UNIVERSITY OF NEW MEXICO HEALTH SCIENCES CENTER
CONSENT TO PARTICIPATE IN RESEARCH

A COMPARISON OF HYDROCHLOROTHIAZIDE AND METOLAZONE IN COMBINATION WITH FUROSEMIDE IN CONGESTIVE HEART FAILURE PATIENTS

PURPOSE AND BACKGROUND

Joe R. Anderson, Pharm.D., who is the Principal Investigator and Co-Investigators James J. Nawarskas, Pharm.D., and associates from the College of Pharmacy, and Robert Taylor, M.D., from the College of Medicine are conducting a research study to compare the effectiveness of hydrochlorothiazide or metolazone in combination with furosemide. Patients with heart failure suffer from swelling because of too much fluid in the body. Furosemide, hydrochlorothiazide, and metolazone are all water pills used to treat the swelling. For most patients, taking furosemide alone is successful. However, sometimes patients need to add another water pill. Doctors usually add either metolazone or hydrochlorothiazide. It is not clear which water pill is better when added to furosemide. The purpose of this study is to determine which water pill when added to furosemide is the best at reducing excess fluid in the body. You are being asked to participate in this study because you have heart failure and are taking furosemide. Approximately 26 patients from the University Hospital will participate in this study.

PROCEDURES

If you volunteer to participate in this study, the following things will happen:

While participating in this study you will have two hospital stays. Starting three (3) days before each hospital stay, you must agree to eat only foods given to you by the University of New Mexico (UNM) General Clinical Research Center (GCRC). The foods contain a specific amount of sodium (salt). Salt intake must be controlled during the study since sodium influences water retention.

You will then be admitted to the UNM GCRC for a period of five (5) days on two separate occasions (one week apart).

You will be asked about what types of medications you are taking. You will continue taking your regular medications throughout this study. On the first day of admission you will continue taking your regular medications.

You will then be assigned by chance (like flipping a coin) to receive your first study treatment. There are two treatments (hydrochlorothiazide and metolazone) in this study and you will be taking both treatments.

For days two, three, and four of each admission you will be given either hydrochlorothiazide or metolazone one hour before taking your first dose of furosemide. After four days, the study treatment will be discontinued and you will be discharged to home on all of your regular

medications. You will then be scheduled to return to the hospital at least one week later. For the first 24-hours on your second visit you will continue taking your regular medications. For days two, three, and four you will be given hydrochlorothiazide or metolazone, whichever you did not receive the first time. The two drugs will look the same and neither you nor the investigators will know which you are taking.

If you are taking potassium or magnesium supplements, the investigators may need to increase the dose of these supplements during the study treatment period. If you are not taking potassium or magnesium supplements, the investigators may need to provide you with supplements during the study treatment period.

At each hospitalization, the following will occur: you will have a physical examination, your medical chart will be reviewed, blood and urine will be collected for laboratory tests, and an electrocardiogram will be done to determine the electrical activity of your heart. A catheter (a small tube used for drawing blood) will be inserted into a vein in your forearm to obtain blood for laboratory tests and will be removed at the end of the hospitalization. In addition, your blood pressure and weight will be monitored. On days one and two, your blood pressure will be measured every hour for the first six hours, then every 2 hours for the next 6 hours, and then every 4 hours for the remainder of the 24 hours for each day. On days one and two, your weight will be measured initially and then at 2 hours, 6 hours, 12 hours, and 24 hours.

You will need to have your blood drawn for laboratory analysis of blood chemistry and kidney function (sodium, potassium, creatinine, etc) as well as for neurohormones. Neurohormones are substances normally produced by your body. Previous studies have shown that these substances are elevated in heart failure patients. During this study, a blood sample of approximately two tablespoonfuls of blood will be drawn from your arm four times each day on days one and four. Approximately one teaspoonful of blood will be drawn four times on day two and two times on day three. Some blood samples will be sent to an out of state laboratory for analysis, however, your name and medical record number will be removed from the sample and labeled instead with a unique code number before being sent. The reason for analyzing your blood chemistry and neurohormones is to determine a baseline for our study and to monitor any changes that may occur during the study. You will be allowed to walk around following each blood draw, but must relax quietly, lying in bed, for at least 30 minutes prior to each blood draw on days one and four and prior to the first blood draw on day three.

Your urine will be collected each of the four days. The reason for collecting your urine is to measure the amount of fluid leaving your body and to determine your kidney function.

You will have an electrocardiogram done four (4) times on each day of each hospital stay. The reason for analyzing your electrocardiogram is to determine if either of the study treatments affects the electrical activity of your heart.

You will be placed on a low salt diet (< 3,000 mg per day) and can drink up to 12 glasses of fluid each 24-hour period while you are in the hospital.

Approximately 35 tablespoons (2 and ¼ cups) of blood will be drawn throughout the study (1 cup for each hospital visit). This amount is slightly less than the amount provided for a standard blood donation.

Participation in the study will take a total of about 228 hours over a period of 21 days (10 total days in the hospital). All study procedures will be done at the UNM GCRC.

You cannot participate in this study if you are pregnant or breastfeeding. If you are a woman of childbearing age, a pregnancy test (1 teaspoon blood or 1 Tablespoon urine) will be done prior to participation in this study. You must agree to use an effective form of birth control throughout the study period.

Table 1: Description of study procedures

Procedure	Day 0	Day 1	Day 2	Day 3	Day 4
	Admit to hospital				
Study Medication			X	X	X
Physical Examination	X				
Weight	X	X	X	X	X
Blood pressure	X	X	X	X	X
Blood Samples		X	X	X	X
24 Hour Urine Collection		X	X	X	X
Electrocardiogram		X	X	X	X

RISKS AND DISCOMFORTS

While receiving hydrochlorothiazide, a possible side effect is low potassium levels. This effect occurs in less than 10% of persons receiving the drug in previous human studies. Other side effects that are possible include low blood pressure, dizziness, sensitivity to the sun, allergic reactions, cardiac arrhythmias, and high blood sugar. These effects have occurred in less than 1% of persons receiving the drug in previous human studies.

While receiving metolazone, the side effects that are possible include dizziness, headache, low potassium levels, and muscle cramps. These effects have occurred in less than 10% of persons receiving the drug in previous human studies. Other side effects include low blood pressure, drowsiness, sensitivity to the sun, rash, nausea and vomiting, allergic reactions, cardiac arrhythmias, and high blood sugar. These effects have occurred in less than 1% of persons receiving the drug in previous human studies.

Frequent risks associated with blood drawing include temporary pain and discomfort at the site of the needlestick, and occasional bruising, sweating, or lightheadedness, and in rare cases, faintness or infection.

You may experience some discomfort or bruising from the inflation of the blood pressure cuff when taking a blood pressure measurement.

Your participation in this research study involves the following risks: emotional distress, stress, inconvenience, loss of privacy. Your information will be handled as confidentially as possible.

BENEFITS

Although you may or may not benefit directly from this research, your participation may lead to information that could help other people suffering from heart failure.

Based on experience with previous human studies, researchers believe that the combination of two water pills in some cases is the best way to reduce swelling. However, because each person responds differently to therapy, this cannot be guaranteed. Upon completion of the study, if it is determined that your symptoms are better with the combination of water pills, your primary care provider will be notified and you will be given the opportunity to continue treatment with the combination of water pills.

ALTERNATIVES TO PARTICIPATION:

Your alternative to participating in this study is simply deciding not to participate. Your doctor can prescribe other treatments and other combinations of therapy used in this study if your doctor thinks they are needed.

CONFIDENTIALITY

Participation in research will involve a loss of privacy, but information about you will be handled as confidentially as possible. Representatives from the University of New Mexico Health Science Center Human Research Review Committee that oversees human subject research will be permitted access to your records. Also, your participation in the study and information in your study records may be shown to your doctors and nurses, and may be disclosed as otherwise provided by law. However, your name will not be used in any published reports about this study.

COSTS OF STUDY

You will not be charged for any of the study treatments or procedures. The costs of hydrochlorothiazide, metolazone, the physical exam, blood tests, electrocardiogram, and hospital stay will be covered by the study.

EMERGENCY TREATMENT AND COMPENSATION FOR INJURY:

If you are injured as a result of this study, the University of New Mexico Health Sciences Center (UNMHSC) will provide you with emergency treatment at usual charge. No commitment is made by the UNMHSC to provide free medical care or money for injuries to participants in this study. If you have any questions about these issues, or believe that you have been treated

carelessly in this study, please contact the the University of New Mexico Health Sciences Center (UNMHSC) Human Research Review Committee (HRRC) University of New Mexico, Albuquerque, New Mexico, 87131, at (505) 272-1129.

PAYMENT FOR PARTICIPATION:

In return for your time and effort for participating in this study, you will receive $550.00. If you do not complete the study, you will be paid for the parts of the study you complete. You should receive payment within 6 weeks of your completion of the study. If you do not receive payment by this time, please contact Dr. Anderson at (505) 272-3664.

NEW FINDINGS

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

WITHDRAWAL

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

QUESTIONS

You have the right to ask questions concerning this study at any time, and you are urged to do so. If you have any questions about the research study, please contact Dr. Anderson at telephone number (505) 272-3664 from 8 AM-5 PM Monday-Friday. At any other time and on weekends, please call the UNM Hospital operator at 272-2111 and ask for the cardiologist on call. If you have any question regarding your legal rights or injuries, please contact the University of New Mexico Health Sciences Center (UNMHSC) Human Research Review Committee (HRRC) University of New Mexico, Albuquerque, New Mexico, 87131, at (505) 272-1129.

CONSENT

You will be given a copy of this consent form to keep. By signing this consent form, you are not waiving any of your legal rights, claims, or remedies. If you have questions about your legal rights as a research subject, please contact the University of New Mexico Health Sciences Center (UNMHSC) Human Research Review Committee (HRRC) University of New Mexico, Albuquerque, New Mexico, 87131, at (505) 272-1129.

A copy of this consent form will be kept in your permanent medical record.

I have read (or someone has read to me) the information in this consent form. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. By signing this consent form, I willingly agree to participate in the study."

_____
Name of Subject (type or print)

_____ _____
Signature of Subject Date

_____
Name of Witness (type or print)

_____ _____
Signature of Witness Date

I have explained the research to the subject or his/her legal representative, and answered all of his/her questions. I believe that he/she understands the information described in this consent form and freely consents to participate.

_____
Name of Investigator/Research Team Member (type or print)

_____ _____
Signature of Investigator/Research Team Member Date