**Tranexamic Acid Reduces Blood Loss and Transfusion in Patients Undergoing Total Knee Arthroplasty without Tourniquet: A Prospective Randomized Controlled Trial**

**Fernando Biodyeguli,1,2, Guillermo Arce,2, Alfonso Lugones,1 Sebastián Pereira1 and Gabriel Vindver1,2**

Bleeding represents the most common cause of postoperative morbidity after total knee arthroplasty (TKA), increasing transfusion requirements and prolonging length of hospitalization. Tranexamic acid (TA) is a synthetic derivative of the amino acid lysine that inhibits fibrinolysis by competitively blocking the lysine-binding sites of plasminogen. Numerous studies have demonstrated that the administration of tranexamic acid, either topically or systemically, diminishes bleeding following an array of surgical procedures, including TKA, without predisposing to thromboembolic complications.

In our institution, we performed this procedure without applying a tourniquet. We are not aware of any prospective, randomized, controlled trial that has evaluated the efficacy of tranexamic acid in reducing blood loss in patients undergoing TKA without the use of pneumatic tourniquet. Therefore, we designed a randomized controlled study to evaluate the use of this agent in patients undergoing TKA without tourniquet. The primary outcome measure was transfusion rate, secondary outcome measures were drain output, hematocrit/hematocrit levels.

**Methods**

We enrolled patients in a consecutive prospective manner on a voluntary basis. The study was conducted between September 2011 and July 2012. Candidates for the study were patients with a diagnosis of osteoarthritis scheduled to undergo primary, unilateral TKA. All patients had normal preoperative platelet count, prothrombin time, partial thromboplastin time and international normalized ratio. We randomized 50 patients to the study drug or placebo in a 1:1 ratio. The treatment group received TA 15mg/kg (diluted in 100 cc of normal saline) 10-minute intravenous infusion before the incision, followed by 15 mg/kg/8 hours thereafter. The control group received normal saline 10-minute intravenous infusion. We measured platelet function using the thromboplastin time and international normalized ratio. We randomized 50 patients to the study drug or placebo in a 1:1 ratio. The treatment group received TA 15mg/kg (diluted in 100 cc of normal saline) 10-minute intravenous infusion before the incision, followed by 15 mg/kg/8 hours thereafter. The control group received normal saline 10-minute intravenous infusion. We measured platelet function using the thromboplastin time and international normalized ratio.

**Results**

Postoperatively, hematocrit and hemoglobin levels were significantly higher at 24, 48 and 72 hours in the treatment group. Blood drained during the first 24 hours was lower in the treatment group (p<0.001). This results into zero transfusion requirement for the treatment group and 32% (8/25, 2.32 odds, 95% confidence interval 1.56-3.44) in the control (p=0.002); with 2.12 (range 1-4) transfused units. Six out eight transfused patients had a postoperative hematocrit level < 8 g/dl, while 2 patients had a hematocrit < 9 g/dl associated with significant comorbidities. None of the patients in the treatment group reached these transfusion thresholds. There were no thrombotic, embolic or infectious complications during hospitalization and at six-month follow-up.

**Outcome Measures**

The primary endpoint was transfusion rate during hospitalization. Patients were transfused in the event of a hemoglobin level <8 g/dl or <9 g/dl associated with either patients instability or with prior cardiac history. We also recorded data regarding the total drain output at twenty-four hours and the serial changes in hematocrit and hemoglobin (baseline, first, second and third postoperative days) for the hospital stay as well as adverse events related both to the wound and to any medical complications.

**Discussion**

TKA is associated with considerable intraoperative and postoperative need for blood transfusion. Several strategies have been used to diminish transfusion requirements such as the use of pneumatic above-the-knee tourniquet, postoperative blood salvage, hypotensive anesthesia, use of femoral intramedullary plug, cryotherapy or use of Jones bandage along with the administration of topical agents (fibrin-based or thrombin-based). TA affects the fibrinolytic system by inhibiting the proteolytic action of plasmin, which stabilizes clot formation and diminishes blood loss. Intravenous administration of this agent has dramatically reduced the rate of bleeding during TKA. Several investigators have also demonstrated its efficacy as a topical agent. In a recent TKA study, five different intravenous drug regimens were tested. This study clearly suggests the need for an intravenous preoperative dose of tranexamic acid to obtain the strongest effect. In line with these results, we used double-dose scheduled regimen with a preoperative dose and second dose 3 hours after the procedure, but in contrast with prior studies, we did not apply tourniquet.

To our knowledge, this study is the first to test the clinical safety and efficacy of this agent in patients undergoing TKA without pneumatic tourniquet. In conclusion, tranexamic acid reduces postoperative blood loss and the need for blood transfusion in patients undergoing TKA without the adjunctive use of an pneumatic compression tourniquet. We observed no increase in symptomatic thromboembolic phenomena in our patients.

**References**