Approved
10-Jan-2022
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09-Jan-2023

INFORMED CONSENT AND AUTHORIZATION

Postpartum management of gestational hypertensive disorders using furosemide: A randomized controlled trial

Investigator(s) name, Degree, University Department, & address:

- Zachary G Candela, DO, Wright State University Boonshoft School of Medicine, OBGYN
- Sheela Barhan, MD, Wright State University Boonshoft School of Medicine, OBGYN
- Samantha Wiegand, MD, Perinatal Partners, Miami Valley Hospital
- Rose Maxwell, PhD, Wright State University Boonshoft School of Medicine, OBGYN

Site(s) where study is to be conducted:

- Miami Valley Hospital, Dayton, OH
- Five Rivers Center for Women's Health, Dayton, OH

Phone number for subjects to call for questions

- (937) 208-2965 - Wright State Physicians/ WSU-BSOM OBGYN Department
- (937) 208-8000 after hours

Introduction

The purpose of this consent form is to give you information about this research study. It will describe the purpose, procedures, benefits, risks, and discomforts of this study. The principal investigator and/or the study staff will discuss this study with you and explain everything in detail. Please ask them to explain any words or information that you do not clearly understand.

It is up to you to decide whether or not to take part in this study. If you choose not to participate your decision will not affect your current or future relationship with Wright State University or Premier Health nor will it affect your health care at Premier Health. If you decide to participate, you are free to withdraw at any time without affecting that relationship. Please read this entire consent form and take your time to make your decision. We encourage you to talk to your doctor, your family, and/or your friends before you decide.

Who is conducting and funding this research study?

Wright State University (WSU) will be conducting this trial under the direction of Dr. Zachary Candela, principal investigator. This study is being carried out with funds received from the WSU Department of OBGYN.

Why is this research study being done?

The purpose of this study is to compare standard treatment of postpartum gestational hypertensive disorders using labetalol vs experimental treatment using labetalol plus furosemide, which is an FDA approved diuretic, to see if there is a difference in blood pressure control.

Why am I being asked to participate in this research study?

You are being asked to take part in this study because you have elevated blood pressures that are caused by a gestational hypertensive disorder such as pre-eclampsia or gestational hypertension. You may benefit from this experimental treatment regimen.

How many people will be in this study?

Approximately 192 women will participate in this study (96 in the labetalol arm and 96 in the labetalol plus furosemide arm).

What will happen if I take part in this research study?

If you agree to be in this study, the following will happen:

BEFORE YOU BEGIN THE STUDY – SCREENING PROCEDURES

You will have the following things done:

- History and physical examination which will include checking your heart rate, blood pressure and temperature.
- Weight measurements
- Review of medications and supplements you are currently taking.

These are part of your regular care.

DURING THE STUDY

This research will take place at Miami Valley Hospital.

If the screening exams, tests or procedures show that you can continue to be in the study, and you choose to take part, then the following will be done.

If you agree to take part in this study, you will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance (like pulling numbers out of a hat). A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group (also referred to as an “arm”) you will be in. You will have an equal chance of being placed in any group.

If you are in **Arm A** you will be given the current standard treatment for gestational hypertensive disorders which consists of **labetalol.** You will take labetalol as long as your doctor recommends that you need it to control your blood pressure.

If you are in **Arm B** you will be given the experimental treatment for gestational hypertensive disorders which consists of **labetalol plus furosemide.** You will take labetalol as long as your doctor recommends that you need it to control your blood pressure. You will take furosemide for 5 days.

The following procedures will be completed:

- You will receive labetalol twice daily and if you are in the furosemide arm, you will receive one dose of furosemide daily.
- Your urine output will be measured every twelve hours. This will require you to urinate into a collection unit while sitting on the toilet.
- You will be asked questions about your medical history, and information about any drugs that you are taking from your last visit.
- A physical exam including vital signs (blood pressure and heart rate), will be performed.
- You will have blood drawn for routine lab work. (About 6mL or 2 teaspoons of blood will be drawn).

How long will I be in this research study?

If you choose to take part, you will be in the study for the duration of your hospital stay and up to 1 week when you have your blood pressure check appointment. Typically, postpartum patients remain in the hospital somewhere between 2-4 days. We will also ask that you come in for a routine one week blood pressure check to see how you are doing after discharge from the hospital.

Can I stop being in this research study?

If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without any penalty. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled. If you withdraw from the study, or the study medication is stopped for any reason:

- You will need to alert your treatment team (nurse, resident, attending, study coordinator) that you are electing to leave the study
- You will no longer receive the study medications, but your treatment team will still take care of you and give you the current standard of care for gestational hypertensive disorders including blood pressure checks, medications and routine follow up.

The principal investigator or study staff may also withdraw you from the study and the study medication may be stopped [if applicable], without your consent for one or more of the following reasons:

- Failure to follow the instructions of the research study staff.
- Pregnancy.
- You need treatment not allowed in the study.
- The study is cancelled.
- The principal investigator believes it is in your best interest.

What are the potential risks and discomforts from being in this research study?

Although highly unlikely, there is a small risk of loss of privacy regarding this study (revealing to others that you are taking part in this study) or confidentiality (revealing information about you to others to whom you have not given permission to see this information).

Risks and side effects of furosemide (Lasix):

More common reactions:

- Fatigue (tiredness)
- Urinary frequency
- Dizziness
- Nausea/vomiting
- Muscle cramps
- Hypokalemia (low levels of potassium in the blood)
- Hypotension, orthostatic (low blood pressure when standing up)
- Diarrhea
- ALT, AST elevated
- Blurred vision
- Anorexia (eating less from loss of appetite)
- Abdominal cramps
- Pruritis (itching)
- Rash
- Hyperuricemia (high levels of uric acid in the blood)
- Hyperglycemia (high blood sugar)
- Hypocalcemia (low levels of calcium in the blood)
- Hypomagnesemia (low levels of magnesium in the blood)
- Tinnitus (ringing in the ears)
- Paresthesia (feeling of tingling, tickling, prickling or burning)
- Photosensitivity (increased sensitivity of the skin to light)

Less common reactions:

- Hypokalemia, severe (low levels of potassium in the blood)
- Electrolyte imbalance, severe (abnormal levels of electrolytes such as sodium, potassium, calcium)
- Metabolic alkalosis (increased pH in tissues)
- Hypovolemia (decreased blood volume) /dehydration
- Ototoxicity (toxic condition affecting the inner ear or the auditory nerve)
- Thrombocytopenia (abnormally low levels of platelets in the blood)
- Anemia, hemolytic (anemia due to having fewer red blood cells)
- Aplastic anemia (anemia due to bone marrow producing very few new red blood cells)
- Leukopenia (abnormally low number of white blood cells in the blood)
- Agranulocytosis (abnormally low number of granulocytes/neutrophils tha may lead to increased risk of infection)
- Thrombosis (blood clots)
- Anaphylaxis (allergic reaction)
- Vasculitis (inflammation of blood vessels)

- Pancreatitis (inflammation of the pancreas)
- Stevens-Johnson Syndrome (severe inflammation of the skin and mucous membranes)
- SLE exacerbation (worsening of symptoms lupus)
- Toxic epidermal necrolysis (severe skin reaction involving the top layer of skin separating from lower layers of the skin)

Please let your doctor know if you are experiencing new onset weakness, fatigue, muscle cramping, dizziness or heart palpitations as these can be signs of hypokalemia, a side effect from taking furosemide.

Unknown:
There may be risks from furosemide that are not known at this time.

Are there benefits to taking part in this research study?

You may not receive any personal benefit from being in the study. It is possible that you may benefit by having better control of your blood pressures in the postpartum period. It may also lead you to have a shorter hospital stay and lower your rate of being readmitted for blood pressure control later. However, there is no guarantee that you will benefit from being in this study.

The researchers hope that information learned from your participation in this study will increase knowledge about which way is best to treat patients like you. This knowledge will help make it possible to provide the best type of treatment for patients in the future. While you may or may not personally benefit from being in this study, your participation will provide a benefit to others with this condition and to society.

What other options are there?

If you decide not to participate in this study, you will receive the standard of care treatment for your condition.

What about privacy and confidentiality?

The people who will know that you are a research subject are members of the research study staff, and if appropriate, your physicians and nurses. No information about you, or provided by you, during the research, will be disclosed to others without your written permission, except if necessary, to protect your rights or welfare or if required by law. The following groups will have access to study records that identify you:

- Food and Drug Administration (FDA)
- Wright State University Institutional Review Board (IRB, including the WSU IRB Office and the Office of Research and Sponsored Programs
- Office of Human Research Protections, under the Department of Health and Human Services

A possible risk of the research is that your participation in the research or information about you and your health might become known to individuals outside of the research team.

Identifiers might be removed from your identifiable private information (or/and identifiable biospecimens). After such removal, the information could be used for future research studies or distributed to another investigator for future research studies without your (or your legally authorized representative's) consent.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

FDA Clinical Trial Registry

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.

What if I am injured as a result of my participation in the research study?

If you feel that you have been injured as a result of participating in the research, contact the researcher Dr. Zachary Candela at (937) 208-2287 to talk to them about your illness or injury. In the event of an emergency, dial 911 or go to your nearest emergency department.

There are no plans for Wright State University to provide free medical care or to pay for research-related illnesses or injuries, or to provide other forms of compensation (such as lost wages or pain and suffering) to you for research related illnesses or injuries.

You or your insurance company will be billed for this medical care. Your insurance company may not pay for some or all of this medical care because you are participating in a research study.

By signing this form you will not give up any legal rights.

What are the costs for participating in this research study?

You or your insurer will be responsible for paying for the cost of the following**:**

- Daily basic metabolic panel blood test

The cost for the furosemide will be paid by the study.

Will I be reimbursed for any of my expenses or paid for my participation in this research?

You will not be reimbursed for participating in this research study.

Will I be told about new information that may affect my decision to participate in this research study?

During the course of the study, you will be informed of any significant new research information (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the research. If new information is provided to you, you may be asked to sign a consent form that includes the new information.

Who should I contact if I have questions?

Contact the researcher, Dr. Zachary Candela, at (937) 208-2287 if you have any questions about this study or your part in it or if you have questions, concerns or complaints about the research.

If you have any questions about your rights as a research subject, you may call the Wright State University Institutional Review Board (IRB) at (937) 775-4462. The IRB is an independent committee composed of members of the University community, staff of the institutions, as well as lay members of the community not connected with these institutions. The IRB has reviewed this study.

What are my rights/responsibilities as a research subject?

As a subject, your responsibilities include:

- Follow the instructions of the research study staff.
- Take the study drug as instructed.
- Keep your routine one week postpartum blood pressure check appointment. If it is necessary to miss an appointment, please contact the Five Rivers Women's Health Center staff to reschedule as soon as you know you will miss the appointment. You can reach them at **(937) 208-2007**.
- Tell the research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Contact your doctor you have any of these side effects: new onset of weakness, fatigue, muscle cramping, dizziness or heart palpitations.
- Ask questions as you think of them.
- Tell the research staff if you change your mind about staying in the study.

While participating in this research study, you should not take part in any other research project without approval from the research staff of each study.

Authorization to Use and Disclose Your Health Information

State and Federal laws, including the Health Insurance Portability and Accountability Act (HIPAA), require researchers to protect the privacy of your health information. This section of the consent form describes how researchers, with your authorization (permission), may use and release (disclose or share) your protected health information (PHI) for this research study. **Please read this section of the consent form carefully.**

If you sign this document, you give permission to Dr. Zachary Candela and his research team to use or disclose (release) the following protected health information:

- Your medical records for past medical conditions and medications related to your cardiovascular health
- All information (research records and medical records) created during your participation in this research study
- All information related to illness, readmissions and/or hospitalizations that occur during your participation in this study

The research team needs this information to conduct the study. This is a study that looks at controlling blood pressures in the postpartum state by adding a diuretic (furosemide) to current standard of care.

To maintain the integrity of this research, you might not have access to any health information developed as part of this study until it is completed. At that point, you generally would have access to your health information.

Disclosure of your protected health information

If you sign this form, the researchers may share your health information during the conduct of the study with:

- Non-WSU/PH researchers or organizations working with WSU/PH researchers.
- Law enforcement or other agencies, when required by law
- WSU's Institutional Review Board (or other IRB of record), which oversees our research
- Representatives of government agencies in the United States and other countries (i.e. Food and Drug Administration and the Office of Human Research Protection)
- Other authorized WSU/PH Officials who oversee research and clinical care

The people listed above will use and share your health information to review the quality, safety, and results of the research and may also do additional research.

Please understand that these persons/organizations who may receive your health information may not be required by U.S. Federal privacy laws (such as HIPAA) to protect it and may share your information with others without your permission.

This authorization does not have an expiration date.

However, you can change your mind and cancel this authorization at any time. To cancel this authorization, you must write the study investigator listed at the beginning of this consent form.

If you cancel this authorization, you will no longer be allowed to take part in the research study. If you cancel this authorization, health information you had already allowed us to obtain may still be used and disclosed by researchers in order to maintain the integrity and reliability of the research, and to report any adverse (bad) effects that may have happened to you.

Right to refuse to sign this Authorization

You have the right to refuse to sign and give your authorization. If you do not sign this form, your non-research related treatment, payment or enrollment in any health plans, or your eligibility for other medical benefits at Premier Health will not be affected in any way.

However, if you do not sign this form, you will not be able to participate in this research study.

Signature of Subject

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to participate in this research and authorize the use and disclosure of my protected health information for this study. I will be given a copy of this signed and dated form.

_____ _____
Signature Date

_____
Printed Name

_____
Signature of Person Obtaining Consent and Authorization

_____
Date

_____
Printed Name of Person Obtaining Consent and Authorization