Informed Consent

Pilot Study of Loop Diuretics Among Individuals Receiving Hemodialysis

NCT number NCT04622709
Document Date 04/14/2020

Adult Consent Form

University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Consent Form Version Date: 4/14/2020
IRB Study # 19-3550

Title of Study: Pilot Study of Loop Diuretics among Individuals Receiving Hemodialysis
Principal Investigator: Jennifer Flythe
Principal Investigator Department: Medicine-Nephrology
Principal Investigator Phone number: (919) 445-2656
Principal Investigator Email Address: jenny_flythe@med.unc.edu
Funding Source and/or Sponsor: National Institutes of Health

SHORT STUDY SUMMARY

This study is being done to understand if the diuretic drug, furosemide (or "Lasix") is safe for dialysis patients and will help them increase the amount of pee/urine they produce. Increasing the amount of pee/urine can potentially help patients reduce fluid overload and the need for rapid fluid removal during dialysis treatments. Participation in this study lasts a total of 22 weeks. If you choose to participate in this study, your participation would help us better understand your experience as a dialysis patient and understand the right drug dose that will be both safe and effective for dialysis patients. If you experience furosemide-related improvements in the amount of pee (or urine) you produce, blood pressure control, and/or fluid volume-related symptoms during dialysis, the drug could be added to your dialysis prescription by your treating nephrologist if they believe it is a good long-term treatment for you.

If you choose to participate in this study, you would come to your regular dialysis treatments 3 times per week like you normally do, and you would be given the study drug (furosemide) to take by mouth two times a day for 18 weeks. You would also be asked to do a 24-hour urine collection 4 times throughout the study, and answer questions about your hearing and about the symptoms you may experience on dialysis. A dialysis clinic nurse would draw extra tubes of blood 10 times throughout the study (no extra needle sticks).

The risks related to the study drug furosemide include unusual electrolyte changes (potassium, magnesium, calcium, for example), low blood pressure, rash, ringing in the ears and other hearing changes including deafness, and other symptoms. Patients who already have a high risk of furosemide side effects will not be asked to participate in this study. There is minimal risk of loss of confidentiality. Efforts to protect you as a participant in this study are discussed below.

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary. You may refuse to join, or you may take back your consent to be in the study, for any reason, without penalty.

Research studies are designed to gain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to understand if furosemide, sometimes called Lasix, (a drug that helps patients pee or make urine) is safe for hemodialysis patients and effective at increasing the amount of pee (or urine) they produce. Increasing the amount of pee (or urine) can potentially help with fluid overload and potentially reduce the need for rapid fluid removal during hemodialysis treatments. Furosemide is approved by the U.S. Food and Drug Administration (FDA) for the treatment of high blood pressure and swelling in people who make urine. It is not known how well it works in dialysis patients who make urine. Your participation will help us better understand your experience as a dialysis patient and understand the right drug dose that will be both safe and effective for dialysis patients.

Are there any reasons you should not be in this study?

You should not be in this study if you are not a hemodialysis patient who receives in-center treatment, if you don't make at least 1 cup of urine per 24-hours, if you are pregnant, if you are incarcerated (prisoner), if you get dialysis treatments more than 4 times per week, or if you eat natural licorice.

How many people will take part in this study?

If you decide to be in this study, you will be one of approximately 30-40 hemodialysis patients who participate in this study.

How long will your part in this study last?

If you decide to participate in this study, you would be involved in the study only during your regularly scheduled dialysis treatments 3 times per week, for a total of 22 weeks.

You will not be contacted again. There is no study follow-up after the 22 weeks. However, if you desire, we will send you a summary of the study results by email, mail, or in person once the study has finished and results analyzed.

What will happen if you take part in the study?

If you choose to participate in this study, you will be asked about your medical history, including questions about your medications and health problems. At the start of the study, you will also be asked questions about symptoms you experience during dialysis and about your hearing, and you will be asked to do a 24-hour urine collection and bring the jug back to the study team. A sample of your blood will be taken from your vascular access (dialysis fistula, graft, or catheter). Aside from doing the 24-hour urine collection at home at the beginning and then 3 times during the study, your involvement in this study will happen only during your routinely scheduled dialysis treatments 3 times per week.

During the study, you will receive the study drug furosemide at your regularly scheduled dialysis treatments, along with instructions on how to take the drug. If it is safe to do so, the drug dose will increase 3 times (every 14 days) over 6 weeks, and then you will continue taking the highest dose of the drug for another 12 weeks until the end of the study. You will be told when the dose increases and you will have the chance to tell the study team if you do not feel well. The dose increases help the study team understand how much of the drug is needed to help dialysis patients pee (or urinate) more and not have bad side effects.

At the beginning of the study, you will start with a low drug dose for the first 2 weeks, and then, if it is safe and you agree to it, you will take a higher drug dose for 2 weeks. If it is safe and you agree to it, you will then take a higher drug dose for the last 2 weeks. If, after the first 6 weeks, it is safe and you agree to it, you will then continue taking the highest drug dose for another 12 weeks until the end of the study.

This study will not make changes to your normal dialysis prescription. Your blood pressure will be monitored during treatments like it always is. Your weights will be checked before and after dialysis like they always are. You will be asked to answer questions about your hearing and about symptoms that you may experience during dialysis treatments. You will be asked to do a 24-hour urine collection 4 times throughout the study. You will have extra blood drawn (2 tubes, each with 2.5 mL (1/2 teaspoon) of blood each) from your vascular access (no extra needle sticks) during your dialysis treatments 10 times throughout the study.

Study Activities and Timeline					
Study Period	**Before starting on study drug**	**Take study drug at increasing levels**			**Continue taking study drug at highest safe level**
Study drug	None	Lowest dose	Increase dose if safe	Increase dose again if safe	Highest safe and effective drug dose
# of Weeks	2-4 weeks	2 weeks	2 weeks	2 weeks	12 weeks
What you will be asked to do		Take study drug every day			Take study drug every day
	Get blood drawn (1 time)	Get blood drawn (6 times)			Get blood drawn (3 times)
	Do 24-hr urine collection (1 time)	Do 24-hour urine collection (2 times)			Do 24-hour urine collection (2 times)
	Answer questions about your symptoms (1 time)	Answer questions about your symptoms (6 times)			Answer questions about your symptoms (6 times)
	Answer questions about your hearing (1 time)	Answer questions about your hearing (3 times)			Answer questions about your hearing (3 times)
		Answer a question about continuing the study drug (6 times)			Answer a question about continuing the study drug (6 times)

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge, and results from this study could potentially benefit future dialysis patients. There may be no direct benefit to you from participating in this study in addition to your usual dialysis treatment care. Possible benefits to you from being in this study may be having the opportunity to discuss your dialysis experience in a supportive environment, and possible increased interest or engagement in your own care. If you experience furosemide-related improvements in the amount of pee (or urine) you produce, blood pressure control, and/or fluid volume-related symptoms during dialysis, the drug could be added to your dialysis prescription by your treating nephrologist if they believe it is a good long-term treatment for you.

What are the possible risks or discomforts involved from being in this study?

Risks related to the study drug furosemide include unusual electrolyte changes (potassium, magnesium, calcium, for example), low blood pressure, rash, ringing in the ears, other hearing changes including deafness, and other symptoms such as cramps, dizziness, unusual tiredness or weakness, chest pain, nausea/vomiting, diarrhea, and numbness/tingling. Patients who already have a high risk of furosemide side effects will not be asked to participate in the study.

You may experience the normal risks associated with your normal hemodialysis treatment, such as low blood pressure, abnormal heart rhythm, bleeding or bruising at the blood access (dialysis fistula or

graft), infection, or symptoms like cramping or feeling tired. All study monitoring is low risk and part of regular dialysis care. This study involves an additional blood draw, which will be taken from your vascular access by a dialysis clinic nurse and will not require a separate needle stick. The main risk with the blood draw is bruising or bleeding at the vascular access. This study also involves additional 24-hour urine tests, which will be done by you and returned to the study team. The main risk with the 24-hour urine test is embarrassment related to collecting, storing, and transporting the urine jug. Occasional 24-hour urine tests are required as part of regular dialysis care, so this risk is minimal.

There is minimal risk of loss of confidentiality. Every effort will be taken to protect your identity as a participant in this study, and we are taking multiple steps to protect your privacy as detailed below. You should report any problems you experience to the research team.

What are the risks to a pregnancy or to a nursing child?

All female patients who are eligible to participate in the study will be asked about their pregnancy status before the study starts. Women who are pregnant or planning to get pregnant will not be asked to participate in the study. We do not know the effect of the study drug on babies before they are born, or on nursing children. Many drugs can get into the mother's milk. You should not breastfeed your child while taking the study drug. If you are a man, there is no known risk to fathering children while on furosemide (or "Lasix"). If you become pregnant during the study you should notify the researcher right away.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

Will I receive any clinical results from this study?

The study Principal Investigator or your nephrologist may choose to share some study results with you if they are determined to be medically important to your dialysis or general health care.

How will information about you be protected?

Information collected for this study (including medical information, blood and urine samples, and your responses to questions) will not be placed in your medical record. Your information will be kept confidential in a separate research study chart. A study identification number will be used to link information collected for this study to your name. Your name will not be directly associated with your information. You will not be identified in any report or publication of this study or its results. Your study data will be transferred to a secure computer. Study information will be stored on secure password-protected computers, blood and urine samples will be stored in secure UNC freezers, and both will be accessible only to study staff. All blood and urine samples will be sent to a UNC laboratory to be tested for electrolyte and study drug levels in your blood (to make sure they are at safe levels) and then stored in secure UNC freezers using a study identification number for 12 months after the study ends. Participation in this study will not affect your medical care. Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

By signing this informed consent document, you agree that some of the information created by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you (nephrologists, dialysis care staff, for example). This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use. The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?

You can stop participating in the study at any time, without penalty. If you stop participating in the study before it is done, study staff may ask you your reasons for ending your participation. The researchers also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or your care is transferred to another dialysis clinic that is not part of the study, or because the entire study has been stopped. If you choose to stop participating in the study or the study team stops your participation in this study before the study is done, the study team will keep all data collected up until the point of stopping. No additional information will be collected unless you provide additional written permission for further data collection at the time you stopped taking part in the study.

Will you receive anything for being in this study?

You will receive $199 total for participating in the full study including bringing back all four 24-hour urine collection jugs to the study team. You will receive $159 total if you participate in the full study but do NOT bring back any of the four 24-hour urine collection jugs.

If you participate in the entire study, you will receive study payments 4 times. For each of those study payments, you will receive $10 more each time you bring back your 24-hour urine collection jugs. If you bring back your 24-hour urine collection jugs, you will receive $50 at the beginning of the study, $40 during the first part of the study (6-week period), $40 during the 2nd part of the study (12-week period), and $69 at the end of the study. If you do NOT bring back your 24-hour urine collection jugs each time, you will receive $40 at the beginning of the study, $30 during the first part of the study (6-week period), $30 during the 2nd part of the study (12-week period), and $59 at the end of the study.

You will receive the full payment amounts for each part of the study even if you stop participating in the study before the end of each period (1 time at the beginning, 1 time during the 6-week period, 1 time during the last 12-week period, and 1 time at the end of the study).

Will it cost you anything to be in this study?

It will not cost you anything to be in this study.

Who is sponsoring this study?

This research is funded by the National Institutes of Health (NIH). This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with NIH or in the final results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, or concerns, you should contact the researchers listed on the first page of this form. A description of this clinical trial will be available on 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.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____

Signature of Research Participant **Date**

_____

Printed Name of Research Participant

_____ _____

Signature of Research Team Member Obtaining Consent **Date**

_____

Printed Name of Research Team Member Obtaining Consent