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ORIGINAL PAPER

The efficacy of autologous platelet gel in pain control and blood loss in total knee arthroplasty

An analysis of the haemoglobin, narcotic requirement and range of motion

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Abstract Biological materials used to assist in haemostasis following total knee arthroplasty have been the subject of much recent research. Autologous platelet gel is a substance that is derived from platelet-rich plasma extracted from the patient's blood and centrifuged perioperatively, and is applied to exposed tissues, synovium and the lining of the wound at closure. Concentrating and applying these factors directly to the wound at the end of a total knee arthroplasty procedure may lead to more complete haemostasis, a reduction in perioperative blood loss, accelerated tissue repair and decreased postoperative pain. In this study, 98 unilateral total knee arthroplasties were evaluated retrospectively, 61 of which involved the intaroperative use of platelet gel, and 37 of which served as control subjects. Outcomes analysed were postoperative haemoglobin changes, intravenous and oral narcotic requirements, range of motion on discharge and total days in hospital. Patients receiving platelet gel during surgery had less postoperative blood loss as measured by differences in the preoperative and postoperative haemoglobin on day 3 (2.7 vs. 3.2 g/dl; P=0.026). The narcotic requirement was less in the platelet gel group for both intravenous (17.0 vs. 36.3 mg/day; P=0.024) and oral (1.84 vs. 2.75 tabs/day; P=0.063) medication. This group also achieved a higher range of motion prior to discharge (78.2 vs. 71.9; P=0.052) and were discharged an average of 1 day earlier than their control counterparts. Though further prospective trials are necessary, this study indicates that the application of autologous platelet gel may lead to improved haemostasis, better pain control and a shortened hospital stay.

Résumé Le gel de plaquettes autologues est une substance dérivée des plaquettes plasmatiques extraites du sang du patient et centrifugées dans la période péri-opératoire, destiné à être appliquée sur les tissus exposés , la synoviale, et la ligne d'incision à la fermeture. Le but est d'avoir une meilleure hémostase, une réduction de la perte sanguine, une accélération de la réparation tissulaire et une diminution des douleurs post-opératoires. Dans cette étude 98 arthroplasties totales de genou ont été évaluées rétrospectivement, avec utilisation du gel plaquettaire dans 61 cas, les 37 autres servant de groupe témoin. Les éléments étudiés étaient le taux d'hémoglobine, la prise orale ou intraveineuse d'antalgiques et la durée d'hospitalisation. Les patients recevant le gel avaient moins de perte sanguine, mesurée sur le taux d'hémoglobine pré-opératoire et au 3eme jour (2,7 vs 3,2 g/dl; P=0,026). La nécessité d'antalgiques était moindre dans le groupe avec gel tant par vois orale (1,84 vs. 2,75 tabs/j; P=0,063) que par voie veineuse (17,0 vs. 36,3 mg/j; P=0,024). Le groupe avec gel atteignait une meilleure amplitude avant le départ (78,2° vs 71,9°; P=0,052) et celui-ci se situait en moyenne un jour plus tôt que dans l'autre groupe. Bien que des essais prospectifs restent nécessaires, l'application du gel plaquet-

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taire semble pouvoir améliorer l'hémostase, le contrôle de la douleur et raccourcir la durée d'hospitalisation.

Introduction

A successful outcome in total knee arthroplasty (TKA) requires adequate intraoperative haemostasis in order to avoid haematoma formation and minimise blood loss through suction drains. Achieving a satisfactory postoperative range of motion may depend largely upon adequate primary soft tissue haemostasis [1]. Persistent bleeding may lead to postoperative pain, wound haematoma and seroma formation, and arthrofibrosis, which have all been shown to be associated with suboptimal outcomes after TKA [2–5]. Postoperative pain is often treated with narcotic medications, which are effective, but are associated with a number of side effects, such as sedation, respiratory depression and constipation. Furthermore, these effects may be exacerbated in the elderly, who comprise a significant portion of the TKA patient population. Perioperative techniques that decrease the demand for narcotics may be very useful because they limit sedation and allow for earlier physical therapy, and possibly lead to shorter hospital stays.

Haemostasis is an important consideration in TKA, which may lead to perioperative blood loss as high as 1,500 ml and often necessitates transfusions [6–9]. Homologous transfusion carries a small but definite risk of viral infection, including the possibility of human immunodeficiency virus, hepatitis or cytomegalovirus transmission. Transfusion reactions are also known to occur. Predonated autologous blood does not carry a risk of viral infection, but the rates of administrative error and bacterial overgrowth are similar to those with homologous blood [10]. It has also been reported that the use of autologous instead of homologous blood may result in considerable additional cost without a concomitant increase in health benefits [11]. Consequently, efforts have been made to develop biological methods of haemostasis during the procedure.

The role of tourniquet use and the timing of release on perioperative blood loss have been studied extensively. In a prospective randomised study, intraoperative tourniquet release and electrocautery haemostasis were found not to be effective in reducing total blood loss in TKA [12]. Additional retrospective studies have shown that tourniquet release prior to wound closure followed by haemostasis is associated with significantly greater blood loss, higher rates of transfusion and longer operating times compared to tourniquet release after skin closure and compressive bandaging [13, 14]. Low-dose vasopressors in conjunction with drains have also been used to attempt to minimise perioperative blood loss. Ryu et al. used vasopressors to decrease postoperative blood loss after TKA by clamping the suction drain and infusing saline containing a low concentration of epinephrine in a retrograde fashion [15]. Saline infusion alone resulted in a significant decrease in postoperative bleeding compared to the controls, and the addition of epinephrine further increased the haemostatic effect [15].

Recently, fibrin tissue adhesive (or "fibrin glue") has been shown to be a particularly effective and relatively safe means of reducing the blood loss associated with TKA. In a prospective randomised study designed to evaluate the haemostatic efficacy of fibrin glue in patients undergoing TKA, patients who received fibrin glue exhibited a mean decrease of 518 ml of total blood loss compared to the controls, a significantly smaller drop of haemoglobin postoperatively, and a lower risk for transfusion, despite preoperative thromboprophylaxis with low-molecular weight heparin [9], an effect that accorded with other studies [16, 17].

Despite its apparent benefits, fibrin glue is made from human plasma and may contain blood-borne viral agents [18–21]. Though the risk of transmission is minimised by screening plasma donors and by inactivating and removing certain viruses, the potential for infection with viruses such as parvovirus B19 has been reported to be as high as 20% [21]. Considering the value of externally applied fibrin products in minimising blood loss associated with TKA, we sought to explore the use of an alternative autologous method. Treatment with autologous platelet gel (APG) involves obtaining and centrifuging the patient's blood perioperatively to isolate the factor-rich buffy coat. This component of blood contains concentrated platelets and their factors, specifically platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β), which have been associated with many beneficial haemostatic and wound-healing effects [22–24]. Both by mechanically sealing the tissues, vessels and lymphatics and by augmenting the healing cascade [25], platelet gel used during TKA may decrease both blood loss and pain medication requirements, thereby accelerating the recovery of the range of motion. Furthermore, since it is prepared directly from the patient's own blood, the risk of infection is essentially nonexistent.

Materials and methods

Platelet gel is a platelet-based biological clot that uses the platelet-rich buffy coat harvested from centrifuged autologous whole blood. One unit (approximately 450 ml) of blood was drawn perioperatively into an anti-coagulation bag containing citrate, phosphate and dextrose. The blood was centrifuged in the operating room using the Medtronic Sequestra 1000 Autotransfusion System (Medtronic, Inc.,

Minneapolis, MN). The buffy coat was then suspended in 30–50 ml of plasma and separated from the red blood cell mass and the platelet-poor plasma. When ready for application, 8 ml of the platelet concentrate was mixed with 0.5 ml of calcified thrombin, significantly less than the concentration used in spray thrombin preparations, and was rapidly applied to the dried surfaces [26].

A medial parapatellar approach to the knee was used, and the patella was everted. A cruciate-sacrificing prosthesis was used, intramedullary femoral alignment and extramedullary tibial alignment were employed, and both components were cemented. A tourniquet was used, and after cementing, it was deflated, haemostasis was achieved with electrocautery, and the wound was dried. Platelet gel was then initially applied to the posterior recess, the gutters and the exposed surfaces of the femur and tibia. The wound was closed in layers without the placement of any drains, and the remaining platelet gel was placed on the repaired extensor mechanism and prepatellar fat. Postoperatively, the knee was immobilised in bulky dressings for 24 h, and then a continuous passive motion device was applied at 0 to 40° and advanced as tolerated. Lateral retinacular releases, while not specifically quantified, were performed very infrequently.

The hospital records and charts were reviewed for 98 consecutive patients who underwent unilateral TKA by the senior author (PAM) between 1995 and 1999. The study group comprised 61 patients in whom APG was used during TKA, and the control group consisted of the remaining 37 patients who underwent TKA without APG. The cohort without APG was treated consecutively prior to the authors' use of APG. Data collected from patient charts include the following: patient age, date of surgery, discharge date, preoperative haemoglobin concentration, postoperative day 3 haemoglobin concentration, range of motion (ROM) on the first 3 postoperative days, ROM at discharge, patient-controlled anaesthesia (PCA) pump intravenous morphine requirement and oral oxycodone/acetaminophen (5/325 mg).

A Student's t-test was used to evaluate the study patients versus control patients based on five different parameters. The change in the patient's haemoglobin was evaluated and calculated as the difference between the postoperative day 3 value and the preoperative value. The number of milligrams of intravenous morphine required as well as the number of oxycodone/acetaminophen tabs required during hospital stay were tabulated. Lastly, both discharge ROM in degrees of flexion and the length of hospital stay from the date of surgery to the discharge date were analysed. All patients were evaluated postoperatively by the same physiotherapy team and placed on similar mobilisation regimens, and all patients were entered into the same algorithm for a target discharge of 4 days.

Results

The patients who had APG were an average of 73.3 years old, and the control group an average of 72.9 years old. The sex of the subjects in the APG group was 73% female and 27% male (45 females and 17 males), and in the control group, 77% were female and 23% were male (34 females and 10 males). All patients required TKA for due to end-stage osteoarthritis.

Patients receiving APG had a smaller decrease in postoperative haemoglobin (2.68 vs. 3.16 g/dl) compared to the controls. This difference was statistically significant (P=0.026). The study group required fewer intravenous (17.0 vs. 36.3 mg/day) and oral (1.84 vs. 2.75 pills/day) narcotics than the control group. The P-values were 0.024 and 0.063, respectively. Functional ROM achieved by discharge was greater in the APG-treated TKAs (78.2° vs. 71.9°) relative to the control TKAs (P=0.052). Patients treated with APG were discharged earlier, averaging one less hospital day (4.04 vs. 5.29 days) than their control counterparts (P=0.002).

Discussion

APG is derived from blood collected from the patient in the perioperative period. It contains a high concentration of platelets, can be used in individuals who are not candidates for blood bank donation and carries no risk of infection. We postulated that APG use in patients undergoing TKA would improve various outcome profiles. Our results indicate that the administration of APG has immediate benefits in the postoperative course for TKA and may result in a shorter hospital stay.

Numerous strategies for decreasing postoperative blood loss have been employed for major orthopedic procedures such as TKA. In our study, the haemoglobin decrease from the preoperative level to the third postoperative day was used as an estimate of blood loss. This was based on the assumption that significant haemodilution occurred during this period, so that haemoglobin concentration accurately mirrored blood loss. Patients who were not treated with APG had a significantly greater drop in haemoglobin concentration compared to those who were treated with APG, indicating that blood loss may have been minimised because of the APG treatment.

Relief of postoperative pain is an important criterion in the overall success of a TKA, and many potential postoperative complications may be manifested by excessive pain. In this study, patients treated with APG required lower doses of intravenous morphine than patients who did not receive platelet gel. This may have been due to accelerated haemostasis, with fewer and smaller hemarthro-

ses resulting. All patients were started on a standard PCA protocol immediately after surgery, with the same demand-dose and lockout interval. Patients who require fewer narcotics are likely to be less lethargic, start active rehabilitation sooner and more productively, and may have a lower risk for the pulmonary complications associated with excess narcotic sedation, though these parameters were not specifically quantified in this protocol. Similarly, the oral pain medication requirement in study subjects was also decreased. Early conversion to oral analgesics may be one of the factors significantly contributing to the shorter length of the hospital stay for patients in the study group. No patients who were taking narcotic pain medication, intravenously or orally, were concurrently taking non-steroidal anti-inflammatory therapy.

Assessment of immediate post-surgical outcome can be somewhat subjective, but early functional ROM may indicate a successful short-term postoperative course. Patients who received APG achieved a greater range of motion despite a shorter length of stay than the control group. The final ROM was measured on the day of discharge, allowing controls a longer recovery time and an additional day of physical therapy.

Prolonged hospital stay may be associated with exposure to virulent infectious agents, patient depression and increased cost to society. Protocols that lead to shortened hospital stay are beneficial to the patient and physician, as well as to the hospital and health care field. Use of APG led to a shortened length of the hospital stay when compared to controls that did not receive the treatment. The aforementioned parameters of decreased blood loss, decreased narcotic requirement and improved functional ROM support earlier discharge.

The potential beneficial effects associated with APG use may have been due to the growth factors, cytokines and fibrin products present in the platelet-rich plasma concentrate. Other studies have confirmed the efficacy of concentrating platelets by centrifugation of whole blood and harvesting of the platelet-rich plasma layer. Marx et al. [26] conducted platelet counts on patients' whole blood and compared them to the platelet counts of the platelet-rich plasma. Patients in the study averaged platelet counts of 232,000/ml (range, 111,000 to 523,000), and the buffy coat counts averaged 785,000/ml (range, 595,000 to 1,100,000), which was an average increase of 338% [26]. In addition to the growth factors present in platelet-rich plasma, other proteins elicited from platelets include thromboxane A2, thrombin and adenosine diphosphate. These attract additional platelets to the wound site, potentiating the activity of the originally applied platelets in forming a platelet plug, augmenting the inflammation cascade, and allowing for earlier haemostasis and repair [23]. The buffy coat, which is sequestered in the process, also contains concentrated leucocytes, which may add an anti-bacterial component to the gel, although this has not been substantiated [23]. It is suspected that platelets provide a concentrated and directed supply of growth factors that stimulate the migration and maturation of mesenchymal and epithelial cells [24]. In a goat model experiment to evaluate the effects of the addition of a platelet-rich clot around titanium implants used to anchor dental prostheses, histochemical studies on biopsy sections showed more dense bone with better organized trabeculae at 2–3 months in the experimental group [27].

Beyond clinical applications, APG use also has several practical and economic benefits. The process of perioperative donation eliminates clerical errors in the blood bank. Additionally, because the red blood cell mass may be returned to the patient, those who are unable to donate a unit of blood to the blood bank may still undergo platelet gel treatment. The materials cost approximately $180 per use, require less than 1 h of technician time, and the procedure adds about 10 min to the total operating room time.

Several limitations are inherent in this study. First, this was a retrospective analysis, and future work should include prospective, randomised controlled trials, which are necessary to identify the benefits of APG use more clearly. Furthermore, the degree of pain was measured indirectly, via the use of analgesics rather than by a pain-rating scale. We have no records of the preoperative ROM, so a direct comparison between pre- and postoperative ROM cannot be made, though due to the relatively large patient groups and the similarity in the age and pathology of all patients, it is unlikely a significant difference exists in the preoperative ROM between the groups. Also, this ROM was measured only in the short term, and additional studies will require longer follow-up. Finally, it is not known just how much aspirin and other anti-platelet compounds modify the effects of APG.

In conclusion, the application of autologous platelet-rich plasma is a simple perioperative procedure that can be used in total knee replacement. Platelet gel applied directly to the operative site after knee replacement seals the tissues and delivers platelets directly to the wound. Though further investigation is warranted, it appears that APG may have substantial benefits in patients undergoing total knee arthroplasty.

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