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Evaluation of The Use of Tranexamic acid to Reduce Blood Loss in Unicompartmental Knee Arthroplasty

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Research Article

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ABSTRACT

Tranexamic Acid (TXA) has been associated with the ability to reduce blood loss in patients undergoing Total Knee Arthroplasty (TKA); however, publications assessing the efficacy and safety of TXA in Unicompartmental Knee Arthroplasty (UKA) are limited. We performed a retrospective chart review of 30 patients to evaluate the effect of TXA on blood loss and transfusion rates in UKA between January 2013 and January 2014. Use of TXA did not equate to a statistically significant difference in postoperative haemoglobin between the control group and the TXA group. There were no venous thromboembolic events or pulmonary embolisms reported in either group and no patients received blood transfusion. Although the use of TXA did not increase complications in the study, its use does not confer significant benefit.

INTRODUCTION

The main indication for which patients undergo knee arthroplasty is either osteoarthritis or Rheumatoid arthritis. In the United States, approximately 700,000 total knee replacement procedures are performed annually and Unicompartmental Knee Arthroplasties (UKA) make up 10%-15% of the total number of knee arthroplasties. UKA is an option for patients who have osteoarthritis limited to only one compartment of the knee [1-3]. Although the blood loss associated with UKA is not quantitatively comparable to that of TKA, the risk of bleeding complications requiring allogeneic blood transfusion still exist. Blood transfusion is attributed to multiple 3 complications such as transmission of HIV, Hepatitis B and C, ABO incompatibility, hemolysis, Transfusion-Related Acute Lung Injury

(TRALI), Transfusion Related Circulatory Overload (TACO) and even increased mortality [4]. As a result, various blood-conserving techniques including controlled hypotension, regional anesthesia, intraoperative blood salvage, erythropoietin, and anti-fibrinolytic agents have been implemented [5,6].

Synthetic lysine-analogue tranexamic acid (TXA, Trans-4-aminomethylcyclohexane-1-carboxylic Acid), was first patented by S. Okamoto in 1957[7]. TXA is not a pro-thrombotic agent but rather acts as an antifibrinolytic by reversibly binding to lysine receptor sites on plasminogen which then prevents plasmin from binding to and degrading fibrin. The binding of TXA to plasminogen is 6 to 10 times more potent that of e-aminocaproic acid, another antifibrinolytic agent [8]. The main purpose of TXA is the reduction of perioperative bleeding and transfusion requirements in both cardiac and non-cardiac surgery. It's application in cardiac surgery is well established in the past and recent meta-analyses confirm this belief [9,10]. An additional patient population which has experienced benefit from TXA as evidenced by the crash-2 collaborators are the trauma patients [11]. The pharmacological use of TXA in Orthopaedic surgery has gained much popularity due to the importance of reduction in blood loss especially in hip or TKA [12,13]. Numerous prospective and meta-analysis studies have investigated the efficacy of TXA in TKA and total hip arthroplasty and supports the routine use of TXA in such procedures; however, there is minimal literature to date on the use of TXA in UKA [14].

MATERIALS AND METHODS

After obtaining institutional review board approval, a retrospective cohort study was performed at Henry Ford Macomb Hospital comparing elective UKA patients who received TXA to those who did not receive TXA. The study population includes all patients 18 years of age or older who underwent elective UKA between January 2013 and January 2014. Patients were excluded if they had an active history of severe ischemic heart disease, chronic renal failure, cirrhosis, bleeding disorders, DVT or stroke, or any of the following contraindications of TXA, hypersensitivity to TXA or any component of the formulation, or acquired defective color vision, or active intravascular clotting, or subarachnoid hemorrhage. Patients were identified using ICD-9 codes corresponding to the listed surgeries. All procedures were performed by one fellowship-trained surgeon at a single institution who used a tourniquet control. The tourniquet was inflated prior to incision and was released after the application of dressing. Preoperative erythropoietin and intraoperative drains were not utilized. In both the control group and the TXA group standard fluid management per hospital protocol was followed. In addition, in both groups a multimodal pain management was utilized consisting of preoperative analgesia with typically spinal anesthesia and oral celecoxib, pregabalin, acetaminophen, and oxycodone, intraoperative dexamethasone and a periarticular injection with ropivicaine, epinephrine, and ketorolac. For postoperative thromboembolism prophylaxis, aspirin 325 mg twice daily for 4 weeks was utilized. Patients in the TXA group received 1 gram of TXA five minutes before incision and 1 gram in the post anesthesia care unit.

Data collected included demographic information, preoperative and postoperative haemoglobin and haematocrit levels, change in hemoglobin, units of allogeneic blood transfusions received, length of hospital stay, and development of venous thromboembolic. The need for 5 transfusions was indicated if the hemoglobin was less than 7 g/dL, or if hemoglobin was between 7-8 g/dL accompanied by hypovolemic signs and symptoms (headache, light-headedness, dizziness and systolic blood pressure less than 90). The primary endpoint was intraoperative and postoperative blood loss and number of allogeneic blood transfusions. Secondary endpoints were: length of stay, change in hemoglobin from baseline, duration of surgery, and adverse events (venous thromboembolism, and post-

surgical complications). Ordinal variables were compared using chi-squared tests and nonparametric Wilcoxon tests were used to compare continuous variables.

RESULTS

Nine and twenty-one patients were included in the TXA and control groups respectively. Demographic and baseline data for the TXA and control groups are shown in Table 1.

Table 1. Patient demographics and baseline variables of the patient groups.

Variable	Control (n=21)	TXA (n=9)	P-value
Gender (% females)	66.7	88.9	0.374
Age (years ± SD)	66.3 ± 8.3	56.1 ± 7.8	0.007
Pre-operative hemoglobin (g/dL ± SD)	13.5 ± 1.4	13.2 ± 1.3	0.587
Weight (kg ± SD)	87.8 ± 16	90.4 ± 6.5	0.635
Anesthesia (%spinal)	85.7	77.8	0.622

All patient demographic and baseline variables were not statistically significant except age; patients in the TXA cohort were younger compared to the control group (66.3 ± 8.3 *vs*. 56.1 ± 7.8, P= 0.007). Primary and secondary outcomes are illustrated in Table 2.

Table 2. Results of outcome measures between the patient groups.

Variable	Control (n=21)	TXA (n=9)	P-value
Average hemoglobin postoperative day 1 (g/dL)	11.8 ± 1.4	12.2 ± 1.1	0.353
Average hemoglobin drop postoperative day 1 (g/dL)	1.7 ± 0.9	1.0 ± 0.5	0.03
Transfusion rate, n (%)	0 (0)	0 (0)	0.236
Duration of surgery (hour ± SD)	1.5 ± 0.2	1.7 ± 0.1	0.09
Length of stay (day ± SD)	2.3 ± 0.5	2.0 ± 0	0.078
Venous thromboembolic events	0	0	N/A

There was no statistically significant difference in postoperative day 1 hemoglobin between the control group and the TXA group (11.8 ± 1.4 g/dL *vs* 12.2 ± 1.1 g/dL, respectively). The mean hemoglobin drop for the control group was 1.7 ± 0.9 g/dL, which was significantly greater than the TXA group at 1 ± 0.5 g/Dl (P=0.03). No patients in either the control group or the TXA group required allogeneic blood transfusion.

The length of hospital stay post-surgery was shorter in patients who received TXA in comparison to the control group (2.0 *vs*. 2.3 ± 0.5, P=0.078). Duration of surgery between the 6 two patient groups was not significantly different (1.7 ± 0.1 *vs*.1.5 ± 0.2, P=0.090). No incidences of VTE, pulmonary embolism, or postoperative infections were found in either group.

DISCUSSION

Orthopedic surgeries are associated with significant blood loss. The risk of bleeding complications with UKA is lower in comparison to other orthopedic operations. Several methodologies to reduce intraoperative blood loss have been implemented and the administration of TXA is one of the most recent interventions. TXA has gained attention for attenuating blood loss in total hip replacement as well as TKA, but currently there are limited published data on its role in UKA [12-14].

In our study, patients receiving TXA were administered 1 g intravenously 5 minutes before incision and 1 g intravenously in the post anesthesia care unit. We found that use of TXA did not result in a statistically significant difference in postoperative hemoglobin. We did however find that patients in the control group had a greater drop in hemoglobin from baseline than the patients in the TXA group. The administration of TXA in TKA and total hip arthroplasty has been identified with a significantly decreased requirement of allogeneic blood transfusion [15-17]. This relationship between TXA and blood transfusion is not consistent to what we found with patients in our study. More specifically, no patients in either the control or the TXA group required blood transfusion. The above finding can be attributed to the fact that patients undergoing UKA have less blood loss in comparison to patients undergoing TKA or total hip arthroplasty.

One theoretical concern in using TXA is its potential to cause VTE on the account of its mechanism of action. Even though TXA is an inhibitor of fibrinolysis, there were no studies supporting the notion that the administration of TXA increases the risk of thromboembolic complications. A recent meta-analysis looking at the use of TXA in total knee arthroplasty illustrated no significant difference in the occurrence of deep-vein thrombosis or pulmonary embolism compared to placebo [6]. Furthermore, also demonstrated the above conclusion in patients undergoing total hip replacement [12,13,18]. In our study, albeit not powered to detect a difference in the rate of thromboembolic complications, we did not find an association with the administration of TXA. Routine screening with Doppler ultrasound was not performed at our hospital, but patients with signs and symptoms of venous thromboembolism were evaluated appropriately with a venous doppler per hospital protocol.

We acknowledge that there were several limitations with our study. One inherent limitation is the retrospective nature of the study which allows confounding variables to make impacts on the findings in our study. To limit the effects of confounding variables, the surgical procedure was performed by a single surgeon, and there were no use of other blood conserving methodologies or drains. Second, with a small sample size, our study was not powered to detect differences that may have otherwise existed. Thirdly, we used hemoglobin as a marker for blood loss since the estimated blood loss is merely an estimate and drains were not used to determine blood loss. Factors such as body mass index, hemodilution, wound drainage, and hematomas could have impacted the hemoglobin levels.

CONCLUSION

In conclusion, this retrospective study at a community hospital is the first that we are aware of to assess the efficacy and safety of TXA in UKA. It was found that TXA leads to higher 8 postoperative hemoglobin levels compared to the control group, however no effect was seen on the number of transfusion. More studies are warranted to further assess the utility of TXA in UKA.

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