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Review

CONTEMPORARY RECOMMENDATIONS ON PATIENT BLOOD MANAGEMENT IN JOINT ARTHROPLASTY

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SUMMARY – Hip and knee replacement surgery are a common and effective procedure for the relief of pain and loss of function. The number of procedures is increasing and great interest is given how to improve outcome following hip and knee replacement surgery. Last two decades have been characterized by many innovations in hip and knee replacement surgery including minimally invasive technique but also by improvements in anesthetic technique and blood management.

The patients undergoing hip and knee replacement surgery are commonly elderly and have cos-existing organ dysfunctions. These procedures are characterized by great perioperative disturbances including cardiovascular complications, high incidence of thromboembolic complications, possible significant perioperative blood loss, possible bone cement effect and high level of postoperative pain.

Anesthetic assessment of patients include preoperative preparations, intraoperative and postoperative care. In this article, all problems of perioperative blood management are discussed. The recent data of advantages of blood management for every patient are outlined. Blood management include preoperative preparation, use of autologous blood in perioperative period and administration of drugs for minimizing intraoperative blood loss. The final result of improvements in blood management is reducing in blood loss and need for allogeneic blood and significant reduction in perioperative morbidity.

Key words: *joint replacement surgery, blood management, autologous blood, tranexamic acid.*

Introduction

Total hip replacement (THR) and total knee replacement (TKR) surgeries are become routine procedure with increasing number being performed each year all around world. Since its introduction in the 1960s, THR and TKR are standard treatment for patients with osteoarthritis providing significant improvement in physical status and health. THR and TKR are associated with many conditions and complications of which the anesthesiologist must be aware and many investigations are performed to design optimal conditions for this procedure. (1)

Current surveys from the United States and Europe report continued growth in the use of THRs

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from the 1990s to early 2000. Current projections for the United States suggest that from 2005 to 2030 the number of THRs will increase by 174 %, to nearly 600.000 procedures per year. (2) Similar situation is with TKR in many other countries as result of increasing number of people in age over 65 years. Most of patients scheduled for THR and TKR are elderly, and commonly have associated medical problems like heart disease or coexisting organ dysfunction what can compromise their outcome after procedure. In study performed in UK is estimated that in patients undergoing primary hip replacement 63 % were American Society of Anesthesiologists (ASA) grade 2, 14 % were grade 3 or worse, and this figure rose to 59 % and 26 % for revision procedures.(3). THR and TKR are associated with a large amount of blood loss. According to many studies, THR patients had a mean total true blood loss of 1510 mL, with a calculated hidden blood loss of 471 mL (4). TKR patients had a blood loss of 1450 mL; hidden blood loss reached 465 mL (5). In many patients perioperative blood transfusion in needed to maintain or restore the hematocrit and level of hemoglobin close to normal. In last two decades modern anesthesia techniques include blood management procedures for patient with joint arthroplasty in order to minimize complications of allogenic transfusion like risk of viral and prion transmissions, administrative errors, risk of bacterial contamination of blood products. A correlation has been reported between allogeneic blood transfusion and postoperative infection. Allogeneic blood also adds to the cost of an operation, it has been shown with increased morbidity and prolonged hospital stay (6). In contrast to advances in knowledge of blood management many procedures for reducing blood transfusion are developed.

Preoperative considerations

Problems in multiple systems are common because most patients are elderly. Preoperative assessment and planning should minimize potential anesthetic problems, optimize co-morbidity and provide the most appropriate anesthetic for the patient. All patients should be assessed preoperatively two to three weeks before the scheduled procedure and meticulous preoperative assessment must be performed. However, the elective nature of the surgery allows enough time for a thorough work-up, and effective treatment can be initiated when it is necessary. Assessing patients preoperatively includes a detailed history, a physical examination and any indicated laboratory tests. Investigations of cardiovascular and respiratory system, liver and renal function, musculoskeletal and airway status are important. A detailed history of drugs used and allergy should be taken.

The prevalence of preoperative anemia in patients undergoing elective hip or knee replacement surgery is in range between 23 and 70 % (7). When anemia is detected the subsequently laboratory tests are directed at identifying iron deficiency or other nutritional deficiencies (folic acid and or vitamin B12), chronic kidney disease or chronic inflammatory disorders. It is recommended that elective surgery is not performed in patients who are anemic until the anemia has been correctly treated. Most popular methods are iron therapy. There is statistically significant increase in preoperative Hb level following the administration of oral iron supplementation. The problem is that oral iron supplementation requires a long time to replenish the exhausted iron stores and is associated with intolerability in about 70 % of patients. In contrast, intravenous (IV) iron supplementation allows for a large quantity of iron to be administered over a few dose. Some of studies confirmed that IV iron therapy is effective in correcting anemia and limiting transfusion requirements (8) but in others systematic reviews is found little evidence that IV iron therapy is effective at reducing transfusion in patients undergoing major orthopedic surgery (9). It should be remembered that hypersensitivity reactions to IV iron are reported in some cases potentially life threatening. Preoperative iron therapy is also used as supplement therapy when erythropoietin is administered. Meta-analyses of placebo controlled RCT indicate that erythropoietin with or without iron is effective in reducing the number of patients requiring allogenic transfusion (10). In summary in adult patients with iron-deficiency anemia, oral iron therapy has been found to be effective in the treatment of preoperative anemia, in reducing transfusion needs and in some cases, also reducing the duration of hospitalization.

Preoperatively is important discontinuation of anticoagulants and antiplatelet agents. In consultation with an appropriate specialist discontinuation of anticoagulation therapy (warfarin, antiXa drugs, antithrombin agents) should be performed. If clinically possible discontinuing nonaspirin antiplatelet agents (thienopyridines such as clopidogrel, ticagrelor or

prasurgel) for a sufficient time in advance of surgery. The literature is insufficient to evaluate the effects of discontinuing aspirin before surgery, although two RCTs comparing aspirin with placebo before surgery report equivocal findings for perioperative blood loss, transfusion requirements or postoperative adverse effects (11).

Preoperative autologous donation (PAD) remains the most widely known, but no longer the most widely used of the autologous options for surgical blood conservation. Interest in all forms of autologous transfusion beginning as early as 1983. By 1993, when participation in PAD peaked, approximately 6 percent of all blood collected in United State was intended for autologous use. This percentage declined to 0.4 percent in 2013 and 0.2 percent in 2015. PAD program currently have marginal value and cost effectiveness, should be restricted to healthy individuals with long life expectancies requiring blood, intensive procedures or to individuals for whom crossmatch-compatible blood in unavailable (a rare occurrence) (12).

Anaesthetic technique

THR and TKR surgery can be performed under general, spinal or epidural anesthesia, and a combination of techniques is often used. The type of anesthesia should be determined at preoperative anesthetic assessment. Spinal anesthesia is the most commonly used technique, usually in combination with intravenous sedation. Epidural blockade or a lumbar plexus block are also widely used, alone or in combination with general anesthesia. There are many advantages of regional anesthesia, such as reduced intraoperative blood loss and reduced requirement for blood transfusion, reduced incidence of postoperative deep vein thrombosis and pulmonary embolism, improved postoperative analgesia (especially if a spinal or epidural catheters are used), improved outcome from surgery and anesthesia, reduction in the effects of general anesthesia and systemic opioid analgesia on pulmonary function (basal atelectasis, hypoxemia and pulmonary infection) and reduced incidence of postoperative nausea and vomiting. (1,3)

There are many advantages of regional anesthesia for patients scheduled for THR and TKR but there is still debate in literature does regional anesthesia improve outcome. In meta-analysis of 66 articles is confirmed that use of spinal anesthesia resulted in significantly less estimated blood loss (EBL) ($p<0.0001$) compared with epidural anesthesia (EA), which, in turn resulted is significantly less EBL compared with general anesthesia (GA) or combined GA-EA (13).

Intraoperative considerations

There is possibility of significant blood loss in joint replacement surgery. The average blood loss in THR ranges from 300 to 1000 mL intraoperatively and rise to total of 1500 mL in 24 hours postoperatively. Blood transfusion is relatively uncommon during surgery in patients with an adequate preoperative Hb. Intraoperative blood loss is in correlation with systolic blood pressure. Many methods are popular for decreasing blood pressure and blood loss: regional (spinal or epidural) anesthesia and deliberate hypotension with many drugs (inhaled anesthetics, vasodilator drugs like sodium nitroprusside, nitroglycerin, prostaglandins, calcium channel blockade). Some antifibrinolytics drugs like tranexamic acid, epsilon-aminocaproic acid and aprotinin have all been used in the last 20 years and have resulted in significant decrease in the need for transfusion. Intraoperatively many methods for reducing blood loss and allogeneic blood transfusion can be used.

Acute normovolemic hemodilution (ANH) is a blood conservation technique that entails the removal of whole blood from a patient after induction of anesthesia, with maintenance of normovolemia using crystalloid/colloid replacement fluid. The amount of blood removed typically varies between one and three units. ANH can be used as the sole blood conservation technique, but can be combined with other methods to minimize or avoid transfusion. ANH can be used in patients with normal or high initial hemoglobin levels. A prospective study that included 50 patients undergoing total hip or total knee surgery noted that patients in ANH group had a lower rate of allogeneic blood transfusion (16 versus 60 percent) and fewer postoperative complications compared with controls (14).

Intraoperative autotransfusion is method when shed blood during joint replacement surgery is salvaged and reinfused to patients. The intraoperative blood salvage machine (commonly referred to as a "cell saver") separates washes and concentrates salvaged RBCs. Several steps are involved, including suctioning of shed blood from surgical field, addition of an anticoagulant, separation and washing of RBCs (to remove the anticoagulant, free hemoglobin,

thrombogenic substances and cellular stroma), concentration of the blood and reinfusion to patient. During the reinfusion a 40-micron microaggregate filter are used. Intraoperative blood salvage is suggested in surgical procedures having a likelihood of significant blood loss (> 1000 mL). It is usually done in operating room without direct involvement of the transfusion service. Contraindications include use of fluids such as sterile water (or any hypotonic solution), hydrogen peroxide, alcohol or povidone/iodine because RBC hemolysis can occur. Blood salvage cannot be used during suctioning of blood from surgical field if there is any potential for collection of hemostatic products such as topical thrombin, fibrin glue of microfibrillar bovine collagen-based products. In a 2010 systemic review including 75 trials (36 involving orthopedic procedures) the absolute reduction in the use of allogeneic red blood cell transfusion was 21 percent (95 % CI 15-26 percent) (15). Intraoperative blood salvage has strong indication for selective cases, especially if any massive blood loss is expected during surgery. It is useful for a revision arthroplasty or simultaneous bilateral primary THR (in both cases anticipated intraoperative blood loss of more than 1000 mL).

Systemic hemostatic agents have been used in an attempt to decrease blood loss and need for transfusion. Desmopressin, a synthetic vasopressin analogue, has been used in cardiac surgery where the reduction in blood transfusion is reported. The results in joint replacement surgery are controversial. A Cochrane systematic review concluded that there was no convincing evidence that desmopressin reduced allogenic blood transfusion in patients who did not have congenital bleeding disorders. (16).

High-dose aprotinin, a fibrinolytic inhibitor, was found to reduce blood loss in total joint replacement surgery. Its use has been limited because of its high cost and possible allergic reactions and a reported risk of acute renal failure. Conflicting reports have been published regarding the effectiveness and safety of aprotinin in patients undergoing orthopedic surgery. In meta-analysis performed in 2014, the effectiveness was evaluated. In this study, eighteen randomized controlled trials involving 1276 patients were include. The use of aprotinin reduced total blood loss by a mean of 498.88 mL, intraoperative blood loss by a mean of 246.11 mL, postoperative blood loss by a mean of 169.11 mL, the number of blood transfusions per patient by 0.93 units. Aprotinin led to a significant reduction in transfusion requirements and no increase in the risk of DVT (17). Is not widely used in joint replacement surgery but there are many reports of aprotinin use in spine surgery.

The most popular antifibrinolytic drug used in joint replacement surgery is tranexamic acid (TXA) which has been used for more than 20 years in various fields such as dentistry, gynecology, cardiac surgery and liver transplantation. Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible blockade of lisyne binding sites on plasminogen molecules. This process may also potentially enhance the risk of venous thromboembolic events by promoting thrombosis and many RTC are performed evaluating the efficacy and possible complications of its use in joint replacement surgery. The route of administration include intravenous, local and peroral use. The protocol for use of the tranexamic acid is not yet formalized. Its efficiency on the bleeding is dose dependent, especially when the doses are repeated. The duration of postoperative fibrinolysis after THR a TKR: it is about 18 hours with a peak at the 6th hour after the end of surgery. Thus, it seems rightful to propose a protocol including repeated injections of tranexamic acid of 15 mg/kg in the incision, then at the third hour, then every 4 hours during the first night; this protocol should be modified in case of renal failure or significant postoperative thrombotic risk. In meta-analysis reduction in blood loss, relative risk of transfusion (RR 0.52) and no increased risk of thromboembolism, the dose of TXA administered ranged between 10-15 mg/kg (18). In other studies, it was confirmed that patients who received TXA had lower rates of blood transfusion (7.7 vs 20.1 %), fewer thromboembolic events (1.6 vs 1.8 %) and reduced incidence of acute renal failure (1.9 vs 2.6 %). (19). TXA can be administered topically. Topical administration results in a ten-fold less plasma concentration of TXA when compared to intravenous route with a potential reduction in adverse effects. The topical dose of TXA is in range 2 to 3 gr. Meta-analysis of topical TXA showed reduced perioperative blood loss and need for transfusion (20). In the recent studies peroral route of TXA administration is investigated. Transfusion rates decreased from 15.4 % in the no-oral TXA to 9.6 % in the single dose oral TXA group and 7 % in 2-dose group ($p<.001$). (21)

With the use of TXA, there are concerns about the risk of venous thromboembolic complications.

In meta-analysis performed in 2020 large number of 9.067 patients were analyzed in 140 articles. The route of administration were intravenous, intraarticular and oral. No differences in terms of thromboembolic complications were detected between TXA and control group (22).

Postoperative procedures

Thoracic surgeons initially studied postoperative reinfusion of shed blood in an attempt to reinfuse blood lost form mediastinal drainage. In joint replacement surgery, method is used from 1980s and now is popular in TKR surgery. The main advantage of postoperative collection and reinfusion is this methods simplicity. Postoperative shed blood is collected usually 6 hours postoperatively, after collection the blood is reinfused to patients. There is no need for anticoagulants. During reinfusion, 40-micron microaggregate filters are used. Development of efficient systems for collecting, anticoagulating and filtering blood for reinfusion has increased interest in salvaging blood after major orthopedic surgery, despite residual concerns regarding the safety of unwashed blood. Blood reinfused after simple filtration has a low hematocrit and contains large concentrations of inflammatory mediators, histamine, eosinophil cationic protein, activated complement factor C3, cytokines, various coagulation factors and split products, as well as free Hb. It is generally accepted that no more than 1000 mL of drained blood should be reinfused, and that blood drained more than six hours after the end of surgery should not be reinfused. In many studies, plasma hemoglobin was measured and found be > 25 %, also affirming the reinfusion would provide a significant amount of red cells. The survival of red cells is similar to intraoperative retrieval. When postoperative autologous blood collection is used the need for allogeneic blood is reduced what is confirmed in many RTC (need for allogeneic blood products in patients underwent TKR is less than 10 %) (23).

Conclusion

As mentioned in this article, the number of THR and TKR increased dramatically in last 20 - 30 years. It will continue to rise in future, so appropriate patient blood management is essential to prevent blood loss and further complications. Blood management include preoperative preparation, use of autologous blood in perioperative period and administration of drugs for minimizing intraoperative blood loss. Although the techniques vary from preoperative to intra/postoperative procedures, they all have in common that they reduce blood loss and the need for allogeneic transfusion. To conclude, in all patients underwent total joint replacement surgery blood management techniques are essential nowadays and should be use accordingly when needed.

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Sažetak

SUVREMENE PREPORUKE ZA PRIMJENU KRVI KOD ARTROPLASTIKE ZGLOBOVA

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Ugradnja umjetnih zglobova kuka i koljena je česta i uspješna metoda liječenja kod poremećaja velikih zglobova praćenih boli i gubitkom normalne funkcije. Broj ovih operacija je u stalnom porastu te se velika pažnja posvećuje poboljšanju perioperacijskog liječenja. U zadnja dva desetljeća mnoge inovacije kao minimalno invazivna kirurška tehnika su uvedene u kliničku praksu, a došlo je i do znatnog napretka u aneteziološkom i transfuzijkom liječenju.

Bolesnici kojima se ugrađuje endoproteza kuka i koljena su često starije životne dobi i imaju značajan komorbiditet. Operacijski zahvat karakteriziraju značajni perioperacijski poremećaji kao kardiovaskularne promjene, velika učestalost tromboembolijskih komplikacija, moguće je značajno perioperacijsko krvarenje, poremećaji uzrokovani koštanim cementom te visok nivo postoperacijske boli.

Posebna pažnja posvećuje se problemima značajnog perioperacijskog krvarenja i provođenju metoda kojima se smanjuje perioperacijsko krvarenje te potrošnja alogene krvi. U ovom članku pokazuju se postupci koji se provode prijeoperacijski (korekcija anemije postupci prijeoperacijske autologne donacije), intraoperacijski (akutna normovolemička hemodilucija i intraoperacijska autrotransfuzija) te postoperacijski (postoperacijska autotransfuzija). Posebno se opisuje primjena lijekova (antifibrinolitici) koji smanjuju intraoperacijsko i postoperacijsko krvarenje.

Konačan rezultat napretka u anesteziji i transfuzijskom liječenju je smanjenje perioperacijskog krvarenja i potrošnje alogene krvi, te posljedično smanjenje perioperacijskog morbiditeta, kraće vrijeme hospitalizacije kao i brži oporavak bolesnika.

Ključne riječi: *endoproteze kuka i koljena, autotransfuzija, traneksamična kiselina.*