Bleeding in orthopaedic surgery: the role of blood transfusion and erythropoietin alpha

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Abstract. High energy trauma is often responsible for acute bleeding. Long bone and pelvis fractures are correlated with increased blood loss. Hypovolaemia could become a life threatening complication especially in elderly patients because of the reduced physiological response. Furthermore it could compromise the course of associated morbidities. Haemorrage is also associated in both comminuted fractures and osteoporosis. An increased intraoperative bleeding often occurs when a prolonged surgical time is required to obtain an appropriate ostheosynthesis. The final consequence of a mayor bleeding is hypovolaemic shock. The reduced oxygen tension of the tissue may be responsible for heart attack, arrhythmia, stroke, multi organ deficiency. For these reasons, it is important to immediately recognize and correct all potential bleeding in order to avoid complications. (www.actabiomedica.it)

Key words: Erythropoietin, high energy trauma, bleeding

Introduction

High energy trauma is often responsible for acute bleeding. The final consequence of major bleeding is hypovolaemic shock. 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 (1, 2).

It is important to specify that total blood volume is about 7% of human weight; for example, a 70 Kg male has about 25 blood unit (5000 cc) (3).

Haemorrhagic classification is very helpful for the treatment management (4):

- class I: blood loss up to 4 units. Minor physiological solution infusion should be employed.
- class II: blood loss between 4 and 8 units. Physiological solution infusion or plasma expander is always required.
- class III: blood loss between 8 and 10 units. Blood infusion is necessary to prevent hypovolaemia.
- class IV: blood loss greater than 10 units. This is a life threatening condition. An operative treatment is necessary to correct the cause of bleeding.

Principles of treatment

The Advanced Trauma Life Support is the best procedure in treating polytrauma patients.

According to Tscherne et al. trauma management may be divided into 4 phases (5): Resuscitation (1 to 3

hours), Stabilization (1 to 72 hours), Regeneration (between 3 to 8 days), Rehabilitation (after 8 days).

During the first phase, particular attention is reserved to breath, circulation and neurologic survey. Haemodynamic instability should be evaluated with an operative intervention.

During the Stabilization phase, the patient should return to spontaneous breath and a stable haemodynamic condition. Afterwards, all controls and treatments should be started. Bleeding is intended as a consequence of a primary pathology, thus treatment should be targeted (6). Multiple fractures should be treated in the following order: tibia, femur, pelvis, spine, upper arm (7). During the Regeneration phase, blood volume is reconstituted by endogenous erythropoietin. At this time all minor surgery should be performed in order to complete the treatment. During the Rehabilitation phase, bleeding is absent and erythropoiesis returns to be preponderant (8, 9).

Treatment of acute bleeding

Acute bleeding is best managed with arterial embolization (10). Unknown massive bleeding with associated haemodynamic instability always requires surgical exploration. These treatments are usually reserved in the first and second phases with massive bleeding (Class III and IV). Blood infusion is always required. During the Regeneration phase, there may be a lack of endogenous blood volume reconstitution. Blood infusion may be an option. The decision is primarily based on the clinical status. Symptomatic hypovolaemia always presents with dyspnoea, exhaustion, and angina pectoris (11).

Elective treatments

In orthopedics the elective treatments in the management of hypovolaemia are different. Historically, blood was replaced, when needed, with banked blood. It is known that complications of infections as well as reactions to transfusion have led to the development of preoperative autologous donation programs. However, preoperative autologous donation has been associated with scheduling difficulties: the limited shelf life of the blood, perioperative anemia (12), and bacterial contamination (13). 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 allogeneic blood (14). Recent techniques have been employed in order to optimize blood conservation, including the use of pharmacologic agents (15), hemodilution (16) and perioperative blood salvage (17). In the United States, around 20 million haematic transfusions are performed yearly.

The role of Human Erythropoietin

The most extensively evaluated pharmacologic agent is recombinant human erythropoietin. Erythropoietin is a glycoprotein that is excreted by the kidney, which stimulates the production of red blood cells. Various studies have shown its efficacy in the treatment of renal, chemotherapy, and retroviral-related anemia (18). During postoperative trauma this treatment can reduce the need for blood transfusion. Goodnough et al estimated a 40% reduction of transfusion (19). Usually after the treatment, haemoglobin levels increases about 0.5-1.4 gr/dl within 7-10 days (20). In orthopedic 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 (21, 22). When combined with preadmission donation, erythropoietin increases the amount of blood that is predonated, while reducing the risk of perioperative anemia.

Discussion

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 (23). 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 (24). 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 (25). 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) (26). 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 orthopedic 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 epoetin alfa (EPO) and iron. EPO is used scheduled orthopedic 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.

Chronic blood loss results in iron deficiency, which can be effectively treted with iron supplementation. This principle has been extended to the management of acute blood loss. However, there is evidence that iron supplementation is not effective for the treatment of postoperative anaemia in emergent hemiarthroplasty or in elective total joint replacement (27). Furthermore, significant adverse effects was reported in over 20% of patients (28). 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 (29). 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 (30, 31).

Bierbaum et al. (32) 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. (33) 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 allogeneic blood transfusions and may have a higher incidence of postoperative infections and a longer duration of hospitalization (34). In addition, Gurson et al. (35) 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 is best managed with surgical exploration and allogenic blood transfusion. 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 allogeneic blood. The stimulation of red blood cell (RBC) production by erythropoietin therapy is one means of treating anemia pre and post operatively. Epoetin alfa can be administered perioperatively as primary blood management strategy to accelerate RBC production and increase haemoglobin concentration.

Erythropoietin is effective in reducing allogenic transfusion and have a important role during the Reconstitution and Rehabilitation phases.

In elective surgery, erythropoietin combined with preoperative autologous blood donation lowers allogenic blood requirements more effectively than erythropoietin or preoperative autologous donation alone.

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