The Effect of Combined Intravenous and Topical TXA in Major Multilevel Spine Surgery: A Prospective Randomized Trial

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STUDY INFORMATION:

Study Title: High Dose Intravenous TXA vs. Combined Intravenous and Topical TXA in Major Multilevel Spine Surgery: A Prospective Randomized Trial

Study site(s): Mount Sinai West, 1000 10th Avenue, New York, NY 10019

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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

The purpose of this research study is to evaluate the effect of tranexamic acid, a medication routinely used in orthopedic surgeries to reduce blood loss by promoting blood clots formation, in reducing blood loss in patients undergoing multilevel spine surgery using different dosing regimens. Specifically, we will compare tranexamic acid given only intravenously (administered via veins) at a lower dose vs. given only intravenously at a higher dose vs. given both topically (applied directly to wounds) and intravenously at a lower dose. You will be randomized to one of these three groups. The use of tranexamic acid in orthopedic surgeries including multilevel spine surgery is currently the standard of care to reduce blood loss. There are currently no standards or guidelines for specific dosage and route of administration for tranexamic acid in multilevel spine surgeries and its efficacy in reducing blood loss which is the focus of this research study. The intravenous tranexamic acid regimen has been used in prior studies. The combined topical and intravenous tranexamic acid regimen has not been used in prior spine studies to our knowledge, and hence is investigational.

If you choose to take part, your participation in this research study is expected to last from the day of surgery to first post-operative visit at the surgeon's office.

There will be no additional costs associated with participation and there is no compensation.

If you choose to take part, the main risks to you are reactions and side effects of the study agent (tranexamic acid) which include hypersensitivity reaction and chances of any thromboembolic vascular events.

You may benefit from taking part in this research. Some potential benefits are possible reduced blood loss during and after your surgery by being assigned to either of the two study groups.

Instead of taking part in this research, you may receive your surgery as planned per standard of care.

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

STUDY PARTICIPATION:

You may qualify to take part in this research study because you are between the ages of 18 and 80 and undergoing multilevel spine surgery. Funds for conducting this research are provided by Mount Sinai.

Your participation in this research study is expected to last from the day of surgery until the day of hospital discharge or until three days after surgery during hospital stay, whichever is earlier.

There are 75 people expected to take part in this research study at Mount Sinai West.

Funds for conducting this research study are provided by, Mount Sinai.

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.

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to take part in this research study, here is what may be involved:

On the day of your surgery your anesthesia provider will perform a history and physical. This involves discussing your medical and surgical history and reviewing your allergies as well as your medications along with a focused physical exam. A small catheter, known as an intravenous (IV) line, will be placed in one of your veins in preparation for your surgery. All patients undergoing anesthesia are required to have an intravenous line placed.

After discussing the anesthetic plan with your anesthesia provider, you will be entering the operating room. You will be randomly assigned to receive one of the three dosing regimens of tranexamic acid (TXA): 1) low dose of intravenous TXA throughout the surgery and topical placebo in the form of salt water before the end of surgery, 2) high dose of intravenous TXA throughout the surgery and topical placebo in the form of salt water before the end of surgery or 3) low dose of intravenous TXA throughout the surgery and topical TXA before the end of surgery. Throughout the duration of the procedure, the intravenous TXA will be administered to you by infusing through the IV line that was inserted in your vein. By the end of the procedure, the topical TXA or placebo in the form of salt water will be poured over 5 minutes at the surgical wound prior to closure. You will randomly be assigned to one of the three treatment groups and each subject has an equal chance of being in any group. Randomization will occur via a computer software number generator that will assign you to either of the groups.

The amount of blood loss, fluid and/or blood transfusion during your entire surgery will be recorded. Blood loss will be measured in terms of number of lap pads used and blood collected in the canister.

The only thing(s) that are experimental in this study are the dosing regimen of the tranexamic acid. Your post-surgery follow-up and care are standard of care. After surgery you will be transferred to the post anesthesia care unit (PACU) also known as the recovery room. Your pain scores (level of pain you report) will be assessed and treated by PACU physicians and nurses.

The amount of blood loss, fluid and/or blood transfusion if needed, and the lab results of complete blood count (CBC) during the first 24, 48 and 72 hours during your hospital stay will be recorded. The number of days of hospitalization will be recorded. Post-operative complications including wound complication, deep venous thrombosis, pulmonary embolism and any other thromboembolic event if any will be recorded. Further chart review will be done to collect data regarding wound complication, wound healing time, incidence of infection, need of readmission and reoperation.

Because this research study involves the use medication, a note must be included in your electronic medical record that you are taking part in the research. This way, anyone involved in your medical care will know that you are a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.

Randomization

No one, not you, or anyone from your medical team or from the research team will be able to choose what group you are assigned to or what study drug regimen you get. It will be by chance, like pulling names out of a hat You will have a(n) equal chance of being given each study drug regimen. Neither you nor the Lead Researcher or your own doctor will know which study drug regimen you are getting. If there is an emergency, they can get this information.

USE OF YOUR DATA AND/OR SAMPLES:

The research team will never use or share your personal information (such as, name, address, date of birth, social security number), study data and/or samples (blood, tissue, urine, saliva, or any other body matter) that are collected as part of this study for future research, even if your identity is removed. Your data and/or samples will only be used to complete this study and then they will be destroyed.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study, you will be responsible for the following things:

Your participation in the research study involves the time from the day of surgery until the day of hospital discharge or until three days after surgery during hospital stay, whichever is earlier.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You will not be paid for taking part in this study. Being in this study will not cost you anything extra. Researchers will not pay you for your travel or the time it will take for you to be in the study.

POSSIBLE BENEFITS:

There is a chance this study may benefit you, but this is not guaranteed. Others may benefit from what researchers learn from the study. Possible benefits to you include: reduced blood loss during and after your surgery in either group.

POSSIBLE RISKS AND DISCOMFORTS:

Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

As with any medication, there is a possibility of an allergic reaction. Although rare, possible complications include bleeding or local site infection, hypersensitivity reaction (undersirable reactions produced by normal immune system, such as hives, difficulty breathing, low blood pressure,

palpitation), seizures, and chance of any thromboembolic vascular event, such as stroke, deep vein thrombosis (DVT), pulmonary embolism (PE).

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study. If you decide not to take part, this will not affect the clinical care you receive at Mount Sinai. The choice is totally up to you.

If you choose not to participate in this study you will receive your surgery as planned with TXA regimen per standard of care.

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you believe that being in this research study has harmed you, you should contact the Lead Researcher. Their contact information is listed at the beginning of this consent form.

If you are injured or made sick from taking part in this study, you will get medical care. The group funding this research study will pay you for any reasonable and necessary medical expenses to diagnose and treat research-related injury or illness. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff. You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the

first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you stop being in the research study, the research team may not remove information they have already placed in the study database, and may continue to use that data as part of this study. The research team may ask you whether they can continue to collect information from your medical record.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not to be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If your data and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number **212-523-6915**

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others?

As part of this study, the research team at the hospital(s) involved in the research will collect your name, address, telephone number, dates directly related to the individual (birth, admission, discharge, date of death, etc.), and medical record number.

The researchers will also get information from your medical record including pertinent medical history, type of surgery and type of anesthesia delivered.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.

Why is your PHI being used?
Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let

others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your information.
- If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?
As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- Other collaborating research center(s) and their associated research/clinical staff who are working with the researchers on this project: Mount Sinai Hospital, Mount Sinai St. Luke's
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors,

auditors, the IRB, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access.* The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI? Your authorization for use of your PHI for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will not be able to access your medical records. This is done to prevent the knowledge of study results from affecting the reliability of the study. Your information will be available should an emergency arise that would require your treating physician to know this information to best treat you. You will have access to your medical record and any study information that is part of that record when the study is over or earlier, if possible. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff. The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection

regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 416-0197. These agencies are responsible for protecting your rights.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

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

ADULT PARTICIPANT:

Your signature below documents your permission to take part in this research study and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of Participant	Printed Name of Participant	Date	Time [required if used for FDA documentation purposes]

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:

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 participant, and that consent was freely given by the participant.

Signature of Witness	Printed Name of Witness	Date	Time