INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Full Study Title:
The HeLiX (Hemorrhage during Liver resection: tranexamic acid) Trial: Tranexamic Acid (TXA) Versus Placebo to Reduce Perioperative Blood Transfusion in Patients Undergoing Liver Resection: A Randomized Controlled Trial

Principal Investigator: Dr. Paul Karanicolas, Surgical Oncology, 416-480-4774

Funder: This study is being funded by the Canadian Institutes of Health Research (CIHR)

Emergency Contact Number (24 hours/7 days per week): Dr. Paul Karanicolas (pager: 5452)

INFORMED CONSENT

You are being asked to consider participating in a research study. A research study is a way of gathering information on a treatment, procedure or medical device or to answer a question about something that is not well understood.

This form explains the purpose of this research study, provides information about the study drug (tranexamic acid), the tests and procedures involved, possible risks and benefits, and the rights of participants.

Please read this form carefully and ask any questions you may have. You may have this form and all information concerning the study explained to you. If you wish, someone may be available to verbally translate this form into your preferred language. You may take as much time as you wish to decide whether or not to participate. Feel free to discuss it with your friends and family, or your family doctor. The study staff will tell you if there are any study timelines for making your decision. Please ask the study staff or one of the investigator(s) to clarify anything you do not understand or would like to know more about. Make sure all your questions are answered to your satisfaction before deciding whether to participate in this research study.

Participating in this study is your choice (voluntary). You have the right to choose not to participate, or to stop participating in this study at any time, without giving reason(s) and with no negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

INTRODUCTION

You are being asked to consider participating in this study because you will be undergoing liver surgery.

Despite improvements and advances in liver surgery, many patients require a blood transfusion during or after their operation due to blood loss from surgery. While blood transfusions are generally safe, they do carry serious risks and should be avoided if possible.
We are studying the effect of a drug named tranexamic acid on blood loss and the need for blood transfusion after liver surgery. Many studies have examined tranexamic acid in patients having other types of surgery and it appears to be safe and effective at reducing blood loss and the need for blood transfusions. However, the effects of tranexamic acid have not been well-studied in patients having liver surgery, therefore it is not commonly used during this procedure.

Health Canada has allowed the use of tranexamic acid in this research study, although it has not been approved for use in patients undergoing liver surgery at this time.

WHAT IS THE USUAL TREATMENT?

Treatment during liver surgery does not regularly involve the use of tranexamic acid, although it has been used at Sunnybrook many times for different types of operations, including the one you are having. Your doctors will use the routine standard ways of trying to keep blood loss to the lowest possible amount.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine the effects of tranexamic acid on blood loss and on blood transfusion in patients undergoing liver surgery.

WHAT WILL HAPPEN DURING THIS STUDY?

This is a placebo-controlled study. A placebo looks like the study drug but does not have any active or medicinal ingredients. The placebo in this study will be the same colour and consistency (clear liquid) as tranexamic acid, but is not expected to have any effect on your condition. The placebo for this study will be saline (salt water solution). A placebo is used to eliminate bias (the possibility of the study investigator(s) unintentionally influencing the study results because of a belief in the effectiveness of the treatment) and makes the results of the study more reliable. Participants in this study will be randomly (by chance, like the flip of a coin) placed in one of the two study groups: experimental (tranexamic acid) or control (saline). Neither you, the study staff, the investigator(s), nor your doctors or nurses can influence, or will know, which group you are in. However, in case of an emergency the study treatment can be identified. You will have a 50% chance of getting placebo during the entire study.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that 1230 people will participate in this study at a minimum of 5 centres across Canada. About 450 to 770 people will participate in this study at Sunnybrook. The study is expected to take about 4-5 years to enroll participants. The primary results should be known in 30-42 months, and the secondary results should be known in approximately 7-9 years.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you decide to participate in this study you will be asked to provide written and informed consent in the surgical clinic. If you are a woman of childbearing potential (which means you have experienced menarche, you are not permanently sterile, and you are not postmenopausal, which is defined as 12 consecutive months with no menses without an alternative medical...
cause), you will be asked to take a urine pregnancy test before the study commences. The test result must be negative for you to participate in the study.

Before your liver surgery, study staff will ask you some questions about your medical history. You will also be asked to complete quality of life assessment questionnaires. You can complete this in person or at home depending on your preference and it will take approximately 10 minutes to answer.

On the day of your liver surgery, your preoperative preparation will be the same as standard procedure. Once you are in the operating room and asleep, the anaesthesiologist (the doctor who administers the sleeping medication) will give you a bolus (a dose of medication given intravenously) of the study drug (tranexamic acid or saline). You will then receive a continuous intravenous infusion of study drug for the next eight hours. No other study specific medications or study procedures are required for the study after that time. Your blood levels and other parameters will be monitored as they typically would be following liver surgery while you are in hospital. This information will be recorded by a study representative.

You will have a postoperative visit with your surgeon (approximately 30 days and 90 days after surgery), which is standard care for patients who are undergoing liver surgery. The study specific portion of the follow-up visit will consist of only questions, which may take place in person, via phone, or online. You will be asked if you have experienced any surgery-related complications and if you have been readmitted to the hospital since your discharge from the hospital. You will also be asked to complete the quality of life assessment questionnaires at each of these postoperative visits. Depending on your responses, these questions could take approximately 15 minutes to answer.

There will also be a 5 year long-term follow up to study the potential effect of tranexamic acid on the rate of cancer recurrence and survival postoperatively. You do not have to attend study-related hospital visits and will have no added risks. A study representative will request any medical records following your surgery from either Sunnybrook Health Sciences Centre or your most recent treating hospital and review them for cancer recurrence and survival. The study representative will review your medical records at 6 month intervals for up to 5 years following your surgery. If we are unable to locate any recent medical records, we will contact you by phone to update our records.

No additional visits or time commitments will be required if you participate in this study.

WHAT ARE THE RISKS OR HARMs OF PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be other side effects that are not expected. If you decide to take part in this study, you should contact your doctor or the study’s Principal Investigator, Dr. Paul Karanicolas (Surgical Oncology, 416-480-4774) about any side effects or study-related injuries that you experience.

Known side effects include nausea and diarrhoea (less than 1 in 10,000 patients). Both of these are usually mild and improve after stopping the medication. Rarely, and at higher doses than the dose you will receive, seizures have occurred. These high doses were given for open heart surgery. The chance of this happening in this study is extremely small.
There are no other reasonably foreseeable risks, harms, discomforts or inconveniences to participants in this study. The effects of tranexamic acid on unborn babies or sperm are unknown. You should not take part in this study if you are pregnant or planning pregnancy.

If any new information that could reasonably affect your willingness to continue to participate in this study becomes available to the study staff, they will notify you.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

You may or may not benefit directly from participating in this study. Your participation may help other people undergoing liver surgery in the future.

WHAT OTHER CHOICES ARE THERE?

If you decide not to participate in this study, you will undergo your liver surgery as planned by your surgeon, which could include the use of tranexamic acid.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The investigator(s) may decide to remove you from this study without your consent. If you are removed from this study, the investigator(s) will discuss the reasons with you and plans will be made for your continued care outside of the study.

You can also choose to end your participation at any time without having to provide a reason. If you choose to withdraw, your choice will not have any effect on your current or future medical treatment or health care. If you withdraw voluntarily from the study, you are encouraged to contact the Principal Investigator, Dr. Paul Karanicolas, by phone at 416-480-4774 immediately.

WHAT ARE THE COSTS OF PARTICIPATING IN THIS STUDY?

Participation in this study will not involve any additional costs or time.

WHAT HAPPENS IF I HAVE A RESEARCH RELATED INJURY?

If you become sick or injured as a direct result of your participation in this study, your medical care will be provided. Financial compensation for such things as lost wages, disability or discomfort due to this type of injury is not routinely available.

By signing this consent form, you do not give up any of your legal rights.

ARE STUDY PARTICIPANTS PAID TO PARTICIPATE IN THIS STUDY?

You will not be paid to participate in this study.

HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

You have the right to have any information about you and your health that is collected, used, or disclosed for this study to be handled in a confidential manner.
If you decide to participate in this study, the investigator(s) and study staff will look at your personal health information and collect only the information they need for this study. Personal health information is health information about you that could identify you because it includes information such as your:

- name,
- date of birth,
- new and existing medical records, or
- types, dates and results of various tests and procedures.

You have the right to access, review and request changes to your personal health information.

The following people may come to the hospital to look at your personal health information to check that the information collected for the study is correct and to make sure the study has followed the required laws and guidelines:

- Representatives of the Sunnybrook Research Institute, Sunnybrook Health Sciences Centre or the Sunnybrook Research Ethics Board, because they oversee the ethical conduct of research studies at Sunnybrook; and
- Representatives of Health Canada, the group of people who oversee the use of drugs in research in Canada.

Access to your personal health information will take place under the supervision of the Principal Investigator.

Study data is health information about you that is collected for the study, but does not directly identify you. Any study data about you that is sent outside of the hospital will have a code and will not contain your name or address, or any information that directly identifies you. Study data that is sent outside of the hospital will be used for the research purposes explained in this consent form.

The investigator(s), study staff and the other people listed above will keep the information they see or receive about you confidential, to the extent permitted by applicable laws. Even though the risk of identifying you from the study data is very small, it can never be completely eliminated.

The Principal Investigator will keep any personal health information about you in a secure and confidential location for 25 years and then destroy it according to Sunnybrook policy.

When the results of this study are published, your identity will not be disclosed.

You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of the results of this study, please contact the Principal Investigator, Dr. Paul Karanicolas (416-480-4774).

A description of this clinical trial will be available on [http://www.ClinicalTrials.gov](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.

**DO THE INVESTIGATORS HAVE ANY CONFLICTS OF INTEREST?**
The investigators have no conflicts of interest to declare related to this study.

**WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?**

You have the right to receive all information that could help you make a decision about participating in this study. You also have the right to ask questions about this study and your rights as a research participant, and to have them answered to your satisfaction, before you make any decision. You also have the right to ask questions and to receive answers throughout this study.

If you have any questions about this study you may contact the person in charge of this study, the Principal Investigator, Dr. Paul Karanicolas (Surgical Oncology) by phone at 416-480-4774.

The Sunnybrook Research Ethics Board has reviewed this study. If you have questions about your rights as a research participant or any ethical issues related to this study that you wish to discuss with someone not directly involved with the study, you may call the **Chair of the Sunnybrook Research Ethics Board** at (416) 480-4276.
DOCUMENTATION OF INFORMED CONSENT

You will be given a copy of this informed consent form after it has been signed and dated by you and the study staff.

**Full Study Title: The HeLiX (Hemorrhage during Liver resection: tranexamic acid) Trial:**
Tranexamic Acid (TXA) Versus Placebo to Reduce Perioperative Blood Transfusion in Patients Undergoing Liver Resection: A Randomized Controlled Trial

Name of Participant (print): ________________________________________

Participant/Substitute Decision-Maker
By signing this form, I confirm that:
- This research study has been fully explained to me and all of my questions have been answered to my satisfaction
- I understand the requirements of participating in this research study
- I have been informed of the risks and benefits, if any, of participating in this research study
- I have been informed of any alternatives to participating in this research study
- I have been informed of the rights of research participants
- I have read each page of this form
- I authorize access to my personal health information, medical record and research study data, as explained in this form
- I have agreed, or agree, to allow the person I am responsible for, to participate in this research study
- This informed consent document may be placed in my medical records

____________________________        ____________________________        _____________________
Name of Participant/Substitute Signature Date
Decision-Maker (print)
ASSISTANCE DECLARATION

Was the participant assisted during the consent process? ☐ Yes ☐ No

☐ The consent form was read to the participant/substitute decision-maker, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant/substitute decision-maker.

☐ The person signing below acted as a translator for the participant/substitute decision-maker during the consent process. He/she attests that they have accurately translated the information for the participant/substitute decision-maker, and believe that the participant/substitute decision-maker has understood the information translated.

____________________________        ____________________________        _____________________
Name of Person Assisting (print)    Signature                 Date

Person Obtaining Consent
By signing this form, I confirm that:
• This study and its purpose have been explained to the participant named above
• All questions asked by the participant have been answered
• I will give a copy of this signed and dated document to the participant

____________________________        ____________________________        _____________________
Name of Person Obtaining Consent (print)    Signature                 Date

Statement of Investigator
I acknowledge my responsibility for the care and well-being of the above participant, to respect the rights and wishes of the participant as described in this informed consent document, and to conduct this study according to all applicable laws, regulations and guidelines relating to the ethical and legal conduct of research.

____________________________        ____________________________        _____________________
Name of Investigator (print)    Signature                 Date