THE GEORGE WASHINGTON UNIVERSITY

WASHINGTON, DC

Informed Consent for Participation in a Research Study

Title of Research Study: Prevention of postpartum hemorrhage (bleeding): pharmacokinetics and pharmacodynamics of Tranexamic Acid

Investigator: Dr. Homa Ahmadzia

Investigator Contact Information:

Phone: 202-741-2500

Email: hahmadzia@mfa.gwu.edu

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

We invite you to take part in a research study because you are having a Cesarean section at the George Washington University Hospital and have been identified at risk for bleeding after delivery

What should I know about a research study?

- Someone will explain this research study to you. You may ask all the questions you want before you decide whether to participate.
- Participation is voluntary; whether or not you take part is up to you.
- You can agree to take part and later change your mind.
- Your decision not to take part or to stop your participation will not be held against you.
- Your decision will not affect the medical care you receive from GW. If you decide not to take part, you can still receive medical care from GW.
- You may take this document home to read or to discuss with your family members or doctor before deciding to take part in this research study.

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who can I talk to if I have questions?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the Principal Investigator at ***202-741-2500.***

This research is being overseen by an Institutional Review Board ("IRB"). You may talk to them at 202-994-2715 or via email at ohrirb@gwu.edu if:

- You have questions, concerns, or complaints that are not being answered by the research team or if you wish to talk to someone independent of the research team.
- You have questions about your rights as a research subject.

Why is this research being done?

After delivery bleeding causes significant problems for mothers after delivery and is worldwide responsible for approximately 10 maternal deaths every hour. Prediction for who is at risk for severe bleeding is not reliable based on current methods. Aside from medications that help the uterus decrease in size for treatment and/or prevention, few other simple medical solutions exist.

Tranexamic acid (TXA) is an inexpensive and easy to administer drug that prevents blood clots from breaking down, routinely used in cardiac, trauma and orthopedic patients to prevent bleeding and reduce deaths. Most of the evidence to support dosing recommendations for clinical studies are based on drug level data from non-pregnant patients. High dose exposure to TXA among non-pregnant patients is associated with stomach side effects, seizures and a potential increase in blood clotting risk. Thus, US obstetricians and anesthesiologists are less likely to use TXA around delivery for prevention of after delivery bleeding due to uncertainty about the best dose to prevent bleeding and limit side effects.

The purpose of this study is to find out about drug levels of TXA when given for prevention at time of delivery. Three doses will be tested, (5, 10 and 15mg/kg). There is no standard dose; in previous studies using pregnant women the standard dose often ranges from 10-15mg/kg.

In addition, we aim to determine the impact TXA has on your blood taken in the period after delivery. This will involve some bleeding/clotting tests to be performed in the laboratory. This research may provide a method to make a common and necessary procedure safer and potentially reduce your risk for the need to receive a blood transfusion.

How long will I be in the study?

We expect that you will be in this research study for approximately 6 weeks, from the time you consent to the study until 6 weeks after your Cesarean section.

How many people will take part in this research study?

We expect 45 participants to take part in the entire study.

What happens if I agree to be in this research?

If you agree to take part in this research, the following study procedures will take place:

1. You will be asked to review and sign the study's consent form. This form also contains a HIPAA authorization permitting us to access your medical records as necessary to the study.
2. You will be assigned to one of the following three groups to determine what dosage of TXA you will be given at your scheduled Cesarean section:
    a. Participants in Group 1 will receive 5 mg/kg of TXA
    b. Participants in Group 2 will receive 10 mg/kg of TXA, up to a maximum dose of 1 gram
    c. Participants in Group 3 will receive 15 mg/kg of TXA, up to a maximum dose of 1 gram
3. On the day of your scheduled Cesarean section, you will receive your assigned dosage of TXA after the baby has been delivered. If recommended by your physician, a blood sample will be collected prior to delivery to measure your kidney function.
4. The amount of estimated blood loss (EBL) or total bleeding during and after delivery will be calculated.

5. Six blood samples will be taken in the first 8 hours and one taken at 24 hours after drug administration to determine the effect of the study drug. A second IV will be placed in one of your veins, in order for these blood samples to be collected. We will most likely collect this from the intravenous tubing you will have already in place.

   Breast milk samples will be taken after feedings during the after delivery hospital stay when is convenient for you after feeding the baby. A very small amount (<2ml) sample will be obtained 2-4 times in total. This can be obtained via breast pump or self-expression.

6. You will be evaluated during your hospital stay as well as by phone 1-2 weeks after delivery, and in person at 6 weeks for any signs or symptoms related to blood clots. We will ask about the health of your baby during these evaluations.

If you take part in this research, you will be responsible for fully understanding the study prior to agreeing to participate. There will be no additional visits taking place outside of the scheduled time for your Cesarean section, so you will not be responsible for returning to the clinic for follow up visits outside of the normal care.

What other choices do I have besides taking part in the research?

An alternative to participating in the study is to not participate. All persons approached for this study will receive the same level of high quality care regardless of whether they choose to participate.

What happens if I agree to be in research, but later change my mind?

You may refuse to participate or you may discontinue your participation at any time without penalty or loss of benefits to which you would otherwise be entitled.

If you decide to leave the research, contact the investigator so that the investigator can ensure no additional study procedures occur. To formally rescind your consent to participate, you must put this request in writing. You may do so by either emailing Dr. Homa Ahmadzia at hahmadzia@mfa.gwu.edu or you may write a letter and send it to:

Dr. Homa Ahmadzia, MD-MPH

2150 Pennsylvania Ave. NW Suite 6A Washington DC, 20037

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

What determines my eligibility to participate in this study?

Participants are pre-selected for the study if they meet the following eligibility criteria:

Inclusion Criteria:

a. Women who are undergoing medically indicated cesarean section at greater than 34+0 weeks gestation or women undergoing elective cesarean section at 39+0 weeks gestation in accordance with recommendations from the American Congress of Obstetricians and Gynecologists
b. Women who are undergoing elective or non-urgent cesarean delivery greater than 34+0 weeks gestation.
c. Pregnant women with normal kidney function

A patient will not be asked to participate in this study if they are found to have one or more of the following non-eligibility criteria:

Exclusion criteria:

a. Patients younger than 18 or older than 50
b. women with active blood clot or blood clotting disease
c. Women with a history of blood clot
d. Women with blood clotting problem or a medical condition that makes them more likely to have a blood clotting problem (i.e. lupus, antiphospholipid syndrome)
e. Women with a brain bleed
f. Women with acquired defective color vision (problem with seeing certain colors)
g. history of seizure disorder
h. known kidney problems (serum creatinine >0.9)
i. Twin or triplet pregnancies
j. Abnormal over-reaction to Tranexamic acid or similar medications
k. History of known liver problems

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

Possible risks and discomforts you could experience during this study include:

- Psychological: you may experience emotional discomfort if you are worried that a different level of care will be given to those who do or do not participate in this study. However, all efforts will be made to assure patients that participation in this study will not affect the quality of care received.
- Privacy: There is also a risk of breach of your private medical information. All efforts will be made to ensure that private medical information is protected. Risk of breach of privacy will be minimized by undertaking both recruitment and consent in the clinic and hospital, at your appointment in a private office or exam room. The research coordinator and the clinicians will practice discretion in choosing when to discuss the patient's involvement in the study. Furthermore, all patients who participate in the study will receive a special study number, and any study data collected will be labeled with that patient's special study number and stored in secure password protected digital locations. The only connection between your name and your special study number will be a code log. This log will be stored in a locked file cabinet in the research coordinator's locked office at the MFA, separate from any other documents relating to this study.

Physical: Risks of tranexamic acid include nausea, vomiting, diarrhea, seizures, and an allergic reaction. Tranexamic acid has been studied in a broad range of surgical and obstetrics studies and the risk for blood clots in the veins is thought possible but has not actually been shown. In the small randomized trials thus far in obstetric literature, there is no increased risk for blood clots found. Your baby will be exposed to the study drug. There may be other risks associated with this drug not yet known/published. Participants will be immediately unenrolled from the study under the following conditions:

Subject Discontinuation Criteria:

Women who experience any serious adverse side effect such as

a. unknown drug reaction or sensitivity
b. hives
c. severe trouble breathing

d. swelling in face or
e. sudden blood clot,

while undergoing TXA infusion will be removed from the study and the infusion of study drug will be stopped immediately. There is no optimal dose in pregnancy and that is why we are doing the study. The doses will be given in increasing fashion, meaning that participants enrolling early in the study will be given relatively low doses of the study drug and participants enrolling later will receive higher doses. Your assignment to a group is based on when you join the study rather than a medical decision made by the research team. The maximum dose being studied in this study is equal to the maximum dose being used in another large study using this drug for prevention where they plan to include 4,000 pregnant women.

Tranexamic acid is an FDA approved Category B drug, which means that it is not thought to harm the fetus. In this study, your baby will be exposed to TXA just before birth and TXA may transfer into breast milk in much smaller amounts. The effects of TXA in breast milk are currently unknown but to date there has been no evidence of harm to the newborn.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

What happens if I believe I am injured because I took part in this study?

The researchers have taken steps to minimize the known or expected risks. In spite of all precautions, you still may experience medical complications or side effects from participating in this study. You should promptly notify the study doctor in the event of any illness or injury as a result of being in the study.

If you believe that you have been injured or have become ill from taking part in this study, you should seek medical treatment from GWU Hospital and/or the GWU MFA or through your physician or treatment center of choice. Care for such injuries will be billed in the ordinary manner to you or your insurance company.

You will not receive any financial payments from GWU, GWU Hospital and/or the GWU MFA for any injuries or illnesses. You do not waive any liability rights for personal injury by signing this form.

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 decreased complications, decreased need for blood transfusions, and faster recovery if tranexamic acid does minimize blood loss during cesarean section. Additionally, as many patients with cesarean sections may get repeat operations for delivery during their lifetime, results of this study may inform management of repeat cesarean sections in the future.

The potential indirect benefits of the study are also significant. This research may provide a method to make a common and necessary procedure safer. It may potentially help future studies designed to identify the lowest safest dose for women to use during childbirth for prevention of after delivery bleeding.

Can I be removed from the research without my permission?

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 a change in your medical history between

the time you agree to participate and when you are scheduled for your scheduled cesarean section which, in the opinion of the investigator, no longer makes you a good candidate for our study. We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What happens to my information collected for the research?

To the extent allowed by law, we limit your personal information to people who have to review it. We cannot promise complete secrecy. The IRB and other representatives of this organization may inspect and copy your information. Others include the Food and Drug Administration (FDA), and the Department of Health and Human Services (DHHS).

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

How will my privacy and health information be protected?

The Health Insurance Portability and Accountability Act (HIPAA) requires that researchers and health care providers protect the privacy of information that identifies you and relates to your past, present and future physical and mental health or conditions, or the provision of health care. If you agree to participate in this research, protected health information will be used and shared with others for purposes of the study. Below is more detailed information about how your health information will be shared and protected. By signing this form, you are allowing the people and groups that are listed in the next paragraphs to use your health information for this research study. Your information will only be used or shared as explained in this authorization form

The use and release of protected health information is for the purpose of collecting data for this study.

Protected Health Information to be shared with researchers for the purposes of this study: email and phone number (for recruitment purposes only), name, medical record number, age, date(s) of medical procedures, race/ethnicity, gender, blood samples (for lab analysis).

Who may disclose your protected health information: The researcher and the other members of the research team may obtain your individual health information from:

Hospitals: The George Washington University Hospital

Clinics: The Medical Faculty Associates

And from hospitals, clinics, health care providers, and health plans that provide health care to you during the study.

By signing this form, you allow the use, sharing, copying, and release of your protected health information in connection with this study by:

- The members of the research team;
- Other healthcare providers such as labs which are part of the study;
- Institutional officials who are responsible for compliance; Some of the tests in this study would have been done as part of your regular care. These test results will be used both to treat you and to complete this research. The test results will be recorded in your medical record. These study results will be included in your medical record. Results of tests and studies done solely for this research study and not as part of your regular care will not be included in your medical record.

Once your health information has been disclosed to others outside of the hospitals and medical practices by your authorization or communication, the information may no longer be covered by the federal regulation that protects privacy of health information.

Not signing this form or later canceling your permission will not affect your health care treatment outside the study, payment for health care from a health plan, or ability to get health plan benefits. However, if you do not give permission to use your health information, you may not take part in this study because your health information is needed in order to conduct this study.

This Authorization does not have an expiration date.

However, you may cancel this authorization at any time. Even if you cancel this authorization, the researchers may still use the protected health information they already have about you; however, no new health information or new biological specimens will be collected from you after you cancel your permission.

To cancel your permission, you will need to send a letter to Dr. Homa Ahmadzia stating that you are canceling your authorization. This letter must be signed and dated and sent to this address:

Homa Ahmadzia
2150 Pennsylvania Ave NW
Suite 6A
Washington DC, 20037

Are there any costs for participating in this research?

There is no cost to you for participating in this research study.

Will I be paid for my participation in this research?

If you agree to take part in this research study, we will pay you $200 in the form of a Visa gift card *or* instead of the gift card you will receive a Medela breast pump valued at $250 for your time and effort. You will receive this compensation after you have undergone delivery and all blood samples are collected.

What else do I need to know?

This research is being funded in part by GWU School of Medicine and Health Sciences. Results of this study will be made publicly available on www.clinicaltrials.gov.

By signing below, you agree that the above information has been explained to you and you have had the opportunity to ask questions. You understand that you may ask questions about any aspect of this research during the course of the study and in the future. Your signature documents your permission to take part in this research. Your signature documents your permission to take part in this research.

_____
Printed name of subject

_____ _____
Signature of subject Date

_____ _____
Signature of person obtaining consent Date