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Tranexamic Acid to Improve Same-day Discharge Rates After Holmium Laser Enucleation of the Prostate (HoLEP)

10/29/2021

Protocol

PROTOCOL TITLE: Tranexamic acid to improve same-day discharge rates after Holmium Laser Enucleation of the Prostate (HoLEP)

PRINCIPAL INVESTIGATOR:
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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	Tranexamic acid
IND / IDE / HDE #	
Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	110
Funding Source	Department of Urology
Indicate the type of consent to be obtained	☒ Written ☐ Verbal/Waiver of Documentation of Informed Consent ☐ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process
Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐ Yes ☒ No
DSMB / DMC / IDMC	☐ Yes ☒ No

OBJECTIVES:

This study is designed to assess if there is a significant difference in same day discharge rates after Holmium Laser Enucleation of the Prostate (HoLEP). We attempt to perform HoLEP as a same-day discharge (SDD) procedure, but at NM, our SDD rate is currently approximately 60%. The limiting factor in SDD is hematuria. Tranexamic acid (TXA) is a clot promoting drug that is commonly used by orthopedic, cardiac and obstetric surgeons to prevent bleeding. Our

primary outcome will be to assess if there is a difference in SDD rates in those who receive TXA vs. those who do not.

Secondary outcomes will assess bleeding complications (defined as unplanned ED visit/clinicvisit/procedure/admission related to bleeding, clot retention, clot evacuation, need for perioperative transfusion) between patients who receive TXA vs. those do not. We will also assess differences in perioperative complications associated with TXA including but not limited to: deep venous thrombosis, pulmonary embolism, cerebrovascular events, between the groups. We will also assess for the duration of postoperative hematuria between groups. Additionally, we will assess for differences in operative times between the groups.

We anticipate that there may be up to a 25% increase in SDD rates in those who receive TXA vs. those who do not.

BACKGROUND:

Holmium Laser Enucleation of the Prostate (HoLEP) is a size-independent treatment option for bening prostate hypertrophy (BPH) as recommended by the American Urological Association (AUA) Guidelines.[1] Furthermore, HoLEP is one of the few surgical options that is recommended by the AUA for patients on active anticoagulation given its superior hemostatic properties.[1] Dr. Krambeck's research team has previously shown that same-day catheter removal and same-day discharge (SDD) was successful in approximately 87% of patients.[2] This study was performed in a limited cohort of 207 patients. Dr. Krambeck was recently recruited to Northwestern Medicine to introduce HoLEP to Chicago. Our current SDD rate is approximately 60%. Factors limiting discharge are primarily related to the degree of hematuria and patient anxiety.

Tranexamic Acid (TXA) is an indirect fibrinolytic inhibitor and was discovered in the early 1960s.[3] Although it was initially only used in women with heavy menstrual blood loss and those with hereditary bleeding disorders, it is now widely used in trauma situations and orthopedic, cardiac, otolaryngologic, and obstetric surgeries as it is cheap, safe, and effective.[3] Oral, IV, topical and combined methods of TXA administration also reduced blood loss and risk of transfusion compared to placebo for patients undergoing total hip arthroplasty.[4] TXA is safe, but high doses of TXA (80-100 mg/kg) or TXA use in those with poor renal function have been associated with an increased risk of seizures.[5] While there is no clear evidence of increased risk of thromboembolic events[6], it should be used cautiously in those with a history of embolic events, those on hormonal contraceptives [7]

Use of TXA in Urologic literature has been limited. One prospective, randomized controlled trial studied the use of TXA in 40 men undergoing transurethral resection of the prostate (TURP).[8] The authors found that TXA resulted in significantly less postoperative serum hemoglobin drop, less hemoglobin loss per gram of resected tissue, shorter OR time, and more resected tissue.[8] In another prospective, randomized controlled trial, the authors randomized 136 men undergoing TURP to receiving TXA or not.[9] The authors found TXA resulted in reduced operative blood loss, the amount of blood loss per gram of resected tissue, and shorter OR time. Interestingly, TXA did not decrease length of stay or catheter duration.[9] In one systematic review analyzing the effects of TXA after transurethral resection of the prostate, the authors included nine studies in their meta-analysis and found that TXA reduced intraoperative estimated blood loss as well as the transfusion rate.[10] The use of TXA in percutaneous nephrolithotomy (PCNL) has also been studied. A randomized, double-blinded, placebo-controlled trial enrolled 192 patients with Guy's stone scores III-IV. Patients were given 1g of IV TXA vs. placebo at time of anesthetic induction. The authors found that TXA administration during PCNL resulted in reduced blood transfusion rate, and higher stone free rates in the immediate postoperative period and at 3 months.[11]

Although HoLEP is one of the few surgical options recommended by the AUA for patients at high risk of bleeding due to its excellent hemostatic properties, for patients undergoing same-day discharge, hematuria is often the rate limiting factor. Currently, no studies have examined the use of TXA during HoLEP. Therefore, we would like to study if the use of TXA during HoLEP will increase our SDD rates.

STUDY ENDPOINTS:

Primary:

1) Difference in same-day discharge and same-day catheter removal rates

Secondary:

2) Difference in medical events: defined as unplanned ED visit/clinic visit/procedure/admission related to bleeding, clot retention, clot evacuation, need for perioperative transfusion
3) Duration of postoperative hematuria
4) Difference in operative, enucleation and morcellation times
5) Adverse events related to TXA (thrombotic events (DVT, PE, stroke), seizures,

PROCEDURES INVOLVED:

Visit 1 – Screening (Day -45 – Day 0)

i. Patients will complete:
   1) Patient Informed Consent Form,
   2) HIPAA form,
ii. Investigative site will complete: patient demographics, medical history, Inclusion/Exclusion Criteria
iii. Randomization and instructions to patients on whether or not to receive TXA

Visit 2 – HoLEP (Day 0)

iv. Inclusion/Exclusion Criteria to reconfirm eligibility (only if Screening and HoLEP are not on the same day)

v. Adverse Events secondary to TXA

Catheter Removal (Day 0 or 1)

Assessment of same day discharge and catheter removal rates

Week 1 through resolution of hematuria

The patient will receive a weekly computed generated text from Twilio (secure software integrated to REDCap) asking them to report their hematuria and dysuria after the procedure. It will also ask if they have had any unplanned visits or interventions. This will continue until 12 week post HoLEP survey

Visit 3 – One month follow-up (Day 30)

If patients have already reported resolution of hematuria, they will receive an additional questionnaire 30 days postoperatively to assess for bleeding complications and symptoms.

Visit 4 – Follow-up (12 weeks Post HoLEP)

vi. Patient will be assessed for BPH symptom related questionnaires in addition to urinary parameters. Will also confirm if there were or were not bleeding or other complications in first 90 days postoperatively.

Early Withdrawal Patients: The investigator will make reasonable attempts to ensure all enrolled patients complete the study.

****If the patient is unable to complete the questionnaires by text, they will be contacted by phone call for questionnaire completion.**

The HoLEP procedure is performed in a similar fashion by all surgeons with similar postoperative care plans. Duration of postoperative catheterization is determined by the treating surgeon, with respect to time of surgical case completion, need for inpatient observation, and patient preference. The portions of the case will not be altered regardless of patient being on anticoagulation or not, however the surgeon will not be blinded to the patient's status of anticoagulation therapy, as this knowledge would be paramount in postoperative management if there were complications.

DATA AND SPECIMEN BANKING

Data will be collected and stored electronically in REDCap. Quality assurance steps will include testing of database including any potential data calculated by command functions within REDCap (ex: age of patient at time of surgery calculated by using patient's date of birth and date of surgery) by study team prior to moving to production mode. The following quality control methods will be used: 1) single entry of data with random checks of accuracy, and 2) extraction and cleaning of data on a monthly basis that will be used for analysis every 3 months until completion of enrollment.

Data will be accessible to only authorized members of the study team. Any presentations on the study or published findings will use only de-identified data.

Data will be stored for 7 years after the end of the study. After this period, electronic data will be deleted.

SHARING RESULTS WITH PARTICIPANTS

Study results will not be shared with participants.

INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria

- Males 18 -89 undergoing HoLEP
- Willing to sign the Informed Consent Form
- Able to read, understand, and complete patient questionnaires**,** pain texts, and medication diary.

Exclusion Criteria

- Allergy or hypersensitivity to TXA, history of acute venous or arterial thrombosis, intrinsic risk for thrombosis or thromboembolism, history of thromboembolic disease, hereditary thrombophilia, use of hormonal agents
- Patients having a concurrent ureteroscopy +/- laser lithotripsy, percutaneous nephrolithotomy, or non-urologic surgery at the time of their HoLEP
- Anticipated need for perineal urethrostomy at the time of HoLEP
- Patient not undergoing catheter removal and voiding trial at Northwestern Memorial Hospital

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed

			to Address the Research Question
Local	0	110	110
Study-wide	0	110	
Total:	0	110	110

RECRUITMENT METHODS
Enrollment into the study will be performed by a qualified research coordinator.

After the patient completes their pre-surgical enrollment paperwork in the clinic, they will then be met in a private room away from the treating physicians by a qualified research coordinator who will discuss their potential enrollment and complete any research paperwork. Some patients may be approached via telephone with virtual consent.

Therefore, the initiation of enrollment will begin at the time of the office consultation visit. The patient will remain enrolled until she/he has completed the post-procedure follow up clinic/virtual visit at week 12. Data will not be collected beyond when the patient is seen at the postoperative clinic visit. If the patient is unable to have a physical or virtual visit, a text follow-up will be performed.
After consenting, patients will be randomized to one of two groups.

Group 1 (control): Receive intraoperative 1g TXA
Group 2 (experimental): No TXA

Randomization to **Group 1** or **Group 2** will be allocated through REDCap.[12] The stratified randomization list will be created and provided by the study statistician before the start of patient recruitment.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES
Patients will not be compensated for participating in this research.

WITHDRAWAL OF PARTICIPANTS
If a subject wishes to withdraw from the study, he/she may do so by verbal request to the research team. A subject may be withdrawn from the study by a physician-investigator if determined to be in the subject's best interest for medical reasons.

RISKS TO PARTICIPANTS
The risks in this study are no greater than the risks incurred during a HoLEP. AUA and EAU guidelines support HoLEP as a size independent treatment option for BPH.

Common side effects of TXA are nausea, vomiting, diarrhea, and muscle pain.

POTENTIAL BENEFITS TO PARTICIPANTS
Patients in the TXA arm may have higher rates of success with same day discharge and same day catheter removal.

DATA MANAGEMENT AND CONFIDENTIALITY
Data will be collected and stored electronically in REDCap. Quality assurance steps will include testing of database including any potential data calculated by command functions within REDCap (ex: age of patient at time of surgery calculated by using patient's date of birth and date of surgery) by study team prior to moving to production mode. The following quality control methods will be used: 1) single entry of data with random checks of accuracy, and 2) extraction and cleaning of data on a monthly basis that will be used for analysis every 3 months until completion of enrollment.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS
Data will be collected and stored electronically in REDCap and will only be accessible to members of the study team.

Data resulting from this study will not be linked to subjects. Subjects will not be referred to by name of initial in any publications.

CONSENT PROCESS
Enrollment into the study will be performed by a qualified research coordinator.

After the patient completes their pre-surgical enrollment paperwork in the clinic, they will then be met in a private room away from the treating physicians by a qualified research coordinator who will discuss their potential enrollment and complete any research paperwork. Some patients may be approached via telephone with virtual consent.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)
HIPAA authorization will be obtained as part of the consent. PHI from medical records and information collected from research and tumor samples will be protected by using coded subject numbers. The coded identifiers will be stored on a password protected spreadsheet stored on the FSM Urology server.

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11. Batagello CA, Vicentini FC, Monga M, et al. Tranexamic acid in patients with complex stones undergoing percutaneous nephrolithotomy: a randomized, double-blinded, placebo-controlled trial. *BJU Int*. Feb 25 2021;doi:10.1111/bju.15378