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Effect of Injecting Tranexamic Acid from a Drain to the Joint and Drain-Clamping to Reduce Blood Loss during Bilateral Cementless Total Knee Arthroplasty

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Abstract

Purpose: Our purpose was to clarify the effect of immediately postoperatively injecting tranexamic acid (TA) to the knee joint and drain clamping on reducing postoperative bleeding. Allogeneic blood transfusion requirement after bilateral cementless total knee arthroplasty (TKA) was also evaluated.

Methods: This nonrandomized, retrospective study included 50 patients who underwent simultaneous bilateral primary cementless TKA. They were equally divided into a study group given an injection of TA (1000 mg) from drain to knee joint and drain clamping postoperatively (study group) and a control group who did not undergo this treatment. Postoperative total blood loss, drainage volume, hemoglobin level and transfusion amounts/rates were recorded.

Results: Total blood loss, total drainage, and mean allogeneic transfusion volume and rate were lower in the study group than in controls (P<0.05). Hemoglobin level on postoperative day (POD) 14 was similar in the two groups but was higher in the study group on PODs 1 and 7 (P<0.05).

Conclusions: Injection of TA from drain to knee joint and drain clamping at the end of the operation effectively reduced blood loss and allogeneic blood transfusion after bilateral cementless TKA.

Keywords: Intra-articular injection; Tranexamic acid; Drain-clamping; Blood loss; Bilateral cementless total knee arthroplasty

Introduction

Total knee arthroplasty (TKA) is usually associated with marked postoperative blood loss [1-3]. Blood loss is expected to be higher after bilateral TKA than after unilateral TKA and for cementless TKA than for cemented TKA [4-10]. The requirements for allogeneic blood transfusion increase for these patients. The administration of tranexamic acid (TA) to reduce blood loss and the need for allogeneic blood transfusion after TKA have been evaluated by two meta-analyses [11,12] of clinical trial results. It was concluded that TA appears to be a safe method for reducing blood loss-and thereby the need for allogeneic blood transfusion-without increasing thromboembolic complications. Tranexamic acid inhibits tissue fibrinolysis for up to 17 hours, consequently diminishing the possibility of clots entering the extravascular space and accumulating in tissues [13]. We therefore performed immediately postoperative intra-articular retrograde injection of TA from the drain and drain clamping in patients after unilateral cementless TKA [14]. The method reduced postoperative blood loss and the need for blood transfusion.

Only a few papers have evaluated the effect of TA for bilateral cemented TKA [9,10]. The effect of injecting TA from the drain to the knee joint on reducing postoperative bleeding after bilateral cementless TKA has not been reported. Our hypothesis was that intra-articular administration of TA via the drain would reduce postoperative bleeding and the need for allogeneic blood transfusion after bilateral cementless TKA. The purpose of this study was to determine if injecting TA from the drain to the knee joint and drain clamping reduces postoperative bleeding and the need for allogeneic blood transfusion in patients undergoing bilateral cementless TKA.

Methods

This study, conducted from July 2007 through October 2012, was nonrandomized and retrospective. It included 50 patients (100 knees) undergoing simultaneous bilateral primary cementless TKA. The patients gave written informed consent for publication of this report and any accompanying images. Exclusion criteria were a known allergy to TA, cemented TKA, unilateral TKA, and posterior stabilized TKA. After these exclusions, 50 patients remained. They were divided into two groups. The study group underwent injection of TA from the drain to knee joint at the end of the operation but before tourniquet release, followed by clamping the drain for 1 hour (n=25). The control group did not undergo this treatment (n=25). The preoperative characteristics, including age, sex, knee disease, height, weight, preoperative femorotibial angle, range of motion of the knee, and hemoglobin levels 1 day before surgery were comparable in the two groups (Table 1). The backgrounds of the patients in the groups were not significantly different except for their height and the femorotibial angle of the right knee. All surgery was performed or supervised by two surgeons (H.M. for the right knees, K.I. for the left knees).

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Parameter	Study group (*n* = 25)	Control group (*n* = 25)	*P*
Age (years)	70.7 ± 7.2	71.6 ± 6.4	NS
Sex (male/female)	7/18	5/20	NS
Disease (OA/RA)	25/0	25/0	NS
Height (cm)	154.2 ± 7.0	148.9 ± 6.7	0.008
Body weight (kg)	64.3 ± 11.4	63.0 ± 9.6	NS
Preoperative FTA (°) Right Left	 185.2 ± 4.0 187.0 ± 3.9	 188.9 ± 6.0 188.3 ± 4.9	0.015 NS
Preoperative ROM (°) Right Left	 112.4 ± 20.4 112.2 ± 21.4	 115.4 ± 15.9 118.4 ± 15.0	 NS NS
Preoperative Hb (g/dl)	12.9 ± 1.0	12.8 ± 1.1	NS

OA: Osteoarthritis; RA: Rheumatoid Arthritis; FTA: Femorotibial Angle; ROM: Range of Motion; Hb: Hemoglobin, Results are the mean ± SD

Table 1: Patient profiles.

All patients were given general anesthesia. In all 100 knees, the patellae were not replaced, the posterior cruciate ligaments were retained, and components were fixed without cement. Surgery was performed under tourniquet control. A medial parapatellar approach was used after a midline skin incision. An intramedullary alignment rod was used for femoral cutting and an extramedullary guide system for tibial cutting. The femoral canal for intramedullary guidance was routinely plugged with bone. We did not use intraoperative blood salvage system "cell savers." The implants for all patients were the Scorpio NRG CR HA (Stryker Howmedica Osteonics, Allendale, NJ, USA) or the NexGen CR (Zimmer, Warsaw, IN, USA). Even if either implant is used, it is not different in quantity of osteotomy.

Because of the reduced blood loss, the tourniquet was not released until skin closure and application of a compressive dressing in all knees [15]. Intraoperative blood loss was negligible in the patients because the tourniquet was not deflated until wound closure. We used a vacuum bag (J-VAC suction reservoir 450 ml; Johnson & Johnson K.K., Tokyo, Japan) as an intra-articular drain. In the study group, TA was injected intra-articularly from the drain before releasing the tourniquet, after which the drain was clamped for 1 hour [16]. The drain-clamping was performed for keeping the TA in the joint. One ampoule of TA (10% Transamin, 10 ml, 1000 mg; Daiichi-Sankyo, Tokyo, Japan) of TA was injected to each knee-a dose found to be acceptable in previous studies [4-12]. The drains were removed 48 hours after the operation in both groups. Sutures were removed from all patients 2 weeks after the surgery.

All patients underwent postoperative intravenous prophylactic antibiotic therapy consisting of 1 g cefazolin every 12 hours for 3 days. Standard thromboprophylaxis was also prescribed. Starting 24 hours after the operation, each patient was given 1.5-2.5 mg fondaparinux sodium (Arixtra® Injection; Glaxo-Smith-Kline, Brentford, Middlesex, UK) subcutaneously. The regimen comprised this dose every 24 hours for 10 days. Thromboembolic prophylaxis also included use of a foot pump (Novamedix A-V Impulse System; Kobayashi Medical, Osaka, Japan) and antiembolic stockings (Ansilk®; Alcare, Tokyo, Japan) [16,17]. As part of the postoperative care for both groups, continuous passive movement was started on postoperative day (POD) 3, and standing and full weight-bearing walking were allowed 1 week after surgery.

If possible, autologous blood was collected on preoperative day 4 or earlier. Indications for preoperative autologous blood donations were based on the Standards for Preoperative Autologous Blood Donations (2007) developed by the Japanese Society of Autologous Blood Transfusions. A blood hemoglobin level of ≥ 11.0 g/dl or a hematocrit of ≥ 33% was required. No age limit was established. Supplemental iron (80 mg) was given by injection at the time of blood collection. When collection of ≥ 800 ml of blood took ≥ 1 week, 24,000 units of recombinant human erythropoietin (ESPO®, epoetinum alfa; Kyowa Kirin, Tokyo, Japan) were administered subcutaneously. The collected autologous blood was transfused back to each patient on POD 1.

We used the principle of allogeneic blood transfusion based on the criteria and guidelines for perioperative transfusion suggested by the National Institutes of Health Consensus Conference, which states that the decision to transfuse blood depends on clinical assessment aided by laboratory data indicating that the patient has symptoms and signs associated with acute anemia [18]. Our indication for blood transfusion was set at a hemoglobin concentration of 8.5 g/dl or a postoperative hemoglobin level of 8.5-9.0 g/dl with clinical evidence of acute anemia [19]. These levels may be adjusted according to the patient's cardiovascular status. One unit of allogeneic transfusion was calculated as 200 ml transfusion.

Blood loss by drainage, total postoperative blood loss, the need for autogenic and/or allogeneic blood transfusions, and the transfusion rate were recorded. Hemoglobin levels were measured on PODs 1, 7, and 14. A formula proposed by Nadler et al. [20] and Sehat et al. [21] was used to calculate the total postoperative blood loss. It was based on the maximum postoperative decrease in hemoglobin level adjusted for the weight and height of the patient.

We monitored the operating time, the wound condition (hematoma, infection), and the possibility of deep venous thrombosis (DVT) and/or pulmonary embolism (PE) for 4 weeks after the operation.

Statistical Analyses

Student's t-test was used to analyze parametric data, and the Mann-Whitney U-test was used for nonparametric data. $P<0.05$ was considered to indicate a significant difference.

Results

The results are summarized in Table 2. Total blood loss was less in the study group than in the control group (1156.3 ± 396.7 ml vs. 2318.0 ± 733.4 ml, $P<0.001$), as was total drainage (430.9 ± 284.6 ml

Parameter	Study group (*n*=25)	Control group (*n*=25)	*P*
Postoperative Hb (g/dl)			
POD 1	11.4 ± 1.2	10.8 ± 1.1	0.024
POD 7	10.4 ± 1.1	9.3 ± 1.6	0.003
POD 14	10.8 ± 1.1	10.4 ± 1.0	NS
Blood loss (ml)			
Drained	430.9 ± 284.6	1111.2 ± 319.3	<0.001
Total	1156.3 ± 396.7	2318.0 ± 733.4	<0.001
Transfusions (ml)			
Autologous	288.0 ± 245.5	472.0 ± 528.8	NS
Allogeneic	112.0 ± 216.6	776.0 ± 721.8	<0.001
Total	400.0 ± 200.0	1248.0 ± 361.8	<0.001
Transfusion rate (%)			
Autologous	64.0	48.0	NS
Allogeneic	24.0	60.0	0.006
Total	88.0	100.0	NS
Complication rate (%)	4.0	14.0	0.041

POD: Postoperative day
Results are the mean ± SD

Table 2: Postoperative data for all patients.

vs. 1111.2 ± 319.3 ml, $P<0.001$). There was a greater reduction in allogeneic transfusion rates in the study group than in the control group (24.0% vs. 60.0%, $P=0.006$). The mean amount of transfusion per patient for allogeneic transfusions was less in the study group than in the control group (112.0 ± 216.6 ml vs. 776.0 ± 721.8 ml, $P<0.001$). Autologous transfusion rates and the mean amount per patient were not significantly different in the two groups. The mean amount of transfusion per patient for total transfusions was less in the study group than in the control group (400.0 ± 200.0 ml vs. 1248.0 ± 361.8 ml, $P<0.001$). The total transfusion rates were not significantly different in the two groups. The hemoglobin level on POD 14 was not different in the two groups. On PODs 1 and 7, however, the hemoglobin level was higher in the study group than in the control group (POD 1: 11.4 ± 1.2 g/dl vs. 10.8 ± 1.1 g/dl, $P=0.024$; POD 7: 10.4 ± 1.1 g/dl vs. 9.3 ± 1.6 g/dl, $P=0.003$).

The operating time for the left knee was shorter in the study group than in the control group (81.8 ± 13.7 min vs. 95.8 ± 13.1 min, $P<0.001$). The operating times for the right knee were not significantly different in the two groups (89.5 ± 18.2 min in the study group vs. 92.8 ± 10.9 min in the control group, $P>0.05$). Neither symptomatic DVT nor PE was observed in either group. Wound complications, including infection and hematoma, occurred less often in the study group (wound infection in two knees) than in the control group (deep infection in one knee, wound infection in one knee, hematoma in five knees) (4.0% vs. 14.0%, $P=0.041$).

Discussion

The most important finding in this study was that injecting TA from the drain to the knee joint and drain clamping at the end of the operation effectively reduced postoperative blood loss and the need for allogeneic blood transfusion after bilateral cementless TKA.

One of the main problems after TKA is the need for allogeneic blood transfusion. Although the incidence is low, serious complications involving allogeneic blood transfusions (e.g., viral infections, graft-versus-host disease, and electrolyte imbalance) have been reported [22]. Because the need for allogeneic blood transfusion was reduced using our method, the incidence of transfusion-associated complications was reduced. Also, hemoglobin levels on PODs 1 and 7 were higher in the study group than in the control group. Because the general condition of the patients in the study group can be superior to that in the control group, aggressive rehabilitation may start earlier for the study group patients. Using our method in patients with bilateral cementless TKA is more cost-effective than the conventional method because it does not use cement, there is a single hospitalization, and the need for allogeneic blood transfusion was reduced.

The fibrinolytic system is activated transiently after any surgery [23]. TA is a synthetic amino acid that inhibits fibrinolysis by reversibly blockading lysine-binding sites on plasminogen molecules, thereby inhibiting activation. This situation prevents plasmin from binding with fibrinogen and fibrin structures after clot formation [24]. Because of its antifibrinolytic effects, the risk of increasing venous thromboembolism when using TA is a cause for concern [25,26]. TA, however, does not influence fibrinolytic activity in vein walls [26]. Therefore, neither our study nor previous studies observed an increased incidence of venous thrombosis in patients treated with TA [27-29].

Hematomas can lead to infection after TKA [30], but the incidence of postoperative infections and hematomas was lower in the study group than in the control group. Hematomas can be reduced using this method. A retrospective review of bilateral TKA compared incidences of symptomatic PE in simultaneous and staged procedures [31]. PE developed in 0.81% of patients who had undergone a single procedure and in 1.44% of patients who had undergone a simultaneous procedure. We combined subcutaneous administration of fondaparinux sodium with TA, a foot pump, and antiembolic stockings for successful thromboembolic prophylaxis [16,17]. Although randomized controlled trials with large numbers of patients are needed, we believe that our method for bilateral cementless TKA is safe, easy to perform, and suitable for these patients.

In our study, the operating time for the left knee was longer in the control group than in the study group. This finding may have been influenced by the use of different implant types. Although it is unclear whether there was greater blood loss in the control group, a longer operating time does not imply a greater chance of postoperative bleeding [32]. Further investigations using the same implant may be required.

The study has some limitations. It was a retrospective study. There also were differences in patient characteristics regarding their height and femorotibial angle and the implant types in the two groups. Therefore, selection bias was not completely excluded. Another limitation was the small number of patients. Randomized controlled trials with more patients are needed. Also, investigations using thromboembolism screening tests, such as ultrasonography, may be required.

Conclusion

Injection of TA from the drain to the knee joint and drain clamping at the end of the operation effectively reduced postoperative blood loss and the need for allogeneic blood transfusion after bilateral cementless TKA.

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