the 13 women). Another one experienced minor allergic reaction with generalized self-limiting erythematous rash.

CONCLUSIONS:
Intravenous iron sucrose is safe and effective for treating puerperal anemia and following gynecological surgery.
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Recommendations & future directions to consider
Objective

- To provide guidance on the indication of blood transfusion and avoid patients having unnecessary exposure to adverse reactions and complications related to blood transfusion.
- To provide recommendations on measures to optimize patient’s haemoglobin (Hb) level and iron store at the peri-operative and peri-partum period.

Definitions of Iron deficiency anemia

- Anemia is defined as $Hb < 12g/dL$ in non-pregnant patients.
- During pregnancy, anemia is defined as $Hb < 11g/dL$ in the first trimester, $<10.5g/dL$ in the second and third trimester, and $<10g/dL$ in the post-partum period.
- In general, serum ferritin level $< 30ug/L$ is the diagnostic criteria for ID.
Iron therapy

Oral iron

- Oral iron is the first line treatment.

- Ferrous sulphate (FeSO4) is the first line oral iron therapy (300mg once daily, which contains 60 mg elemental iron per 300mg tab).

- A rise in Hb by >=1 g/dL after taking oral iron for 14 days or more indicates positive response to oral iron therapy.

- Consider second line oral iron in case a non-responder is due to poor tolerance to ferrous sulphate:

  Ferrum Hausmann (iron(III)-hydroxide polymaltose complex) chewable tablet 100mg (contains 100mg elemental iron) or
  Ferrum Hausmann (iron(III)-hydroxide polymaltose complex) drops, 1-2ml per day (which contains 50mg elemental iron per ml)
IV iron

Indications:

- Patient does not respond to second line oral iron therapy and recurrent bleeding is also excluded.
- Patient who cannot tolerate or absorb oral iron
- Patients unable to adhere to oral iron treatment
- There is a clinical need to deliver iron rapidly (e.g. patient with severe iron deficiency in third trimester of pregnancy or severe anemia pending major gynaecological operations)
- Patient with chronic kidney disease using erythropoiesis-stimulating agents

- In HA hospitals, both Iron Isomaltoside (Monofer®) and Ferric saccharate (Venofer®) are available
- Calculation of total iron dose based on Ganzoni formula or body weight
- Guidelines on monitoring during IV iron therapy, pre-medications and management of hypersensitivity reactions
- Treatment response should be monitored by checking CBC at least 4 weeks after giving IV iron as maximum haemoglobin response is observed at 3 weeks post treatment
Indications for blood transfusion

- Patients with **acute blood loss**, who are **haemodynamically unstable** - Single unit blood transfusion is recommended and then reassess; once haemostasis is achieved and patient is **haemodynamically stable**, intravenous or oral **iron** is recommended

- Patients with **acute blood loss**, who are **haemodynamically stable**, but ongoing bleeding is anticipated

- Patients with **chronic blood loss**, who are **haemodynamically unstable OR** there are clinical **evidence of acute coronary syndrome (ACS) or heart failure**
Chronic anemia with symptom

- **IV Iron therapy** is the first line treatment for patient who is haemodynamically stable.

- Transfusion may be considered in case of severe anemia (Hb < 7 g/dL).

- Adopt single unit blood transfusion and reassess before further unit is ordered. When anemic symptoms resolve, IV or oral iron are recommended to restore Hb to normal.

Chronic anemia without symptom

- For patient with Hb >= 7 g/dL, oral iron is the preferred choice of treatment. Give IV iron if doubtful about patient’s compliance to oral iron.

- For patient with Hb < 7 g/dL, IV iron remains the first line treatment and is an effective way to restore the iron depletion rapidly.

- Only consider transfusion if IV iron is contraindicated and adopt single unit blood transfusion and reassess before further unit is ordered.
Optimization of patient’s haemoglobin level before major gynaecological operation

- All gynaecology patients with menorrhagia resulting in anemia should have a **long term management plan** to treat the menorrhagia and avoid the risk of recurrent anemia and transfusion.

- If surgery is indicated, **early operation** should be arranged before they become severely anemic again.

- Consider **GnRHα** to render patient temporary amenorrhoea before operation.

- Prescribe **oral iron for 6-8 weeks** to anemic patient while they are waiting for operation.

- For patient undergoing operation with a high risk of estimated blood loss > 500ml, it is recommended to **check CBC 4 weeks before operation**.

- **IV iron** should still be considered even < 2 weeks from operation date.

- Consider **blood transfusion** to top up haemoglobin promptly before major gynaecological operation **only if patient is haemodynamically unstable**.
Optimization of maternity patient’s haemoglobin level before delivery

- **Ferritin** should be checked to look for any iron deficiency when **low MCV** is found in antenatal patient in addition to the checking of haemoglobinopathy.

- **Oral Iron** replacement therapy should be given to pregnant women diagnosed with **iron deficiency anaemia or iron deficiency without anemia**. Haemoglobin response should be checked, preferably **4-6 weeks before delivery** to monitor the treatment response, with sufficient time to correct any persistent anemia before delivery.

- If the **response to oral iron is inadequate**, **IV iron** should be considered except in the first trimester of pregnancy.

- IV iron is preferred when rapid restoration of Hb and iron stores is required.

- In maternity patient **who require iron therapy for treatment of anemia**, the routine addition of **folic acid is not recommended**.

- **Multivitamin preparations** such as Materna should not be recommended as a sole therapy for iron deficient anemia because the calcium, phosphorus and magnesium salts contained in iron-containing multivitamin pills can impair absorption of elemental iron.
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A retrospective review on the use of intravenous iron infusion among menorrhagic patients with severe anaemia

Recommendations & future directions to consider
Use of intravenous Iron infusion with a simplified dose-standardized protocol in menorrhagic patients with severe iron-deficiency anaemia - A retrospective pilot cohort study

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- Although the efficacy and safety of intravenous (IV) iron therapy in general medical patients with iron-deficiency anaemia has been well documented, the optimal protocol of IV iron therapy among menorrhagic patients, who have cyclical blood loss due to menses compared with general patients, has yet to be established.

- A relatively simple protocol for IV iron therapy for menorrhagic patients, without complicated dose calculation or prolonged hospitalization, is worth exploring for.

- KWH OG - started IV iron therapy for Gyn patients with severe iron-deficiency anaemia with a standardized protocol in October 2017.
Objectives

To evaluate the

(1) efficacy
(2) safety
(3) patient acceptability

of intravenous iron infusion in menorrhagic patients with severe iron-deficiency anaemia using a simplified dose-standardized protocol
Materials & methods

- Retrospective cohort analysis
- **Haemodynamically-stable menorrhagic** patients suffering from iron-deficiency anaemia with haemoglobin (Hb) level 6-8 g/dL, admitted to Kwong Wah Hospital between October, 2017 and October, 2018
- Patients were given the choice of blood transfusion versus iron infusion
- All patients who had chosen IV iron therapy received 2 doses of IV iron (Venofer®), 200mg each, within 2 weeks, together with oral iron supplement
- Outcome criteria - Hb, Ferritin and Total Iron Binding Capacity (TIBC) levels taken before treatment and 4 weeks after the first dose of IV iron infusion, as well as resolution of anaemic symptoms
Patients with Hb 6-8 g/dL (n=182)

Blood Transfusion (n=44, 24.2%)

IV Iron (n=138, 75.8%)

n=114 (study population)

Exclude n=24 (incomplete data, Tx not completed, blood transfusion in same index admission)
## Results - Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Mean +/- S.D.</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44.0 +/- 7.9</td>
<td>46</td>
<td>16 - 54</td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>58.3 +/- 9.3</td>
<td>57</td>
<td>43.6 - 89.9</td>
</tr>
<tr>
<td>Interval between 2 IV iron doses (days)</td>
<td>12.8 +/- 4.4</td>
<td>13</td>
<td>1 - 14</td>
</tr>
<tr>
<td>Uterine size (weeks)</td>
<td>8.0 +/- 5.2</td>
<td>8</td>
<td>4 - 26</td>
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</tbody>
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- Uterine fibroids: 52 (45.6%)
- Adenomyosis: 23 (20.2%)
- Dysfunctional uterine bleeding: 39 (34.2%)
Results - Treatment efficacy

Haemoglobin level:

A significant rise in mean Hb level (3.4 g/dl) was observed at 4 weeks after starting IV iron infusion

- Pre-treatment: $7.1 \pm 0.7$ g/dL
- Post-treatment: $10.5 \pm 1.2$ g/dL

* Wilcoxon Signed Rank Test, $p < 0.001$
Results - Treatment efficacy

Ferritin level:

Significantly increased by 34.4 ng/mL

- Pre-treatment: $6.8 \pm 9.4$ ng/mL
- Post-treatment: $41.2 \pm 28.1$ ng/mL

* Paired Sample t-test, $p<0.001$
Results - Treatment efficacy

Total Iron Binding Capacity (TIBC):
Significantly reduced by 12.7 μmol/L

- Pre-treatment: 75.2 ± 10.6 μmol/L
- Post-treatment: 62.5 ± 9.2 μmol/L

* Paired Sample t-test, p<0.001
Results - Treatment efficacy

Symptomatic resolution:

✓ Among the 103 patients with anaemic symptoms before IV iron therapy, 102 (99%) had their symptoms resolved after treatment.
Results - Patient Acceptability

✓ 75.8% (138 out of 182) patients opted for IV iron therapy after counselling on the options of IV iron therapy versus blood transfusion

✓ No patients declined continuing treatment after the first dose of Venofer®
Results - Patient Safety

- *One patient* reported skin rash after first dose of IV iron
  -> treated with antihistamine and
  2
  nd
dose of IV iron withheld

- No anaphylactic reaction observed
Conclusions

- Intravenous iron infusion using a simplified, dose-standardized protocol is an effective, safe and well-accepted treatment option for selected group of menorrhagic patients with severe iron-deficiency anaemia.

- Combining IV iron therapy with subsequent oral iron supplement may be a more cost effective way to improve patient blood management.
  - avoid unnecessary blood transfusion
  - drug cost can be reduced compared with giving a much higher dose of IV iron alone

- Although the role of combined IV and oral iron treatment appears to be promising, further subgroup analysis is warranted to identify which patients are suitable for this protocol and which patients are unlikely to benefit from it.
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Recommendations & future directions to consider
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- Review of HA Guideline on iron-deficiency & iron-deficiency anaemia - compliance, further amendments

- Cost-effectiveness of treatment / clinical service
  - Review the optimal regime of IV iron treatment (dosage, way of administration)
  - Streamline admission / clinic procedure

- Increase manpower and resources to shorten the OT waiting time for definitive treatment of various causes of menorrhagia

- Improve patient & staff education on
  - Dietary advice
  - Taking oral iron supplement
  - Taking medication to reduce menstrual flow
Raise Hb safely, effectively with sustained efficacy
Avoid repeated blood transfusions

Early definitive OT

Patient education

Optimization of iron therapy

Healthcare professionals education
An essential prerequisite ....

Good team work!
Patient Blood Management in O&G ......