



HOW DO I TREAT ANEMIA IN THE PERISURGICAL SETTING?

By Shaughn Nalezinski, MS, MLS(ASCP)^{cm}SBB^{cm}, MLS(AMT)

Department of Laboratory Medicine Transfusion Services

Concord Hospital

Concord, NH

ANEMIA AND PREVALENCE

Anemia is the insufficiency of red blood cells or the dysfunction of red blood cells, which affects oxygen-carrying capacity and tissue perfusion. The World Health Organization (WHO) defines anemia as having a hemoglobin (Hgb) of <13g/dL in men and a Hgb of <12g/dL in women.¹ Throughout the world, approximately 22.8% of individuals are anemic.² Anemia can manifest in various forms, with multiple causes, including common nutritional deficiencies. In fact, iron deficiency anemia accounts for the majority of anemia cases worldwide.³

In patients undergoing surgery, the rate of anemia varies greatly but is notably higher than the general population. In a 2016 study, Kansagra and Stefan showed that the prevalence in surgical patients varied with medical conditions.⁴ For example, in elderly patients with hip fractures, approximately 45% were found to be anemic, whereas those with advanced colon cancer had a prevalence of approximately 75%.

Anemia in the surgical setting is especially of concern due to the nature of the patient population since, generally, some comorbidities are likely to exist. In addition, surgery can exacerbate anemia by contributing to blood loss. Orthopedic surgeries, for example, carry the risk of about a 1 L blood loss perioperatively. This exacerbation of anemia puts the patient at a higher risk of needing a blood transfusion during admission.⁴

OUTCOMES WITH ANEMIA

In a 2021 study, Bulte et al. found an association between moderate to severe anemia and the length of hospital stay in non-cardiac patients. They found that patients who were anemic were more likely to have a longer duration in the hospital. When correcting confounding variables in their cohort, the authors found that patients with preoperative anemia had an independently increased hospital stay ($P < 0.001$).⁵ In addition to increased hospital admissions, those with perioperative anemia also had an increased risk of postoperative complications and an increased risk of mortality.³ Even patients with mild anemia perioperatively had an increase in postoperative morbidity and mortality when confounders were adjusted.

Perioperative anemia tied with surgical blood loss increases the need for allogeneic blood transfusions. Munoz et al. found that perioperative anemia was a major independent positive predictive factor for the need for perioperative blood transfusions. Critically ill and surgical patients who received blood – even a single unit of blood – had an increased risk of mortality, wound problems, pulmonary complications, postoperative renal dysfunction, systemic sepsis and composite morbidity.³

PERISURGICAL ANEMIA

Preoperative testing is important in identifying those with anemia before surgery. A screening risk assessment should be used to identify those at an increased risk so that testing can occur earlier. Earlier detection of anemia is important for treatment before the patient's operation. Patient risk factors that should be considered are active malignancy, chronic kidney disease, heart failure, inflammatory bowel disease, recent unintentional weight loss and chemotherapy treatment. Surgical factors should also be considered, such as if the patient undergoes major abdominal surgery, hepatic resection, or if the estimated blood loss (EBL) is >500 mL.⁶

Laboratory evaluation of anemia should start with a complete blood count. This provides the patient's Hgb level, mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC). Hgb levels and MCV can help determine which testing route the clinician should take to uncover the causative agent of their anemia. For example, low Hgb and low MCV indicate microcytic anemia. Iron deficiency anemia is the most common cause worldwide and is microcytic anemia. Therefore, iron studies should be done to determine which therapy would be best to correct a patient's anemia before their operation. Other studies include reticulocyte counts and may include a reticulocyte hemoglobin concentration. A normal reticulocyte count in the presence of anemia may indicate that the bone marrow response is inadequate to correct anemia. A reticulocyte hemoglobin can give insight into iron incorporation in erythropoiesis in iron-deficient states.

Peripheral blood smear evaluation can also be beneficial when investigating the cause of anemia. For example, polychromasia, hyper-segmented neutrophils, ovalocytes and microcytes can be observed on the peripheral smear. These morphological findings have been associated with different forms of anemia. Other laboratory tests for anemia include ferritin, total iron binding capacity (TIBC), B12 and folate levels.

The timing of presurgical testing is critical to treating patients before surgical interventions, and starting three to four weeks before the procedure is ideal. However, if iron therapy or erythropoiesis-stimulating agents are to be used, testing is likely to have the most benefit if it is conducted four to five weeks before the operation.⁶

IRON

Iron can be taken by patients orally and parentally, with the latter having the most efficacy for the short-term correction of iron deficiency anemia (IDA). Functional iron deficiency can increase patients' inflammatory processes. In addition, those with anemia or chronic disease have decreased hepcidin, a regulatory iron hormone. Intravenous (IV) administration is most effective due to the iron bypassing hepcidin-regulated mechanism for absorption.⁶ IV iron administration also negates potential side effects, such as abdominal cramping, nausea and black stools, which may deter patients from continuing therapy. Iron dosing recommendations for different formulations can be seen in Table 1.

B12

Vitamin B12 supplementation can occur both orally and intramuscularly. Both methods are effective and safe for most patients. In patients with chronic gastric inflammation or other gastrointestinal issues, intramuscular B12 administration is preferred due to an increased chance of absorption. Intramuscular dosing is 1,000 ug per week for eight weeks, and retesting would be needed following eight weeks and reevaluation of dosing. Oral dosing of B12 is typically 1,000 ug per day. Follow-up must be maintained to ensure adequate repletion of B12.⁶

FOLATE

Folate (vitamin B6) supplementation is generally done through oral supplements. In most cases, 400 ug daily is sufficient for red blood cell production. It can be purchased over the counter and is relatively cheap. As with B12, follow-up is vital to check for adequate repletion and red cell production.⁶

ERYTHROPOIESIS-STIMULATING AGENTS (ESAs)

ESAs are synthetic analogs of endogenously produced erythropoietin. The administration of ESAs is beneficial, specifically in patients undergoing orthopedic surgery.⁶ While there is a debatable risk of venous thromboembolism (VTE) following ESA use, it has not been shown to increase VTE risk in this patient population. Of note, ESAs should be avoided in specific patient populations, such as patients with cancer, when deep vein thrombosis (DVT) prophylaxis is omitted. There has been an increased risk of VTE in patients with cancer and in patients with myelodysplastic syndrome, who may be at an increased risk for VTE following ESA administration at higher doses. There is also a concern that ESA administration may worsen certain malignancies, although this has not been proven.

Before initiating ESA therapy, a patient's iron store must be checked. Iron stores should be adequate before starting treatment since erythropoiesis is unlikely to occur in the setting of iron deficiency. It is recommended that patients who are identified as candidates for ESA therapy receive at least 600 U/kg three weeks before their procedure to correct their anemia adequately.

SUMMARY

Anemia in the perisurgical setting has been linked to transfusion and poor outcomes. It is essential to identify populations at risk for anemia and screen them early. At-risk populations include those with chronic kidney disease, recent blood loss (i.e., gastrointestinal bleeding), the elderly, cancer, inflammatory disease and patients who have had bariatric surgery. It is recommended that presurgical testing be performed at least three to four weeks before the scheduled procedure. This ensures enough time to uncover the etiology of anemia and correct it. Follow-up testing must be performed to confirm it has been corrected. If anemia is still present, non-emergent surgeries should be postponed.

Table 1.: IV iron formulations and dosing considerations.^{6,7}

Formulation	Dose	Infusion Duration (mins)
Injectafer (carboxymaltose)	750 mg x 2 doses >4 weeks between doses	60
INFeD (iron dextran)	1,000 mg once	90
Feraheme (ferumoxytol)	510 mg x 2 doses >3 days between doses	60
Ferrlecit (ferric gluconate)	250 mg x 4 doses maximum 1 dose/week	120
Venofer (iron sucrose)	1,000 mg divided into 3 doses over 28 days	90
Monoferic (ferric derisomaltose)	1,000 mg as single dose or 3 doses of 500 mg over 7 days	≥30

-
1. World Health Organization. (n.d.). *Anaemia*. World Health Organization. https://www.who.int/health-topics/anaemia#tab=tab_1
 2. Gardner W, Kassebaum N. Global, Regional, and National Prevalence of Anemia and Its Causes in 204 Countries and Territories, 1990–2019. *Current developments in nutrition*. 2020;4(Supplement_2):830-830. doi:10.1093/cdn/nzaa053_035
 3. Muñoz M, Gómez-Ramírez S, Campos A, Ruiz J, Liumbruno GM. Preoperative anemia: prevalence, consequences, and approaches to management. *Blood transfusion = Trasfusione del sangue*. 2015;13(3):370-379. doi:10.2450/2015.0014-15
 4. Kansagra AJ, Stefan MS. Preoperative Anemia: Evaluation and Treatment. *Anesthesiology clinics*. 2016;34(1):127-141. doi:10.1016/j.anclin.2015.10.011
 5. Bulte CSE, Boer C, Hemmes SNT, et al. The effects of preoperative moderate to severe anemia on length of hospital stay: A propensity score-matched analysis in non-cardiac surgery patients. *European Journal of Anaesthesiology*. 2021;38(6):571-581. doi:10.1097/EJA.0000000000001412
 6. Borgmeier E, Lawrence H, Morton C, McEvoy MD. Perioperative anemia management. *International anesthesiology clinics*. 2022;60(1):1-7. doi:10.1097/AIA.0000000000000350
 7. “UpToDate.” www.uptodate.com, www.uptodate.com/contents/ferric-derisomaltose-iron-isomaltoside-drug-information?topicRef=7148&source=see_link#. Accessed 15 June 2023. (Subscription required)