Article Title: Tranexamic Acid for Prevention of Hemorrhage in Elective Repeat Cesarean Delivery – A Randomized Study

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Consent to be part of a Research Study
To be conducted at
The University of Texas Southwestern Medical Center
Parkland Health & Hospital System

Key Information about this Study

This study is being done to find out whether a drug called tranexamic acid (TXA) given through your IV can decrease your risk of bleeding from your cesarean delivery.

Abnormal bleeding can happen after giving birth, and affects 11 out of every 100 deliveries. Tranexamic acid is a medication that works by keeping the body from breaking down blood clots (also known as an antifibrinolytic). It has been shown to decrease bleeding during surgery.

This study will last two days. We will look at your medical record to learn more information about you. You will receive two doses of the study drug while you are in the operating room. You will have your blood drawn twice on the day of your cesarean delivery, and once the day after your cesarean delivery to see how well your blood is clotting.

The benefit to you of participating in this study is that the information we learn from the study can help limit blood loss in women like yourself who have cesarean deliveries in the future. If you receive active study drug, it may decrease the risk of bleeding during your cesarean delivery.

There are risks to this study described in this study. Some risks include: nausea, muscle and joint pain, headache, blood clots and allergic reaction.

If you are interested in learning more about this study, please continue reading below.

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is Olutoyosi Ogunkua MD, Department of Anesthesiology and Pain Management at University of Texas Southwestern.

Funding

Simmons Sister Fund, a non-profit organization is funding this study. This organization is providing money to University of Texas Southwestern so that the researchers can conduct the study.

Purpose – "Why is this study being done?"

Women who have more than one cesarean delivery increase their risk of bleeding. Bleeding after cesarean delivery is called postpartum hemorrhage and affects up to 11 out of every 100 deliveries. It is the leading cause of death and injury in pregnant women. This study is being done to find out whether a drug called tranexamic acid given through your IV can decrease your risk of bleeding from your cesarean delivery. The body has the ability to form and break down blood clots. Tranexamic acid works by stabilizing blood clots, and prevents bleeding.

You are asked to participate in this research study of the effect of tranexamic acid on prevention of bleeding in cesarean delivery. Severe bleeding during cesarean delivery is currently treated by medication to help your uterus contract, and blood transfusions. Current treatment focuses on replacing blood lost during cesarean delivery. Our study wants to prevent blood loss during cesarean delivery.

The researchers hope to learn if tranexamic acid decreases the amount of blood loss during cesarean delivery.

The following definitions may help you understand this study:

- Randomization means you will be placed by chance (like a flip of a coin) in one of the study groups
- Double-blind means that you nor the researcher will know if you receive tranexamic acid or placebo.
- Placebo means a substance or treatment with no therapeutic effect.
- Placebo-controlled means that some participants will get a placebo. A placebo looks like the investigational drug but it includes no active ingredients.
- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Investigational Use of Drug or Device
This study involves the use of an investigational drug called tranexamic acid. "Investigational" means that the tranexamic acid has not yet been approved by the U.S. Food & Drug Administration (FDA) for preventing bleeding in cesarean delivery.

This study will compare the effects, good and/or bad, tranexamic acid has on people who use it and if it decreases bleeding after cesarean delivery when compared to placebo. The safety of this drug in humans has been tested in prior research studies; however, some side effects may not yet be known.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you are pregnant, age 18 years and older and you are having a scheduled cesarean delivery.

How many people are expected to take part in this study?
This study will enroll approximately 150 study participants.

Information about Study Procedures – "What will be done if you decide to be in the research?"

Screening – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You will be told which results we will obtain and which procedures will not have to be repeated. Many of the procedures are described below as "**standard care**" and would be done even if you do not take part in this research study. You will be told which ones are for "**research only**".

Screening Procedures

If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including medications you take and any surgical procedures you have had.

You may also have to fill out certain forms or have the following exams, tests or procedures (all of the following are standard of care whether you chose to participate of not):

- Physical exam and medical history;
- Vital signs;
- Blood tests;
- Demographic information (age, sex, ethnic origin).

Assignment to Study Groups –

Group Assignment
If the researchers believe you can take part in this study, you will be assigned randomly (like a flip of a coin) to receive either tranexamic acid or placebo. You have a 1 in 2 chance of receiving tranexamic acid or placebo. A placebo is an inactive, harmless substance that looks like the other study drugs.

If you decide to participate in this study you will either have:

- A medication named tranexamic acid in normal saline that may decrease blood lost during your

cesarean delivery

Or

- Normal saline without medication that has no effect on bleeding during cesarean delivery

Neither you nor the researchers will know whether you are receiving the study drug or a placebo. In the event of an emergency, there is a way for the researcher to find out which you are receiving.

Study Procedures - as a participant, you will undergo the following procedures:

Patients in the study will receive either tranexamic acid or placebo by slow intravenous injection over 10 minutes. A second dose of tranexamic acid or normal saline will be given at placental delivery.

There will be 12 ml (2 teaspoon) of blood drawn from your arm before the first dose of the drug. Another 12 ml of blood will be drawn after the delivery of your baby. The day after you have the baby, another 12 ml of blood will be drawn. The blood will be used to study markers of clot formation and clot breakdown.

The study will last for two days. After the two doses of medication or placebo, and after the final blood draw, your medical record will be reviewed to obtain necessary information for the researchers to determine if the medication worked.

You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

The researchers will discuss your options for medical care when your participation in this study ends.

Risks – "What are the risks of participation in the research?"

Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

Most of the side effects of tranexamic acid are not common, this means it occurs in less than fifteen out of every one hundred patients.

A potentially serious side effect of tranexamic acid is blood clots. However, in studies completed to date, the likelihood of developing blood clots is the same in patients who have been treated with tranexamic acid and those who received placebo.

Potential Risks:

	Frequent (30% of subjects)	Uncommon (<15% of subjects)
Major		Tranexamic acid: • Hypotension (rare) • Thromboembolism (Maternal **AND** fetal) (rare) • Seizures (rare) • Anaphylaxis (rare) Venous blood draw: • Excessive bleeding (rare) • Infection (rare) • Fainting (rare)
Minor		Tranexamic Acid: • Stomach discomfort • Nasal congestion • Headache • Joint and Muscle Pain • Vision changes Venous blood draw: • Discomfort at the needle site • Bruising • Clotting

TXA can pass through your blood or breast milk, and reach your baby, However, other research studies similar to this have never found medication given to mom causing blood clots in babies.

Tranexamic acid may cause some, all or none of the side-effects listed above. If you are concerned about other, unknown side effects, please discuss this with the researchers.

Side effects from this study will usually go away soon after you stop taking tranexamic acid. In some cases, side effects can be long lasting or may never go away.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately, about any side effect that you have while taking part in the study.

We will tell you about any significant new findings which develop during the course of this research which may relate to your willingness to continue taking part.

Are there Risks related to withdrawing from the study?

There are no risks to withdrawing from the study. If you decide to withdraw from this study early, please discuss your decision with the principal investigator.

Are there risks if you also participate in other research studies?
Being in more than one research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

What if a research-related injury occurs?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – "How could you or others benefit from your taking part in this study?"
The possible benefit of your participating in this study is decreased risk of bleeding during your cesarean delivery. There is no guarantee or promise that you will receive any benefit from this study. We hope the information learned from this study will benefit other people with similar conditions in the future.

Costs – Will taking part in this study cost anything?

The sponsor will provide the study drug free of charge during this study.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information that would make it possible to figure out whose it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include:

Medical/surgical history such as pre-existing medical problems
Obstetrical history: information on previous pregnancies if any
Current pregnancy complications: current problems with pregnancy
Information regarding side effects or complications
Results of blood test
Imaging
Information given during interviews
Demographic information like your age, race, etc.

We will get this information by asking you, asking your doctor, by looking at your chart at Parkland Health & Hospital System.

How will your PHI be shared?
Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- Data Safety Monitoring Board, the committee that checks the study data on an ongoing basis, to determine if the study should be stopped for any reason.
- The members of the local research team.
- The Institutional Review Board, Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out.
- The Research offices at the University of Texas Southwestern Medical Center, Parkland Health and Hospital System.
- The Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.
- Representatives of domestic and foreign governmental and regulatory agencies may be granted direct access to your health information for oversight, compliance activities, and determination of approval for new medicines, devices, or procedures.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of Parkland Health & Hospital System for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties but you will not be allowed to participate in the study.
After you enroll in this study, you may ask the researchers to stop using your health information at any time . However, you need to say this in writing and send your letter to Olutoyosi Ogunkua MD, Department of

Anesthesiology and Pain Management at UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75390. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

Because of the type of research, you can only access your PHI when the study is done. At that time, you have the right to see and copy the medical information we collect about you during the study, for as long as that information is kept by the study staff and other groups involved.

How long will your PHI be used?

By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends and all required study monitoring is over.

Contact Information – Who can you contact if you have questions, concerns, comments or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact:

Dr. Olutoyosi Ogunkua
University of Texas Southwestern Medical Center
Department of Anesthesiology & Pain Management
5323 Harry Hines Blvd. Dallas, TX 75390-9068
Olutoyosi.ogunkua@utsouthwestern.edu
Office:(214) 648-6400 * Pager: (214) 746-0821

To use the pager, you need to have a touch tone (push button) telephone. Dial the pager number as you would any phone number. When you hear 3 short high pitched beeps, dial in the number where you want the doctor to call you back. Push the # button, hang up and wait for the doctor to return your call.

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the HRPP by calling the office at 214-648-3060.

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research, sign this section. You will be given a copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE FOLLOWING STATEMENTS ARE TRUE:

- You have read (or been read) the information provided above.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.
- You have freely decided to participate in this research or you are voluntarily giving your consent for another person to participate in this study because you believe this person would want to take part if able to make the decision and you believe it is in this person's best interest.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.
- You authorize the collection, use and sharing of your protected health information (another person's protected health information) as described in this form.

Adult Signature Section

Printed Name of Participant	Signature of Participant	Date	Time AM PM
Printed Name/ Employee ID of Person Obtaining Consent	Signature of Person Obtaining Consent	Date	Time AM PM

Blind or Illiterate Signature Section *At the time of consent, also complete this section if consent is obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English (e.g., blind, physically unable to write, etc.)*

Declaration of witness:

By signing below, I confirm I was present for the entire consent process. The method used for communication (e.g., verbal, written, etc.) with the subject was: _____ .

The specific means (e.g., verbal, written, etc.) by which the subject communicated agreement to participate was: _____.

Printed Name of Witness	Signature of Witness	Date	Time AM PM