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ORIGINAL ARTICLE

Polysaccharide hemostatic system reduces blood loss in high-body-mass-index patients undergoing simultaneous bilateral total knee arthroplasty

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Abstract
Background To investigate the efficacy of a topically applied hemostatic agent used to reduce blood loss in patients undergoing simultaneous bilateral total knee arthroplasty (TKA).
Methods Thirty-two patients (5 male, 27 female) mean age 65 ± 9.3 (46–80) undergoing single-stage bilateral TKA were enrolled in the study and divided in two groups. Groups 1 and 2 consisted of patients with body mass index (BMI) <30 and >30, respectively. Polysaccharide hemostatic agent (PHA; 3 g) was applied topically to the right knees of each patient intraoperatively. The left knees were used as controls. A negative suction drain was used and the effect of PHA and BMI on postoperative bleeding was evaluated.
Results Blood loss was significantly higher ($p = 0.027$, $r = 0.397$) for patients with higher BMI. Treatment by local application of PHA to potential bleeding sites significantly reduced blood loss—314 ± 151 ml (50–600) for the right knees versus 468 ± 140 ml (150–700) for the left knees ($p = 0.007$) in group 1; 420 ± 251 ml (100–900) for the right knees versus 620 ± 229 ml (350–1125) for the left knees ($p = 0.036$) in group 2. Blood loss reduction between the right and left knees was no different between the two groups ($p = 0.173$).
Conclusions By reducing blood loss and the need for postoperative blood transfusion in patients with high BMI, PHA can be of value as adjuvant therapy in new blood-management procedures in major joint-replacement surgery.

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Introduction

Despite preoperative, intraoperative, and postoperative blood-loss management techniques, the need for allogenic blood transfusion remains substantial—34 % for bilateral total knee arthroplasty and 20 % for bilateral total hip arthroplasty (THA) [1–3]. Substantial blood loss has been recorded during bilateral total knee arthroplasty (TKA) compared with unilateral TKA because numerous bone cuts, much soft tissue release, and violation of tibial and femoral medullary canals occur. Unfortunately this excessive blood loss in bilateral TKA procedures is associated with increased use of allogenic blood transfusion and remains a major problem for patients and surgeons [4–6].

Single-stage bilateral total knee arthroplasty has been advocated by orthopaedic surgeons in recent years for patients with bilateral knee osteoarthritis, because it has numerous advantages over two-stage procedures. Compared with bilateral procedures performed in two stages, simultaneous bilateral TKA does not increase the overall need for transfusions and significantly reduces the duration and cost of hospitalization [7–9].

Despite the advantages of this procedure, blood loss is still excessive and there is no standard strategy for prevention of blood loss. Blood loss directly effects the success and outcomes of bilateral TKA, especially for patients who are prone to bleeding. Attention to effective blood-management techniques is mandatory especially if the institutional policy is to use allogenic blood transfusion.

Besides unfavorable minor side effects, allogenic transfusion can lead to problems such as transmission of human immunodeficiency and hepatitis viruses, and transfusion-related allergic and immunmodulatory reactions, and can be life threatening. Among numerous methods used to reduce the need for postoperative blood transfusion, four have been proved effective: preoperative administration of epoetin alfa, preoperative autologous donation (PAD), reinfusion of postoperative drainage, and use of tranexamic acid. Despite these methods, patients undergoing simultaneous bilateral TKA still often need allogenic blood transfusions.

Although the above mentioned methods are known to be effective, they are not ideal; each method has its advantages and disadvantages. Adjuvant therapy and a standard blood-management strategy for patients undergoing simultaneous bilateral TKA is a necessity in orthopaedic surgery.

The polysaccharide hemostatic system is a medical device comprising absorbable modified polymer particles (AMP^{TM}). These particles, which are derived from purified plant starch, are biocompatible and nonpyogenic. AMP particles rapidly absorb water from the blood. This dehydration process results in a high concentration of platelets, red blood cells, thrombin, and fibrinogen, which accelerates the normal physiological clotting cascade. In contact with blood, AMP particles support the formation of a gelled, adhesive matrix which provides a mechanical barrier to further bleeding. Absorption needs several days and AMP particles are degraded by histaminases, including amylase and glucoamylase.

This study was performed to determine whether PHA can be of value as an adjuvant in new blood-management procedures to reduce the need for postoperative blood transfusion.

Materials and methods

Thirty-two patients mean age 65 ± 9.3 (46–80) diagnosed with osteoarthritis who underwent simultaneous primary bilateral TKA were divided in two groups equal in number and evaluated prospectively in this study. Patients of group 1 (13 female, 3 male) mean age 65.9 ± 9.3 (47–80) consisted of patients with BMI <30. Patients of group 2 (14 female, 2 male) mean age 65.1 ± 9.7 (46–80) consisted of patients with BMI ≥30. Units of BMI were kg/m^2.

Data consisting of gender, BMI, age of the patient, hemoglobin, hematocrit levels, prothrombin, partial prothrombin time, and platelet count were noted before surgery. Patients with a history of bleeding disorder, previous use of medication that can effect perioperative bleeding, and preoperative hgb levels <9 g/dl were excluded from the study.

Correlation between BMI and blood loss was evaluated by use of Pearson correlation analysis. Regional anesthesia (combined spinal and epidural anesthesia) was preferred by all patients. The duration of the procedure was also noted. Sterile disposable tourniquets were used during all procedures A posterior cruciate retaining design with cemented femoral and tibial components was used. All procedures were performed by the same surgeon using the same technique. Hemostasis was achieved by coagulating any active vessels with an electrocautery device. Before closure all excess blood is removed from the joint and irrigation is performed. After drying the tissues with sterile gauze AMP particles were applied directly over the wound of the right knees, especially at sites at risk of postoperative bleeding (supracondylar synovial tissue, geniculate vessels, origo of patellar tendon and adjacent sites of tibia). All patients had bone grafting of the femoral medullary canal. An intra-articular negative suction drain was used in all knees. The amount of bleeding was recorded from suction drains immediately after the tourniquets were released. Drains were kept active until there was no active drainage. Blood loss between the two groups was evaluated by use of the Mann–Whitney U test. The need for postoperative transfusion was determined for healthy patients mainly by evaluating clinical anemia symptoms. Postoperative transfusion was also conducted for patients with coronary heart disease and congestive heart failure with postoperative hemoglobin level <9 g/dl. Our postoperative blood transfusion regimen consists of allogenic red-blood-cells (RBC) transfusions. All patients received anticoagulation therapy from the first day until the day of discharge (low molecular weight heparin 0.4 ml s.c.) Data accumulation was in conformity with the Institutional Ethics Committee and the study was in adherence to the tenets of the declaration of Helsinki. The study complied with Onkoloji Training and Research Hospital Ethics Council regulations and was approved by the Ethics Council. The objective of the study was described and informed consent was obtained from the parents before their inclusion to the study.

Results

Blood loss was significantly higher ($p = 0.027$, $r = 0.397$) for patients with BMI >30. In both groups postoperative drain output was found to be lower for the right knees of patients who received PHA. In group 1 blood loss was 314 ± 151 ml (50–600) for the right knees compared with 468 ± 140 ml (150–700) for the left knees ($p = 0.007$). In group 2, blood loss for the right knees was 420 ± 251 ml (100–900) compared with 620 ± 229 ml (350–1125) for the left knees ($p = 0.036$) (Table 1; Fig. 1). The total amount of blood lost (right + left knees) had a positive

Table 1 Drain outputs for the right and left knees in groups 1 and 2

	Group 1, BMI <30 ($n = 16$)	Group 2, BMI >30 ($n = 16$)
Right knee blood loss (ml)	314 ± 151 (50–600)	420 ± 251 (100–900)
Left knee blood loss (ml)	468 ± 140 (150–700)	620 ± 229 (350–1125)
p value (Mann–Whitney U)	$p = 0.007$	$p = 0.036$

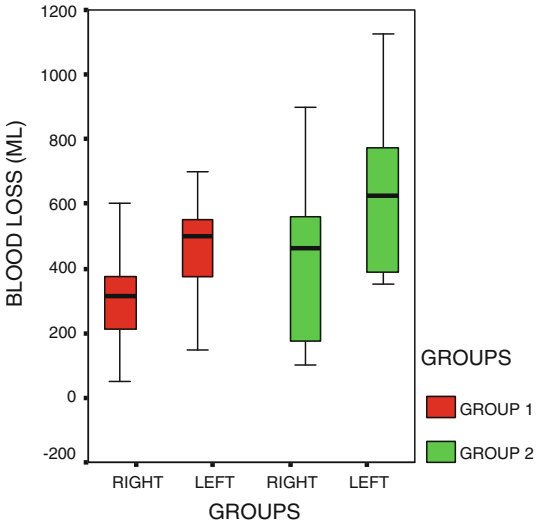

Fig. 1 Blood loss in groups 1 (BMI <30) and 2 (BMI >30) for the right and left knees

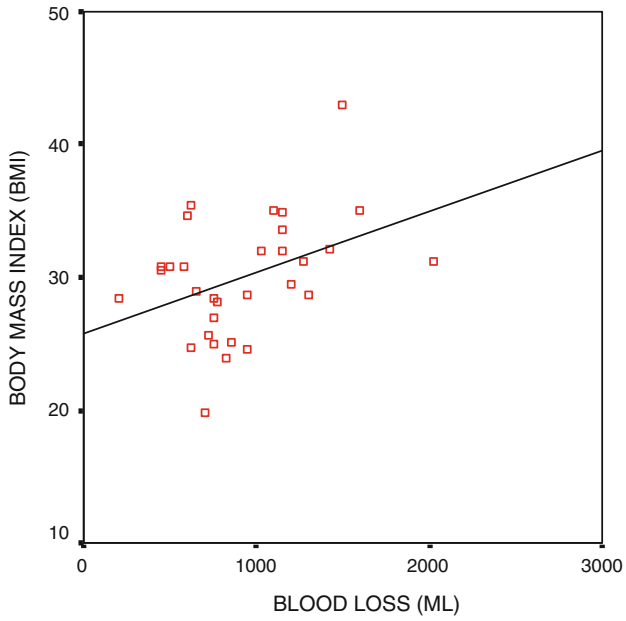

Fig. 2 Correlation between BMI and amount of blood loss (right + left knee) for each patient

correlation with BMI, irrespective of preoperative hemoglobin levels (Fig. 2). The blood loss reduction between the right and left knees was no different between the two groups ($p = 0.173$). The PHA system was found to be effective in reducing postoperative bleeding in patients with high BMI. The need for allogenic transfusion was greater in the BMI ≥30 group at 41 % than in the BMI <30 group at 31 %, but this difference was not statistically significant ($p = 1.0$).

Discussion

TKA is associated with substantial blood loss and a need for transfusion, and bilateral TKA increases the risk further. Single versus two-stage bilateral total knee arthroplasty has also recently been discussed in the literature. Findings suggest that single-stage bilateral knee arthroplasty has numerous advantages over the two-stage procedure. In our center we prefer the single-stage TKA procedure for patients with symptomatic bilateral knee osteoarthritis. One of the compelling issues for this procedure is blood-loss management; especially, avoiding the need for allogenic blood transfusion is essential. Preoperative hemoglobin and advanced age are known to be factors associated with increased postoperative need for allogenic transfusion, but the effect of BMI is controversial. Although some studies suggest that BMI has no correlation with perioperative bleeding, Bowditch and Villar and Marulanda et al. suggest that BMI ≥30 patients bled significantly more than those of optimum weight (BMI <26). Contrary to Bowditch and Villar, Parvizi et al. concluded that patients with low BMI were more prone to bleeding. There is still no consensus regarding the effects BMI on perioperative bleeding. It is certain that BMI is only one of the multiple factors that effect the amount of blood lost [10–12]. In this study we demonstrated that blood loss was greater for patients with higher BMI. The positive correlation between amount of blood lost and BMI can be explained by the greater amount of soft tissue dissection needed and the thickness of the subcutaneous fat tissue. Regarding these data, as well as preoperative hgb levels and advanced age, patients with high BMI are also at risk of postoperative allogenic blood transfusion. Attention must be paid to BMI >30 patients before surgery, because the adverse effects of increased blood transfusion and low hgb levels have been well demonstrated. Keating et al. [13] reported a 5.42 g/dl drop in hemoglobin in patients who underwent bilateral TKA compared with a 3.85 g/dl decrease for a unilateral group. In the bilateral TKA group 82 % of patients with baseline hemoglobin levels of 10–13 g/dl received a transfusion compared with 60 % of patients with baseline hemoglobin >13 g/dl. Regarding

these data, blood-loss management for patients undergoing single-stage bilateral TKA with preoperative hgb levels <13.0 g/dl are at high risk of requiring postoperative allogenic blood transfusion. This issue is critically important for orthopaedic surgeons, because a variety of transfusion-related morbidities can adversely effect the outcome of a technically successful procedure [14, 15]. Concerns about allogenic blood transfusion, for example transfusion-transmitted infectious disease, fluid overload, and prolonged hospital stay remain a major problem for patients undergoing bilateral TKA [16]. Immunomodulation leading to downregulation of host immunity by transmission of foreign antigens is also of concern to orthopedic surgeons [17, 18].

Keating et al. described the development of a vigor scale for use with postoperative patients and demonstrated a correlation between postoperative hematocrit levels and postoperative vigor and muscle strength. Higher postoperative hematocrit levels were significantly associated with favorable results. In the light of these findings we must focus on minimizing postoperative blood loss, especially after major joint-replacement procedures.

In recent studies, a combination of reinfusion drains, weekly epoetin alfa injections, autologous blood transfusion before surgery, and use of tranexamic acid has been advocated to control blood loss. All of these methods have been shown to reduce the need for allogenic transfusion but, unfortunately, none of these methods is accepted as being sufficient alone. PAD is time-consuming, logistically difficult, may increase the risk of allogenic transfusion, and wastage is as high as 50 % [5]. Parvizi et al. [12] reported that PAD seemed to be effective in reducing allogenic transfusions only after THA but not TKA. Use of epoetin alpha is time-consuming and expensive [19, 20]. Tranexamic acid is administered with two-dose slow intravenous injections and is believed to be effective only for the first 6 h [21, 22].

When we consider current blood-loss strategies for major orthopaedic procedures, there is still a need for a simple and effective method to reduce postoperative bleeding and the related need for allogenic blood transfusion. Patients undergoing bilateral TKA with preoperative hgb under 13 mg/dl, advanced age, and high BMI may also be regarded as candidates for an effective procedure for reduction of blood loss.

During the TKA procedure the surgeon can only interfere with visibly active bleeding and use a electrocautery system for hemostasis. This conventional method has thermal side effects, and it is difficult to coagulate diffuse bleeding. Although the surgical technique is important, the major percentage of the total amount of blood loss occurs when the tourniquet is released. In this study we focused on the use of a topical hemostatic agent (PerClot™) to reduce postoperative blood loss. Although topical PHAs have been widely and effectively used in neurosurgery, cardiovascular surgery, urology, and laparoscopic and endoscopic surgery, this is the first use in major orthopaedic surgery. When applied intraoperatively, mostly to the known bleeding sites mentioned above, PHA reduced postoperative blood loss in patients with high BMI who are more prone to bleeding. No side effects were observed and the PHA was practical in use. PHAs can be applied safely and easily in conjunction with a bipolar electrocautery device.

Asymptomatic deep-vein thrombosis (DVT) has been reported in up to 50–70 % of patients who received total knee arthroplasty. The reported incidence of DVT in Europe and North America ranges from 17 to 57 % after TKA, even when using an accepted form of prophylaxis, and 4.0 % in Japanese patients [23–25]. Adverse events, including venous thrombosis, have been reported in fewer than 5 % of the PHA population, especially if the PHA is applied to blood vessels. In accordance with the above mentioned data it is highly possible that DVT occurred in our patients; it was, however, clinically asymptomatic. With regard to this criterion there was no difference between cases that received PHA and cases that did not. In this study the patients were not routinely screened by venography or B-mode ultrasonography, merely observed for any clinical signs of DVT (calf tenderness, swelling, fever, increased pulse rate, tachypnea). More accurate and reliable data can be obtained by using these screening methods to assess the possible risk of venous thrombosis in patients that use PHA.

The relationship between BMI and postoperative blood loss and the beneficial effects of a topically applied hemostatic agent on blood loss in a single-stage bilateral TKA are discussed for the first time in this paper. PHA can be regarded as adjuvant therapy in blood-loss management for patients undergoing simultaneous TKA. By reducing blood loss PHAs may also improve postoperative vigor, and reduce the incidence of infection, rehabilitation time, and hospital stay.

Conflict of interest The authors declare that they have no conflict of interest.

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