

Strategies for Minimizing the Use of Allogeneic Blood During Orthopedic Surgery

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Abstract

Selected orthopedic surgical procedures, such as total joint arthroplasty and spinal instrumentation, have some of the highest perioperative transfusion rates of all surgical procedures. Blood transfusions carry the risk of complications, including the transmission of disease, immunomodulation, and hemolytic and non-hemolytic reactions. Strategies that reduce or remove the risk of allogeneic transfusion include preoperative autologous donation, acute normovolemic hemodilution, perioperative cell salvage techniques, deliberate hypotension, and pharmacologic interventions. This paper will review the current status of these therapies in the orthopedic surgical patient.

Key Words: Orthopedic surgery, allogeneic blood transfusion, hemodilution, red cell salvaging techniques.

Preoperative Autologous Donation

PATIENTS MAY CHOOSE to have their own (i.e., autologous) blood processed and stored in the weeks prior to their intended surgery. While advanced age had been considered a relative contraindication to predonation because of the presence of anemia and concurrent diseases, a study of 1,073 patients over 65 years of age revealed an incidence of cardiac and vasovagal complications of only 0.6% (1). In fact, studies of predictors of vasovagal reactions during blood donations reveal that younger age, lower weight, and first-time donations, rather than repeat donations, were the independent predictors for the risk of vasovagal reactions (2). Anginal and vasovagal events requiring hospitalization after blood donation do occur at a 12-fold higher rate for autologous donation (0.006%) than for allogeneic donation (0.0005%), with first time donation in the autologous group being, again, identified as a risk factor (3).

The availability of autologous blood does not ensure that the patient will not experience adverse reactions associated with transfusion. Over a 6-year period, the experience of one

large academic medical center revealed that 12 of 27,859 (0.0435%) transfusion reactions were associated with preoperative autologous donation (PAD) and transfusion. These reactions included one episode of acute hemolytic transfusion reaction secondary to clerical error and four allergic transfusion reactions (two of which occurred in patients who had a history of allergy to plastic and/or latex, which are found in blood collection bags). Five febrile non-hemolytic reactions and two non-febrile, non-hemolytic reactions occurred, but were not associated with positive blood cultures (4).

PAD has been shown to alter transfusion patterns. Early studies demonstrated that the availability of autologous red cells resulted in more conservative approaches to transfusion. PAD was effective in protecting 77.6% of 134 patients undergoing orthopedic surgical procedures from exposure to allogeneic blood (5). More recently, several studies have found that even though allogeneic transfusion rates were greater in patients who did not predonate blood, overall transfusion occurred more frequently in those who had PAD than in those who did not (6, 7). This is probably related to lower preoperative hematocrits in those patients who predonated, and may reflect a more liberal transfusion policy when autologous blood is available. The Practice Guidelines for blood component therapy (8), developed by the American Society of Anesthesiologists Task Force, state that "the indications for transfusion of autologous red blood cells may be more liberal than for allo-

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genic red blood cells because of the lower (but still significant) risks associated with the former.”

PAD in orthopedic procedures has not been determined to be cost effective, with a calculated cost of \$235,000 per quality-adjusted year of life saved by avoidance of transfusion-associated infectious disease (9). It is more expensive to produce an autologous unit, due to the costs involved with collection (scheduling donations, longer screening interviews of patients with complicated histories), special labeling, and storage considerations. Costs are also incurred with the disposal of unused PAD units, more than half of which are discarded. Patients may not meet requirements of community volunteer donors. Units may become outdated since they are donated weeks before the planned procedure and must be available until the patient is discharged from the hospital. Healy et al. found PAD to be cost-effective if one considers the expense incurred by longer hospitalizations necessary to treat postoperative infections that result from the immunosuppressive effects of allogeneic blood (10). The incalculable benefits associated with decreased anxiety of patients regarding allogeneic transfusion will continue to make PAD a principal intervention.

Acute Normovolemic Hemodilution

Acute normovolemic hemodilution (ANH) requires the withdrawal of whole blood at the beginning of a surgical procedure and its simultaneous replacement with crystalloid or colloid solution, to maintain intravascular volume. Blood is removed into sterile citrate-containing bags according to the formula by Gross:

$$\text{EBV} \times \frac{\text{volume to be removed} = \text{initial Hct} - \text{minimum allowable Hct}}{\text{average Hct}}$$

where EBV is estimated blood volume and Hct is hematocrit (11).

The units of whole blood are stored with the patient, thereby eliminating the possibility of clerical error. It is thought that dilution decreases the number of red cells lost for each volume of blood shed during surgery. Thus, ANH conserves red blood cells. This technique is inexpensive and convenient, and it preserves all of the components of autologous blood.

Decreased viscosity of blood with a hematocrit of 5 g/dL is associated with decreased sys-

temic vascular resistance and increases in heart rate, stroke volume and cardiac index in healthy volunteers (12). Reductions of hemoglobin to 7 g/dL resulted in no detectable changes in cognitive function in 9 healthy volunteers, but further reductions to 5 g/dL did cause reversible increases in reaction times and impairments in immediate and delayed memory (13).

Patients undergoing surgery, with or without ANH, experience small changes in prothrombin time and partial thromboplastin time, and increased concentrations of prothrombin fragment 1 β 2 and thrombin-antithrombin III complex (markers for coagulation), and D-dimer and plasmin-alpha 2-antiplasmin complex (markers for fibrinolysis). Surgery itself can activate both the coagulation and fibrinolytic systems secondary to inflammation and to the mobilization of fat and bone debris. Thus, ANH has not been implicated in the derangement of hemostasis that accompanies it (14). Interestingly, Bombardini et al. found a 13-fold reduction in fatal pulmonary thromboembolism in 4,653 patients who underwent elective orthopedic surgery with ANH, to hemoglobin levels > 6 g/dL, compared with a non-ANH cohort (15). This may be secondary to the depletion of coagulation factors, increased regional blood flow or improved rheological properties of the blood.

Ness et al. randomized 50 patients to donate PAD of 3 units of red blood cells or to undergo ANH prior to radical retropubic prostatectomy (16). They found that ANH could safely replace or augment PAD as a means of decreasing the use of allogeneic blood, and they consider their results applicable to any surgical procedure in which a 1,000 mL blood loss is anticipated. In a randomized trial of patients undergoing total knee arthroplasty who predonated either one unit of blood for unilateral, or two units for bilateral knee procedures, or who underwent ANH to a hematocrit of 28%, Good-nough et al. found no differences in the amount of allogeneic blood transfusions among the PAD and ANH cohorts, for all 32 patients (17). Conversely, a meta-analysis of all 24 eligible prospective randomized trials (1,218 patients) comparing ANH with control groups was undertaken. ANH effectively reduced the likelihood of exposure to at least 1 unit of allogeneic blood in cardiac and miscellaneous procedures, but not in orthopedic surgery. The overall results of this analysis were inconclusive since sample sizes in the trials were small, variable amounts of blood were withdrawn (18), and tri-

als involving different surgical procedures had to be pooled.

Perioperative Red Cell Salvage

Perioperative red cell salvage (PCS) is a technique that has been widely used in the United States and Europe since the 1970s. It involves the collection and reinfusion of red cells lost during and after surgery. Intraoperative salvage during orthopedic surgical procedures involves washing prior to reinfusion to remove the bone, fat, hemolytic byproducts, methylmethacrylate monomer, and other debris. The use of this technology had been shown to be effective in reducing allogeneic blood use, and also reducing the risk of transmission of infectious disease and preserving the allogeneic blood reserves (19). The use of allogeneic blood was investigated in a meta-analysis of 16 studies in which patients were randomized either to undergo, or not to undergo, PCS for orthopedic surgery. Huet et al. found that devices that wash, or do not wash, salvaged blood both decrease the proportion of patients who require allogeneic transfusion (20).

Advantages of PCS include avoiding the cost and inconvenience of repeated preoperative donations and of discarding blood. Its use is precluded when blood is contaminated with bacteria or tumor. Hansen et al. recovered malignant cells in blood salvaged from 57 of 61 patients undergoing oncologic surgery; only 26% of those patients had evidence of circulating malignant cells (21). He showed, *in vitro*, that irradiation of salvaged blood with gamma radiation was effective in inactivating tumor cells from salvaged blood (22). Continued research may provide a basis for the use of cell salvage during orthopedic oncologic procedures.

Postoperative blood salvage devices collect blood from surgical drains, with reinfusion without processing; this blood may contain cytokines, free hemoglobin and debris. The utility of postoperative devices had been challenged by Umlas et al. (23), who found that in 51 patients undergoing hip or knee arthroplasty, the red blood content of drainage of the first 6 postoperative hours was small (55 ± 29 mL for hip and 121 ± 50 mL for knee replacements). They determined that the potential annual national expenditure for 6-hour collections of this low volume of blood return would be approximately \$31–35.5 million dollars. Thus, the cost of the devices does not justify routine use, and may only be indicated for use during bilateral joint replacements.

Deliberate Hypotension

Controlled hypotensive anesthesia can be achieved by decreasing vascular tone or cardiac output. The reduction in mean arterial pressure (MAP) has been associated with reduced blood loss and relatively bloodless operative fields, which may contribute to decreased operative times. In orthopedic procedures, another potential advantage is that the reduced amount of blood in the cement-bone interface during total joint arthroplasty may improve the quality of fixation of the prosthesis to the bone.

Hypotensive techniques have been shown to be particularly effective in reducing transfusion requirements in patients undergoing spinal surgery. One hundred forty-five patients undergoing spinal surgery, in whom the mean arterial pressure (MAP) was reduced by 20 mm Hg, experienced a 50% reduction in blood loss and a 36% reduction in the need for blood replacement (24). Lawhon et al. studied 264 posterior spinal fusions in adults in whom hypotension to a MAP less than 80 mm Hg was achieved using nitroprusside or trimethaphan; they found that blood loss was reduced by 33% (25).

Greater levels of hypotensive anesthesia have been advocated to further decrease blood loss. Sharrock et al. (26) randomized 40 patients undergoing primary total hip arthroplasty to target MAPs of 50 or 60 mm Hg. They found a significant decrease in intraoperative blood loss in the 50 mm Hg group, with subjective improvements in the amount of surgical bleeding during the dissection of the hip joint and reaming of the femur and acetabulum. Hypotensive epidural anesthesia to MAPs of 45–55 mm Hg has been shown not to affect cognitive function, including memory, psychomotor and language skills, in a study of elderly patients undergoing elective primary total hip replacement (27).

Complications of hypotensive techniques include reactionary hemorrhage, persistent hypotension, and cardiac ischemic injury. Ischemic optic neuropathy (ION) has been described following orthopedic (particularly spinal) surgery (28–30). Etiologies of ION may include lower mean blood pressure (from deliberate hypotension) and increases in intraocular pressure (from positioning) which could result in lower perfusion pressure to the optic nerve head. Hypoxia leads to destruction of axonal integrity, and free radicals that accumulate during reperfusion from ischemia may further damage the optic nerve. Patients who have a small cup-to-disk ratio (associated with

compression of structures secondary to swelling) may be anatomically predisposed to developing ION (31). The American Society of Anesthesiologists has created a postoperative visual loss registry to collect information regarding ocular complications from non-ophthalmologic surgery in an attempt to determine the parameters that contribute to the occurrence of ION.

Pharmacological Interventions

Recombinant human erythropoietin is a glycoprotein that stimulates erythropoiesis. Four hundred ninety patients who were scheduled to undergo total joint arthroplasty were randomized to either preoperative erythropoietin or PAD groups (32). The patients who received erythropoietin had fewer transfusions with allogeneic blood and had significantly higher mean hemoglobin levels both preoperatively and on the first postoperative day. The widespread use of erythropoietin, however, is limited by its high cost. Economic analysis revealed that use of erythropoietin alone in orthopedic surgery patients led to only modest incremental benefit compared with no intervention. Thus, the routine use of erythropoietin is not justified (33).

Antifibrinolytic agents have been employed to reduce blood loss during orthopedic surgery. A single dose of 10 mg/kg of tranexamic acid administered to patients undergoing total knee arthroplasty, prior to the release of the tourniquet, was associated with a significantly decreased mean blood loss and the need for fewer transfusions (34, 35). Aprotinin, a serine protease inhibitor, is usually administered as 2 million kallikrein inhibitor units (KIU) prior to surgery. Lower doses have proven effective in reducing blood loss during cardiac surgery (36), but doses of 20,000 KIU/kg do not seem to be effective for patients undergoing primary unilateral hip arthroplasty (37).

Combination Therapies

Multiple studies have looked at the advantages of combining blood conservation strategies. The use of erythropoietin allows the safe predonation of more autologous units of blood than can be deposited without it (38). The combined use of PCS, PAD, and hypotensive anesthesia prevented the need for allogeneic blood in 50 patients who underwent spinal instrumentation and fusion (39). Blais et al. added the use of apheresis (red cells, plasma and platelet concentrates) to ANH and intraop-

erative cell salvage, and compared this combination of techniques to both the use of intraoperative cell salvage alone and to a retrospective cohort of patients who received conventional transfusion therapy. They found that the combination of strategies decreased the quantity not only of allogeneic red cells transfused, but also of other blood products in those patients undergoing reconstructive spinal surgery (40). Schmied et al. (41) looked at the effect of red cell scavenging, hemodilution and active warming in 821 elective total joint arthroplasties. Both univariate and regression analyses indicated that each treatment contributed to a more than twofold reduction in transfusion requirements. By combining PAD, PCS, and hemodilution, Borghi et al. were able to restrict the use of allogeneic blood to only 184 of 2,303 (8%) of patients undergoing major orthopedic procedures over the last twenty years (42).

In the future, combined therapies may include "augmented acute normovolemic hemodilution." This term describes the use of one of the new oxygen-carrying solutions (either stroma-free hemoglobin or perfluorocarbon emulsions) instead of currently-available crystalloids and colloids for maintaining intravascular volume during ANH.

Conclusions

Many therapies and techniques are available to prevent or reclaim the blood lost during orthopedic surgical procedures. Understanding the advantages and limitations of these interventions permits their rational use and can markedly decrease or obviate the need for allogeneic transfusion. Cooperation between anesthesiologists and surgeons in identifying and enrolling patients is an integral part of a successful blood conservation program.

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