1) Protocol Title

Topical Intranasal Tranexamic Acid for Epistaxis in the Emergency Department

02/06/2017

2) Author of Protocol
UC Davis Researcher:

Aimee Moulin, MD
Brian Dang, PharmD
Brittany Traylor, PharmD
Christopher Adams, PharmD
Verena Schandera, MD
Howard McKinney Jr, PharmD
James Catlin, PharmD

3) IRB Review History

This protocol has not been submitted for review by an external IRB.

4) Objectives

Determine the efficacy and safety of topical intranasal tranexamic acid for patients with epistaxis that present to the emergency department.

The primary outcome of the study will be the time to control of bleeding after the administration of tranexamic acid. The secondary outcomes will be the length of stay in the emergency department, re-bleeding within first 24 hours and one week. Safety endpoints will include the incidence of thromboembolic events within one week and the incidence of any other drug-related adverse event.

The hypothesis is that topical administration of tranexamic acid will have comparable if not better time to control of bleeding, length of stay in the emergency department, re-bleeding at 24 hours and one week as well as minimal adverse effects compared to placebo.

5) Background

Epistaxis is defined as a nasal bleed of any cause, and is a commonly occurring condition that is usually self-limiting and rarely requires medical attention. Nares are highly vascularized mucosa with intricate folds and irregularities in the interior surface, and blood vessels closest to the surface of the mucosa are most prone to breakage and rupture. [1-2] The majority of epistaxis occurs anteriorly near the Kiesselbach's plexus; however, posterior epistaxis, which occurs at a lower incidence, usually occurs around the sphenopalatine artery and may result in airway compromise and aspiration of blood. [1-3] The causes of epistaxis are often due to mucosa dryness/irritation, nose picking, or facial traumas. Additionally, there are

disease states that place patients at a higher risk of epistaxis such as blood dyscrasia (i.e. platelet disorders), hemophilia, neoplasms or other disease states that require anticoagulants (i.e. warfarin, heparin, etc.).[1-2] It is estimated that epistaxis results in 4,500,000 emergency department visits per year throughout the United States.[3]

The standard of care and initial treatment of epistaxis is to applying direct pressure to the front of the nose. For patients that require additional medical intervention, the currently recommended treatment options include chemical or electrical cautery, nasal packing, hemostatic foams and gels, and topical vasoconstrictive agents.[4-6] Silver nitrate sticks applied to the location of the bleed is the usual method for chemical cauterization; however, the complications from this procedure are rhinorrhea, crusting, ulceration and possibly even perforation of the septum. Nasal packing with gauze or nasal tampons can also be performed to mitigate the bleeding, although this procedure may have complications such as the development of bacterial infections since the nasal packing becomes a viable living environment for bacteria. Additionally, extraction of the packing may result in the removal of the formed clot and could cause resumption of epistaxis. A more effective way to prevent re-bleeding is the use of hemostatic agents such as Surgicel®, Gelfoam®, and Avitene® which promote thrombogenesis and can be left in the nares. Additional treatment options are topical vasoconstrictive agents, such as oxymetazoline, which stimulates alpha adrenergic receptors in the nares resulting in vasoconstriction of the arteries and reduction of bleeding. Topical vasoconstrictors are usually not effective alone and are often used in combination with other modalities. Over use of vasoconstrictive agents may also result in worsening of epistaxis. Due to the pitfalls of these treatment options, tranexamic acid may be considered an attractive option.

Tranexamic acid (TXA) has been used in a variety of different hemorrhagic disease states. TXA is FDA approved for treatment of menorrhagia and tooth extraction for hemophilia patients[7]; however, there are many off-label uses of this drug especially for surgical and trauma patients. TXA is a synthetic amino acid that reversibly blocks the lysine binding site on plasminogen.[7] When this happens plasminogen is still converted to plasmin but has no proteolytic activity; therefore, TXA allows for the stabilization of a clot and prevents clot degradation. TXA is available as a 100 mg/mL intravenous solution as well as a 650 mg oral tablet. The half-life of TXA is between 2 to 11 hours and is excreted in the urine primarily as unchanged drug.[7-8] TXA is a well-tolerated drug with minimal adverse effects. Thromboembolic events are reported rarely; <1% occurrence for all formulations.[7-8] Other reported adverse effects include diarrhea, vomiting, and visual disturbances.[7-8]

TXA has been used in previous studies and case reports of epistaxis. White et. al. used oral TXA for the treatment of epistaxis.[9] Patients received TXA 1,000 mg by mouth three times a day for 10 days. The result of the trial showed that oral TXA reduced the amount of mild re-bleeds. Adverse events from oral TXA were minimal, but it was noted that one person developed superficial thrombophlebitis of

both legs following discharge from the hospital. Another study by Tibbelin et. al. used TXA gel (1,500 mg/15 mL) applied to the nasal cavity once for ongoing nosebleeds.[10] The study found no difference in resolution of bleeding within 30 minutes or re-bleeding at 3 and 8 days; however, the TXA group had patients with more moderate and severe bleeds than the placebo group ($P<0.01$). There were no adverse events observed in their study. A more recent study by Zahed et. al. used a cotton pledget soaked in 500 mg/5 mL of TXA and then anteriorly packed into the nares.[11] The results of the study showed that more patients had resolution of bleeding within ten minutes, more patients were discharged from the hospital at two hours, and there were fewer incidents of re-bleeding at 24 hours and at one week. No drug-related adverse events occurred during the study. From this data, we can extrapolate that the use of TXA seems to be beneficial for epistaxis with minimal risk of adverse events for patients.

In this study, TXA will be applied topically into the affected nares of patients with epistaxis. The advantage of topical TXA compared to nasal packing is that it is a quick, simple procedure that can be performed by a physician. Additionally, minimal manipulation of the nostrils is required and the risk of removing or disrupting the forming clot is also minimal. The goal of this study is to determine the efficacy and safety of topical TXA for patients with epistaxis that present to the emergency department.

6) Inclusion and Exclusion Criteria

Data will be prospectively collected from patients aged 18 years of age or older that are seen in the emergency department and diagnosed with anterior epistaxis. Patients that will be excluded are those unable to consent, do not have a valid telephone number, pregnant women, prisoners, cognitively impaired individuals, diagnosis of posterior epistaxis, major trauma, bleeding disorder such as thrombocytopenia or hemophilia, hemodynamically unstable, and a known hypersensitivity to study medication.

Patients will be screened for inclusion and exclusion criteria once patients have been assigned a room/location in the emergency department. Screening of patients will be done by the Emergency Medicine Research Associate Program (EMRAP), medical staff, and study investigators. The study investigators will perform informed consent of potential subjects and enrollment in the study.

7) Number of Subjects

a) Study- Wide:

Not applicable, as this is a single-center study.

b) Local:

All patients that have signed the consent form will be enrolled in the trial. We estimate that we will enroll a total of 70 patients in a 1:1 ratio in the study group to placebo group. Assuming time to control of bleed for the TXA group to be 10 minutes (SD ± 5 minutes) and the placebo group to be 15 minutes, the study will need to enroll 16 patients in each arm to obtain 80% power with an alpha of 0.05.

8) Recruitment Methods

a) Study-Wide:

Not applicable, as this is a single-center study

b) Local:

Patients that present to the emergency department during the enrollment time (Jan 2016 – January 2020) will be asked if they would like to be included in the study. If so the patient will be requested to fill out an informed consent form (HRP-502) and HIPAA Authorization Research form (see attachment).

c) HIPAA:

In order to identify prospective subjects for the study, the screeners and investigators will only need to know the primary diagnosis of epistaxis, age, and health conditions. No other health information will be accessed without consent. It would be impractical to get HIPAA Authorization prior to looking at diagnosis due to the high volume of patients that present at the emergency department.

All personal health information (PHI) will be de-identified and stored in an encrypted file to which only the primary investigator and primary study personnel have access. PHI, electronic, and hard copies will be deleted upon completion of the study. PHI will not be reused or disclosed to any other person or entity.

PHI to be accessed will include name, medical record number, age, medication administration record (MAR), laboratory data, patient flowsheets, patient history/demographics, medications profile and progress notes found within the electronic medical record (EMR). Name and medical record will not be attached to the other described data to minimize risk of loss of confidentiality.

9) Compensation to the Subjects

If a subject is injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by the University or the study sponsor or may be billed to the patient's insurance company just like other medical costs. The

University and the study sponsor do not normally provide any other form of compensation for injury.

10) Study Timelines

Date	Activity
December 2015	UCDMC IRB approval
February 2016 – January 2020	Recruitment, data collection
February 2016 – January 2020	Data analysis
November 2016 – January 2017	First interim analysis
TBD (at completion of study)	Study presentation and manuscript preparation

11) Study Endpoints

Primary efficacy endpoint:

- Time from administration of intervention until control of bleeding

Secondary efficacy endpoints:

- Length of stay in the emergency department
- Re-bleeding within the first 24 hours
- Re-bleeding within one week

Safety endpoints

- Incidence of thromboembolic events
- Incidence of other drug-related adverse events

12) Procedures Involved

Prospective, randomized, single-center, double-blinded, placebo controlled study comparing efficacy and safety of topical intranasal tranexamic acid.

Screening of subjects will be done by EMRAP, medical staff, and study investigators. Once a diagnosis of epistaxis is identified, the research personnel will screen for inclusion and exclusion criteria. If inclusion criteria are met, the study investigators will request consent from the patient for participation in the study.

Upon completion of consent, investigator will collect the following baseline characteristics: Age, sex, past medical conditions, home medications, laboratory values (complete blood count, coagulation values), and pertinent home medications.

Following collection of baseline characteristics, computerized randomization will assign patients to either receive topical intranasal TXA or placebo. The Investigational Drug Services (IDS) will set up block randomization using randomizer.org. IDS will not be involved in administration of TXA or placebo to the patient. Both groups will have

medical personnel apply direct pressure to both nares prior to starting the study and during the treatment period using standard of care procedures and/or equipment, with or without an ice pack. For patients within the two study groups, study protocol will then be initiated for whichever study arm the patient is randomized to. In case of emergency, the subject's data will be unblinded.

IDS will be in charge of storage, dispensing, labeling, and distribution of all study medications. IDS standards will be in place to ensure the integrity of the study.

For patients randomized to the TXA treatment arm, medication will be prepared as follows: TXA 1-2 mL will be drawn up into intranasal mucosal atomization device.

For patients randomized to the TXA treatment arm, medication will be administered as follows: Physician will administer 1 mL (100 mg) to each affected nostril(s) via the atomization device. Additional doses may be repeated up to two times to each affected nostril (TXA 100 mg/1 mL) at providers' discretion.

For patients randomized to the placebo treatment arm, medication will be prepared as follows: Normal Saline 1-2 mL will be drawn up into intranasal mucosal atomization device.

For patients randomized to the placebo treatment arm, medications will be administered as follows: Physician will administer 1 mL to each affected nostril via the atomization device. Additional doses may be repeated up to two times to each affected nostril(s) (Normal Saline 1 mL) at providers' discretion.

Following 30 minutes following administration of the medications, the provider will be allowed to provide additional medical intervention as they feel is necessary.

Patients will be monitored during this time for tolerability and safety.

Data collected will include: time of administration of drug or intervention(s), time to control of bleeding, length of stay in the emergency department, additional interventions required, and any incidence of adverse events. Data will be collected on a data collection form (see attached), which will then be transcribed into an electronic data form.

Prior to patient discharge, a valid telephone number will be obtained and patients will be informed that they will be contacted via telephone within one week to inquire about incidences of re-bleeding or any complications.

13) Data and/or Specimen Management and Confidentiality

All procedures regarding data management and confidentiality will apply locally at UCDMC. All data for this study will be retrieved and reviewed from electronic

medical records and documented on data collection forms. Patient sensitive information will be coded with a unique, anonymous identification number and kept on an encrypted UCDMC computer or on the encrypted Research Electronic Data Capture (REDCap server) with passwords only accessible by the research personnel directly associated with this study. The code sheet will be kept secure and separate from the dataset. Information will be stored on the UCDMC password-protected servers within password-protected electronic folders. This information will be accessible to study personnel only. Any patient-sensitive information on hard copies will be locked and stored in a work area accessible only to authorized study personnel.

Upon completion of the full-scale research study, all identifiers in hard copy format will be disposed of in the patient confidentiality bins and later shredded. Electronic data will be permanently deleted from any UCDMC computers and the REDCap server.

14) Data and/or Specimen Banking

No biological specimens will be banked for later use. All data information will be banked for a future study. All patient identifiers will be stripped from the data collected and only anonymous identifiers will be kept. Data will be stored on an encrypted UCDMC computer Data will be kept until the completion of a larger study. Data will not be released to any other entity outside of UCDMC.

15) Provisions to Monitor the Data to Ensure the Safety of Subjects

The study investigators will review data at 15%, 25%, 50%, and 75% of enrollment period to ensure patient safety. Upon findings of increased potential for patient harm or adverse events, the study investigators will report findings to IRB immediately. The study investigators will review documentation of adverse events noted during the treatment timeframe as well as during one week follow-up phone calls. If over 50% of the patient population requires emergent medical attention that is directly related to study medication, the study will be suspended until analysis of adverse event is complete.

16) Withdrawal of Subjects

Subjects have the right to withdraw from the study at any time. Subjects may withdraw from the study by informing the investigator and/or the treating physician.

Subjects may be withdrawn from the research without their consent if there are any major deviations from study protocol that jeopardizes the integrity of the study. This may include but is not limited to: incorrect dose of study

medication, incorrect administration of study medication, incomplete documentation, and inability to contact patient during follow-up.

17) Risks to Subjects

Reasonably foreseeable risks associated with intranasal administration are nasal irritation and allergic dermatitis. Due to the small volume and amount of intranasal TXA that will be used, we do not anticipate any side effects of parenteral TXA to be associated with intranasal TXA.

Foreseeable economic risk may be due to re-admission to the emergency department or hospital due to re-bleeding.

For both arms of the study, if epistaxis continues even after administration of TXA or placebo the risk are blood volume loss which may cause anemia, longer length of stay in the ED, requirement for additional interventions, and patient discomfort.

No foreseeable psychological or social risk.

18) Potential Benefits to Subjects

Direct potential benefits to the patients may be faster control of bleeding, decreasing need for invasive procedure, decrease risk of re-bleed, faster time to discharge, and fewer adverse effects.

19) Vulnerable Populations

This study will not include vulnerable populations.

20) Multi-Site Research

This study will only be a single-center study.

21) Community-Based Participatory Research

The community has not and will not be involved in the development of this research design.

22) Sharing of Results with Subjects

Research results will not be provided to the subjects involved.

23) Setting

Research will be conducted inside the emergency department at the University of California, Davis Medical Center (UCDMC) located at 2315 Stockton Blvd, Sacramento, CA 95817. Investigators will identify patients and recruit potential patients inside the emergency department. All medication preparation, medication administration, and procedures will be performed by the IDS or within the emergency department.

No community advisory board will be involved with this study.

24) Resources Available

Aimee Moulin, M.D. is currently an attending physician in the Emergency Department as well as the Assistant Emergency Medicine Residency Program Director, Coordinator of Intern Rotations, and Assistant Professor at for the UC Davis School of Medicine. Dr. Moulin received her Doctorate of Medicine at the University of Southern California and completed her emergency medicine residency at USC + LA County Medical Center. Dr. Moulin has had several years of clinical experience in the UC Davis Emergency Department providing clinical care as well as research support identifying, and participating in clinical research. In addition, Dr. Moulin has had experience in quality improvement both as the Quality Improvement Director for the ED at Sutter Sacramento and through quality improvement projects involving faculty from the Department of Psychiatry and the Psychiatric Evaluation Service at UCDMC. Dr. Moulin also serves as a board/committee member for many different professional organizations including the California American College of Emergency Physicians, Western Journal of Emergency Medicine, Emergency Care Psychiatric Committee for the Sierra Sacramento Valley Medical Society, and the California Office of Statewide Health Planning and Development. Additionally, Dr. Moulin has had multiple articles published in journals including: Western Journal of Emergency Medicine, American Journal of Emergency Medicine, and the Journal of Emergency Medicine.

Brittany Traylor, Pharm.D., BCPS is the director for the PGY2 Emergency Medicine Pharmacy Residency at UCDMC. Dr. Traylor joined the UCDMC team in 2012 following her PGY2 training at The University of Arizona Medical Center in Tucson, Arizona in emergency medicine. Dr. Traylor is currently responsible for the oversight of planning, implementing and management of clinical pharmacy practice in the emergency department, assuring efficient and effective clinical services among ED pharmacists, residents, and students. In addition to her responsibilities in the ED at UCDMC, she has since obtained faculty positions at UC San Francisco School of Pharmacy as a Health Sciences Assistant Professor. In 2013, Dr. Traylor was recognized by her colleagues by being awarded the Pharmacy Service Excellence Award.

Christopher B. Adams, Pharm.D. is currently an Emergency Department clinical pharmacist at UCDMC. During his formal pharmacy education he was a co-investigator evaluating diagnostic criteria in heart failure patients. His research efforts during his residency training culminated in a presentation at the Western States Pharmacy Residency Conference, an abstract published in Clinical Toxicology (DOI: 10.3109/15563650.2014.940163) and poster presentations at the ASHP Midyear Clinical Meeting and Exposition (Dec 2011 and Dec 2014), United Healthcare Consortium Conference (Dec 2012), The ACCP Annual Meeting (Oct 2013) and the America Academy of Clinical Toxicology's Annual Meeting of the North American Congress of Clinical Toxicology (Oct 2014). Dr. Adams was awarded the 2014 ASHP Pharmacy Resident Practice-Based Research Grants for his work on "Survey of Emergency Medicine Pharmacy Education Opportunities for Students and Residents" (doi: 10.1310/hpj5008-690) and was a co-authored on an editorial entitled "Student Commentary: Purpose and Impact of Introductory Pharmacy Practice Experiences," which was accepted for publication in Pharmacotherapy in 2011.

Verena Schandera, M.D. is currently a Post-Graduate Year Two Emergency Medicine Resident at UCDMC. Dr. Schandera completed her Bachelors of Science in Human Biology and also completed her Doctorate of Medicine at the University of California San Diego (UCSD). During medical school, she was involved in clinical research with the UCSD Neuroscience Department; which involved measuring hippocampal volume in children with cystinosis and evaluating memory function. Dr. Schandera presented her findings from this study at the UCDS Summer Research Conference. While at UCDMC, Dr. Schandera has been involved in quality improvement projects in the Emergency Department looking at safe patient sign outs.

Howard McKinney Jr, Pharm.D. is currently a clinical pharmacists in the emergency department at UCDMC. Dr. McKinney completed his Bachelor of Arts with a major in biology and minor in Spanish literature at the University of California San Diego and completed his Doctorate of Pharmacy at the University of California San Francisco. Dr. McKinney was also one of the founding staff

members of the San Francisco Regional Poison Control Center, a Poison Information Specialist, and a member of the Board of Directors for the American Board of Applied Toxicology (ABAT). In addition, Dr. McKinney is also a member of the American Academy of Clinical Toxicology, International Society of Toxicology, and North American Society of Toxicology.

James Catlin Pharm.D. is currently a Post-Graduate Year One Pharmacy resident at UCDMC. Dr. Catlin received his Doctorate of Pharmacy at the University of Florida. After completion of his PGY-1 year, Dr. Catlin will be the incoming PGY-2 Emergency Medicine Pharmacy resident 2016-2017. During his PGY-1 year, he completed his retrospective study regarding initial dose of diuretics for patients with heart failure that present to the emergency department. His results were presented at the Western States Conference in San Diego, CA in May 2016.

25) Prior Approvals

This study has not had prior approvals.

26) Provisions to Protect the Privacy Interests of Subjects

All steps will be taken to ensure privacy interest of the patient. Patients will be informed of their rights to place limits on whom they interact or whom they provide personal information to. It is within their right to request any research personnel to be removed or become involved with their care during the treatment period.

All healthcare professionals and research personnel involved in the patient's care are obligated to answer any questions or concerns the patient may have during the treatment period and into the follow-up period.

Research team will be permitted to access patient information that pertains to the care of the patient or relevant to the study's objectives after the consent and HIPAA forms are signed by the patient.

27) Compensation for Research-Related Injury

Due to minimal risk of research-related injury, no compensation will be provided.

28) Economic Burden to Subjects

Subjects are responsible for all medical care outside of study medication cost and supply.

29) Consent Process

The consent process will take place within the emergency department. Once prospective subjects are identified and all criteria are met, investigator will obtain consent as soon as possible. Since this study will require access to personal health information, subjects are required to sign a HIPAA Authorization for

Research form at the time of consent. For the enrollment of non-English speaking subjects, the study will follow HRP-090 SOP – Informed Consent Process for Research.

30) Process to Document Consent in Writing

The study will follow the SOP: Written Documentation of Consent. Consent for participation in this study will be documented by the attached HRP-502 form. Following agreement of consent, paper document will be filed in patient's unique identifier folder.

31) Drugs or Devices

☒ I confirm that all investigational drugs will be received by the Investigational Drug Service (IDS). The IDS will store, handle, and administer those drugs so that they will be used only on subjects and be used only by authorized investigators.

☒ I confirm that all investigational devices will be labelled in accordance with FDA regulations and stored and dispensed in such a manner that they will be used only on subjects and be used only by authorized investigators.

References

1. Morgan DJ, Kellerman R. Epistaxis: evaluation and treatment. Prim Care. 2014;41(1):63-73.
2. Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. Drugs. 1999;57(6):1005-32.
3. Pallin DJ, Chng YM, Mckay MP, Emond JA, Pelletier AJ, Camargo CA. Epidemiology of epistaxis in US emergency departments, 1992 to 2001. Ann Emerg Med. 2005;46(1):77-81.
4. Kucik CJ, Clenney T. Management of epistaxis. Am Fam Physician. 2005;71(2):305-11.
5. Villwock JA, Jones K. Recent trends in epistaxis management in the United States: 2008-2010. JAMA Otolaryngol Head Neck Surg. 2013;139(12):1279-84.
6. Singer AJ, Blanda M, Cronin K, et al. Comparison of nasal tampons for the treatment of epistaxis in the emergency department: a randomized controlled trial. Ann Emerg Med. 2005;45(2):134-9.
7. Lexicomp Online®, Hudson, Ohio: Lexi-Comp, Inc.; August 28, 2015.
8. Tranexamic acid [package insert]. Acella Pharmaceutals, LLC. Alpharetta, Ga.
9. White A, O'reilly BF. Oral tranexamic acid in the management of epistaxis. Clin Otolaryngol Allied Sci. 1988;13(1):11-6.

10. Tibbelin A, Aust R, Bende M, et al. Effect of local tranexamic acid gel in the treatment of epistaxis. ORL J Otorhinolaryngol Relat Spec. 1995;57(4):207-9.
11. Zahed R, Moharamzadeh P, Alizadeharasi S, Ghasemi A, Saeedi M. A new and rapid method for epistaxis treatment using injectable form of tranexamic acid topically: a randomized controlled trial. Am J Emerg Med. 2013;31(9):1389-92.
12. Utkewicz MD, Brunetti L, Awad NI. Epistaxis complicated by rivaroxaban managed with topical tranexamic acid: case report and literature review. Am J Emerg Med. 2015
13. Klepfish A, Berrebi A, Schattner A. Intranasal tranexamic acid treatment for severe epistaxis in hereditary hemorrhagic telangiectasia. Arch Intern Med 2001;161:767-767.
14. Aguilera X, Martínez-zapata MJ, Hinarejos P, et al. Topical and intravenous tranexamic acid reduce blood loss compared to routine hemostasis in total knee arthroplasty: a multicenter, randomized, controlled trial. Arch Orthop Trauma Surg. 2015;135(7):1017-25.
15. Waldow T, Szlapka M, Haferkorn H, et. al. Prospective clinical trial on dosage optimizing of tranexamic acid in non-emergency cardiac surgery procedures. *Clin Hem Micro* 2013;55:457-468.
16. Wolfe TR, Braude DA. Intranasal Medication Delivery for Children: A Brief Review and Update. *Pediatrics* 2010;126:532-537.

Title of research study: Topical Intranasal Tranexamic Acid for Epistaxis in the Emergency Department

Investigator: Aimee Moulin, MD, Brittany Traylor, PharmD, Christopher Adams, PharmD, Verena Schandera, MD, Howard McKinney Jr, PharmD, and James Catlin, PharmD

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you have presented to the emergency department with a nosebleed.

What should I know about a research study?

Experimental Subject's Bill of Rights

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any drug or device to be used.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
  - Other procedures, drugs, or devices that might be helpful, and their risks and benefits compared to this study.
  - Medical treatment, if any, that is available for complications.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document**.**

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, you may talk to the Principal Investigator or the Research Coordinator at (916-734-6498). In the case of an emergency, dial 911 from any phone.

For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to Emergency Department Clinical Pharmacist or you may call (916) 703-6110. Emergency Department Clinical Pharmacist is available from 7 am to 1 am, 7 days a week including holidays. If you are unable to contact a pharmacist, you may leave a voicemail and someone will return your call promptly. In the case of an emergency, dial 911 from any phone.

This research has been reviewed and approved by an Institutional Review Board (“IRB”). Information to help you understand research is on-line at

For IRB Use

http://www.research.ucdavis.edu/policiescompliance/irb-admin/.You may talk to a IRB staff member at (916) 703-9151, IRBAdmin@ucdmc.ucdavis.edu, or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

We are interested in evaluating the benefits of topical intranasal tranexamic acid for patients with epistaxis (nosebleeds). Tranexamic acid is not currently approved by the FDA for the treatment of nosebleeds.

How long will the research last?

We expect that you will be in this research study for one week following your discharge from the emergency department.

How many people will be studied?

This study will only be conducted at UCDMC and we expect to enroll about 70 people.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for reporting back to emergency department if you have a major nosebleed lasting over 20 minutes after discharge and informing the study investigator of any adverse events.

What happens if I do not want to be in this research?

You may decide not to take part in the research and it will not be held against you.

Instead of being in this research study, your choices may include: continue standard treatment at the discretion of the caring provider.

Potential risk of alternatives includes but is not limited to: more invasive procedure, nasal discomfort, prolonged bleeding, infection, and longer time to discharge from the emergency department.

Potential benefits of alternatives include but are not limited to: faster resolution of bleed, faster time to discharge from the emergency department, and less discomfort.

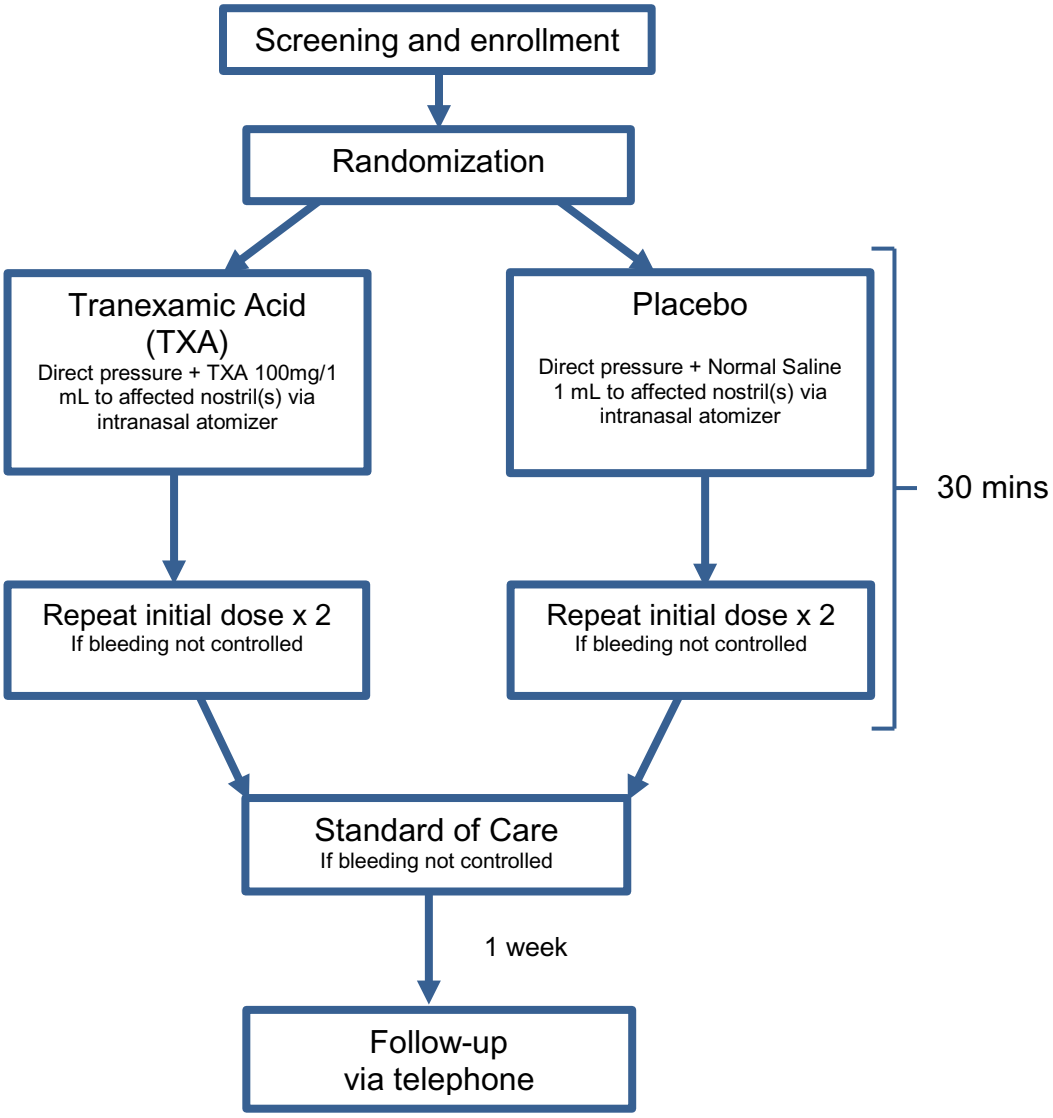
What happens if I say yes, but I change my mind later?

You can leave the research at any time and it will not be held against you. All data that has been collected up until the time you decided to withdraw consent will still be used but no further data will be collect.

For IRB Use

What happens if I say yes, I want to be in this research?

- If you agree to be in the study, below is a diagram illustrating the flow and pathways of the study.



- If you meet the inclusion criteria and agree to be in the study, the treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what treatment you get. You will have an equal chance of being given each treatment.
- In addition to direct pressure to the nares, you will receive tranexamic acid or placebo, which will be administered as a spray into the affected nostril(s). The study drug or placebo will be administered by an intranasal atomization device, which will spray a fine mist into your nostril(s). The study doctor will have the option of repeating this step twice during the first 30 minutes if bleeding is not controlled. The repeat doses will be the same as the initial dose.

For IRB Use

- If you are still bleeding after 30 minutes from the start of treatment, the study doctor may decide to perform other treatment options to stop the bleeding. Some standard treatment options are chemical or electrical cautery, nasal packing, hemostatic foams or gels, and/or topical vasoconstrictive agents.
  You will be contacted within a week from your initial visit via telephone for follow-up. The investigator will ask you questions regarding re-bleeding occurrences and if you have experienced any side effects.

- We estimate that the length of the treatment period will be around 30 minutes; however, your duration of stay in the emergency department may vary depending if you require additional treatment or have other medical needs.
- The doctor may order blood draws prior to the start of the study and may order additional blood draws at his/her discretion. The usual blood volume for a blood draw is approximately 6 mL.
- During the study you may interact with many healthcare providers in the emergency department such as but not limited to doctors, nurses, and pharmacists.
- The study will only be conducted at UCDMC during your stay in the emergency department.
- In case of an emergency, your study doctor can find out which treatment you were given.

Is there any way being in this study could be bad for me?

Tranexamic acid is a medication that is generally very well tolerated and many patients do not have any side effect to the drugs at all. Some rare side effects that have been reported are: nausea, vomiting, and diarrhea. Side effects that happen even at a lower frequency are: blood clots, visual changes, and seizures. If the bleeding continues even after administration of TXA the risk are blood volume loss which may cause anemia, longer length of stay in the ED, requirement for additional interventions, and patient discomfort.

There is a potential risk to privacy; however, the research team takes your privacy very seriously and will keep confidentiality as a top priority. The data collected will be de-identified and password-protected.

Your economic risks for participating in this study is that you may have to come back to the emergency department or seek medical attention if you have a re-bleed that last over 20 minutes after discharge.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

Risk of Ranodmization – This study involves two different treatments. Some people in the study will get a placebo instead of TXA. There is a risk that the treatment you receive may be inferior or may cause more side effects than the other treatment.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include faster resolution of nose bleed, faster time to discharge from emergency department, and decreasing your chances of having a re-bleed.

What happens to the information collected for the research?

Efforts will be made to limit use or disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the IRB and other University of California representatives responsible for the management or oversight of this study.

During your participation in this research, data will be collected about you. The de-identified data and any specimens, such as blood or tissue, are taken from you for this study; they will become the property of the University of California. The specimens may be used in this research, may be used in other research, and may be shared with other organizations. The specimens could lead to discoveries or inventions that may be of value to the University of California or to other organizations. Under state law you do not have any right to money or other compensation stemming from products that may be developed from the specimens.

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your research records to conduct and oversee the study. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your research records may be looked at by the sponsor of this study and government agencies or other groups associated with the study. They may not copy or take your personal health information from your medical records unless permitted or required by law.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/compliance/pdf/notice.pdf) and in an attached document.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include incorrect dose of study medication, incorrect administration of study medication, incomplete documentation, and inability to contact patient during follow-up.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

For IRB Use

What else do I need to know?

The cost of tranexamic acid will be covered by the study but you or your health plan will be billed for the costs of routine medical care you received during the study. These cost may include operating room fees, other pharmacy charges, treatments, hospitalizations, scans, etc. You will be expected to pay for the usual deductibles and co-payments, and for any routine care that is not covered. Only the costs of research or experimental procedures will be paid by the study**.** You will be charged for standard medical care including but not limited to: diagnostic labs, procedures, and medical supplies. You will not be charged for study medication and the medical supplies used to administer these medications.

For more information about possible costs, please contact the research team. The research team can follow UC Davis Uninsured Non-Emergency Estimate Policy (Policy ID 1883) to work with their department and Decision Support Services to get you a cost estimate.

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may call the IRB Administration at (916) 703-9151 or email at IRBAdmin@ucdmc.ucdavis.edu.

You will not be compensated for taking part in this study.

For IRB Use

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

[Add the following block if a witness will observe the consent process. E.g., short form of consent documentation or illiterate subjects.]

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	Date
Printed name of person witnessing consent process	

For IRB Use