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Background

There is accumulating evidence of a strong association between blood transfusion and adverse patient outcomes. Patient blood management aims to achieve improved patient outcomes by avoiding unnecessary exposure to blood products through effective conservation and management of a patient's own blood.

Objective

To introduce the general practitioner's role in patient blood management.

The GP's quide

Discussion

There are a number of ways in which GPs can contribute to patient blood management, particularly in the care of patients scheduled for elective surgery. These include awareness, identification, investigation and management of patients with or at risk of anaemia; assessment of the adequacy of iron stores in patients undergoing planned procedures in which substantial blood loss is anticipated; awareness and assessment of medications and complementary medicines that might increase bleeding risk; and awareness of and ability to discuss with patients, the possible risks associated with blood transfusion and alternatives that may be available.

Keywords

blood transfusion; anaemia; preoperative assessment; iron/deficiency

Patient blood management (PBM) is the timely application of evidence based medical and surgical concepts designed to maintain haemoglobin concentration, optimise haemostasis and minimise blood loss in an effort to improve patient outcomes.¹ Patient blood management principles are particularly relevant to the care of patients scheduled to undergo elective surgical procedures in which significant blood loss is anticipated. Effective conservation and management of a patient's own blood requires a proactive, multidisciplinary, team based approach. General practitioners play a unique role as care coordinator,

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advocate and referrer of their patients. *Table 1* outlines the questions GPs should consider when intending to refer a patient for elective surgery.

Why do we need patient blood management?

Many factors have led to the uptake of PBM. There is increasing evidence of the potential risks and adverse outcomes associated with blood transfusion, as outlined in *Table 2.*² Evidence also suggests that use of blood products is not always in accordance with clinical guidelines.³ Rising costs and demand for blood products, from a limited donor base, is putting increasing pressure on supply.^{2,4} Patient blood management optimises the use of donor blood and reduces transfusion associated risk.

New Australian patient blood management guidelines

A review of the 2001 National Health and Medical Research Council/Australasian Society of Blood Transfusion *Clinical practice* guidelines for the use of blood components³ is currently being undertaken by the National Blood Authority (NBA) on behalf of Australian governments. A series of six modules will comprise the new patient blood management quidelines. The modules are intended to assist and guide clinical decisions and coordination of healthcare across the primary, secondary and tertiary care settings for patients requiring blood products.⁵ Three modules are currently published and the remaining modules are expected to be released over the coming months. Module 2 -Perioperative,⁶ is particularly relevant to GPs. A number of recommendations and practice points contained in this module are discussed in this article. The guideline also includes a preoperative haemoglobin assessment and optimisation algorithm (*Figure 1*)⁶ to assist with the assessment and management of preoperative anaemia and suboptimal iron stores.

Preoperative assessment

Surgical patients should be evaluated as early as possible to coordinate scheduling of surgery with optimisation of the patient's haemoglobin and iron stores.⁶ Ideally this should occur a minimum of 30 days before the procedure.

If the haemoglobin is <120 g/L for females or 130 g/L for males the patient should be further investigated to determine the cause of the anaemia and replacement therapy instituted if indicated. Common causes of anaemia include iron, B12 or folate deficiency, anaemia of chronic disease and chronic kidney disease. Resources to assist with the diagnosis and management of these conditions can be found at the end of this article. In cases of significant anaemia where the cause is uncertain specialist referral may be necessary.

Risk factors for transfusion associated with surgery

Three main predictors for red blood cell transfusion have been identified by the Austrian Benchmark Study of blood use in adult patients undergoing elective surgery.⁷ These include patients with preoperative anaemia and those in whom substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated. Procedures associated with substantial blood loss include: cardiac surgery, vascular surgery (eg. abdominal aortic aneurysm repair, femero-popliteal bypass), large joint orthopaedic surgery and major general surgery (eg. bowel resection).

The strategies to address these risks, as outlined in *Table 3*, are referred to as the 'three pillars of patient blood management'.

Anaemia and its potential adverse effects on patient outcomes

The first pillar of PBM can readily be addressed in the primary care setting. Anaemia is common, with prevalence rates increasing rapidly after the age of 50 years, and reaching over 20% at age \geq 85 years.⁸ It needs to be considered in all

Table 1. Questions to consider when referring a patient forelective surgery

- Is the surgery likely to result in significant blood loss?
- Does my patient have anaemia or are they at risk of anaemia?
 What are my patient's iron stores?
- Are there comorbidities that may contribute to adverse outcomes if anaemia develops?
 - If so, what steps are needed to optimise these conditions (eg. cardiac disease)?
- Are there chronic conditions that may impede a haematopoietic response (eg. chronic kidney disease, inflammation or bone marrow pathology)?
- What medications and complementary medicines is my patient taking that might increase their bleeding risk?
- Is my patient informed about the possible risks associated with blood transfusion and alternatives that may be available?

Table 2. Risks and adverse outcomes associated with blood transfusion²

Infectious risks

- Known infectious agents (HIV, hepatitis C and B)
 - risk has been reduced to very low levels, however the blood supply will always remain vulnerable to emerging infectious agents
- Bacterial contamination
 - also low risk, however this is still an important consideration, particularly with platelet transfusion

Non-infectious risks

- Acute haemolytic reaction (eg. incorrect blood component transfused)
- Allergic, including anaphylactic, reactions
- Transfusion associated circulatory overload
- Transfusion related acute lung injury
- Delayed haemolytic transfusion reaction
- Transfusion associated graft versus host disease

Adverse outcomes - red blood cell transfusion has been associated with:

- Increased morbidity and mortality
- Increased ICU and hospital length of stay
- Increased incidence of postoperative infection
- Transfusion related immunomodulation

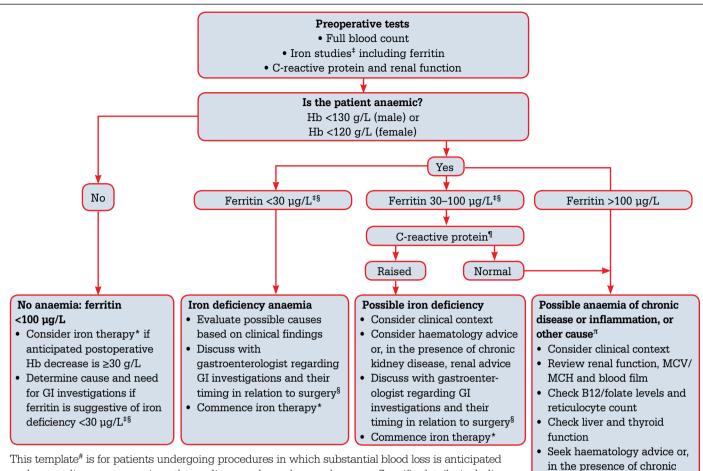
Note: The major source of morbidity and mortality relating to transfusion in Australia is from the non-infectious risks and adverse outcomes

For further information and updates on adverse events go to www.transfusion.com.au/adverse_events

Table 3. Relationship between the predictors of red blood cell transfusion and the three pillars of patient blood management

Predictors for red blood cell transfusions	Pillars of patient blood management
Preoperative anaemia	Optimisation of red cell mass
Volume of surgical blood loss	Minimisation of blood loss
Failure to adopt a more restrictive threshold for transfusion	Optimisation of the patient's tolerance of anaemia

kidney disease, renal advice



such as cardiac surgery, major orthopaedic, vascular and general surgery. Specific details, including reference ranges and therapies, may need adaptation for local needs, expertise or patient groups

*Iron therapy

Oral iron in divided daily doses. Evaluate response after 1 month. Provide patient information material

IV iron if oral iron is contraindicated, not tolerated or effective; and consider if rapid iron repletion is clinically important (eg. <2 months to non-deferrable surgery)

Note: 1 µg/L of ferritin is equivalent to 8–10 mg of storage iron. It will take approximately 165 mg of storage iron to reconstitute 10 g/L of Hb in a 70 kg adult. If preoperative ferritin is <100 µg/L, blood loss resulting in a postoperative Hb drop of \geq 30 g/L would deplete iron stores

In patients not receiving preoperative iron therapy, if unanticipated blood loss is encountered, 150 mg IV iron per 10 g/L Hb drop may be given to compensate for bleeding related iron loss (1 mL blood contains \sim 0.5 mg elemental iron)

Notes

- # Anaemia may be multifactorial, especially in the elderly or in those with chronic disease, renal impairment, nutritional deficiencies or malabsorption
- ‡ In an anaemic adult, a ferritin level <15 µg/L is diagnostic of iron deficiency, and levels between 15–30 µg/L are highly suggestive. However, ferritin is elevated in inflammation, infection, liver disease and malignancy. This can result in misleadingly elevated ferritin levels in iron-deficient patients with coexisting systemic illness. In the elderly or in patients with inflammation, iron deficiency may still be present with ferritin values up to 60–100 µg/L
- § Patients without a clear physiological explanation for iron deficiency (especially men and postmenopausal women) should be evaluated by gastroscopy/ colonoscopy to exclude a source of gastrointestinal bleeding, particularly a malignant lesion. Determine possible causes based on history and examination, initiate iron therapy, screen for coeliac disease, and discuss timing of scopes with a gastroenterologist
- \P CRP may be normal in the presence of chronic disease and inflammation
- π Consider thalassaemia if MCH or MCV is low and not explained by iron deficiency, or if long-standing. Check B12/folate if macrocytic or if there are risk factors for deficiency (eg. decreased intake or absorption), or if anaemia is unexplained. Consider blood loss or haemolysis if reticulocyte count is increased. Seek haematology advice or, in presence of chronic kidney disease, nephrology advice

Figure 1. Preoperative haemoglobin assessment and optimisation template

patients not just the 'typical' risk groups such as premenopausal females (particularly those with menorrhagia); institutionalised or socially disadvantaged people; and those with poor or restrictive diets or malabsorption disorders.9-11 Using the World Health Organization definition of anaemia of 120 g/L for females and 130 g/L for males,¹² the Austrian Benchmark Study found the overall prevalence of preoperative anaemia in elective surgery (coronary artery bypass graft, total hip and knee replacements) to be 19%. There was no female predominance. The incidence of preoperative anaemia was on average three times higher in patients who received transfusions than in those who did not. A considerable number of patients with preoperative anaemia had not had their anaemia treated.7

Preoperative anaemia has been shown to be associated with an increased risk of adverse outcomes. A retrospective study of 8000 patients undergoing non-cardiac surgery, in which 40% of both male and female patients had preoperative anaemia, found a five-fold increase in 90 day postoperative mortality.¹³ A larger study of 300 000 elderly patients undergoing non-cardiac surgery showed a statistically significant increasing rate of 30 day postoperative mortality with decreasing haematocrit.¹⁴

These statistics highlight the extent and significance of preoperative anaemia, particularly in the older age group in whom the likelihood of need for surgery is increased. In patients undergoing cardiac and non-cardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise red blood cell (RBC) transfusion, which may be associated with an increased risk of morbidity, mortality, intensive care unit length of stay and hospital length of stay.⁶

Iron deficiency

It is important to note that iron deficiency may occur without anaemia, and suboptimal iron stores will impact on the patient's ability to respond to the increase in erythropoiesis associated with blood loss. Surgical patients with, or at risk of iron deficiency anaemia, or with suboptimal iron stores (as defined by a ferritin level <100 μ g/L), in whom substantial blood loss is anticipated, should be treated with preoperative iron therapy.6

The management of iron deficiency involves two concurrent components: iron therapy to correct deficiency and replenish stores, and diagnosis and treatment of the underlying cause.^{9–11,15,16} Key points for the diagnosis and management of iron deficiency are highlighted in *Table 4*.

Table 4. Key messages for the diagnosis and management of iron deficiency

Diagnosis of iron deficiency

- $\bullet\,$ Serum ferritin is the most powerful test for iron deficiency 11
- Serum iron should NOT be used to diagnose iron deficiency¹⁰
- Serum ferritin:
 - <15 µg/L is diagnostic of iron deficiency¹⁰
 - between 15–30 μ g/L is highly suggestive of iron deficiency¹⁰
 - ->100 µg/L iron deficiency is unlikely (but consider functional iron deficiency)¹⁰
 - iron deficiency may be present with levels up to 60–100 μ g/L in the elderly or those with inflammation or systemic illness; C-reactive protein may be useful to identify coexisting inflammation^{6,10}
 - <100 µg/L is considered as suboptimal iron stores in patients awaiting major surgery in whom substantial blood loss is anticipated 6

Investigations

- Iron deficiency is never a final diagnosis in itself and a cause should always be ${\rm sought}^9$
- All patients with iron deficiency anaemia (IDA) should be assessed for coeliac disease.⁹⁻¹¹ For further information on assessment, including interpretation and limitations of screening tests (coeliac serology and IgA), refer to available guidelines^{15,16}
- Upper and lower gastrointestinal investigations should be considered in all postmenopausal female and all male patients where IDA has been confirmed unless there is a history of significant overt non-GI blood loss¹¹
- In premenopausal women with IDA, upper and lower gastrointestinal investigation should be reserved for those aged 50+ years, those with symptoms suggesting gastrointestinal disease, and those with a strong family history of colorectal cancer¹¹

Iron therapy

- Increasing dietary iron intake alone is inadequate to treat frank iron deficiency¹⁰
- Oral iron therapy, in appropriate doses and for a sufficient duration, is an effective first line strategy for most patients¹⁰
 - after the rapeutic doses of oral iron, reticulocytosis should occur within 72 hours, and Hb levels should rise by about 20 g/L every 3 weeks¹⁰
 - oral iron should be continued for 3–6 months beyond normalisation of haemoglobin, so that stores are replenished $^{10,11}\,$
- Patients in whom parenteral (intravenous) iron should be considered include those with:
 - demonstrated intolerance, non-compliance or lack of efficacy with oral iron, despite modification of dose, timing and frequency
 - a clinical need for rapid iron supply (eg. where there is insufficient time to correct iron deficiency before non-deferrable surgery)
 - intestinal malabsorption
 - ongoing iron (ie. blood) losses that exceed absorptive capacity
- The use of intramuscular iron is discouraged unless other approaches cannot be practically delivered $^{10}\,$
- Blood transfusion should be reserved for patients with or at risk of cardiovascular instability due to the degree of their anaemia^{10,11}

Haemostasis management

Many medications such as aspirin, clopidogrel, non-steroidal anti-inflammatory drugs, warfarin and novel oral anticoagulants such as dabigatran and rivaroxaban affect haemostasis. Complementary medicines including garlic, Ginkgo biloba, ginseng and fish oil products may increase bleeding risk^{17–19} and discontinuation before surgery should be considered. The PBM perioperative guidelines provide some guidance on which medications, under what circumstances, may be continued or when they require cessation. They also provide references to other established guidelines for management of patients on warfarin therapy. Hospitals may also have their own guidelines and pathways. Early referral is important in the management of complicated or high risk cases that may require multidisciplinary assessment in order to balance the risk of bleeding and thrombotic events. General practitioners should ensure patients are aware that their medications and complementary medicines may represent a bleeding risk, and that they provide an up-to-date list at specialist review and preoperative assessment.

Additional techniques to reduce or avoid the need for transfusion

In addition to preoperative anaemia and haemostasis management, numerous other techniques, such as acute normovolaemic haemodilution, intra- and post-operative cell salvage, and the use of pharmacological agents may be used to reduce or avoid the need for transfusion. These are further outlined in the PBM perioperative guidelines. It is essential that patients are encouraged to discuss their possible need for transfusion and the availability of additional or alternative techniques with their specialist team before surgery. This will ensure that they are able to provide fully informed consent for treatment.

Preoperative autologous donation no longer recommended

At the time of the emergence of HIV and before robust testing methods being available, predonation of a patient's own blood before surgery had been previously advocated. However, the routine use of preoperative autologous donation is not recommended, because, although it reduces the risk of allogeneic RBC transfusion, it increases the overall risk of receiving any RBC transfusion (allogeneic and autologous).⁶ Collection of predonated autologous blood should only be undertaken in specific circumstances, such as rare blood groups where blood may not be available in the general supply.²⁰

Summary

General practitioners can play a vital role in PBM by helping to ensure that available measures are adopted to reduce or avoid the need for blood transfusion. Of particular importance is the early identification, evaluation and management of anaemia and suboptimal iron stores, particularly in patients awaiting major surgery. Awareness of medications and complementary medicines that affect haemostasis will enable appropriate planning to balance the risk of bleeding and thrombotic events. Educating patients about treatment options, including blood transfusion, and their associated risks and benefits is vital for informed consent. Initiating a PBM approach at the primary care level is the first important step in ensuring optimum outcomes for patients.

Resources

Resources for health professionals

- National Blood Authority patient blood management guidelines – currently available modules and updates: www.nba.gov.au/ guidelines/review.html
- Australian Red Cross Blood Service patient blood management and anaemia management guidelines: www.transfusion.com.au
- WA Health Patient Blood Management Program

 information for health professionals: www.
 health.wa.gov.au/bloodmanagement/home
- BloodSafe clinician resources are available under clinical resources/anaemia management topics including chronic kidney disease management, macrocytosis, normocytic normochromic anaemia and iron deficiency anaemia: www.health.sa.gov.au/bloodsafe/ Default.aspx?tabid=77

Resources for patients

 Australian Red Cross Blood Service – information on anaemia and iron deficiency, having a blood transfusion and giving consent: www.mytransfusion.com.au

- WA Health Patient Blood Management Program

 information about patient blood management:
 www.health.wa.gov.au/bloodmanagement/
 home/good.cfm
- Gastroenterological Society of Australia information about iron deficiency: www.gesa. org.au/consumer.asp?cid=7&id=84
- BloodSafe patient resources iron therapy: www.health.sa.gov.au/bloodsafe/Default. aspx?tabid=86.

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