Blood Loss Reduction After Total Knee Arthroplasty. Comparison Topical Tranexamic Acid vs Platelet Rich Plasma

NCT02650856
Document Date: October 21, 2019
Date of Study Closure: April 26 2017

Statistical analysis Plan

The sample size was calculated using the following characteristics: 90% power and a critical *p* value of 0.05 for a decrease in the transfusion rate of 100% based on a previous report and on the assumption that may abate transfusion requirements.[21] This resulted in a total of 40 patients. Central tendency and dispersion measures were calculated for the numerical variables, and frequencies and percentages were calculated for the categorical variables. The Kolmogorov-Smirnov test was performed to test the normal distribution of all numerical variables. In the case of parametric numerical variables, Student's t-tests, one-way ANOVA, and multiple comparisons ANOVA were performed for related and independent samples. For non-parametric numerical variables, Mann-Whitney U, Wilcoxon, and Kruskal Wallis tests were performed. The Bonferroni sequential correction test was performed in the post hoc analyses. Statistical significance was set at a value of $p < 0.05$. The SPSS version 20.0 (IBM, Armonk, NY) statistical package for Windows 7 was used for the statistical analysis.

Brief Summary

The investigators will include patients who will be schedule for total knee arthroplasty with a diagnosis of osteoarthritis. The patients will be divided in two

groups. In both groups a verbal and clear detailed information will be given on the intraoperative approach. The first group will receive topical tranexamic acid and the second group topical platelet rich plasma; both in the surgical site. Both groups will be assessed before and after the intervention with laboratory results (hemoglobin, hematocrit levels) and drainage drain.

Detailed Description:

Total knee replacement (TKR) surgery is one the most common orthopaedic procedure in the world. Morbility in perioperative TKR is associated to: blood loss, pain, infection, wound complications, stiffness and thrombotic events. Blood loss and transfusion have been associated to increased hospital stay, costs, morbility and mortality of the patient. Indications for blood transfusions are now limited and it is well known that is not a free risk procedure. Complications such as; ABO incompatibility, viral transmission, hemolysis, immunosuppression and wound infection have been reported.

Literature reports have reported blood loss in TKR ranging from 300ml to 1 liter, and transfusion rate varying from 10-38%. In diminishing hospital cost Moskal J. et al reported 53.90% of savings and a 100% reduction in working hours of the hospital staff using topical tranexamic acid in TKR. Tranexamic acid is an antifibrinolytic agent that acts inhibiting the plasminogen, stabilizing the blood clot; it is used to stop surgical or traumatic bleeding like in the CRASH-2 trial, demonstrating its efficiency in the polytraumatized patients. Tranexamic acid has been used in the last years for blood loss with good results. Due to its systemic effects and past medical history of myocardial infarction, stents and previous thromboembolic events its intravenous use is limited. In this study the investigators

will use topical tranexamic acid and its use has been proven in clinical trials as secure strategy por blood loss reduction in TKR, without excluding patients with previous thromboembolic events.

Platelet rich plasma (PRP) is an orthobiologic that has played an important role over the past decade in different areas like; spinal fusion, ACL reconstruction, osteoarthrosis and tendinopathies. The use of platelet rich plasma (PRP) in orthopaedics is overrated and true indications for its use and cost benefit are still unclear. Retrospective studies like Pace T et al in 268 patients did not demonstrated differences in hospital stay, Postoperative hemoglobin levels, range of motion with the use PRP in TKR. Morishita M. Et al in a clinical trial of 40 patients, using intralesional PRP didn´t show any benefits for blood loss reduction in TKR, but good clinical results were observed in clinical scores like KOOS and VAS compared to the control group. Other studies have demonstrated the efficacy of topical PRP in blood loss reduction in TKR.

Due to its high platelet concentration and growth factors contained in the alfa granules; it is used as an hemostatic, analgesic and antiseptic agent in TKR.

There is a variety of blood loss prevention strategies for TKR and this strategies can be divided in preoperative, intraoperative or postoperative. The aim of this study is to compare the use of topical tranexamic acid versus topical platelet rich plasma.

An Insall knee approach, parapatellar medial will be used in all the patients. After the final cuts of the femoral, tibial and patellar and before placing the final cemented components the experimental intervention of the study will begin.

Group 1. A dosis of 2 gr of tranexamic acid (1000mg/10mL X-GEN

pharmaceuticals inc.) is diluted in 80mL of physiologic solution and will be divided in two applications:

First application: 40mL of the solution previously prepared is applied over the surgical site and it will be left for five minutes then drained out completely by suction.

Second application: The rest of 40mL of solution previously prepared is applied after placing the final TKR cemented components (femoral, tibial and patellar), over the surgical site and leaving it there without draining it by suction.

Group 2. In the preoperative room with previous premedication, a total of 55cc of total venous blood is obtained from the forearm (cubital o basilic veins). The blood is carried on 12 steriles tubes using sodium citrate at 3.8% as anticoagulant (BD, Vacutainer; Becton, Dickinson and Company, NJ). Blood samples are then transported to the Bank of Tissue (Banco de hueso Dr. José E. Gonzalez) where by centrifugation at 1800 rpm for 10 minutes (HeraeusMegafuge 1.0R; ThermoElectronCorporation) the separation of the 3 layers (White, yellow and red). The superior layer rich in plasma will be collected in 50 microliters polypropylene tubes (Corning,NY). A final volumen of 16 ml of platelet rich plasma is obtained and will transferred to airtight tubes (BD Vacutainer; Becton, Dickinson and Company, NJ). The manipulation of the blood samples is made on laminar flow cabin biosecurity class II (Logic 3440801; Labconco, KC). The platelet rich plasma will be activated with calcium gluconate at 10% (Pisa Farmacéutica, Jalisco, México) before using it is placed in the surgical site topically. The PRP simple will be divided in two applications, initiating the intervention after the final cuts of the TKR components (like the tranexamic acid group).

First application: 8 mL of PRP are applied over the surgical site and are left for five minutes then drained out completely by suction.

Second application: The rest of the 8 mL are applied over the surgical site after placing the final TKR cemented components (femoral, tibial and patellar), over the surgical site and leaving it without draining.

Then a primary closure of the wound is performed (capsule, fascia, subcutaneous tissue and skin) in both groups. A close drainage (Drenovac, NEdren S de R.L. de C.V.) is left intraarticular and fixed to the skin. The drainage will be clamped for 2 hours and removed at the 48 hours of the surgery. Thromboprophylaxis (low weight heparin) will be initiated after 6 hours of the end of the surgery. In the postoperative follow up, any patient with hemoglobin levels less than 9mg/dl with anemic syndrome will be transfused.

References:

Levine BR, Haughom B, Strong B, Hellman M, Frank RM. Blood management strategies for total knee arthroplasty. J Am Acad Orthop Surg. 2014 Jun;22(6):361-71. doi: 10.5435/JAAOS-22-06-361. Review. PubMed ID: 24860132

Wind TC, Barfield WR, Moskal JT. The effect of tranexamic acid on blood loss and transfusion rate in primary total knee arthroplasty. J Arthroplasty. 2013 Aug;28(7):1080-3. doi: 10.1016/j.arth.2012.11.016. Epub 2013 Mar 28. PubMed ID: 23541868

Frisch NB, Wessell NM, Charters MA, Yu S, Jeffries JJ, Silverton CD. Predictors

and complications of blood transfusion in total hip and knee arthroplasty. J Arthroplasty. 2014 Sep;29(9 Suppl):189-92. doi: 10.1016/j.arth.2014.03.048. Epub 2014 May 24. PubMed ID: 25007727

Moskal JT, Harris RN, Capps SG. Transfusion cost savings with tranexamic acid in primary total knee arthroplasty from 2009 to 2012. J Arthroplasty. 2015 Mar;30(3):365-8. doi: 10.1016/j.arth.2014.10.008. Epub 2014 Oct 12. PubMed ID: 25458093

CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, El-Sayed H, Gogichaishvili T, Gupta S, Herrera J, Hunt B, Iribhogbe P, Izurieta M, Khamis H, Komolafe E, Marrero MA, Mejía-Mantilla J, Miranda J, Morales C, Olaomi O, Olldashi F, Perel P, Peto R, Ramana PV, Ravi RR, Yutthakasemsunt S. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet. 2010 Jul 3;376(9734):23-32. doi: 10.1016/S0140-6736(10)60835-5. Epub 2010 Jun 14. PubMed ID: 20554319

Sheth U, Simunovic N, Klein G, Fu F, Einhorn TA, Schemitsch E, Ayeni OR, Bhandari M. Efficacy of autologous platelet-rich plasma use for orthopaedic indications: a meta-analysis. J Bone Joint Surg Am. 2012 Feb 15;94(4):298-307. doi: 10.2106/JBJS.K.00154. Review. PubMed ID: 22241606

Patel JN, Spanyer JM, Smith LS, Huang J, Yakkanti MR, Malkani AL. Comparison of intravenous versus topical tranexamic acid in total knee arthroplasty: a prospective randomized study. J Arthroplasty. 2014 Aug;29(8):1528-31. doi: 10.1016/j.arth.2014.03.011. Epub 2014 Mar 21. PubMed ID: 24768543

Chimento GF, Huff T, Ochsner JL Jr, Meyer M, Brandner L, Babin S. An evaluation of the use of topical tranexamic acid in total knee arthroplasty. J Arthroplasty. 2013 Sep;28(8 Suppl):74-7. doi: 10.1016/j.arth.2013.06.037. PubMed ID: 24034510

Georgiadis AG, Muh SJ, Silverton CD, Weir RM, Laker MW. A prospective double-blind placebo controlled trial of topical tranexamic acid in total knee arthroplasty. J Arthroplasty. 2013 Sep;28(8 Suppl):78-82. doi: 10.1016/j.arth.2013.03.038. Epub 2013 Jul 29. PubMed ID: 23906869

Sarzaeem MM, Razi M, Kazemian G, Moghaddam ME, Rasi AM, Karimi M. Comparing efficacy of three methods of tranexamic acid administration in reducing hemoglobin drop following total knee arthroplasty. J Arthroplasty. 2014 Aug;29(8):1521-4. doi: 10.1016/j.arth.2014.02.031. Epub 2014 Mar 6. PubMed ID: 24726174

Alshryda S, Mason J, Sarda P, Nargol A, Cooke N, Ahmad H, Tang S, Logishetty R, Vaghela M, McPartlin L, Hungin AP. Topical (intra-articular) tranexamic acid reduces blood loss and transfusion rates following total hip replacement: a randomized controlled trial (TRANX-H). J Bone Joint Surg Am. 2013 Nov

6;95(21):1969-74. doi: 10.2106/JBJS.L.00908. PubMed ID: 24196467

Pace TB, Foret JL, Palmer MJ, Tanner SL, Snider RG. Intraoperative platelet rich plasma usage in total knee arthroplasty: does it help? ISRN Orthop. 2013 Jul 28;2013:740173. doi: 10.1155/2013/740173. eCollection 2013. PubMed ID: 24971180

Morishita M, Ishida K, Matsumoto T, Kuroda R, Kurosaka M, Tsumura N. Intraoperative platelet-rich plasma does not improve outcomes of total knee arthroplasty. J Arthroplasty. 2014 Dec;29(12):2337-41. doi: 10.1016/j.arth.2014.04.007. Epub 2014 Apr 13. PubMed ID: 24851794

Aggarwal AK, Shashikanth VS, Marwaha N. Platelet-rich plasma prevents blood loss and pain and enhances early functional outcome after total knee arthroplasty: a prospective randomised controlled study. Int Orthop. 2014 Feb;38(2):387-95. doi: 10.1007/s00264-013-2136-6. Epub 2013 Oct 11. PubMed ID: 24114251

Bloomfield MR, Klika AK, Molloy RM, Froimson MI, Krebs VE, Barsoum WK. Prospective randomized evaluation of a collagen/thrombin and autologous platelet hemostatic agent during total knee arthroplasty. J Arthroplasty. 2012 May;27(5):695-702. doi: 10.1016/j.arth.2011.09.014. Epub 2011 Oct 27. PubMed ID: 22035976

Gardner MJ, Demetrakopoulos D, Klepchick PR, Mooar PA. 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. Int Orthop. 2007 Jun;31(3):309-13. Epub 2006 Jul 1. PubMed ID: 16816947