Protocol Title: Intravenous Tranexamic Acid in Total Shoulder Arthroplasty and Reverse Total Shoulder Arthroplasty

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Tranexamic Acid for the Reduction of Blood Loss in Total Shoulder Arthroplasty and Reverse Total Shoulder Arthroplasty

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Specific Aim: To determine whether Tranexamic Acid (TXA) administration reduces (1) blood loss, (2) decrease in hemoglobin, and (3) rate of transfusions following total shoulder arthroplasty (TSA) and reverse total shoulder arthroplasty (RTSA) surgeries via a prospective, randomized, double-blinded, placebo-controlled trial.

Hypothesis: Intravenous TXA will reduce blood loss following TSA and RTSA.

Background/Scientific review:
Anatomic and reverse total shoulder arthroplasty (TSA) is associated with the risk of moderate to significant blood loss that can lead to transfusions. Average estimated blood loss has been reported in the range of 354 to 361 mL intraoperatively, not accounting for additional postoperative blood loss postoperatively in surgical drains.[1,2] Transfusion rates have been reported to range from 2.4% to 9.5% in recent studies, with rates over 30% for revision cases.[1-4]. Tranexamic acid (TXA) is a synthetic antifibrinolytic agent that is an established method of reducing blood loss and transfusion requirement for patients undergoing total hip and knee arthroplasty.[5-9] TXA can be administered intravenously, topically (intraarticularly), or orally, with most available literature addressing intravenous and topical administration. Systematic reviews and meta-analyses of the total hip and knee arthroplasty literature demonstrate approximately a 30% decrease in blood loss and 50% decrease in transfusion rate with topical or intravenous administration of TXA compared to placebo.[5-9] Moreover, the literature demonstrates no increased rate of thromboembolic or other complications associated with TXA administration for hip and knee arthroplasty. [5,6]

Despite proven efficacy in the hip and knee arthroplasty literature, there have been no studies analyzing the ability of TXA to reduce blood loss and transfusion rate following TSA and RTSA.

Study Design:
- Prospective, randomized, double-blinded, placebo-controlled study
- Two identical, parallel studies will be conducted for primary TSA and RTSA patients.

Inclusion Criteria:
- Any patient scheduled for a primary anatomic or reverse TSA

Exclusion Criteria:
- Allergy to TXA
- Acquired disturbances of color vision
- Pre-op use of anticoagulant therapy within five days before surgery
- History of arterial or venous thromboembolic disease; such as DVT, PE, CVA, TIA
- Pregnancy or breastfeeding

- Recent MI (within 6 months of surgery) or any placement of stent regardless of time since placement
- Renal impairment
- Hemophilia
- Refusal of blood products
- Any patient undergoing a revision TSA or revision RTSA
- Patients who decline to participate

Treatment Groups:

TSA

1. Intravenous TXA Group (75 TSAs) – 1 gram TXA IV bolus (10 ml solution) 10 minutes prior to incision
2. Placebo Group (75 TSAs) –10 ml normal saline placebo IV bolus 10 minutes prior to incision

RTSA

1. Intravenous TXA Group (75 RTSAs) – 1 gram TXA IV bolus (10 ml solution) 10 minutes prior to incision
2. Placebo Group (75 RTSAs) –10 ml normal saline placebo IV bolus 10 minutes prior to incision

Surgical Protocol:

- Surgeons and patients will be blinded to TXA versus placebo and will proceed with routine surgical technique for primary TSA and RTSA in all cases.
- A surgical drain will be used according to attending surgeon preference.

Blood Transfusion Protocol

- Based upon clinical status and in conjunction with our internal medicine colleagues

Demographics/Patient Specifics:

- Age
- Sex
- ASA score
- Weight, Height, BMI
- Type of anesthesia
- *Indication for surgery:* osteoarthritis, post-traumatic arthritis, rheumatoid arthritis, rotator cuff arthropathy
- *Co-morbidities:* heart disease, hypertension, diabetes, use of NSAID, use of steroid
- Estimated intra-operative blood loss, Intra-operative fluids (crystalloid, colloid), Operative time, Hospitalization days,
- Pre-operative hemoglobin, hematocrit, PT/INR, Pre-operative PTT, Pre-operative platelet count

Outcome Measurements:

Primary

1. Post-operative blood loss

Secondary

2. Post-operative Hgb
3. Post-operative Hematocrit
4. Number of units transfused
5. Proportion of patients transfused
6. Cost comparison – Cost differences resulted from differences in the blood transfusion rate, length of hospital stay, and management of complications as well as from the cost of the TXA itself
7. Complications
    a. DVT or PE
    b. Return to the OR within 30 days
    c. Re-admission within 30 days
    d. Superficial infection
    e. Deep infection
    f. Periprosthetic fracture
    g. Cerebrovascular accident or Transient ischemic attack
    h. Dislocation

Risks/Benefits

The use of TXA is standard of care to reduce blood loss and transfusion rate in both primary and revision knee and hip arthroplasty surgeries. TXA side effects include of nausea, vomiting and/or diarrhea.

The hip and knee arthroplasty literature indicates no increase in complications with TXA use. Therefore, the only risk involved is the potential for breach of confidentiality and/or privacy. Below is a description of the procedure for maintaining confidentiality. There is no direct benefit to the participants in this study, other than the potential decrease in blood loss and transfusion rate.

Procedures for Maintaining Confidentiality

A breach of confidentiality and/or privacy is a risk of this study. To prevent this, all collected data will be stored electronically in password-protected files to protect patient identity and information. All information will be collected and reviewed by the research team only. Data will be maintained on a password-protected computer that will be accessible only to the study team. No patient identifiers will be maintained in the database.

Statistics

- *Sample size:* 150 TSA and 150 RTSA for the two parallel studies, randomly assigned to TXA and saline placebo.
- *Power analysis RTSA:* Using estimated blood loss from a recent paper at Rush,[1] (mean 353 +/- 232mL), power of 80% to detect a 30% reduction in blood loss at 5%

significance yields a sample size of 58 each for TXA and placebo. To account for attrition, we propose a sample size of 75 RTSA receiving TXA and 75 RTSA receiving placebo.
- *Power analysis TSA:* Using estimated blood loss from a recent paper at Rush,[2] (mean 361 +/- 220mL), power of 80% to detect a 30% reduction in blood loss at 5% significance yields a sample size of 55 each for TXA and placebo. To account for attrition, we propose a sample size of 75 TSA receiving TXA and 75 TSA receiving placebo.
- *Statistical analysis:* Independent sample t-test will be used for continuous variables with normal distribution. Non-parametric tests will be used for non-normal data. Fischer exact test will be used for categorical outcomes. Significance of 5% will be used.

References

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