CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Amlodipine Versus Nifedipine ER for the Management of Postpartum Hypertension: A Randomized Controlled Noninferiority Trial

Study to be Conducted at: Greenville Memorial Hospital
701 Grove Road
Greenville, South Carolina 29605

Prisma Health OB/GYN Center
1120 Grove Road Suite B
Greenville, South Carolina 29605

Sponsor Name: Prisma Health

Principal Investigator: Laura Carlson, MD 864-455-1600

KEY INFORMATION

You are being asked to participate in a research study. Participation in a research study is voluntary. The information in this consent form is meant to better inform you so you may decide whether or not to participate in this research study. Please ask the study doctor to explain anything you do not understand.

Many pregnancies are affected by high blood pressure. Women can be diagnosed with different categories of high blood pressure. Your doctor may have diagnosed you with chronic hypertension (high blood pressure even outside of pregnancy), gestational hypertension (high blood pressure only during pregnancy), or preeclampsia (high blood pressure during pregnancy plus other signs and symptoms). While many forms of high blood pressure improve after delivery, blood pressure usually increases before improving. Many women need to start blood pressure medication after delivery.

This study will compare two different blood pressure medications to be used after delivery, amlodipine and nifedipine ER. The purpose of this study is to compare the effects (good and bad) of amlodipine and nifedipine ER on your blood pressure to see which is better.

This research study is being done because there are currently limited recommended treatment options for managing high blood pressure in postpartum women. It is known that amlodipine and nifedipine ER are both effective in managing high blood pressure in the general population, but amlodipine has not been well-studied for high blood pressure during pregnancy and immediately after delivery.

The risks of the study are that amlodipine is ineffective in managing postpartum hypertension and that it may have an unknown adverse effect on breastfeeding. The potential benefit is that amlodipine is at least as effective as nifedipine ER and that it causes less side effects.

If you choose not to participate in this study and need medications, you will be started on a medication which your doctor chooses based on your particular case (which may include amlodipine or nifedipine ER). Aside from the choice of medication, you will have no other changes in your care. You will have medications added or adjusted as needed and be discharged from the hospital when your doctor feels it is

appropriate. You will follow up in the clinic at the same time regardless of study participation (ideally 3 to 7 days after discharge and 6 weeks postpartum).

The Institutional Review Board of the Prisma-Health Upstate has reviewed this study for the protection of the rights of human participants in research studies, in accordance with federal and state regulations.

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 Web site will include a summary of the results. You can search this website at any time.

PURPOSE

You are being asked to participate in this study because you have high blood pressure following delivery of your baby.

Right now, there are 2 main medications used to treat high blood pressures in women who are immediately postpartum (labetalol and nifedipine ER). Both of these medications are safe and effective, but they are not right for everyone. There are many other medications used to treat high blood pressure in patients who have not recently had a baby. Because these medications have not been specifically studied in postpartum women, their use has been limited. One of these medications is called amlodipine. Amlodipine is a similar medication to nifedipine ER, but studies have shown it causes less side effects. It is one of the first-choice blood pressure medications in non-pregnant patients because it is effective and well tolerated. The purpose of this study is to see if amlodipine is a good treatment option for women in the immediate postpartum period. This study will compare the use of nifedipine ER to amlodipine to see if they have similar outcomes. If amlodipine is as effective as nifedipine ER, it may provide a good treatment alternative for patients with high blood pressures following delivery.

The risks of the study are that amlodipine has not been well-studied for this purpose. If it is not as effective as nifedipine ER, you may require additional medications, a change in medications, or a longer stay in the hospital while your medications are being adjusted. In addition, amlodipine is not well studied in breastfeeding women. If you choose to participate in this study and your blood pressure is high enough that you need started on medications, you will be randomly assigned either to amlodipine or nifedipine ER. This medication may later be discontinued by your doctor if your blood pressure improves.

Your participation will last until your postpartum visit is completed at about 6 weeks after delivery.

This study is being conducted as part of the thesis requirements of the Prisma Health Maternal-Fetal Medicine Fellowship program.

HOW THE STUDY WORKS

- Nifedipine ER is a standard medication used for managing high blood pressure in postpartum women.
- Amlodipine is a standard blood pressure medication in the general population. Its use for high blood pressure specifically in postpartum women is investigational.
- Both nifedipine ER and amlodipine are approved by the Food and Drug Administration (FDA).
- If you are not enrolled in the study, your blood pressure will still be treated with the medication your doctor feels best (typically nifedipine ER or labetalol, although others may be used).

- If you agree to participate, you will be "randomized" into one of the study groups. Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor your doctor will choose what group you will be in. You will have an equal chance of being placed in either group.
- The study will not be blinded, meaning that you and your medical team will know which medication you are taking.
- When your blood pressure is high enough to need medications (>/= 150 mmHg systolic and/or 100 mmHg diastolic on two occasions 4 hours apart, or one severe blood pressure of >160 mmHg systolic and/or 110 mmHg diastolic), your doctor will start you on the assigned study medication.
- You will be started on the lowest recommended medication dose initially – either amlodipine 2.5 milligram (mg) daily or nifedipine ER 30 mg daily.
- Your doctor will increase your medication dose if needed. Your doctor may also treat you with additional blood pressure medications or magnesium, depending on the need.
- When your doctor feels you are ready, you will be discharged home.
- Prior to being discharged from the hospital, you will be asked to complete a side effects questionnaire. If a side effects survey is not completed prior to discharge, study staff may call you to administer the questions over the phone or ask you to complete the questionnaire at your next scheduled appointment.
- You will be seen (either virtually or in-person) for a blood pressure check ideally 3 to 7 days after hospital discharge. Your blood pressure will be assessed at that time and your doctor will decide if you should continue medications.
- You will be seen in-person ideally 4 to 6 weeks after delivery. Your blood pressure will be assessed at that time and your doctor will decide if you should continue medications. You will also be asked to complete a form about your breastfeeding experiences. If this breastfeeding survey is not completed at your visit, study staff may send a survey link to your email or call you in person to administer the questions over the phone.

POSSIBLE RISKS

Any treatment has possible side effects. The treatments and procedures used in this study may cause all, some, or none of the side effects listed. There is always the risk of very uncommon or previously unknown side effects.

The most common side effects for Nifedipine include headache, flushing, dizziness, weakness, and nausea.

The most common side effects for Amlodipine include swelling, dizziness, flushing, irregular heartbeat, fatigue, nausea, abdominal pain, and headache.

The side effects listed above do not include all the possible side effects that can occur from taking these medications, and there are other less common or rare side effects that may occur. If you are interested in a complete list of known side effects, this can be requested from the study investigator. It is important to let your physician know of any possible side effects that you experience as some of these complications can sometimes lead to serious illness requiring hospitalization or lead to death.

As with all medications, side effects may include allergic reactions. Allergic reactions may range from minor itching or rash to major reactions, which can lead to death.

Some of the questions in the survey are personal and may be upsetting to some participants. The study doctor or staff will be available to discuss these questions should you have a concern or problem. You do not have to answer any questions that you do not want to answer.

It is possible that receiving the study drug with your regular medications, supplements, or some food (for example, grapefruit juice) may change how the study drug, your regular medications, or your regular supplements work. It is very important that you tell the study doctor about all medications or supplements you are taking during the study. Tell the study doctor if you are taking any drugs, or non-prescription medications or supplements, including vitamins or herbs, other than those being used in this research study because of the risk of possible and/or serious drug interactions. Tell anyone who gives you medical care that you are participating in a research study.

POSSIBLE BENEFITS
It is not possible to know whether or not you may benefit from participating in this study. The treatment or procedures you receive may even be harmful. The information gained from this study may be useful and may help others.

The particular benefits of receiving the study medication (amlodipine) are uncertain. Potential individual benefits include a shorter hospital stay and less side effects.

If the study medication (amlodipine) is found to be as good as nifedipine ER at managing high blood pressure in postpartum patients, other patients may benefit from this information in the future, since it will give doctors and patients additional treatment options.

ALTERNATIVE (OTHER) TREATMENTS
You can still receive evaluation and treatment for your condition if you do not participate in this study. Discuss any alternative treatments with your regular doctor and/or the study doctor before you decide to participate. The decision is entirely up to you. If you decide not to participate in the study, you will not be penalized or lose any benefits and your decision will not affect your relationship with your doctor or hospital.

Standard of care for patients with high blood pressure following delivery is to start medications when the blood pressure is greater than or equal to 150 mmHg systolic and/or 100 mmHg diastolic on 2 occasions 4 hours apart. Nifedipine ER and labetalol are the routinely used medications. If you do not participate in this study and your doctor feels that you need blood pressure medications, they will choose one that they feel is appropriate.

- You may choose to have the standard of care treatment, which is typically nifedipine ER or labetalol.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated.

Please discuss these choices with your doctor.

NEW INFORMATION
Your doctor will tell you about new information that may affect your willingness to participate in this research study. Alternatives, or other choices, concerning your care will be discussed at that time.

There are no plans to share individual research results with you.

COST TO YOU FOR PARTICIPATING IN THIS STUDY
All of the tests and procedures in this study are considered part of your routine care and will not be paid for by the study. We will bill you or your health insurer for these routine items and services, which you would have received even if you did not take part in the research. You will be responsible for payment of any deductible and copayments required by your insurer.

If you have any question about costs to you that may result from taking part in the research, please speak with the study doctor or staff.

PAYMENT FOR PARTICIPATION
To You:
You will not be paid for participating in this study, but you will be given a pack of diapers for your participation.

To Institution:
Prisma-Health Upstate is being funded by the sponsor for staff and administrative costs associated with conducting this study.

COMPENSATION FOR INJURY AS A RESULT OF STUDY PARTICIPATION
Prisma-Health Upstate will provide you the care needed to treat any injury, or illness, that directly results from taking part in this research study.

Injuries sometimes happen in research even when no one is at fault. The study sponsor, Prisma-Health Upstate, or the investigators as part of this study have no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the 'Contact for Questions' section of this consent.

VOLUNTARY PARTICIPATION
Participation in this research study is voluntary. You may refuse to participate or withdraw from the study at any time. If you refuse to participate or withdraw from the study, you will not be penalized or lose any benefits and your decision will not affect your relationship with your doctor or hospital.

However, if you decide to stop study participation, you are encouraged to talk with your doctor regarding safe removal from the study. Further treatment would be discussed.

If your participation in this research study is stopped, your study doctor will discuss any tests or procedures that might be needed for your health and safety, but you may refuse any or all of these tests or procedures.

Following this discussion with your study doctor, you still have the right to refuse any or all of these tests or procedures.

Sudden withdrawal from the study without starting a different medication for your blood pressure may result in very high blood pressures, which can be dangerous. The consequences of very high blood pressure can include stroke and even death. You should talk to your doctor before stopping a blood pressure medication.

AUTHORIZATION TO USE AND DISCLOSE (RELEASE) MEDICAL INFORMATION

As part of this research study, the study doctor and his/her research team will keep records of your participation in this study. These study records may be kept on a computer and will include all information collected during the research study, and any health information in your medical records that is related to the research study. The study doctor and his/her research team will use and disclose (release) your health information to conduct this study. This study may result in scientific presentations and publications, but steps will be taken to make sure you are not identified.

Some of the organizations/entities that may receive your information are:

- The study sponsor and any company supporting the study (the sponsor's authorized representatives)
- The Institutional Review Board, which is a group of people who review research with the goal of protecting the people who take part in the study

Under federal privacy laws, your study records cannot be used or released for research purposes unless you agree. If you sign this consent form, you are agreeing to the use and release of your health information. If you do not agree to this use, you will not be able to participate in this study. Once your health information has been released, federal privacy laws may no longer protect it from further release and use.

The right to use your health information for research purposes does not expire unless you withdraw your agreement. You have the right to withdraw your agreement at any time. You can do this by giving written notice to the study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

If you have any questions about the privacy of your health information, please ask the study doctor.

CONTACT FOR QUESTIONS

For more information concerning this study and research-related risks or injuries, or to give comments or express concerns or complaints, you may contact the principal investigator, whose information is included below.

You may also contact a representative of the Office of Human Research Protection of Prisma-Health Upstate for information regarding your rights as a participant involved in a research study or to give comments or express concerns, complaints or offer input. You may obtain the name and number of this person by calling (864) 455-8997.

Principal Investigator Name: Laura Carlson, MD

Telephone Number: 864-455-1600

CONSENT TO PARTICIPATE

The study doctor, _____, has explained the nature and purpose of this study to me. I have been given the time and place to read and review this consent form and I choose to participate in this study. I have been given the opportunity to ask questions about this study and my questions have been answered to my satisfaction. I have been given the opportunity to review my study doctor's Notice of Privacy Practices. I agree that my health information may be used and disclosed (released) as described in this consent form. After I sign this consent form, I will receive a copy of it for my own records. I do not give up any of my legal rights by signing this consent form.

_____
Printed Name of Participant

_____ _____ _____
Signature of Participant Date Time

INVESTIGATOR STATEMENT

I have carefully explained to the participant the nature and purpose of the above study. The participant signing this consent form has (1) been given the time and place to read and review this consent form; (2) been given an opportunity to ask questions regarding the nature, risks and benefits of participation in this research study; and (3) appears to understand the nature and purpose of the study and the demands required of participation. The participant has signed this consent form prior to having any study-related procedures performed.

_____ _____ _____
Signature of Investigator Date Time

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