

Perioperative Anemia in the Elderly

Ajay Kumar, MD, MRCP^{a,*}, Jeffrey L. Carson, MD^b

KEYWORDS

- Perioperative Anemia • Anemia • Surgery in elderly
- Management of anemia

Anemia is characterized by less than the normal number of red blood cells (RBCs) (as a result of underproduction, increased loss, or destruction) or decreased quantity of hemoglobin (Hgb) in the blood, thereby reducing the blood's oxygen-carrying capacity.

The World Health Organization has identified less than 13 g/dL of Hgb as the cutoff value for anemia in adult men and less than 12 g/dL of Hgb for nonpregnant women.¹ Anemia is the most frequently encountered hematologic diagnosis among patients before surgery. Anemia is related to either the condition prompting the surgery or the underlying chronic medical condition. The prevalence of preoperative anemia varies widely from 5% in geriatric women with hip fractures to 75.8% in patients with Duke's stage D colon cancer.² However, a large retrospective study by Carson and colleagues³ found preoperative incidence of anemia up to 38.5%. The prevalence of perioperative anemia varies because of differences in the (1) definition of anemia in studies, (2) the types of surgeries studied, and (3) patients' comorbidities. Preoperative anemia is associated with increased risk for death, especially in patients with cardiovascular disease and in elderly patients.^{4,5}

Patients with preoperative anemia are more likely to receive allogeneic blood transfusions than patients with normal Hgb levels.⁶ In addition, preoperative anemia and blood transfusions are associated with a higher incidence of postoperative infections and longer hospital stays.⁷ Therefore, it is prudent to delay major elective surgery until the cause of anemia is identified and, if possible, treated. Evaluation begins with taking a detailed history and physical examination.

^a Internal Medicine Preoperative Assessment Consultation and Treatment Center, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44194, USA

^b Division of General Internal Medicine, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, USA

* Corresponding author.

E-mail address: kumara@ccf.org (A. Kumar).

INITIAL APPROACH

Anemia is not normal and its cause(s) should always be investigated; it is a sign of ill health. The workup should be directed toward answering the following questions:

- Does the patient have any blood loss?
- Is there any evidence of increased RBC destruction?
- Is the bone marrow suppressed?
- Is there any deficiency of iron or vitamins?

History and Physical Examination

Patients should be interviewed to detect onset of anemia, symptoms of anemia, history of previous transfusion, and any underlying disease associated with anemia. The history and physical examination should be focused to look not only for the causes for anemia but also for an increased likelihood of anemia from excessive bleeding in peri-operative period. The following are findings suggestive of anemia:

- Palpitations and tachycardia, which might suggest underlying cardiovascular decompensation
- Fatigue, angina, and dyspnea, which might suggest tissue hypoxia
- Family history of anemia, for example, sickle cell disease
- Bone pain, which might suggest an underlying myeloproliferative disorder or metastatic cancer
- History of blood transfusions, which might explain the circumstances surrounding previous blood loss
- Skin examination for pallor and petechiae
- Enlarged lymph nodes and hepatosplenomegaly, which may suggest disorders often associated with anemia
- History of nonsteroidal anti-inflammatory or anticoagulant drug use which is associated with gastrointestinal blood loss.

Diagnostic Tests

The elderly should have Hgb levels measured within 30 days before major elective surgery. If anemia surgery should be delayed unless the anemia is related to the condition for which surgery is to be performed.⁶ The evaluation focuses on the cause for anemia. The initial evaluation includes a complete blood count, peripheral smear, and corrected reticulocyte count, which will determine whether anemia is hyperproliferative from loss or destruction of RBCs or from a decrease in marrow production (eg, anemia of chronic disease). The mean corpuscular volume can help determine the etiology of anemia, but additional tests such as the following may be necessary:

- Iron (Fe) and total iron binding capacity (TIBC) or transferrin.
Fe and TIBC are low in anemia from chronic disease.
Fe is low and TIBC is high with iron deficiency anemia.
- Ferritin levels of less than 30 ng/mL in men and less than 10 ng/mL in women suggest iron-deficiency anemia.
- Serum B12 and RBC folate levels.
- Peripheral blood smear to detect morphologic changes consistent with hemolysis.
- Fecal occult blood testing to document blood loss from the gastrointestinal tract, but false-positive and -negative results are common with this test.
- Hgb electrophoresis in selected patients.

- If iron-deficiency anemia is suspected in the elderly, they should undergo an upper endoscopy and colonoscopy.
- Type and screen provides information about the patient's blood type and the presence of red cell antibodies. If the antibody screen is positive, additional tests are performed to identify the antibodies present and to rule out other clinically significant antibodies to red cell antigens. These tests can be completed within a few hours or can take days if sent out to a reference laboratory. Completion time and blood availability depends on the number of antibodies present, antibody reactivity, and frequency of the corresponding antigen in the donor population. Once clinically significant antibodies are identified, national standards require the blood bank to provide antigen-negative, cross-match-compatible units for transfusion.
- Type and cross is an order for a type and screen plus a request for a specified number of RBC units. Depending on the results of the type and screen, units may be readily available (when no clinically significant antibodies are identified) or may require special screening for antigen-negative units (when clinically significant antibodies are identified).

PATHOPHYSIOLOGY

Perioperative anemia has many potential causes (**Box 1**), including chronic blood loss, nutritional deficiencies, hematologic abnormalities, and chronic diseases. Many patients who require surgery manifest anemia of chronic disease. Anemia of chronic disease is second only to anemia caused by iron deficiency and occurs in patients who have acute or chronic immune activation.⁸ Anemia of chronic disease is an immune-mediated disease. Cytokines and cells of the reticuloendothelial system induce changes in iron metabolism blocking release of iron from the reticuloendothelial system that leads to relative iron deficiency and reduced erythropoiesis. Other factors that play a part in anemia of chronic disease are reduced erythropoietin production, and ineffective erythropoiesis in the absence of functional iron deficiency.⁹

TREATMENT

Iron and Vitamin Deficiency Anemia

Correction of iron-deficiency anemia can be easily done by supplementing iron in oral or intravenous form. Oral iron is generally well tolerated, but some patients have significant gastrointestinal symptoms and require intravenous iron supplementation. Maximum increase in Hgb levels in the treatment of iron-deficiency anemia with intravenous iron can take up to 2 weeks.¹⁰ Vitamin B12 and folate deficiency can easily be corrected by supplements.

Anemia of Chronic Disease

The availability of recombinant human erythropoietin (rHuEpo) for the treatment of anemia in selected patients offers an option to reduce or eliminate the need for RBC transfusion. Several studies have documented that the use of rHuEpo preoperatively is associated with a significant reduction in the number of blood transfusions in the perioperative period.^{9,11–15}

Despite the track record of rHuEpo in correcting anemia, new safety concerns have emerged. Patients with chronic renal insufficiency, treated with rHuEpo, to a target Hgb level of 13 g/dL, had increased mortality, and in some patients with cancers, it increased tumor progression.^{16,17} Higher risk for thromboembolism has been consistently found in various clinical settings.^{18,19}

Box 1**Causes of anemia***Decreased RBC production*

- Marrow replacement
 - Metastasis
 - Granulomas (tuberculosis)
- Marrow injury (aplastic or hypoplastic)
 - Drug induced
 - Infection
- Nutritional deficiency
 - Vitamin deficiency
- Endocrine hypofunction
 - Pituitary, adrenal, and thyroid hypofunction
 - Anemia of chronic renal failure

Deficient heme-synthesis

- Iron Deficiency Anemia

Deficient globin-synthesis

- Thalassemias
- Hemoglobinopathies

Excessive loss of RBCs

- Hemolytic anemias caused by genetically defective RBCs

Abnormal shape

- Hereditary spherocytosis,
- Hereditary elliptocytosis

Abnormal Hgb

- Sickle-cell anemia
- HbC disease

Abnormal RBC enzymes

- G6PD deficiency

Autoantibodies transfusion reactions

Microangiopathic hemolytic anemia

- Exogenous allergens, as in penicillin allergy

- Excessive loss of normal RBCs

- Hemorrhage

- Hypersplenism

- Miscellaneous diseases (eg, uremia, liver diseases, cancers)

- Mechanical trauma (eg, artificial heart valves, tumor microemboli)

The role of rHuEpo in patients who undergo surgery is uncertain, but it can be used in patients without history of cancer, thromboembolism, or uncontrolled hypertension to achieve a preoperative Hgb concentration 10 to 12 g/dL. These patients must receive prophylaxis for thromboembolism. In patients who are treated with rHuEpo, iron supplementation is generally required for an adequate response.

INTRAOPERATIVE TECHNIQUES

Intraoperative blood conservation is an important step to reduce blood transfusion in patients in whom excessive blood loss is expected. Autologous blood cell salvage (intraoperative autotransfusion) is a widely used strategy to retrieve and reinfuse shed blood after it is washed and filtered. Cell recovery devices have been used extensively in cardiac, orthopedic, vascular, and trauma surgery. The safety of cell saver devices has been studied in patients with malignancy, infections, and cases involving amniotic fluid exposure. In such cases, there is evidence supporting the use of leukocyte depleting filters.^{20,21} It is a cost-effective procedure for anemic patients when excessive blood loss during surgery is expected.

ACUTE NORMOVOLEMIC HEMODILUTION

The acute normovolemic hemodilution (ANH) procedure removes blood from patients just before surgery and replaces intravascular volume with acellular fluid (colloid or crystalloid).²² This is ideal for a patient who has a normal Hgb concentration before surgery, but is expected to have excessive blood loss and has a high likelihood of transfusion. The procedure is usually not recommended for patients with active coronary, pulmonary, renal, or liver disease severe hypertension, infection, or bacteremia.²³ ANH requires minimum preoperative preparation and can be performed at the bedside and in emergency situations.²⁴⁻²⁷ A meta-analysis by Segal and colleagues²⁸ compared the effects of hemodilution to usual care or to another blood conservation method in 42 trials. The proportion of patients receiving an allogeneic transfusion was similar in patients receiving ANH and those receiving usual care, although the absolute number of units of allogeneic blood transfused were fewer in patients undergoing ANH. The safety of the procedure and widespread adoption require additional study because only a third of studies reported on adverse effects.

SURGICAL TECHNIQUE

Intraoperative hemorrhage is a precursor to intra- and postoperative anemia. Unfortunately this is not completely avoidable, though it can be reduced. A precise surgical technique and adherence to the basic principle of surgery including initial control of hemorrhage with pressure, clamping and coagulation helps in reducing intraoperative blood loss. Hypothermia-induced coagulopathy leading to increased allogeneic blood exposure has been observed in orthopedic surgery.²⁹ Hypothermia adversely affects enzymatic activity of the coagulation cascade and induces platelet dysfunction, which leads to increased bleeding.^{30,31}

Topical hemostatic agents such as Gelfoam (The Upjohn Co. Kalamazoo, Michigan), which is a derivative of gelatin, can induce thrombosis. This can be used to stop local vascular bleeding or bleeding in an open surgical wound. Surgicel (Johnson and Johnson, New Brunswick, New Jersey) is an oxidized cellulose which provides a matrix for platelet aggregation and subsequent clot formation. If not removed in time, this can increase likelihood of wound infection.³² Fibrin glue is another commonly used hemostatic agent and is more effective than Gelfoam in reducing the

bleeding time.³³ These agents can be used to limit intraoperative blood loss and reduce the likelihood of postoperative anemia.

Blood Transfusion

The indications for perioperative blood transfusion are controversial because there is only one randomized clinical trial in adults that has evaluated restrictive versus liberal transfusion practice. Patients in ICU randomized to restrictive transfusion group (transfused when Hgb concentration < 7 g/dL) had similar mortality as patients in the liberal transfusion group (transfused for Hgb concentration < 10 g/dL).³⁴ Furthermore, the restrictive group had fewer patients who developed myocardial infarction and congestive heart failure. A second large randomized trial is underway in elderly patients with hip fracture having cardiovascular disease or other risk factors, and the results should be available in 2009.³⁵

The safety of allogeneic blood transfusion remains a concern.³⁶ Infectious risks such as HIV and hepatitis C are rare. However, newly recognized noninfectious adverse events such as transfusion-related acute lung injury and transfusion-associated cardiac overload are more common. It is unclear if allogeneic blood increases the risk of bacterial infections. New data raise the possibility that blood older than 2 weeks may not be as safe as blood stored for less than 2 weeks.³⁷

The American Society of Anesthesiology recently published guidelines³⁸ which recommend:

- No transfusion when Hgb concentration is greater than 10 g/dL
- Transfusion is usually indicated if Hgb concentration is below 6 g/dL
- In patients with Hgb concentration between 6 and 10 g/dL, transfusion is indicated if there is evidence for organ ischemia, there is potential for or actual bleeding, and there are risk factors: risk factors of inadequate oxygenation, such as poor cardiopulmonary reserve.

SUMMARY

Anemia is not normal in the elderly and when identified before surgery requires thorough evaluation. Taking a detailed history, physical examination, and laboratory evaluation usually identifies the cause of anemia. When possible, anemia should be corrected before surgery since anemic patients are more likely to require transfusion. Comprehensive perioperative blood management involves meticulous surgical technique, judicious use of erythropoietin, ANH, cell saver, and RBC transfusion.

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