The Journal of Arthroplasty 29 (2014) 2337–2341

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Intraoperative Platelet-Rich Plasma Does Not Improve Outcomes of Total Knee Arthroplasty

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ARTICLE INFO

Article history:
Received 10 November 2013
Accepted 6 April 2014

Keywords:
platelet-rich plasma
total knee arthroplasty
bleeding
postoperative recovery
functional score

ABSTRACT

This randomized controlled study was conducted to assess the effects of platelet-rich plasma (PRP) on outcomes of total knee arthroplasty (TKA). Forty patients who underwent unilateral TKA were evaluated prospectively; 20 received intraoperative PRP and 20 served as control subjects. The results showed no significant differences in reduction of bleeding, range of motion, swelling around the knee joint, muscle power recovery, pain, Knee Society Scores, and Knee Injury and Osteoarthritis Outcome Score between the 2 groups. Additionally, no distinct clinical characteristics were found in patients who received intraoperative PRP. Therefore, we conclude that intraoperative PRP does not improve outcomes of TKA.

With regard to orthopedic surgery, an increasing number of total knee arthroplasties (TKAs) are performed because of aging of the population [1]. TKA is a well-established surgical procedure associated with a high rate of success [1]; however, several factors remain to improve the quality of TKA. Among the complications of TKA, one of the most critical is bleeding; thus, blood conservation is essential [2] and researchers are continuously attempting to reduce blood loss after TKA [3,4].

As a relatively new autologous source, platelet-rich plasma (PRP) came into the spotlight in nonorthopedic surgical fields for increasing bone, healing wounds, and reducing blood loss [5]. PRP, a so-called buffy coat product prepared from freshly drawn autologous blood, is a mixture of platelet- and leukocyte-rich plasma (activated with thrombin to produce a viscous gel cloth). PRP contains high concentrations of platelets with at least 6 abundant platelet growth factors such as platelet-derived growth factor and transforming growth factor, inside α-granules, each with a specific function during wound repair [6–8]. Activated PRP releases growth factors from the α-granules, which have been suggested to accelerate wound healing after surgery [8]. In this manner, PRP was originally considered a source of regenerative medicine mainly in oral and maxillofacial surgery [9,10]. Unlike other agents such as allogeneic blood products, PRP is autologous and not homologous, which does not impart an overt immune reaction. Additionally, PRP is expected to be effective in hemostasis, including wound and bone healing, pain relief, and infection control, by local administration in a variety of surgical fields [7,8,11,12]. In the orthopedic surgical field, PRP has been adopted in a number of surgeries, including those for tendon injury and spinal fusion, and is expected to improve bone and soft tissue healing, hemostasis, and pain relief [11,13].

Recently, several studies have suggested that application of PRP to the incision during TKA may substantially decrease postoperative bleeding [14–16]. Compared with favorable results, few peer-reviewed reports have demonstrated substantial clinical effectiveness. In addition, whether PRP is related to pain relief or functional outcome remains controversial [17,18]. This randomized prospective study aimed to assess the role of PRP as a hemostatic surgical tool during TKA and in the improvement of clinical outcomes such as pain relief and range of motion (ROM), up to 1 month after surgery. The primary outcome is blood loss, and the next outcome is improvement of clinical outcomes.

Materials and Methods

This study was approved by the institutional review board at our facility, and informed consent was obtained from all patients. From November 2010 to January 2012, 40 patients (40 knees) who were scheduled to undergo primary unilateral TKA were included in this observational study. They were randomly divided into 2 groups: 20 patients were treated with PRP (PRP group) and the remaining 20 were treated without PRP and served as untreated controls (control

The Conflict of Interest statement associated with this article can be found at http://dx.doi.org/10.1016/j.arth.2014.04.007.

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http://dx.doi.org/10.1016/j.arth.2014.04.007
0883-5403/

group). We used table of random numbers for randomization. We approached 40 patients and all the patients agreed to participate in this randomized study. The total number of patients enrolled in this study was chosen based on a previous study in our department on the minimum number of patients required to examine clinical differences, and further backed up by the power analysis for the study (alpha = 0.05; power level = 80%, typical standard deviation = 20%; difference detection = 20%; JMP Statistical Software Version 8.0.1). In all patients, the indication for TKA was osteoarthritis of the knee. Patients who were treated with anticoagulants and antiplatelets or who had bleeding diatheses were excluded from this study. Table 1 shows the demographic data of each group.

Platelet Gel Preparation

In this study, the autologous platelet gel used was prepared from PRP and, according to the manufacturer's protocol, was produced using the Accelerate Concentrating System (Exactech, Gainesville, FL). Briefly, a 60-mL container was filled with 57 mL of fresh whole blood, withdrawn via venous puncture just prior to surgery, and 3 mL citrate to avoid clotting. The 60-mL container was centrifuged at 3500 rpm for 15 min (Tabletop Centrifuge 2420; KUBOTA Corporation, Osaka, Japan) to separate PRP-containing buffy coat layers. The contents were kept until application. After finishing the components implantation, we sprayed the platelet gel (5 mL of PRP combined with 5 mL of 5000 U of thrombin in 2% calcium chloride solution) on all accessible surfaces of the deep wound in each patient in the PRP group (Fig. 1). In the control group, no application was performed, although fresh whole blood was similarly withdrawn from each patient's vein. All patients were blinded to this treatment.

Surgical Procedure

Under spinal anesthesia with an air tourniquet, a medial parapatellar approach was used to expose the knee joint. After intramedullary femoral and extramedullary tibial alignments, rods were employed for a measured resection technique, and a cruciate-sacrificing prosthesis (Advance [5 cases/10 controls], Wright Medical Technology, Arlington, TN; Genesis II [2 cases/0 controls], Smith & Nephew, Mississauga, ON; Low Friction Anatomical [1 case/1 control], Kyocera, Kyoto, Japan; Optetrak [10 cases/9 controls], Exactech; Vanguard [2 cases/0 controls], Biomet, Warsaw, IN) was implanted in all subjects. Both components were fixed with cement, and the patella was not resurfaced. After platelet gel treatment, the joint was closed layer by layer. No surgical suction drains were used in this study. In addition to mechanical prophylaxis with an intermittent pneumatic compression device until postoperative day 1, patients received 10,000 IU of heparin sodium (Ajinomoto, Tokyo, Japan) intravenously to protect against venous thromboembolism. The knee rested in bulky dressings for 1 day after the surgery, and a continuous passive motion device was used to encourage knee motion.

Table 1
Demographic data of PRP group and control group.

	PRP Group (n = 20)	SD	Control Group (n = 20)	SD	*P* Value	Power
Age	72	4.1	74.7	5.7	.09	0.50
Gender (male/female)	2/18		0/20		.15	0.74
Height (cm)	148.8	6.1	150	4.6	.48	0.58
Weight (kg)	58.5	6.3	57	9.5	.55	0.62
BMI	26.5	3.5	25.4	4.4	.36	0.53
Operated side (R/L)	12/8		10/10		.53	0.77
Operation time (min)	113	13.4	102.5	15.5	.03	0.51
Hb (g/dl)	12.7	1.2	12.6	1.0	.66	0.69
Ht (%)	38.4	3.2	38	2.6	.71	0.73
Platelets (×104 μl)	23.4	5.2	23.1	4.4	.82	0.83
CRP (mg/dl)	0.17	0.32	0.13	0.12	.69	0.72

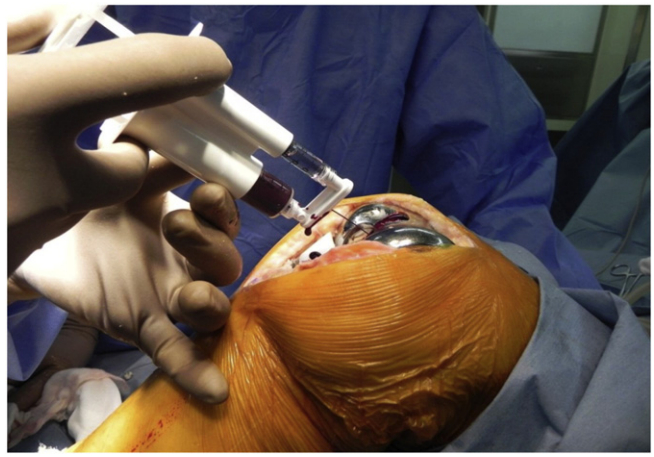

Fig. 1. Injection of PRP. After finishing the components implantation, we sprayed the platelet gel (5 ml of PRP, combined with the 5 ml of 5000 U of thrombin in 2% calcium chloride solution) to all accessible surfaces of the deep wound in PRP group.

Patient Evaluations

Hemoglobin (Hb) and hematocrit (Ht) levels were documented preoperatively and on postoperative days 1, 7, 14, and 28. Estimated blood loss was computed according to the formula of Gross and Sehat [19,20], and each patient's blood volume (PBV) was calculated using the formula of Nadler et al, as follows [21]:

$$V_L = PBV \times \{(H_O - H_F)/H_{AV}\}$$
$$V_L(mL) = estimated\ blood\ loss,\ H_O = preoperative\ Ht,$$
$$H_F = postoperative\ Ht,\ H_{AV} = (H_O + H_F)/2$$
$$PBV(mL) = k1 \times height(m)^3 + k2 \times weight(kg) + k3, k1 = 0.3669,$$
$$k2 = 0.3308,\ k3 = 0.6041\ for\ men;\ k1 = 0.3561,$$
$$k2 = 0.3308,\ k3 = 0.1833\ for\ women$$

C-reactive protein level also was recorded to evaluate inflammation preoperatively and on postoperative days 1, 7, 14, and 28. The affected knee's passive ROM was noted preoperatively and 1 month after surgery. A numeric rating scale was used to measure pain 3 times daily from the day before surgery to postoperative day 7. The highest score on each day was recorded. Muscle strength of knee extension was measured using a handheld dynamometer (Commander Muscle Tester Powertrack II; JTECH Medical, Salt Lake City, UT) preoperatively and on postoperative days 7, 14, 21, and 28. On each day, patients sat on a chair while physical therapists measured open kinetic isometric muscle strength of knee extension with 90° of knee flexion. The handheld dynamometer (HHD) was fixed at the distal third of the patient's lower limb. Measurements were performed 5 times daily, and the mean was used for analysis. For evaluating swelling around the knee joint, knee circumference at the upper pole of the patella and 5 cm and 10 cm above the upper pole of the patella was recorded preoperatively and 1 week after surgery. Differences in the circumferences between the day before surgery and postoperative day 7 were used for analysis. Knee Society Knee Score, Knee Society Functional Score [22], and Knee Injury and Osteoarthritis Outcome Score (KOOS) [19,23] were assessed preoperatively and on postoperative day 28. Additionally, perioperative complication and transfusion rates were recorded. Measurement, collection, and evaluation of all these data were performed by authors who were independent of the treatment.

Statistical analyses were performed using R version 2.8.1 (The R Foundation for Statistical Computing, Vienna, Austria). The nonpaired Student's *t* test was used to examine differences between groups, whereas Pearson's χ^2 test was used to assess frequency tabulations,