Q: Why treat anemia in the preoperative period of joint replacement surgery with erythropoietin?

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A: Recombinant human erythropoietin (epoetin alfa) is an effective therapy approved by the US Food and Drug Administration (FDA) to treat preoperative anemia in patients undergoing knee or hip replacement surgery.

Anemia is linked to poor outcomes

Anemia in the preoperative period is a known predictor of adverse outcomes in surgical patients. Carson et al[1] studied 125 consecutive patients who declined blood transfusions and found that operative mortality was 16 times greater in patients with hemoglobin levels less than 8 mg/dL than in patients with higher hemoglobin levels. Other studies suggest that it is not the anemia itself that is associated with increased mortality, but the practice of treating anemia with blood transfusions.[2]

Blood transfusion used most often, alternatives needed

Allogenic blood transfusion is the most commonly used technique in the United States to correct perioperative anemia. Although several methods are available to reduce the need for blood transfusion, the use of allogenic blood remains very high; for example, 47,456 units of blood products were used in the perioperative period of various orthopedic surgeries at the Cleveland Clinic in 2004.

In the next decade, with the aging of the population, the number of major joint replacements to be performed annually will increase, likely leading to an

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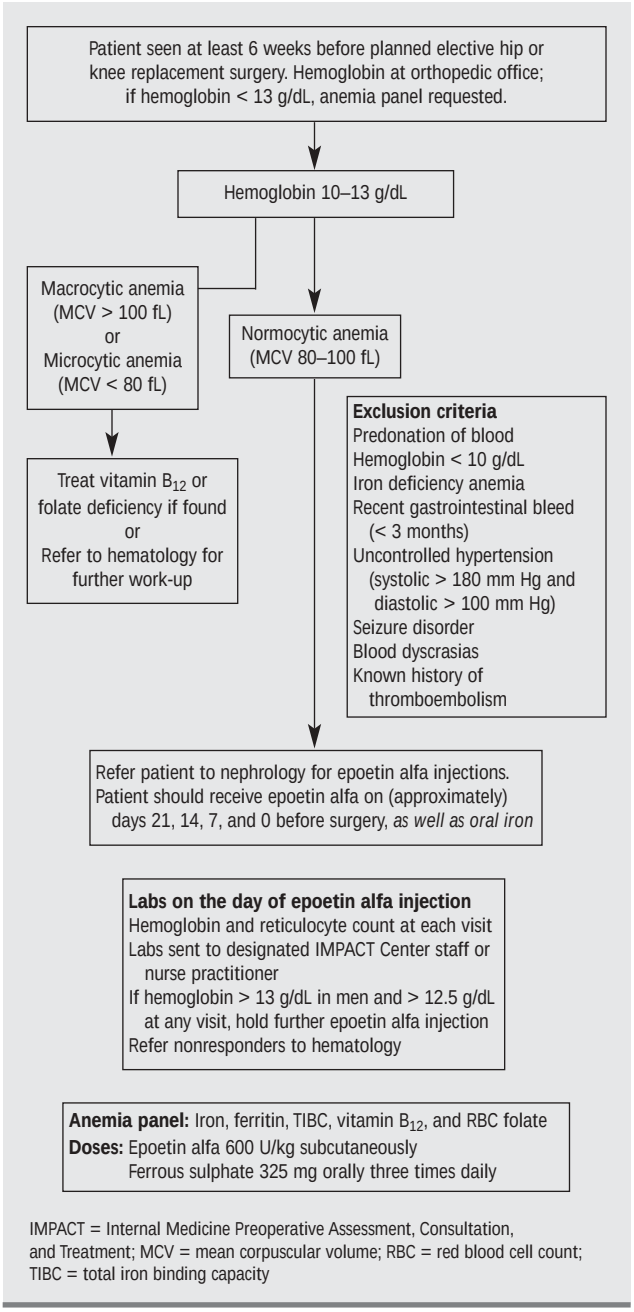

FIGURE. Protocol for management of preoperative anemia at the Cleveland Clinic.

increase in the demand for blood products. Due to the fluctuating supply and the costs and risks associated with the administration of blood products, searching for potential alternatives to transfusions is imperative.

Because blood loss associated with orthopedic surgery is predictable, the application of a carefully designed blood management program is appropriate. However, the usefulness of autologous donations and cell saver machines is limited by incomplete utilization of predonated blood and high cost. Furthermore, allogenic blood transfusions carry certain risks, in particular ABO incompatibility caused by administrative error and transfusion-related lung injuries.[3] Exposure to leukocytes in allogenic blood can also cause immunosuppression.[4] In a large prospective study of 6,301 patients undergoing noncardiac surgery, Dunne et al[5] concluded that the incidence of perioperative anemia in surgical patients is high and is related to an increase in blood utilization. These factors are associated with an increased risk for perioperative infection and other adverse outcomes (including death) in surgical patients.

In a large study by Bierbaum et al,[6] blood management data were collected prospectively on patients who had undergone total hip replacement and knee replacement. Fifty-seven percent of the patients undergoing hip replacement and 39% of the patients undergoing knee replacement received blood transfusions. Patients who were transfused were more likely to have infections, fluid overload, and an increased length of hospitalization compared with patients who did not receive transfusions. The Orthopedic Surgery Transfusion Hemoglobin European Overview study from 225 centers in Europe produced similar results.[7] In this study, allogenic transfusion was associated with a higher rate of wound infection than autologous transfusion (4.2% vs 1%, respectively).

Treatment of anemia and blood conservation

Treatment of perioperative anemia has been shown to decrease the need for transfusion and to improve perioperative outcomes such as postoperative infections, length of stay, and mortality in patients undergoing joint replacement surgery. The efficacy of preoperative erythropoietin therapy for increasing patients' hemoglobin concentrations and reducing exposure to allogenic red blood cell transfusion in orthopedic surgery has been demonstrated in several double-blind randomized clinical trials.[8–11] Synthetic erythropoietin was approved by the FDA and has been used for almost 9 years in orthopedic surgeries as a method to improve hemoglobin levels in anemic patients undergoing surgery, and thus to decrease blood transfusions. Several centers in the United States have adopted this novel therapy to reduce the use of blood transfusions.

At the Cleveland Clinic, patients selected for a blood conservation protocol (Figure) with erythropoietin are eligible for four subcutaneous injections of epoetin alfa (600 U/kg) at days 21, 14, and 7 before surgery and on the day of surgery. Exclusion criteria for preop-

erative erythropoietin treatment are hemoglobin of less than 10 g/dL, iron deficiency anemia, recent gastrointestinal bleed (within 3 months), uncontrolled hypertension, seizure disorder, predonation of blood, blood dyscrasias, and history of thromboembolism.

Reticulocyte count, hemoglobin, and blood pressure should be checked prior to each injection. Iron deficiency may occur during erythropoietin therapy. Normal ferritin but low transferrin saturation may be observed due to an inability to mobilize iron stores rapidly enough to keep pace with the increased erythropoiesis. Supplemental oral or intravenous iron supports erythropoiesis and prevents iron store depletion.

Summary

Treatment of anemia in the perioperative period of major orthopedic surgery decreases the need for blood transfusion and improves perioperative outcomes. Use of epoetin alfa in this setting is FDA-approved and provides significant benefit to qualified and carefully chosen patients.

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