The University of New Mexico Health Sciences Center
Consent to Participate in Research

DIDIT: Diuretic/Cool Dialysate Trial

07/12/2019 (v6.0)

Introduction

You are being asked to participate in a research study that is being done by Dr. Mark Unruh, MD who is the Principal Investigator [Department of Internal Medicine Chair] and his associates.

You are being asked to participate in this study because you are on chronic hemodialysis treatment.

The main functions of your kidneys are filtration and urine production. When kidney filtration drops below 85% of normal, they can no longer filter your blood. When this happens, urine production may also be reduced. If both of these happen, toxins and excess fluid stay in your body. Hemodialysis gets rid of these toxins and excess fluid.

For this study, we are looking to see if changing the temperature of the dialysis fluid and/or taking a diuretic will slow the rate of kidney function decline (urine production), improve quality of life, and reduce overall mortality.

This study will take place during your hemodialysis visits.

Up to 50people will take part in this study. Dialysis Clinic Inc. (DCI) is the funding agency for this study.

This form will explain the research study and the possible risks as well as the possible benefits to you. We encourage you to talk with your family, friends and health care provider before you decide to take part in this research study. If you have any questions, please ask one of the study staff.

What will happen if I decide to participate?

If you agree to participate, the following things will happen:

You will need to confirm that you urinate more than 200 ml (1 cup) daily. If you are a female of childbearing potential you will have a pregnancy blood test done. If you refuse to have a pregnancy test done, you are not allowed to participate in this study.

You will complete the *pre-intervention* visits listed in the table below.

- The 24 Hour Urine Collection results will determine if you can be randomized and complete the study.
- The 24 Hour Urine Collection will tell us if you have enough remaining kidney function to be included in this study.
- If your kidney function is too low for the study, you will be withdrawn from this study at this time.

Once it is decided that you can complete the study, you will be placed by chance (like flipping a coin) into one of these four study arms: (each arm includes a combination of Bumetanide or Placebo and 35.5 or 37 degree Celsius dialysate temperature)

No Diuretic (placebo) and 37°C dialysate	**No Diuretic (placebo) and 35.5°C dialysate**
Diuretic and 37°C dialysate	**Diuretic and 35.5°C dialysate**

This study compares an active drug to a placebo. A placebo is an inactive substance made to look/taste like an active medicine. You will either get the study drug, Bumetanide, or a placebo. Researchers use a placebo to see if the study drug works better or is safer than not taking anything. You will not know if you are taking Bumetanide or the placebo.

- If you get randomized and are currently taking a diuretic, you will discontinue taking your prescribed diuretic prior to starting the study drug.
- If randomized, you will begin taking the "study drug" on the first day of your regularly scheduled weekly hemodialysis sessions (Monday if MWF; Tuesday if TThSat). You will take your "study drug" for 6 months.
- Per randomization, your dialysis temperature will be set for 6 months.

The following events will take place during the study:

Event	Pre Intervention	Intervention Month						Post Study
		1	2	3	4	5	6	
24 Hour Urine Collection	X			X			X	End of Study Evaluation
Pre-dialysis Urine Collection	X			X			X	
Questionnaires	X			X			X	
Blood collection (2 ½ tbsp.)	X			X			X	
Pregnancy Blood Test* (¼ tsp)	X							
History & Physical	X							
Randomization	X							
Bumetanide or placebo (3mg/day-oral)		X	X	X	X	X	X	

**required if subject is female and of "child bearing potential"*

- ***Blood Collections: (3 times during the study: pre-intervention, month 3, month 6)***
  - All of the blood needed for this study will be collected from your hemodialysis tubing port before you are connected to the hemodialysis machine.

- ***History & Physical: (pre-intervention)***
  - A UNM Physician or their designee will perform a History & Physical exam at the time of your first 24-hour urine collection.

- ***Questionnaires: (3 times during the study: pre-intervention, month 3, month 6)***
  - You will complete two questionnaires in person or over the phone
  - Completing these questionnaires will take about 30 minutes

- ***Urine Samples & 24 Hour Urine Collections: (3 times during the study: pre-intervention, month 3, month 6)***
  - Urine samples will be collected at home in the morning before the hemodialysis session.
  - You will be instructed on how to collect urine at home over a one day period (24 hours) for this study.

- ***Post Study (month seven and eight):***

- The following will be reviewed: DCI hemodialysis laboratory results and data, study drug compliance, medication review, adverse events.
- An end of study evaluation index will be collected

What is Bumetanide?

Bumetanide belongs to a group of medicines called loop diuretics. A diuretic is a medicine that increases the amount of urine that you make. Diuretics are often called water tablets. Bumetanide clears excess fluid from your body when your body stores more than it needs. ***Bumetanide is a FDA approved diuretic*.**

Once randomized to a study arm, you will take 3mg Bumetanide, or the placebo equivalent, by mouth once a day for 6 months.

How long will I be in this study?

You will take part in this study for 8 months. Study related procedures will take a total of about 5 hours of your time.

What are the risks or side effects of being in this study?

There are risks of stress, emotional distress, inconvenience and possible loss of privacy and confidentiality associated with participating in a research study.

You may have other side effects not listed below. Everyone taking part in the study will be followed carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious.

Emotional/Privacy:

You may be asked questions that are personal. You can refuse to answer any question(s) at any time. Your participation in this study may include a loss of privacy. We will take steps to keep your study data private.

Hemodialysis:

Hemodialysis may be linked to complications. Hemodialysis can lead to low blood pressure which may result in the following:

- Abdominal discomfort
- Nausea
- Vomiting
- Muscle cramps
- Dizziness
- Anxiety

Furthermore, hemodialysis can lead to:

- Bleeding
- Rapid heart rate or unusual heart beats
- Chemical imbalances
- Blood clotting
- Infection of the vascular access
- Death.

However, these hemodialysis risks may be present even if you do not wish to participate in this study. It is unknown whether changing the temperature of the dialysis fluid with or without taking a diuretic will raise or lower the risk of these complications.

Bumetanide:

The following are possible side effects of Bumetanide

- Muscle cramps
- Severe dizziness
- Changes in hearing (like ringing in the ears)
- Allergic reaction

Cool Dialysate (35.5°C):

The most common complication of being dialyzed with cool dialysate is feeling colder and possible shivering.

Pregnancy:

The risk(s) of cool dialysate and/or Bumetanide on a developing baby are unknown; therefore, if you are currently pregnant, or actively planning to become pregnant in the next 8 months, you are not allowed to participate in this study. If you do become pregnant while on this study, you must notify the study team immediately.

Nursing Mothers:

It is unknown whether Bumetanide is excreted in human milk. Breast feeding should not be undertaken while the participant is on this drug. If you are breast feeding, you are not allowed to participate in this study.

Hemodialysis Access Site Blood Draws:

Collecting blood from a hemodialysis tubing access port may result in infection, bleeding, and possibly damage to the access site.

What are the benefits to being in this study?

Your participation in this research may improve future hemodialysis policies and may lead to better outcomes for all hemodialysis patients. Participants that complete the study will have a residual renal function review letter sent to their Nephrologist.

What other choices do I have if I do not want to be in this study?

Your other choices may include:

- Continue getting your usual medical treatment or supportive care
- Taking part in another study
- Getting no treatment

Talk to your doctor about your choices before you decide to participate or not in this study.

How will my information be kept confidential?

We will take measures to protect the security of all your personal information, but we cannot guarantee confidentiality of all study data.

Your name and other identifying information will be linked to a unique study ID. This study ID will not display any information that can identify you. All of the data we collect from you will be coded using your study ID and kept in a locked cabinet, and/or password protected computer files. The master list linking your identifying information to your study data will be kept in a separate, secure on-site location. Only the UNM study team will have access to the master list. We will keep the link between your identifying information and study data until the end of the research study. This link will only be available to UNM, and will not be accessed by researchers at other institutions.

Your responses to questionnaires will be kept strictly confidential. Dialysis clinic staff will not have any knowledge of your answers to any study questionnaires. While there is a risk that the confidential information we collect could be seen by unauthorized persons, we will take all measures available to us to avoid this risk.

A Data Safety and Monitoring Plan (DSMP) is in place for this study which will involve an Independent Monitor (IM) who will monitor the conduct of this study.

The University of New Mexico Institutional Review Board (IRB) that oversees human subject research and/or other entities such as Dialysis Clinic Inc. (DCI), Food and Drug Administration (FDA) and state regulatory agencies may be permitted to access your records. There may be times when we are required by law to share your information. However, your name will not be used in any published reports about this study.

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.

A copy of this consent will be placed in your DCI medical record.

HIPAA Authorization for Use and Disclosure of Your Protected Health Information (HIPAA)

As part of this study, we will be collecting health information about you and sharing it with others. This information is "protected" because it is not identifiable or "linked" to you.

Protected health information (PHI)

By signing this Consent Document, you are allowing the investigators and other authorized personnel to use your PHI for purposes of this study. This information may include: your name, contact number, dialysis clinic medical records, results of physical exams, medical history, lab results, family history, tests such as ECG, demographic information, emergency contact information. This information may be released by Dialysis Clinic Inc. and other providers.

In addition to researchers and staff at UNMHSC and other groups listed in this form, there is a chance that your PHI may be shared (re-disclosed) outside of the research and may no longer be protected by federal privacy laws. Examples of this include disclosures for law enforcement, judicial proceedings, health oversight activities and public health measures.

Right to withdraw your authorization

Your authorization for the use and disclosure of your health information for this study shall not expire unless you cancel this authorization. Your health information will be used or disclosed as long as it is needed for this study. However, you may withdraw your authorization at any time provided you notify the UNM investigators in writing. To do this, please send a letter notifying them of your withdrawal as well as the reason of your withdrawal to:

Dr. Mark Unruh
MSC 10-5550
1 University of New Mexico
Albuquerque New Mexico 87131

Refusal to sign

If you choose not to sign this consent form and authorization for the use and disclosure of your PHI, you will not be allowed to take part in the research study.

What are the costs of taking part in this study?

There will be no cost to you for your participation in this study. The usual costs of medical care, such as dialysis, will continue to be your responsibility or that of your insurance and may include deductibles and co-payments.

What will happen if I am injured or become sick because I took part in this study?

If you are injured or become sick as a result of this study, UNMHSC will provide you with emergency treatment, at your cost.

No commitment is made by the University of New Mexico Health Sciences Center (UNMHSC) to provide free medical care or money for injuries to participants in this study.

In the event that you have an injury or illness that is caused by your participation in this study, reimbursement for all related costs of care will be sought from your insurer, managed care plan, or other benefits program. If you do not have insurance, you may be responsible for these costs. You will also be responsible for any associated co-payments or deductibles required by your insurance.

It is important for you to tell the Primary Investigator immediately if you have been injured or become sick because of taking part in this study. If you have any questions about these issues, or believe that you have been treated carelessly in the study, please contact the Human Research Review Committee (HRRC) at the University of New Mexico Health Sciences Center, Albuquerque, New Mexico 87131, (505) 272-1129 for more information.

Will I be paid for taking part in this study?

You will be paid for your time and effort to take part in this study. If you complete all parts of the study, you will receive $250*. Payment will be prorated if you withdraw from the study, or are withdrawn by the principal investigator.

You will receive payment for your study participation per the *DIDIT Compensation Table*. Upon enrollment in the study you will be issued a re-loadable study payment card. For each completed study event, the card will be loaded for the amount of the event or events. Payments will be uploaded to your card within 24 hours of completing the event(s) with the exception of weekends and holidays.

DIDIT Compensation Table (*$250)			
Event	Compensation Amount	Number of Events	Total Compensation
24 hour urine collection	$50	3	$150
Phone session 1	$30	1	$30
Phone session 2	$30	1	$30
Phone session final	$40	1	$40
**Additional study visits	$10	Unknown	Unknown

**If you are required to return to the clinic for research specimen collection, you will be compensated for each additional study visit in accordance with the *DIDIT Compensation Table* above.

How will I know if you learn something new that may change my mind about participating?

You will be informed of any significant new findings that become available during the course of the study, such as changes in the risks or benefits resulting from participating in the research or new alternatives to participation that might change your mind about participating.

Can I stop being in the study once I begin?

Your participation in this study is completely voluntary. You have the right to choose not to participate or to withdraw your participation at any point in this study without affecting your future health care or other services to which you are entitled.

If you choose to quit the study early, you need to inform us of that decision (as mentioned above). You may contact Dr. Unruh or a member of the study staff.

Information collected while you are enrolled in this study will remain part of the study.

The investigators have the right to end your participation in this study if they feel that you are no longer a good fit. Some reasons that may end your participation in the research are: physician safety concerns, not following study instructions, and becoming pregnant during the study.

Whom can I call with questions or complaints about this study?

If you have any questions, concerns or complaints at any time about the research study, Mark Unruh, MD, or his associates will be glad to answer them at (505) 272-8300.

If you need to contact someone after business hours or on weekends, please call (505) 272-2111 and ask for the physician on call.

If you would like to speak with someone other than the research team, you may call the UNMHSC HRRC at (505) 272-1129.

Whom can I call with questions about my rights as a research participant?

If you have questions regarding your rights as a research participant, you may call the UNMHSC HRRC at (505) 272-1129. The HRRC is a group of people from UNM and the community who provide independent oversight of safety and ethical issues related to research involving human participants. For more information, you may also access the HRRC website at http://hsc.unm.edu/research/hrpo/.

CONSENT

You are making a decision whether to participate in this study. Your signature below indicates that you read the information provided (or the information was read to you). By signing this consent form, you are not waiving any of your legal rights as a research participant.

I have had an opportunity to ask questions and all questions have been answered to my satisfaction. By signing this consent form, I agree to participate in this study. A copy of this consent form will be provided to you.

_____

Name of Adult Subject (Print)

_____ _____

Signature of Adult Subject Date

INVESTIGATOR SIGNATURE

I have explained the research to the participant and answered all of their questions. I believe that they understand the information described in this consent form and freely consent to participate.

_____

Name of Investigator/ Research Team Member (Print)

_____ _____

Signature of Investigator/ Research Team Member Date