Iron deficiency masterclass: A practical guide to managing iron deficiency anaemia

This meeting report is from a Pharmacosmos-sponsored symposium* that took place at the AAGBI congress, Dublin, Ireland on Wednesday 26th September 2018.

Introduction

Globally, anaemia affects a quarter of the population, accounting for 8.8% of the total global burden of disease, and is associated with substantial risks.¹ In the majority of cases, iron deficiency is the predominant culprit and should be treated upon diagnosis.¹

At a Pharmacosmos-sponsored symposium held on Wednesday 26th September 2018, a multidisciplinary panel of physicians with combined expertise in anaesthesia, haematology and obstetrics convened to provide practical guidance on the management of iron deficiency anaemia (IDA) in surgical patients as well as throughout pregnancy and the post-partum period. The experts also shared their experience of setting up and running anaemia clinics at their centres and embedding them into standard NHS pathways. This report summarises the key learning points from the symposium.

*Speakers received a fee for their involvement in the meeting.

Prescribing Information can be found at the end of this report.
Iron deficiency masterclass: A practical guide to managing iron deficiency anaemia

How you as an anaesthetist can treat anaemia before and after surgery

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In recent years, the role of the anaesthesiologist has evolved as increasing emphasis is placed on peri-operative patient care. An important part of peri-operative medicine is the identification, diagnosis and management of anaemia, which is associated with poor post-operative outcomes, including increased morbidity, mortality and transfusion requirement. The 2016 NICE Quality Standard for Blood Transfusion (QS138), reflects this. It states that patients should have their Hb levels checked at least 2 weeks before surgery and that people with IDA who are having surgery should be offered iron supplementation before and after surgery.

The WHO defines anaemia by the quantified circulating Hb concentration of 13 g/dL in men and 12 g/dL in women. However, I believe this standard is flawed because values were generated from a population average. Since women generally have a lower circulating blood volume and smaller body surface area than men, and are thus more likely to be at risk of anaemia during surgery, I advise aiming for a higher Hb in women to reduce the likelihood of transfusion.

Anaemia is a pathologic condition produced by a decrease in red blood cell mass or a decrease in the amount of Hb. The most common cause of anaemia worldwide is an iron deficiency, which may result from insufficient iron intake, decreased iron absorption or blood loss. The other main cause of anaemia is known as functional iron deficiency (also called anaemia of chronic disease) and occurs in diseases involving acute or chronic immune activation, such as patients with infections, malignancies or autoimmune disorders. These conditions can stimulate hepcidin production and its release from the liver, which in turn reduces the iron carrier protein ferroportin so that access of iron to the circulation is reduced.

After the age of 50 years, the prevalence of anaemia increases with advancing age. Since anaemia of any degree contributes significantly to morbidity and mortality in elderly patients, they are less able to tolerate Hb levels below the normal range.

In the UK, anaemia is a significant problem. Approximately one-third of UK surgery patients are found to be anaemic on pre-assessment. However, a recent UK audit found that only half of elective patients were assessed for anaemia. Of these patients, only 17% underwent screening for serum ferritin – a simple measure of iron stores in the body that can be used to diagnose pre-operative iron deficiency. Low serum ferritin is highly specific for IDA and effectively rules out functional iron deficiency.

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Diagnosing pre-operative anaemia

Hb <130 g/l

Iron tests

Ferritin <30 mg/l

Iron deficiency anaemia

Ferritin 30–100 mg/l + TSAT <20% or CRP >5 mg/l

Anaemia of chronic inflammation with iron deficiency

Ferritin >100 mg/l + TSAT <20% or CRP >5 mg/l

Anaemia of chronic inflammation

Normal

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deficiency (which is diagnosed when anaemia is accompanied by serum ferritin that is not low).^16

The International Consensus Statement on the peri-operative management of anaemia and iron deficiency provides working definitions of peri-operative iron deficiency and anaemia in adult surgical patients. In light of this and other guidelines, the Royal Papworth Hospital operates a peri-operative anaemia clinic that prioritises early evaluation of iron status to allow optimisation of iron levels while the patient is on the surgical waiting list. In the clinic, we perform Hb tests on the same day that the patient meets the surgeon. If Hb is <130 g/l, we also perform transferrin and transferrin saturation tests, and the patient is evaluated for anaemia. Patients diagnosed with anaemia are then referred to our iron clinic for treatment, which may include oral iron and nutritional advice, or IV iron.14

"The whole point of the pre-assessment clinic is to get the blood results early. Patients who are anaemic are called back into the clinic after a week or so – at the beginning of the surgical wait list. So, we have weeks or months in which we can optimise our patients."

Studies have demonstrated that, after surgery, oral iron is ineffective due to its poor absorption caused by increased hepcidin levels as a result of inflammation. Furthermore, current recommendations are to start oral therapy 6–8 weeks before surgery, which is not always possible. For patients who are unable to tolerate oral iron or do not respond in 4 weeks, IV iron should be used.14 IV iron is highly efficacious at replenishing iron stores and increasing Hb levels in IDA.14 While older IV iron preparations were associated with rare but serious allergic reactions that could lead to anaphylaxis, these side-effects appear not to be significant with the newer IV iron preparations such as ferric carboxymaltose, iron isomaltoside and low-molecular-weight iron dextran (LMWID), with no serious adverse events reported in recent RCTs.16 Across the UK, only 1% of anaemic patients presenting for major surgery are receiving IV iron.13

At the Royal Papworth Hospital’s peri-operative anaemia clinic, we treat pre-operative patients with up to 20 mg/kg of Monofer® (iron isomaltoside 1000) 6 weeks before surgery. As a result, Hb levels have been shown to increase by approximately 15–20 g/l.

IV iron has also been shown to be effective in post-operative anaemia management. The international consensus statement on the management of post-operative anaemia after major surgical procedures, provides working definitions of post-operative iron deficiency and easy-to-implement, practical management of anaemia in adult surgical patients.16

"Oral iron is useless in the post-operative period. The only way of treating post-operative iron deficiency in the first 6 weeks is IV iron.1,14,16"
In 2014, the National Clinical Programme for Anaesthesia (NCPA), an initiative that formed part of the Health Service Executive (HSE) speciality programmes, published and launched the Model of Care for Pre-admission Units. This Model of Care included guidelines for governance and management of peri-operative anaemia are in their early stages.

Demonstrating the benefits of the Model of Care through the evaluation of clinical and non-clinical outcomes is a key part of the initiative. The NCPA defined a number of key performance measures, which included same-day surgery rates, day of surgery cancellation, length of hospital stay, readmission rates, waiting list times, percentage of patients entering the clinic, referral to treatment time, identification of high-risk patients, and morbidity and mortality rates, among others.

In light of this initiative, we established a preparation of patients for surgery (POPS) clinic, a dedicated unit for patient pre-assessment and pre-operative preparation, at Cork University Hospital (CUH). Services we provide at the POPS clinic include management of IDA in the pre-operative setting as well as medical assessment, medication management and specialist referrals. We also administer intravenous (IV) iron at a dedicated infusion clinic, which is the POPS clinic’s newest protocol and is in line with the National Institute for Health and Care Excellence (NICE) Quality Standard 138, published in 2016.

In order to gain internal support for the IV iron clinic and embed it into standard care pathways, myself and colleagues at CUH developed a supporting business case to demonstrate the clinic’s viability and benefits. We performed an audit across a range of surgeries to evaluate the prevalence of anaemia in elective patients over a period of 6 weeks. We then calculated administration, consultant and nursing costs of running an IV iron clinic, as well as costs associated with haemoglobin (Hb) testing, equipment and medication. Finally, we extrapolated data on cost savings associated with established IDA treatment centres in the UK into an Irish setting, and economic analysis suggested an overall cost reduction associated with treating IDA.

As a result, our plans to expand the infusion clinic at CUH (two full-time nursing equivalents) were recently approved, and we have developed protocols for the investigation and treatment of IDA.

“The idea is that we have the POPS clinic as a one-stop shop. The patient gets a full medical assessment and admission. They also get a full nursing assessment and admission. On the day of surgery, the last thing they sign is the consent form.”
Iron deficiency anaemia during pregnancy most commonly arises from maternal-foetal transfer of iron, which may be exacerbated by low maternal iron reserves at the beginning of the pregnancy. It can have serious adverse health consequences for the mother and child, and requires effective management throughout pregnancy and the post-partum period. Reflecting this, clinical guidelines recommend that all women should be offered screening for anaemia early in pregnancy (at the appointment booking) and at 28 weeks. It has been proposed that screening should also include serum ferritin to enable early assessment of body iron status; recent guidelines on the treatment of anaemia in pregnancy published in Blood state that a serum ferritin level <30 μg/L should prompt treatment.

While the World Health Organization (WHO) defines anaemia in pregnancy as a haemoglobin concentration of <11 g/dL, I use the definition of 10.5 g/dL as the cut-off from 12 weeks of pregnancy onwards in my clinical practice due to marked plasma expansion that takes place in the second trimester. Following a diagnosis of anaemia, I also recommend performing laboratory testing to further evaluate anaemia for nutritional deficiencies, chronic renal insufficiency, and/or chronic inflammatory disease, as well as screening for haemoglobinopathies in at-risk patient groups.

The Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA) consensus statement highlights that mild-to-moderate IDA (defined as Hb ≥80 g/L) in early pregnancy should be treated with oral ferrous iron (80–100 mg/day elemental iron) and folic acid (400 µg/day). IV iron should be considered in women with severe IDA (Hb <80 g/L) or newly diagnosed IDA beyond 34 weeks of gestation, and in women with confirmed IDA who fail to respond to the correct administration of oral iron, or are intolerant to oral iron treatment, if the gestational age is >14 weeks.

At the High-Risk Haematology Obstetric Clinic at Belfast City Hospital, where we treat challenging cases undergoing general anaesthetic for elective caesarean, we also manage cases of IDA as an add-on service. The focus of this add-on clinic is to maximise Hb at the time of delivery; as such, IV iron is often considered, and frequently given, at around 34 weeks of pregnancy as per current recommendations. My colleagues and I analysed one of the first cohort of patients with IDA who were referred to the High-Risk Haematology Obstetric Clinic and prescribed IV iron. Of these 42 patients, four were on oral iron therapy at the time of referral. By the time they were under consideration for IV iron, their Hb levels had decreased from a mean of 11.1 g/dL at booking, to 8.7 g/dL, and mean ferritin levels were 7.1 µg/L. This indicated profound iron deficiency, even in patients with Hb levels up to 10.3 g/dL, as Hb does not necessarily accurately reflect iron stores in the body. This is because as iron is ingested, it is being utilised to maintain the Hb rather than going into iron storage.

Following treatment with Monofer (iron isomaltoside 1000), 61% of patients achieved an Hb of ≥10.5 g/dL, and at the time of delivery, mean post-infusion Hb was 10.9 g/dL. There are stated precautions for use of Monofer in pregnancy. There are no adequate and well-controlled trials of Monofer in pregnant women, therefore treatment with Monofer should be confined to the second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and foetus.

IV iron preparations can also be used for the treatment of IDA during the post-partum period, a condition that is mainly caused by pre-partum IDA and/or acute bleeding during delivery. The NATA consensus statement recommends that following delivery, IV iron should be used in women who fail to respond to, or are intolerant to, oral iron, and those with moderate to severe post-partum anaemia (Hb <90 g/L).
References

UK Prescribing Information

Monoferr® (iron isomaltoside 1000) prescribing information

This medicinal product is subject to additional monitoring, and healthcare professionals are asked to report any suspected adverse reaction

Note: Before prescribing please read full Summary of Product Characteristics. Pharmacokinetic:
Iron isomaltoside 1000 is a dark brown, non-transparent solution for injection/intravenous. Presentations:
- iron in the form of iron isomaltoside 1000; 100 mg/ ml available in vials of 100 mg/ml, 500 mg/ml and 1,000 mg/ml. Indications: Monoferr® is indicated in patients ≥18 years for treatment of iron deficiency when oral iron preparations are ineffective or cannot be used or when there is a need to deliver iron rapidly. The diagnosis must be based on laboratory tests. Administration: Each iv. iron administration is associated with a risk of a hypersensitivity reaction. Thus, to minimise risk, the number of iron administrations should be kept to a minimum. The cumulative iron dose can be used either the Simplified Table or the Garzoní formula, please consult full Summary of Product Characteristics. Monoferr® may be administered as an iv bolus injection of up to 500 ml at an administration rate of up to 250 ml/hr for up to 3 hours during the first 30 minutes of the infusion. Doses over 500 ml should be administered over >15 minutes up to 1,000 ml must be administered over >30 minutes. In case of iron intolerance, the administration should be stopped by repeating the monoferr® dose. Iron should be used with caution in case of acute or chronic iron deficiency. Monoferr® should not be used in patients with ongoing bacterial infections or signs of intolerance to iron (e.g. arachidonic acid). Hypersensitivity episodes may occur if intravenous injection is administered too rapidly. Caution should be exercised to avoid pulmonary leakage when administering Monoferr®. Pregnancy: Monoferr® should be used during pregnancy unless clearly necessary. The treatment should be confined to the second and third trimester. In rare cases, fetal bradycardia has been observed in pregnant women with hypersensitivity reactions. Undesirable effects: No common (≥10%) undesirable effects listed. Common undesirable effects (1% to <10%): nausea, injection site reactions. For information on other undesirable effects, please consult full Summary of Product Characteristics.

Legal Category: POM. Package Quantities and basic Prices: 5 vials of 1 ml, £84.75, 5 vials of 5 ml, £423.75, 5 vials of 10 ml, £339.00. Marketing Authorisation NumberHolder: PL 18360001, Pharmacosmos A/S, Roenvæjgade 31, DK-4300 Holbæk, Denmark. Date of preparation: June 2017. Further Information is available on request to Pharmacosmos UK. Date of revision: January 2018.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard

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CRP, C-reactive protein; Hb, haemoglobin; IDA, iron deficiency anaemia; RCT, randomised controlled trial; TSAT, transferrin saturation.

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