The Journal of Arthroplasty 29 (2014) 889–894

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Topical Administration of Tranexamic Acid in Primary Total Hip and Total Knee Arthroplasty

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ARTICLE INFO

Article history:
Received 18 July 2013
Accepted 7 October 2013

Keywords:
total hip arthroplasty
total knee arthroplasty
tranexamic acid
blood loss
hemoglobin
blood transfusion

ABSTRACT

Major blood loss is a known potential complication in total hip and total knee arthroplasty. We conducted a prospective, stratified, randomized, double-blind, placebo-controlled trial that evaluated 100 patients undergoing total knee or total hip arthroplasty to evaluate the effect on blood loss using the topical application of tranexamic acid. Participants received either 2 g of topical tranexamic acid or the equivalent volume of placebo into the joint prior to surgical closure. Tranexamic acid resulted in a lower mean maximum decline in postoperative hemoglobin levels when compared to placebo ($P = 0.013$). Patients in the tranexamic acid group demonstrated an improved but non-significant reduction in the units of blood transfused compared to placebo ($P = 0.423$). There was no clinically significant increase in complications in the tranexamic acid group, including no incidence of venous thromboembolism.

In 2010, there were more than 450,000 hip and over 720,000 knee arthroplasty procedures completed in the United States [1]. Major blood loss is a known potential complication of both procedures. Total blood loss as a result of these procedures varies in the published literature due to differences in surgical technique, a lack of standardized definition of blood loss, and differences in measurement of blood loss. Total blood losses in primary total hip arthroplasty (THA) and in primary total knee arthroplasty (TKA) have been documented to average 700 to 2100 mL and systemic postoperative hemoglobin has been reported in the literature to decline by 2.24 to 3.85 g/dL [2–6]. Reducing total blood loss, wound drainage, and the decline in postoperative hemoglobin levels may impact the pace of rehabilitation, the length of hospital stay, and postoperative morbidity [7].

Efforts to reduce surgical blood loss in these patients are relevant from a clinical and economical standpoint. Decreasing postoperative anemia may decrease blood transfusion rates, thus avoiding the risk of transfusion-related reactions, infection, fluid overload, and potential increased duration of hospitalization [8]. In addition, decreasing transfusion rates could lead to a substantial decrease in hospital expenditures. Blood transfusions are expensive, costing an estimated $1100 per unit of blood transfused at our facility. In an attempt to control postoperative blood loss and reduce the need for allogeneic blood transfusions, researchers have explored the use of the antifibrinolytic agent, tranexamic acid (TXA). TXA is a hemostatic agent and is a synthetic derivative of the amino acid lysine. TXA prevents the binding of fibrin to plasmin and preserves and stabilizes the matrix structure of fibrin and diminishes the ability of plasmin to lyse fibrin clots.

TXA has been used to decrease blood loss in various surgical settings. Studies have demonstrated a reduction in blood loss in both total hip and knee arthroplasty with the use of TXA with little or no noticeable side effects. However, the majority of these studies utilized intravenous administration of TXA and many involved the administration of multiple doses [9–24]. Topical TXA using a wound irrigation technique or intraarticular injection has been shown to be effective in lowering blood loss in TKA [23–35]. However, topical application of TXA in THA remains largely unexplored. The use of topical TXA may be preferable due to the potential reduction of systemic side effects such as thromboembolic events, ease of use, and lower cost.

Our primary hypothesis was that topical administration of TXA into the joint space immediately prior to joint closure in total knee and hip arthroplasty would result in a maximum decline in postoperative hemoglobin less than in those patients who received placebo. In addition, we compared the rate of blood transfusions and complications, including the rate of thromboembolic events.

The Conflict of Interest statement associated with this article can be found at http://dx.doi.org/10.1016/j.arth.2013.10.005.

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0883-5403/2905-0006$36.00/0 – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.arth.2013.10.005

Materials and Methods

After receiving Institutional Review Board (IRB) approval, this prospective, stratified, randomized, double-blind, placebo-controlled trial was conducted at a single community hospital. Prior to participating in the trial, all participants provided written informed consent which was obtained in the physician office by the surgeon preoperatively.

Patients of the surgeon author, aged 18 years and older, who were scheduled for a primary TKA or primary THA with or without cement were eligible for inclusion in the trial. Exclusion criteria included revisions, bilateral joint arthroplasty procedures, known hypersensitivity to TXA or its ingredients, active intravascular clotting disorders, and acute subarachnoid hemorrhage. Patients with a history of DVT or PE were not excluded as the current literature does not indicate TXA has an increase risk for thromboembolic events.

From January 2012 through July 2012, 50 patients undergoing TKA and 50 patients undergoing THA were randomized to receive either 2 g TXA in 100 ml of normal saline (NS) or the equivalent volume of placebo (NS) into the joint space prior to surgical closure. Utilizing the statistical program, MINITAB (version 16), 50 patients undergoing TKA were randomized in blocks of ten. In each block, five patients received TXA and five patients received placebo. This same block randomization was completed for 50 patients undergoing THA. All patients, physicians, nurses, anesthesiologists, research personnel, outcome assessors, and other healthcare professionals (excluding the non-research pharmacists and pharmacy technicians who prepared and dispensed the study medications) were blinded to the study arms. The treatment arm was prepared by removing 20 ml of NS from a 100 ml NS IV piggyback and adding 2 g/20 ml TXA to the NS piggyback to provide a total volume of 100 ml. The placebo arm was prepared by removing 20 ml of NS from a 100 ml NS IV piggyback and adding 20 ml NS back into the NS piggyback to provide a total volume of 100 ml. Pharmacy staff prepared all products following approved USP 797 Pharmaceutical Compounding Sterile Preparation techniques.

All procedures were primary total knee and total hip arthroplasties performed by the same surgeon and conducted under general or spinal anesthesia. Total knee arthroplasties were performed through a medial para-patellar approach under tourniquet control. All total hip arthroplasties were performed through an antero-lateral approach. No patients received a lateral release or bone graft. After final washout, the wound was bathed in 100 ml of study drug for two minutes and then just enough fluid was suctioned from the wound to allow joint closure. The tourniquet was released after skin closure and application of bandage in all knee cases. All surgeries were performed without the use of drains and maintenance fluid requirements were replaced with Normal Saline and each patient received a 500 ml bolus of hydroxyethyl starch (Hespan) on post-operative day one per standard practice.

Patients who were taking acetylsalicylic acid, antiplatelet agents, anticoagulants, or nonsteroidal antiinflammatory agents (including cyclooxygenase inhibitors) were advised to discontinue these medications seven days prior to the scheduled surgery. For antibiotic prophylaxis, patients were given cefazolin IV unless a documented allergy was listed, in which case vancomycin IV was administered. For venous thromboembolism prophylaxis, mechanical foot compression was applied in the postoperative recovery room. Unless contraindicated, patients were placed on warfarin while in the hospital and then discharged on aspirin 325 mg orally twice daily for 30 days. Those patients that were on therapeutic anticoagulation therapy prior to surgery were discharged on their pre-surgical anticoagulant regimen. Patients were considered for blood transfusion if they demonstrated symptomatic hypotension, or had a postoperative hemoglobin level less than 7 g/dL. The decision to transfuse was

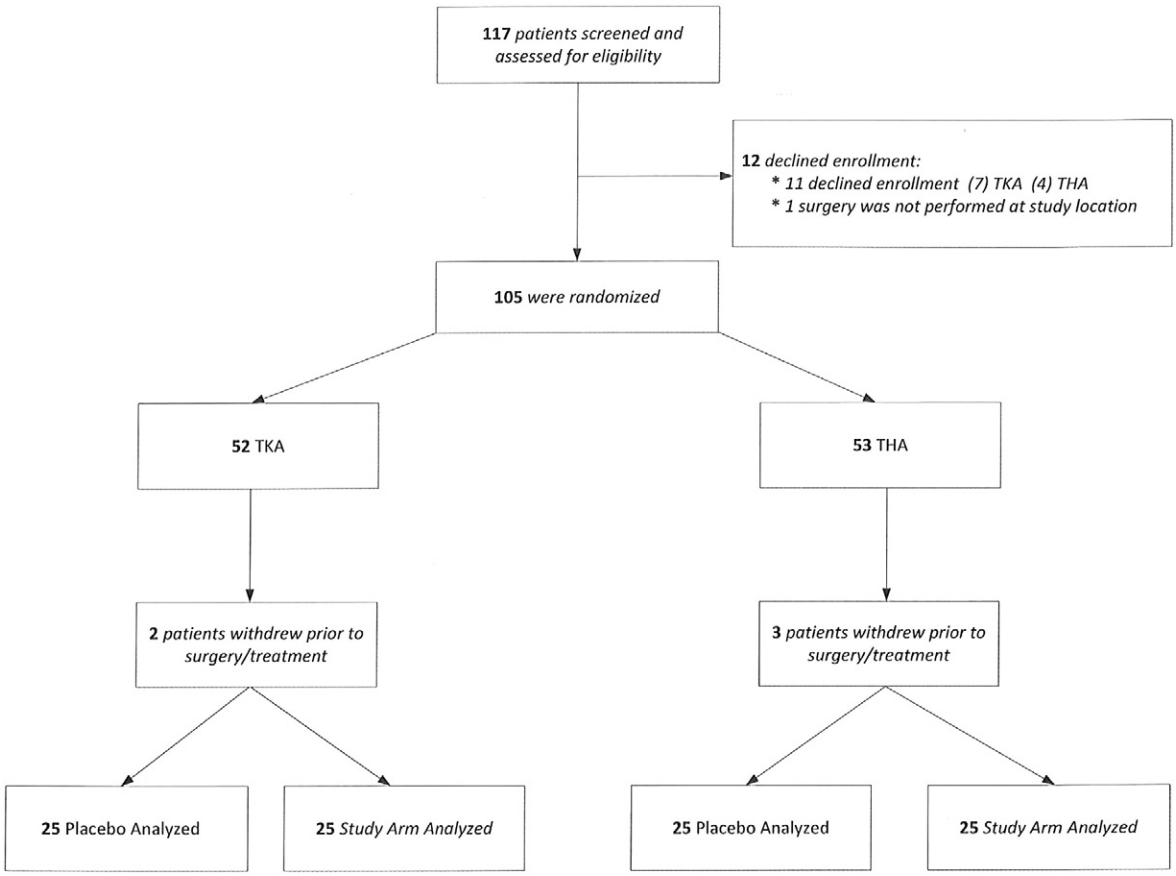

Fig. 1. Flow Diagram of patient enrollment and randomization.