A WHITER SHADE OF PALE – MANAGING PERIOPERATIVE ANAEMIA

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It is widely recognised that red cells are used inappropriately in hospitalised patients and this is associated with adverse outcomes. The core difficulty doctors have in this regard is their attachment to a transfusion trigger of 10g/dl of Haemoglobin (Hb), and the expectancy that the only means of raising it is by a red cell transfusion. While the trigger is undoubtedly incorrect in the majority of patients, there is an element of logic in raising Hb by transfusion in actively bleeding patients. There is very little rationale in raising Hb with a blood transfusion in most other patients.

But it happens every day.

Modern transfusion medicine attempts to improve clinical outcome from the use of blood products by limiting administration to those patients that require it. Reductions in use are mostly attained by focusing on the three "pillars" of blood conservation –

- Elevation of the red cell mass before blood loss
- Reduction of the blood loss through surgical techniques, management of coagulopathy and cell salvage
- Selecting a correct (usually lower) transfusion trigger

Elevation of Hb without transfusion can be achieved with the administration of intravenous iron, if iron deficiency anaemia is identified in a timely manner prior to elective surgery.

What is the Incidence of Iron Deficient Anaemia in Hospitalised Patients?

Anaemia, and iron deficiency with or without anaemia is common in hospitalised patients including those awaiting surgery.

The commonest classification of anaemia is the WHO criteria of <130 g/L in males, and <120 g/L in females. Using these criteria 35% of patients were found to be anaemic when presenting for hip joint surgery,[1] 34% were found anaemic prior to non cardiac vascular surgery and 76% were anaemic with Dukes stage D colon cancer prior to resection. Of note, the majority of these patients had mild anaemia (above 100 g/L) and there was little consideration given to the aetiology of anaemia, or in treating the iron deficient component. While consensus guidelines suggest this group should be investigated and treated, both in the community and before elective surgery, it is obvious this is infrequently performed,[2] especially in elderly patients. The Current GAIHN (Greater Auckland Intergrated Health Care Network) guideline for investigating patients presenting with anaemia suggest referral based on age, sex, and history (see figure 1 and table 1). All anaesthetists undertaking a pre-assessment of a surgical patient that identifies unexpected anaemia should consider referral following these guidelines.

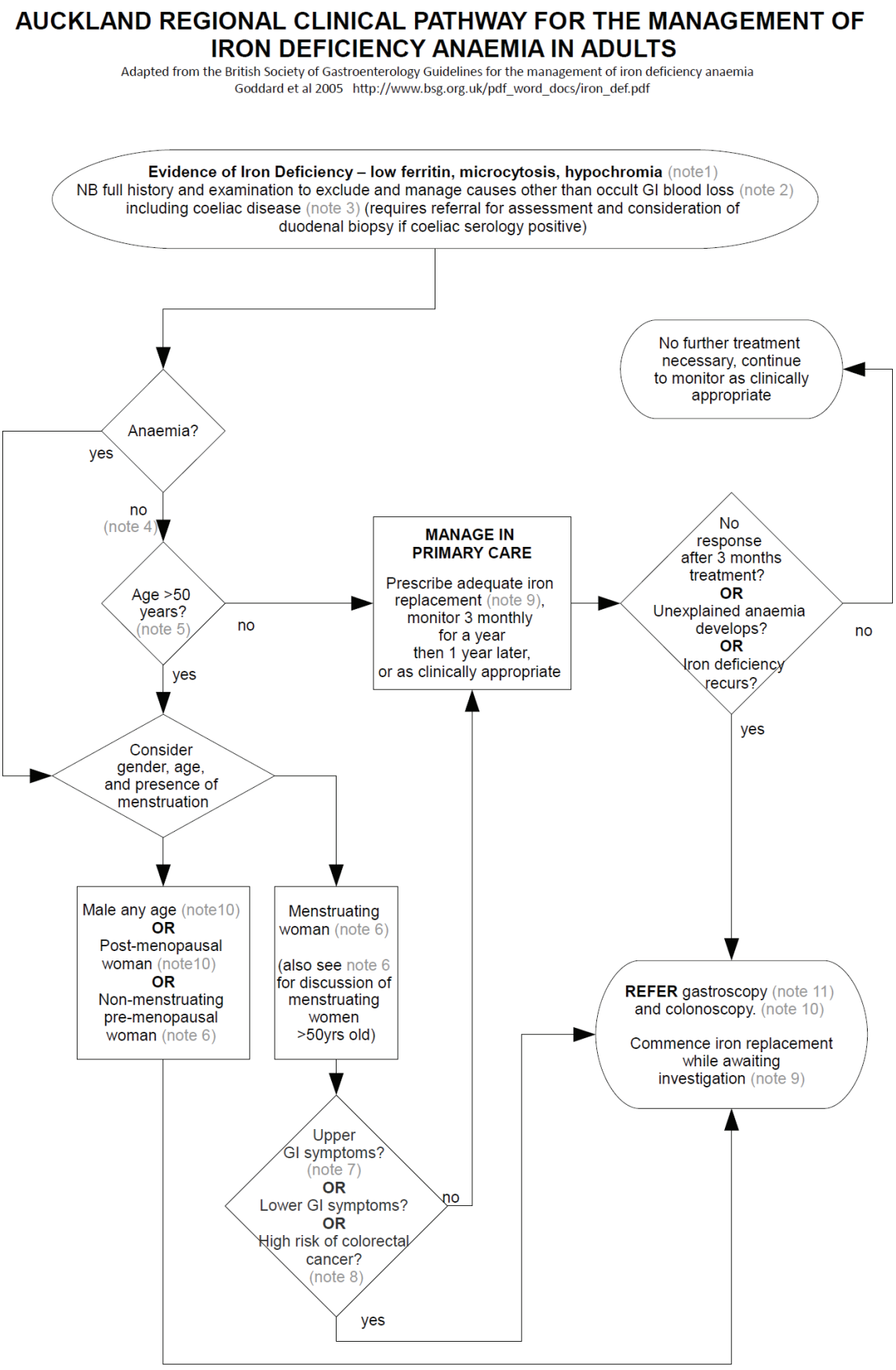

Figure 1. Auckland Regional Clinical Pathway for the Management of Iron Deficiency Anaemia. December 2010

Auckland Regional Clinical Pathway for the Management of Iron Deficiency Anaemia in Adults – Explanatory Notes

1. Iron deficiency should be confirmed by a low serum ferritin, red cell microcytosis or hypochromia in the absence of chronic disease or haemoglobinopathy, eg thalassaemia
2. Full history and examination and consideration of possible causes are recommended before referral for specialist assessment / gastroscopy (see note 11) /colonoscopy –
   - Anaemia is defined as haemoglobin below the lower limit of normal for the laboratory performing the assay. The BSG recommend investigating any level of iron deficiency anaemia
   - Family history may be helpful, eg coeliac disease, bleeding disorder, other rare inherited conditions
   - Consider the presence of chronic disease or haemoglobinopathy, ie the possibility that this is not a true iron deficiency anaemia (IDA). (see note 1)
   - Occasionally chronic iron deficiency may co-exist with anaemia of chronic disease, and in that context iron studies may be equivocal, making it difficult to confirm iron deficiency. Haematologist interpretation of iron studies and soluble transferrin receptor measurements may help to resolve the precise diagnosis – thus discussion with a haematologist is recommended
   - Consider dietary intake, use of aspirin / NSAID's, other significant sources of blood loss (eg heavy menstrual blood loss, frequent blood donation, severe epistaxis)
   - Those with previous gastrectomy commonly have IDA as a result of poor absorption, but also have a 2-3 fold increase in gastric cancer risk after 20 years. Gastroscopy (see note 11) is recommended for investigation of post-gastrectomy patients >50 years with IDA
   - Perform urine dipstix – haematuria from a renal malignancy accounts for ~1% of all cases of IDA and approximately one third of patients with renal cell carcinoma will have anaemia
   - Consider rectal examination
   - Faecal occult blood testing is of no benefit in the investigation of IDA due to its low sensitivity and specificity
3. Coeliac disease accounts for 4-6% of all cases of IDA. This is confirmed at OGD (oesophago-gastro-duodenoscopy), and a biopsy demonstrating gluten enteropathy is necessary for subsidy by Special Authority for funded gluten-free foods (specialist-only application). The lifetime risk of GI malignancy is increased for these patients, and if IDA occurs in such a patient with treated coeliac disease, who is diet-compliant, GI investigation should be considered
4. In iron deficiency without anaemia, there is a very low prevalence of GI malignancy (0.9% of men and post-menopausal women, and 0% of pre-menopausal women). Men >50 and post-menopausal women should be considered for GI screening for the investigation of iron deficiency without anaemia, only after assessment for other causes (see note 2)
5. Age is the strongest predictor of pathology in the iron deficient patient
6. 5-12% of pre-menopausal women who are menstruating have IDA
   - The commonest overall cause of IDA is menstrual blood loss (20-30% of all IDA). ~30-40% of young menstruating women may have low ferritin with usually normal iron studies and no anaemia or microcytosis – this is termed "latent iron deficiency" and is due to a negative iron balance where iron loss due to menstruation exceeds dietary intake
   - Other causes of iron deficiency in this group of women include increased demands in pregnancy and breast-feeding, significant blood loss at delivery, dietary deficiency or coeliac disease (4% of pre-menopausal women with IDA have coeliac disease)
   - Pre-menopausal women with IDA who are not menstruating (eg post-hysterectomy, Mirena, Jadelle or other progesterone-only implant, anovulation) – when assessing a woman in this group consider the length of time that she has not been menstruating and refer if the anaemia is not clearly caused by recent heavy menstrual bleeding or recent pregnancy-related increased iron demands / blood loss (or other causes as in note 2). If significant blood loss or significant increased demands (with inadequate replacement) occurred prior to recent cessation of menses a trial of oral iron and assessment of response to this is recommended. Lack of response within three months should prompt referral for assessment
   - The menstruating woman >50 years old is at higher risk of GI pathology and this should be considered when deciding on a time-frame for trial of iron supplementation before referral
7. Menstruating women with IDA and upper GI symptoms should be referred for gastroscopy (see note 11). Anaemia is an alarm for gastric pathology in the presence of dyspepsia
8. Menstruating women with IDA and lower GI symptoms or those that are at high risk of colorectal

cancer (CRC) according to the NZGG guidelines for CRC screening (see NZGG guideline), should be referred for colonoscopy

9. All patients should have sufficient iron therapy to correct the anaemia and replenish iron stores –
   - This is usually achieved with oral iron – currently ferrous fumarate 200mg bd is the only formulation fully subsidised – until correction of blood parameters, then for a further three months to replenish stores
   - If no response after three months therapy – check compliance, interaction with other medication (eg omeprazole) or dietary components (eg tea)
   - Those intolerant of one formulation of oral iron may do better on another formulation or reduced daily dose
   - Parenteral iron may be considered for those intolerant of oral iron, or non-compliant
   - Patients with symptomatic anaemia should be considered for transfusion, after which oral supplementation is still necessary to replenish stores
   - IDA resistant to therapy or transfusion dependent IDA should be considered for further investigation, eg capsule endoscopy or repeat endoscopy if the former is not available
   - Once fully treated with oral iron – monitoring is recommended every three months for a year, then a year later to check for relapse
10. Blood loss from the GI tract is the commonest cause of IDA in men and post-menopausal women –
    - Common causes are aspirin / NSAID use (10-15%), CRC (5-10%), gastric carcinoma (5%), benign gastric ulceration (5%), and angiodysplasia (5%)
    - Uncommon causes include oesophagitis (2-4%), oesophageal carcinoma (1-2%), and other rare conditions
    - IDA is often multifactorial and dual pathology is not uncommon (1-10%)
11. "OGD" is the more accurate term here – stands for oesophago-gastro-duodenoscopy. However the term "gastroscopy," although essentially inaccurate, is better known and used more commonly in primary care, thus has been chosen for the purposes of this pathway. Gastroenterologists prefer the term "OGD" as it more accurately describes the procedure.

Table 1. Auckland Regional Clinical Pathway for the Management of Iron Deficiency Anaemia. December 2010

How Should We Diagnose the Degree of Iron Deficiency in the Patient Group?

Modern cell counters automatically calculate the Mean Cell Haemoglobin (MCH) and mean cell volume to show microcytosis and hypochromia. MCH is probably more reliable, and if present should indicate iron studies being done. An increased red cell distribution (RCD) often indicates co-committent B_{12} deficiency. Microcytosis and hypochromia are also present in many haemoglobinopathies, especially thalassaemia. These patients will automatically undergo Hb electrophoresis to exclude such haemogloibinopthies. This is important as some patients with thalassaemia have iron overload and should not receive IV Iron. Others however may have a mixed picture and may benefit from iron. Iron studies will separate these groups, mainly distinguished by a low vs high ferritin.

The serum markers of iron deficiency are a low ferritin, low iron and raised iron binding capacity. In cases of pure iron deficiency ferritin is the most important marker to indicate a need to replacement, and a ferritin of less than 40 mcg/L indicates a need for iron. Unfortunately ferritin is an acute phase protein so it rises in the presence of inflammation, so an elevated ferritin may still be present in iron deficiency. In this case, a CRP >5 and a ferritin of less than 100 mcg/ml indicates iron deficiency. A soluble transferring receptor fraction of <15 also indicates the need for iron.

In general all patients who are anaemic, or have known blood loss that may cause iron deficiency should be investigated with iron studies. Strict vegetarians should also be tested, especially in the presence of anaemia.

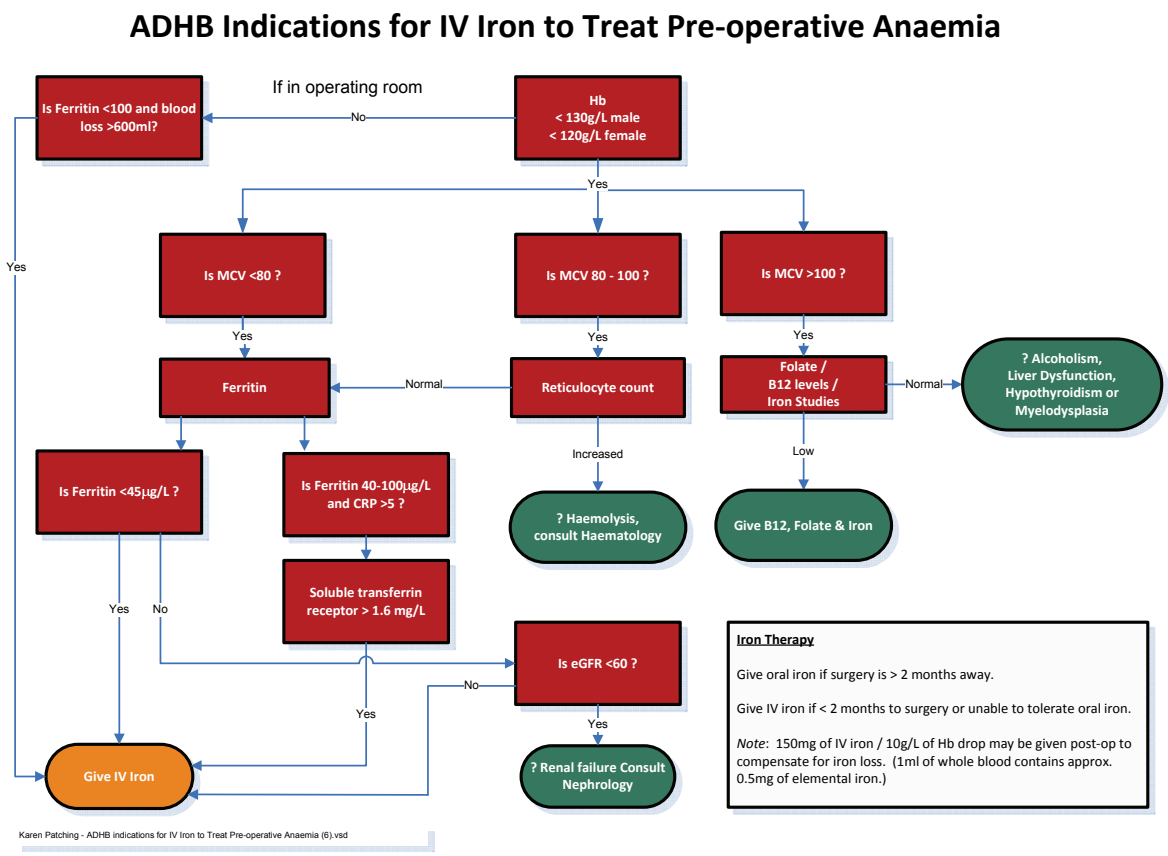

Figure 2. Indications for IV iron to treat pre-operative anaemia

Iron Homeostasis

Under physiological conditions there is a balance between iron absorption, iron transport and storage. Iron deficiency can be absolute or functional. Absolute (true IDA) is where there is iron loss from the body due to blood loss or dietary restriction. Functional iron deficiency (often called “Anaemia of Chronic Disease”) is caused by elevated levels of hepcidin preventing release of iron from cells. Both forms usually respond to iron replacement. Most body iron (2.6g of 3 to 4g) circulates as Hb. One gram is stored in the liver and about 0.4g in myoglobin. Men and non-menstruating women lose about 1mg a day. Menstruating women lose an additional 1mg a day. Iron absorption is down-regulated by hepcidin, to replace the losses. It is usually around 1mg a day, and can rise to a maximum of 5mg a day in anaemic conditions, promoted by erythropoietin. Pregnancy adds about 1000mg to overall requirements. Gastric intolerance and concomitant medications such as proton pump inhibitors which de-acidify the stomach dramatically reduce absorption of oral iron. For unknown reasons post operative absorption of oral iron is also impaired.

Deficits due to blood loss easily overwhelm the ability of oral absorption to cope.

Calculations of Iron Deficits

Total iron deficit [mg] = body weight [kg] x (target Hb - actual Hb) [g/dl] x 2.4 + depot iron [mg]

In most circumstances the target Hb is around 150g/L preoperatively. In this circumstance the table below can be used to calculate the amount (dose) of iron required to make up the deficit.

Body weight (kg)	Hb 60 g/L Dose (mg)	Hb 75 g/L Dose (mg)	Hb 90 g/L Dose (mg)	Hb 105g/L Dose (mg)
35kg	1250mg	1150mg	1000mg	900mg
40kg	1350mg	1200mg	1100mg	950mg
45kg	1500mg	1300mg	1150mg	1000mg
50kg	1500mg	1400mg	1200mg	1050mg
55kg	1500mg	1500mg	1300mg	1100mg
60kg	1500mg	1500mg	1350mg	1150mg
65kg	1500mg	1500mg	1450mg	1200mg
70kg	1500mg	1500mg	1500mg	1250mg
75kg	1500mg	1500mg	1500mg	1300mg
80kg	1500mg	1500mg	1500mg	1350mg
85kg	1500mg	1500mg	1500mg	1400mg
90kg and over	1500mg	1500mg	1500mg	1450mg

As you can see there is a huge deficit in total body iron in a 70kg patient with an Hb of 105g/L (1250mg) and it is unlikely that can be replaced by oral iron in a short period of time when the maximal oral uptake is 5-10 mg/day. In fact, oral replacement should be continued for two months with this degree of deficit, and is a good option if surgery is not anticipated for that length of time.

The Effectiveness of Oral and Intravenous Iron in Treating Anaemia

The correct treatment of iron deficient anaemia is iron. Some studies have looked at the effectiveness of IV and oral iron in elevating Hb. Most of the studies have concentrated on anaemia in the populations of joint replacement surgery, inflammatory bowel disease and bowel malignancy. A summary of the literature includes –

1. Preoperative oral iron given before colorectal surgery was found to raise Hb levels and reduce the proportion of patients receiving blood transfusions compared with the control group. (9.4% vs 27.4%, $p<0.05$).[3] A similar study showed preoperative oral iron for 14 days in this group reduced red cell transfusion from 59% to 29%. A large number of patients are excluded from such studies however due to intolerance of high dose oral iron, or concomitant use of proton pump inhibitors such as omeprazole. Importantly however, if patients are able to take oral iron, they should be given it, as long as there is a minimum of four weeks treatment prior to surgery. Only patients with IDA will benefit, so appropriate investigation and diagnosis is important.
2. Postoperative oral iron is usually ineffective. Inflammatory elevation of hepcidin, or gastric irritation with oral preparations limits the ability to elevate iron stores.
3. Intravenous iron has been shown to improve preoperative anaemia and reduce transfusion requirements in studies. Preoperative IV iron reduced transfusion requirements in pertrochanteric hip fractures by 20-59%.[4,5]
4. No evidence exists for the routine use of IV iron in patients that do not have iron deficiency. Studies need to be done in patients with >600ml blood loss during surgery, as they lose 0.5mg/ml of elemental iron per ml of blood loss (equivalent to 300mg of Iron). As previously indicated, oral iron is ineffectual.

Choice of Intravenous Agent

Previously, concerns regarding IV iron preparations were related to a high incidence of anaphylaxis associated with dextran linkages. These preparations are no longer used in NZ, but their poor reputation persists. Currently the two preparations available in NZ are iron polymaltose (Ferrum H) and iron sucrose (Venofer). Iron carboxymaltose (Ferinject) is currently undergoing registration in NZ but is available in Australia. All are bound to carbohydrate, not dextran.

	Iron Dextran	Iron Sucrose	Iron Polymaltose	Ferric Carboxymaltose
Brand names	Cosmofer, Dexferrum, Imferon (and others)	Venofer, Hemofer, Ferrofer (and others)	Ferrum H, Ferrosig	Ferinject
Presentation	Ampoules containing Fe^{3+} hydroxide dextran complex (50mg/ml). Available in 100mg, 250mg and 500mg doses	100mg elemental iron in 5mls single use ampoule (20mg/ml)	318mg iron polymaltose (100mg elemental iron) in 2ml single use ampoules	50mg/ml ▪ 100mg in 2ml single use vial ▪ 500mg in 10 ml single use vial
Description	▪ Stable iron (III) hydroxide dextran complex analogous to physiologic form of iron (ferritin) ▪ Iron present in non-ionic water soluble form ▪ MW 165kDa	▪ Mixture of polymers – polunuclear Fe^{3+} hydroxide core surrounded by a large number of non-covalently bound sucrose molecules ▪ MW 34-60kDa ▪ 100mg elemental iron / 5ml	▪ Macromolecular spherocolloidal complex of Fe^{3+} hydroxide and carbohydrate polymaltose ▪ MW 462kDa ▪ 100mg elemental iron in 2mls	▪ Complex of polynuclear Fe^{3+} hydroxide surrounded by carbohydrate shell ▪ MW 150kDa
Pharmacokinetics	▪ Infused IV iron dextran is taken up by cells of the RES and Fe is slowly released ▪ IM injection – major portion absorbed via the capillaries and lymphatics within 72 hours with the rest of absorption occurring within the next 3-4 weeks	▪ Obeys first order kinetics ▪ Distribution mainly in blood and a little in extravascular fluid ▪ In patients with IDA, labelled iron (100mg) distributes into liver, spleen and bone marrow ▪ Dissociation of iron and sucrose is in RES cells	▪ IM injection evokes local inflammatory response and iron polymaltose (IPC) is transported via lymphatics into regional lymph nodes ▪ IPC released into blood stream and taken up by cells of RES and ionised to Fe^{3+} and polymaltose. Ferric iron is bound to ferritin or transferrin	▪ Cmax peaked at 20min, 1 hour and 1.2 hours for 500mg, 800mg and 1000mg IV iron dose in 250mls NS infused over 15 minutes respectively ▪ Radiolabelled single 100mg iron dose was distributed to RES within 8 hours and incorporated into RBCs in 6-9 days
Indications	▪ Treatment of IDA when patient cannot tolerate oral iron, or when oral iron show lack of efficacy ▪ When there is a clinical need to deliver iron rapidly	▪ Treatment of IDA in patients undergoing chronic haemodialysis and receiving ESA	▪ Treatment of IDA in adults and paediatric patients when oral iron is contraindicated, patient is intolerant of oral iron, or when enteric absorption of oral iron is defective	▪ Treatment of IDA when oral iron are ineffective or cannot be used
Dosing and Administration	▪ IV: dilute in NS or 5% glucose ▪ 100-200mg in 100mls given over 30min ▪ TDI (</= 20mg/kg) added to 500mls given over 4-6 hours ▪ IM injection: maximum of 2ml (100mg undiluted) daily (weekly in inactive patients) until total required dose given	▪ 100mg elemental iron given during dialysis but no more than 3x per week ▪ Cumulative dose of 1000mg needs to be given over 10 dialysis sessions ▪ Dilution of 5mls into 100ml of NS give over 15 minutes ▪ Can be given as slow IV injection into venous limb of dialysis line undiluted at rate of 1ml/min ▪ Can continue maintenance therapy at lowest dose	▪ Dosing according to calculated total body iron deficits ▪ IM – adults: max of 4 mls (200mg) per injection as daily dose until total dose achieved ▪ IV dosing – only to be used when IM is impractical or unacceptable ▪ IV: max dose of 2500mg in 500mls NS with first 50mls given as slow infusion of 5-10 drops per minute). Infusion rate – max 30 drops/min	▪ IV use only ▪ Undiluted: max of 200mg (4mls) as IV injection no more than 3x per week ▪ Can be given into venous limb of dialysis line ▪ Max single dose of 1000mg (20ml diluted in 250mls NS) can be given over 15 minutes. Not to exceed 15mg/kg in a single infusion ▪ Can continue maintenance therapy at lowest dose

	Iron Dextran	Iron Sucrose	Iron Polymaltose	Ferric Carboxymaltose
Caution	25mg (0.5ml) as test dose must be given before each IM injection or IV administration Total dose infusion is associated with delayed hypersensitivity reactions and should only be given in hospital setting	Should give test dose of 20mg (1ml) diluted in 20mls NS over 15 minutes before administration of therapeutic dose in new patients Potential for life threatening hypersensitivity or anaphylactic reactions	As for any parenteral iron, be aware of potential hypersensitivity reactions	As for any parenteral iron, be aware of potential hypersensitivity reactions
Market	Worldwide and also as veterinary formulations	EU, ANZ	ANZ	EU, Australia. Not in NZ

The key issues associated with using IV Iron preparations are –

1. The side effect profile of the agents available in NZ are nausea, occasionally temporary periods of hypotension, arthralgia and rash
2. Most are best diluted in >200ml of NaCl or similar. They should be given over about one hour with normal monitoring. Iron carboxymaltose can be given as an IV push
3. Total iron dosing can be given in one treatment with Iron polymaltose and iron carboxymaltose (up to 2000mg). Iron sucrose can only be given to a maximum dose of 200mg in one sitting
4. There is a theoretical risk of bacterial infection in preparations with free iron but this has not been shown with use of IV iron

Protocol for the Use of IV Iron

Included at the end of this abstract is a protocol from ADHB for the delivery of iron polymaltose. Other hospitals infuse the agent over longer time periods but recent studies indicate the side effect profile is no different.

Summary

Iron deficiency is present in approximately 35% of pre-operative patients, with many more having reduced iron stores. Patients with inflammatory disease and other chronic illness have a functional impairment to oral iron uptake, that renders oral treatment ineffective. Studies have shown that preoperative anaemia is the strongest predictor of post operative transfusion requirements. IV iron preparations are available, and are relatively cheap and safe to infuse. They could easily be added to the other treatments anaesthetists offer their patients. Reducing the incidence of blood transfusion improves the care of our surgical patients significantly. What is required is a system that identifies, investigates and treats, iron deficient patients under our care. Such a system should be easy to develop under the umbrella of perioperative medicine.

References

1. Goodnough T et al. Detection, evaluation and management of anaemia in the elective surgical patient. Anesth Analg 2005; 101: 1858-61
2. BSG Guidelines in Gastroenterology 2005. Guidelines for the management of Fe deficient anaemia
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AUCKLAND DISTRICT HEALTH BOARD Te Toka Tumai

Adult Intravenous Administration Guidelines

Iron Polymaltose (Rapid Administration)

Iron supplement, treatment of anaemia

Drug guideline

Indications

- Iron deficiency and Iron deficiency requiring supplementation
- Oral Iron intolerance or requirement for rapid increase in Iron stores
- Treatment or prevention of anaemia from excessive blood loss

Dose & Administration

- Dose may be calculated by the following three methods:
  1. Equation
  2. Dosing table
  3. Prescribers may choose to give an arbitrary low dose e.g. 1 gram
- The dose has been capped at 1500mg for the rapid administration protocol.
- Equation method:
  Iron dose (mg) = Body weight (kg) x (Target Hb – Actual Hb in g/L) x 0.24 + Iron depot
  Target Hb = 150g/L for patient over 34kg
  Iron depot = 500mg for patients over 34kg
- Table method: use table below to determine dose using patient weight and actual haemoglobin (Hb)

Body weight (kg)	Hb 60 g/L **Dose (mg)**	Hb 75 g/L **Dose (mg)**	Hb 90 g/L **Dose (mg)**	Hb 105g/L **Dose (mg)**
35kg	1250mg	1150mg	1000mg	900mg
40kg	1350mg	1200mg	1100mg	950mg
45kg	1500mg	1300mg	1150mg	1000mg
50kg	1500mg	1400mg	1200mg	1050mg
55kg	1500mg	1500mg	1300mg	1100mg
60kg	1500mg	1500mg	1350mg	1150mg
65kg	1500mg	1500mg	1450mg	1200mg
70kg	1500mg	1500mg	1500mg	1250mg
75kg	1500mg	1500mg	1500mg	1300mg
80kg	1500mg	1500mg	1500mg	1350mg
85kg	1500mg	1500mg	1500mg	1400mg
90kg and over	1500mg	1500mg	1500mg	1450mg

Please note this table provides the dose in **milligrams** of iron polymaltose. Caution as other references may give the dose in ml or number of ampoules.

Administration

- Dilute drug to 250ml sodium chloride 0.9%
- Infuse test dose at 40ml/hour for 15 minutes. If tolerated, increase infusion rate to 250ml/hour for remainder of infusion.

Iron Polymaltose (Rapid Administration)

Iron supplement, treatment of anaemia

Observation & Documentation

- Anaphylactoid reactions have been reported with parenteral iron . These primarily occur in the first few minutes of an infusion, and present as respiratory difficulty, hypotension and tachycardia.
- Monitor patients every 5 minutes for the first 15 minutes, then every 15 minutes throughout infusion.
- Monitor blood pressure and heart rate
- If infusion related adverse reactions occur, reduce rate to 60ml/hour. If symptoms persist, stop infusion and consult prescriber. If symptoms resolve, the infusion rate may be increased slowly.

Special Considerations

- Rapid administration of iron and infusion volumes < 500ml are outside of the manufacturer recommendations. This protocol has been developed from a single clinical trial and anecdotal reports of efficacy and safety. Clinicians should clearly specify which administration protocol they intend to use when prescribing iron polymaltose at ADHB.
- For information on 'usual' administration rates, see Notes on Injectable Drugs or iron polymaltose datasheet www.medsafe.govt.nz
- Iron polymaltose is contraindicated in the first trimester of pregnancy
- Caution use in patients with infection as iron may increase the pathogenicity of some micro-organisms.
- Ensure the underlying cause of anaemia is established. Iron polymaltose is not useful for treatment of macrocytic or haemolytic anaemia.
- Caution using the rapid administration protocol in patients with inflammatory bowel disease with raised CRP, as there may be an association with infusion related reactions.

Presentation

Iron polymaltose amber ampoules containing 100mg/2ml

Storage

Store unopened ampoules at room temperature. Protect from light.

Diluted solutions for infusion should be prepared as soon as practical before administration. Solutions for infusion must be used within 12 hours.

Reference

- Garg M, Morrison G, Friedman A, Lau A, Lau D, Gibson PR. A rapid-infusion protocol is safe for total dose iron polymaltose: time for change. "Accepted article" Internal Medicine Journal. Accepted 25th July 2010
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This guideline was reviewed by Adele Harrex and Dr Kerry Gunn