Review Article

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# MANAGEMENT OF ANEMIA: BLOOD LOSS IN ORTOPAEDIC SURGERY

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**Abstract**

Major orthopaedic surgery and high energy trauma are often responsible of acute bleeding. Long bones and pelvis fractures are correlated with increased blood loss. The final consequence of a mayor bleeding is hypovolemic shock. The reduced oxygen tension of tissue could be responsible of heart attack, arrhythmia, ictus, multi organ deficiency. For these reasons, it is important to immediately recognize and correct all potential bleeding in order to avoid complications. In orthopaedics the elective treatments in the management of hypovolemia are different. Blood banks and allogenic blood components have had an important impact on operative treatment and health care worldwide. Erythropoietin has been shown in numerous studies to be effective in raising the preoperative hematocrit and reducing the need for allogenic transfusion in major orthopaedic surgery. Erythropoietin may be as good as or better than preoperative autologous donation. The aim of the present article is to describe a simple review of the literature based on our experience

**Keywords:** anemia, erythropoietin, bleeding, hypovolemia, blood loss.

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## Introduction

Anemia is a potent risk factor for mortality and morbidity in surgical patients, and its management has begun to shift away from allogenic blood transfusion in recent years. The serious blood loss, which can occur during major orthopaedic operations, constitutes perioperative blood management one of the main problems for an orthopaedic surgeon is to solve. Also High trauma is often responsible for acute bleeding carries a high cost both economically and socially. The bleeding of the trauma and of the orthopaedic surgery encourage the development of perioperative anemia, has been associated with increased morbidity and mortality, especially in older patients advanced, given the limited response capacity of compensatory mechanisms (1). The average adult has a total blood volume of approximately 5,000 to 6,000 ml (milliliters) and can usually lose 500 ml of blood without serious or lasting effects; but, if the loss reaches 1,000 ml or more, serious acute consequences may result. The reduced tissue oxygen tension may be responsible for heart attack, arhythmia, stroke, multi organ deficiency. For these reasons, it is important to immediately recognize and correct all potential bleeding in order to avoid complications. Haemorrhagic classification is very helpful for the treatment management. Classes of hemorrhage have been defined, based on the percentage of blood volume loss. However, the distinction between these classes in the hypovolemic patient often is less apparent. Treatment should be aggressive and

| | Class I | Class II | Class III | Class IV |
|---|---|---|---|---|
| Blood Loss | Up to 750cc | 750-1500cc | 1500-2000cc | >2000cc |
| % Volume | Up to 15% | 15-30% | 30-40% | >40% |
| Pulse Rate | <100 | >100 | >120 | >140 |
| Blood Pressure | Normal | Normal | Decreased | Decreased |
| Pulse Pressure | Normal or increased | Decreased | Decreased | Decreased |
| Respiratory Rate | 14-20 | 20-30 | 30-40 | >35 |
| Urine Output (cc/hr) | >30 | 20-30 | 5-15 | Negligible |
| Mental Status | Slightly anxious | Mildy anxious | Anxious, confused | Confused, lethargic |
| Fluid Replacement | Crystalloid | Crystalloid | Crystalloid & blood | Crystalloid & blood |

*Tab.1:* Classification of hemorrhagic shock.

directed more by response to therapy than by initial classification (Table 1).

1) Class I hemorrhage (loss of 0-15%):
   - In the absence of complications, only minimal tachycardia is seen.
   - Usually, no changes in BP, pulse pressure, or respiratory rate occur.
   - A delay in capillary refill of longer than 3 seconds corresponds to a volume loss of approximately 10%.
2) Class II hemorrhage (loss of 15-30%):
   - Clinical symptoms include tachycardia (rate >100 beats per minute), tachypnea, decrease in pulse pressure, cool clammy skin, delayed capillary refill, and slight anxiety.
   - The decrease in pulse pressure is a result of increased catecholamine levels, which causes an increase in peripheral vascular resistance and a subsequent increase in the diastolic BP.
3) Class III hemorrhage (loss of 30-40%):
   - By this point, patients usually have marked tachypnea and tachycardia, decreased systolic BP, oliguria, and significant changes in mental status, such as confusion or agitation.
   - In patients without other injuries or fluid losses, 30-40% is the smallest amount of blood loss that consistently causes a decrease in systolic BP.
   - Most of these patients require blood transfusions, but the decision to administer blood should be based on the initial response to fluids.
4) Class IV hemorrhage (loss of >40%):
   - Symptoms include the following: marked tachycardia, decreased systolic BP, narrowed pulse pressure (or immeasurable diastolic pressure), markedly decreased (or no) urinary output, depressed mental status (or loss of consciousness), and cold and pale skin.
   - This amount of hemorrhage is immediately life threatening

**Treatment**

In orthopaedics the elective treatments in the management of hypovolemia are different. Blood banks and allogenic blood components have had an important impact on operative treatment and health care worldwide (2). In orthopaedic operations, packed red blood cells are the most common unit of transfusion. These cells are available in units of 225 to 300 milliliters and are composed of concentrated erythrocytes, leukocytes, and platelets in about eighty milliliters of plasma and anticoagulant. Usually, 100 milliliters of normal saline solution with adenine is combined with the packed red blood cells and plasma to increase the shelf life to forty-two days. Allogenic blood is carefully screened according to standards established by the American Association of Blood Banks (3) (Table 2) The indications for pre and postoperative transfusion involve multiple factors. According to the traditional ten/thirty rule, transfusion is recommended when the level of hemoglobin is less than ten grams per deciliter (110 grams per liter) or the hematocrit is less than 30 per cent. This rule was questioned at the National Institutes of Health Consensus Development Conference (4) in 1988. The recommendation at the Conference was for a lower level of hemoglobin (eighty grams per liter) as the indication for transfusion, and it was suggested that decisions regarding transfusion should include an

assessment of clinical needs and symptoms rather than be based on laboratory values alone. The most common reaction to blood transfusion is a febrile response associated with chills and generalized discomfort or even severe pain. Febrile reactions, which occur after 1 to 3 per cent of approximately four million allogenic transfusions done each year, can be caused by an antibody response against leukocytes in the donated blood (5). A less common reaction to transfusion is an allergic or immune response to donated blood, which produces chills, fever, and urticaria. This reaction is usually seen in patients who have an IgA deficiency; rarely, it progresses to anaphylaxis (6). Immediate hemolysis is a serious and sometimes fatal reaction that occurs in association with one of every 100,000 transfusions of allogenic blood. The symptoms and physical findings include fever, chills, chest pain, circulatory collapse, hemoglobinuria, and coagulopathy (7). The transmission of infectious disease, including acquired immunodeficiency syndrome and hepatitis, is the most feared risk associated with the transfusion of allogenic blood. The reported risk of transmission is one in 200,000 to one in 800,000 for the human immunodeficiency virus (8), one in 200,000 for hepatitis B, and one in 3000 to one in 5000 for hepatitis C (9) (Table 3). Other infectious diseases associated with transfusion of allogenic blood include human T-cell lymphotrophic virus, human immunodeficiency virus-2, malaria, cytomegalovirus, babesiosis, toxoplasmosis, and Chagas disease. These diseases are rare in Europe, but are more common in third-world countries (10). The safest and most effective way to treat blood loss is to give a patient his or her own blood. Preoperative donation of autologous blood is useful before elective operative procedures that have a known potential for blood loss, such as spinal arthrodesis and joint replacement. The advantages include decreased use of banked blood, a decrease in erythrocyte mass and in loss of erythrocytes at the time of the operation, and stimulation of erythropoiesis. However, preoperative autologous donation has been associated with scheduling difficulties: the limited shelf life of the blood, perioperative anemia (11), and bacterial contamination (12). Although it is commonly perceived that blood from a designated donor is superior to allogenic blood, blood from a designated donor may actually be associated with greater risks of infection than allogenic blood (13). Recent techniques have been employed in order to optimize blood conservation, including the use of pharmacologic agents (14), hemodilution and perioperative blood salvage (15). The most extensively evaluated pharmacologic agent is recombinant human erythropoietin. Use of recombinant human erythropoietin (rhEPO) for treatment of pre-operative anemia in anticipation of orthopaedic surgical blood loss has become a routine practice. Use of rhEPO to help manage

| Blood Test | Disease to Be Detected |
|---|---|
| Human immunodeficiency virus-1, human immunodeficiency virus-2 | Acquired immunodeficiency syndrome |
| Human T-cell leukemia/lymphoma virus-1 | Human T-cell leukemia/lymphoma virus or human T-cell leukemia/lymphoma virus-1-associated myelopathy |
| Hepatitis B Ag | Hepatitis B |
| Hepatitis B core Ab | Non-A, non-B hepatitis |
| Serum alanine transaminase | Hepatitis |
| Hepatitis C Ab | Hepatitis C |
| Syphilis serology | Syphilis |

*Tab. 2:* Routine screening practices for allogenic blood donation.

| Risk | Prevalence |
|---|---|
| Transfusion reaction | 5 per cent |
| Fatal hemolytic | <1:1,000,000 |
| Non-fatal hemolytic | 1:25,000 |
| Fever or urticaria | 1 to 3:100 |
| Transmission of disease | |
| Human immunodeficiency virus-1 | 1:200,000 to 1:800,000 |
| Hepatitis B | 1:200,000 |
| Hepatitis C | 1:3000 to 1:5000 |
| Immunomodulation | |
| Infection | 20 to 25 per cent increase postoperatively |

*Tab. 3:* Risk related to transfusion of allogenic blood.

unanticipated blood loss from elective surgery or major orthopaedic trauma is limited by the rate and volume of erythropoiesis that is achievable with exogenously administered rhEPO. The rate and volume of erythropoiesis may be limited by the available population of cells responsive to EPO. Various studies have shown its efficacy in the treatment of renal, chemotherapy, and retroviral-related anemia (16). During postoperative trauma this treatment can reduce the need for blood transfusion. Goodnough et al estimated a 40% reduction of transfusion (17). Usually after the treatment, haemoglobin levels increases about 0.5 - 1.4 gr/dl within 7-10 days (18). In orthopaedic trauma, erythropoietin can be useful during the Regeneration and Rehabilitation phases. Regarding elective treatments such as total joint arthroplasty, randomized studies have shown that the preoperative use of erythropoietin reduces the need for allogenic blood transfusions (19, 20). When combined with preadmission donation, erythropoietin increases the amount of blood that is predonated, while reducing the risk of perioperative anemia.

## Discussion

The bleeding of the trauma and of the orthopaedic surgery encourage the development of perioperative anemia, has been associated with increased morbidity and mortality, especially in older patients advanced, given the limited response capacity of compensatory mechanisms (21). This anemia has been shown have a marked inflammatory component with elevated serum levels of inflammatory cytokines as C-reactive protein (CRP) and various interleukins (22). The amount of bleeding will depend, among other factors, the type of fracture and the surgical technique used for reduction and drug consumption frequent antiplatelet and anticoagulant this population. Also can not ignore the presence frequent deficiency anemia in this population to be to aggravate the anemic box typical of the fracture. The classic treatment of chronic anemia is based on correction of the cause and the replacement of the factors haematinics or lacking erythropoietic or lowered, while that of acute anemia has been the mere blood. This option is not without risks. In addition to the known transmission of infectious diseases, non hemolytic febrile reactions, volume overload, alloimmunization, allergic reactions, inhibition of erythropoiesis recently described a state of Transfusion-associated immunomodulation would favor an increased incidence of bacterial infections in posttransfusion period (23). This fact, coupled with the lack of blood transfusions, frequent in our half, makes it necessary to seek alternative designed to reduce and treat the transfusion rate Perioperative anemia. Among

the alternatives that have been shown to be effective is the use of restrictive transfusion criteria, which involve transfusing when patients present with symptoms or signs of tissue hypoxia or discernible levels hemoglobin (Hb) "low" (less than 7 g / dl in patients non-cardiac) (24). These restrictive transfusion criteria have shown, not only increasing morbidity, or mortality, and costs or stays in surgical patients but even, in certain subgroups patients, be less deleterious. Another alternative measure scheduled effective in orthopaedic surgery is the use drugs that reduce the perioperative bleeding or to correct the anemia or to stimulate erythropoiesis. In this condition with high risk of bleeding, high perioperative anemia prevalence and high risk transfusion seem logical to use some drugs as erytropoetin alfa (EPO) and iron. EPO is used scheduled orthopaedic surgery for several years whereas unscheduled or emergency surgery is only isolated experiences in patients who have rejected blood transfusion. Intravenous iron appears to be the media of choice in the treatment of anemia Perioperative to ensure a rapid supply of iron, directly and effectively to the bone marrow. It has been described recent years their effectiveness in different clinical settings (gynecology, obstetrics, surgical correction of spine, etc.), including patients with fracture hip. Erythropoietin (EPO) is the most potent regulator of red blood cell development, or erythropoiesis. EPO exerts its influence in the bone marrow, where it regulates the proliferation and differentiation of red blood cell precursors. Recombinant human EPO (rhEPO) has been available for exogenous administration since the mid-1980s (25) by 1989, the U.S. Food and Drug Administration had approved its use for treating the anemia associated with chronic renal failure. Renal failure patients were the first obvious targets for treatment with the recombinant protein; their associated anemia is largely attributable to a deficiency of EPO secretion in their failing kidneys. From that point, use of exogenous rhEPO expanded to treating anemias of varied etiologies. There is a strong evidence that erythropoietin therapy promotes haemoglobin recovery and reduces the need for transfusion in patients with pre and post operative anaemia (26). The prevalence of preoperative anemia varies in different populations from 5% up to 76% depending on the trauma, underlying pathology, the population being screened, socioeconomic status, and age (27, 28). Bierbaum et al. (29) reported that 35% had a preoperative hemoglobin level < 13 g/dl. Using a more conservative definition of anemia (men, hemoglobin < 12.5 g/dl; women, hemoglobin <11.5 g/dl), Meyers et al. (30) described a 15% prevalence of preoperative anemia in 225 patients undergoing high orthopaedic trauma. The clinical relevance of preoperative anemia is that anemic patients receive more allogenic blood transfusions and may have a higher incidence of postoperative infections and a longer duration of hospitalization (31). In addition, Gurson et al. (32) have shown that preoperatively, anemic patients had an elevated mortality rate at 6 and 12 months. Therefore, correction of preoperative anemia seems attractive.

## Conclusion

Massive acute bleeding that occurs in trauma and in orthopaedic surgery are best managed with surgical exploration and allogenic blood transfusion. Several options with proven efficacy exist, including acute hemodilution, blood salvage, hypotensive anesthesia, improvements in tissue hemostasis, and pharmacological agents. In addition to reducing the need for and exposure to allogeneic blood, the potential for less blood loss may translate into less swelling, improved range of motion, and earlier return to function. However, all methods come with varying amounts of risk and cost. Because allogeneic transfusions carry risks of viral disease transmission, allergic reactions, and posttrasfusion immunosuppression orthopaedic surgeons have investigated varius blood management strategies in orthopaedic surgery to reduce exposure to allogenic blood. The stimulation of red blood cell (RBC) production by erythropoietin therapy is one means of treating anemia pre and post operatively. Erythropoetin alfa was shown to be an effective treatment for preventing transfusion and reducing the amount of transfused blood required by patients with mild anaemia prior to orthopaedic surgery.

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## LA GESTIONE DELL'ANEMIA: LA PERDITA DI SANGUE IN CHIRURGIA ORTOPEDICA

La chirurgia ortopedica maggiore ed i traumi ad alta energia sono spesso responsabili di emorragie acute. Le fratture delle ossa lunghe e le fratture del bacino sono correlati con la perdita di sangue. La conseguenza finale di un sanguinamento massivo è lo shock ipovolemico. La tensione di ossigeno ridotta nei tessuti potrebbe essere responsabile di infarto, aritmie, ictus, insufficienza multi organo. Per queste ragioni, è importante riconoscere e correggere immediatamente tutti le potenziali fonti di sanguinamento, al fine di evitare complicazioni. In ortopedia i trattamenti elettivi per la gestione di ipovolemia sono diversi. Le banche di sangue e gli emocomponenti allogenici hanno avuto un impatto importante sul trattamento chirurgico e l'assistenza sanitaria in tutto il mondo. L'eritropoietina è stata dimostrata essere efficace nell'innalzare l'ematocrito pre-operatoria e nel ridurre la necessità di trasfusione allogenico in chirurgia ortopedica maggiore. L' utilizzo della eritropoietina può dare ottimi risultati ed anche migliori rispetto la donazione autologa preoperatoria. Lo scopo del presente articolo è di trattare una revisione della letteratura basata sulla nostra esperienza

**Keywords**: anemia, eritropoietina, sanguinamento, ipovolemia, perdita di sangue.

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