VUMC Institutional Review Board Informed Consent Document for Research

Title: Effect of Midodrine vs Abdominal Compression on Cardiovascular Risk Markers in Autonomic Failure Patients

Study Title: Version Date: 8/4/20
PI: Luis Okamoto, MD
NCT number: NCT04620382

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Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
The purpose of this study is to compare the effects of abdominal compression with the medication midodrine, both of which are used to treat orthostatic hypotension (OH, drop in blood pressure on standing). This study includes 3-5 days spent in the Vanderbilt Clinical Research Center (CRC), at least one day of screening tests to make sure it's safe for you to be in the study, followed by 2 study days – one with abdominal compression and one with midodrine. On the study days, you will have instrumentation placed (blood pressure, heart rate) and several tests will be done. We will then place an abdominal binder around you and give you a pill to take. Thirty to sixty minutes later, we will repeat the testing.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have OH.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

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Side effects and risks that you can expect if you take part in this study:

Withholding Medications: Not taking your regular medications for OH may worsen your symptoms and may increase the risk of injury due to fainting. Not taking your regular medications for high blood pressure may cause an increase in blood pressure. The study staff will monitor you during this period. If you cannot tolerate the withdrawal, we will restart your regular medications immediately.

Blood draw: Having a catheter (tube) placed in your vein may cause pain and bruising at the insertion site. Rarely some people faint.

Orthostatic tests and head up tilt table tests: can cause lightheadedness, tiredness, dizziness, or syncope.

Midodrine is a drug approved for the treatment of OH. Taking midodrine results in a rise in blood pressure. Common side effects include goosebumps, itching mainly of the scalp; rare side effects are numbness or tingling and changes in urinary function.

Placebo (sugar pill) - Rarely, people may react to the coloring of the capsules.

Abdominal compression: Applying external pressure to the abdomen may produce some temporary abdominal/back pain, occasional bruising, discomfort, or difficulty breathing deeply. Some people may also experience chest discomfort (such as heartburn and/or acid reflux)**.**

Cardiac output and segmental fluid measurements by impedance: There is no known risk associated with the measurement of heart's pumping capacity by bioimpedance. Measurements are made using patches placed on the skin, similar to ECG measurements.

Blood pressure cuff: Some may find it uncomfortable to hold their arms with an inflated cuff placed around the forearm, or finger in a relatively fixed position or to have the cuff inflated frequently.

Electrodes: Sticky patches on the chest and limbs will be used to record electrocardiograms (a measure of the electrical activity from the heart). The patches might be uncomfortable and may occasionally cause itching or a rash.

Continuous positive airway pressure (CPAP) - You will wear a face mask to apply a low air pressure in your airway. There is no known risk associated with this procedure. The mask might feel uncomfortable

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to wear, and the machine might be noisy. Rarely, CPAP can cause congestion, runny nose, dry mouth nosebleeds, low blood pressure, or feeling claustrophobic. The CPAP device is approved by the Food and Drug Administration (FDA). However, the use of the CPAP in this study is considered investigational (not approved by the FDA).

Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

Good effects that might result from this study:

The benefits to science and humankind that might result from this study: we may learn more about how the body responds to different treatments to be better able to treat OH.

Procedures to be followed:

If you agree to be in the study, we will ask you to stay in the CRC for the duration of the study (up to 5 days). Testing on each study day will take about 3 hours. If you have had some of the procedures listed below recently, they may not need to be repeated. We may ask you not to take your regular medications. The study doctor will tell you which medications you should stop.

We will ask you to come to the CRC. The screening procedures will be done over 1-2 days. These will include:

- A complete physical examination and history.
- We will take about 1 tablespoon of blood from your arm with a needle to be sure it is safe for you to be in the study. We will also ask you for a urine sample.
- If you are a woman who could become pregnant, we will do a blood pregnancy test. If you are pregnant, you will not be allowed to take part in the study.
- We will place sticky patches on your arms and legs for an electrocardiogram (ECG, a measure of your heart's electrical activity).
- We will draw 2 tablespoons of blood from a vein in your arm while you are lying down and after sitting and or standing to determine hormones that regulate the blood pressure. Your blood pressure and heart rate will be measured in these different positions.
- We will do some more tests designed to determine how well your body is regulating your blood pressure and heart rate. During these tests, we will measure your heart rate using an ECG and your blood pressure using a cuff around your arm and/or finger. These tests include asking you to breathe deeply for two minutes and breathing against pressure for 15 seconds. These tests will let us know how well your involuntary nervous system is working.

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- We may perform a tilt table test. This test uses a tilt table, which is a motorized table with a footboard. It moves you to an upright position without you having to use your muscles to stand. You will be asked to lie down on the table and rest quietly while the monitoring equipment is assembled. You will have sticky patches (EKG electrodes) applied to your chest to monitor your heart rate and rhythm. Your blood pressure will be measured with a cuff applied to one of your fingers and/or around your arm. Safety straps will be used to secure you to the table to prevent falling or unsteadiness when the table is moved to an upright position. You will be gradually tilted to an upright position for up to ten minutes, or until your systolic blood pressure drops to 70 mm Hg, or the appearance of orthostatic symptoms such as dizziness, lightheadedness or faintness.

Study Days 1 and 2
The study days will be the same except that on one day you will be given the study medication (midodrine) and on the other day you will be given a placebo (a capsule with no active ingredients).

Before the study starts, you will be asked to empty your bladder. You will then be asked to rest quietly on the tilt table for instrumentation. We will wrap a blood pressure cuff around your upper arm, and a special device around your finger to measure your blood pressure. We will apply sticky patches to the front of your body to measure changes in blood volume within your body (body impedance) and your heart rate (ECG). Safety straps will be used to secure you to the table to prevent falling or unsteadiness when the table is moved to an upright position.

After we have all the monitors in place, you will rest quietly for 15-30 minutes. We will then collect some baseline measurements of your heart rate, blood pressure, and body impedance. We will perform the title table testing. At the end of the test, you will be asked to complete a questionnaire about your symptoms.

We will then have you sit while you take a single dose of medication. You will be given either midodrine, a medication approved by the Food and Drug Administration to treat OH, or a placebo, a capsule with no active ingredients. Which one you are given on study day 1 will be decided by chance, like the toss of a coin. On study day 2, you will be given whichever you did not get on study day one.

We will place a standard blood pressure cuff covered by a commercial abdominal band around your abdomen.

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After 30 minutes, we will repeat the previous measurements. We will again perform the tilt table test, but this time the cuff around your abdomen will be inflated. The amount of pressure is like a very tight belt, much less than what is used on your arm when you have your blood pressure taken. On one study day, the pressure in the cuff will be higher than the other.

At the end of the tilt table test, we may ask you to wear a facemask to apply a low air pressure in your airway [continuous positive airway pressure (CPAP)] for 1-3 minutes. The study doctors may decide not to perform this part of the study.

You will then be done with the study day.

Payments for your time spent taking part in this study or expenses:
You will not be paid to be in this study.

Costs to you if you take part in this study:
There is no cost to you for taking part in this study.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Emily Smith, RN, BSN, MPH at 615-875-1516 or Luis Okamoto, MD at 615-484-3458.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:

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You may be removed from this study without your consent if staying in the study would be harmful to you, if you no longer meet the requirements of the study, or if the study is stopped. If you are removed from the study, you will be told the reason.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:
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 Web site at any time.

Confidentiality:
All efforts, within reason, will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. The study results will be kept in your research record for at least seven years or as long as we need the information for the study. All information on paper will be kept locked in a secure location. Any information kept in a computer will be through the Vanderbilt data system, which has many safeguards. Only members of Dr. Okamoto's research team will be able to see any of the information that would identify you.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.
Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done

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on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:
We will not return any study results to you.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this authorization?
You do not have to sign this authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?

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You may change your mind and cancel this authorization at any time. If you cancel, you must contact the principal investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title

Time: _____