Official Title: Comprehensive Assessment of Vascular and Autonomic Function in Children With Low Vitamin D
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Wake Forest™
School of Medicine

Department of Hypertension

Research Study Informed Consent Form

Comprehensive Assessment of Vascular and Autonomic Function in Children with Low Vitamin D

Hossam Shaltout, PhD., Principal Investigator

You are being asked to take part in a research study carried out by Dr. Hossam Shaltout. Please read this form carefully, taking as much time as you need. Ask the researcher to explain anything you don't understand. This study has been approved for human subjects to take part by the Wake Forest University Health Sciences Institutional Review Board.

You may refuse to give permission, or you may withdraw your permission to be in the study, for any reason. You will also be asked if you would like to take part in this study. Even if you give your permission, you can decide not to be in the study or to leave the study at any time.

What is this research study about?

The purpose of this research study is to gather information on the relationship between low vitamin D levels and the causes of dysautonomia while continually monitoring blood pressure and pulse change and determine if supplemental vitamin D will improve certain symptoms described below. Dysautonomia is a disorder of the central nervous system. The most common symptoms associated with dysautonomia are sudden changes in blood pressure and pulse which may cause fatigue, excessive thirst, lightheadedness, dizziness or vertigo, nausea, feelings of anxiety or panic, and fainting. There are many types of dysautonomia that patients may experience. Orthostatic intolerance (OI) is one type of dysautonomia. OI can be defined as low blood pressure, lightheadedness, weakness, fainting or near fainting after prolonged standing. While medications currently used to treat nausea have proven to be effective in a good number of patients with OI, this may not be the best treatment in all patients particularly because long term use could pose certain risks.

It has been noted that vitamin D deficiency is associated with dysautonomia. We would like to learn more about the link between problems with the nervous system and nausea and determine if supplementation of Vitamin D could improve symptoms.

In order to provide a more specific treatment to patients suffering from nausea and orthostatic intolerance, we will look at blood pressure, pulse, blood tests, and a tilt table procedure which mimics daily life stressors which will be discussed in another section of this consent.

You are being asked to take part in this study because your doctor has determined that you have low levels of vitamin D and dysautonomia.

You cannot take part in this study if you have diabetes, any heart problems that would preclude performing certain tests, certain inflammatory conditions which might be causing your gastrointestinal problems, or unable to discontinue certain medications.

How Many People Will Take Part in the Study?

Wake Forest Baptist Hospital is the only site participating in this study and we plan on recruiting 80 subjects for the trial.

What will I be asked to do in this research study?

If you have not had your vitamin D levels tested recently, we will draw 1 small tube, about 1 tablespoon, of blood at this time. If the results reveal a low vitamin D value, you will be asked to join the study.

This study will involve 2 separate visits. At your first study visit you will discuss any questions or concerns regarding your study participation with the study staff. A medical history, including a review of your current medications, will be obtained from you and we will ask that you complete questionnaires regarding symptoms of your nausea as well as possible anxiety. We will first ask you to undergo various non-invasive vascular tests. These will include lying down and having blood pressure cuffs placed on your arms, legs and ankles. We will also ask you to hold an instrument to measure your hand grip. Another test will use a small rod, placed at different locations of your body where your pulse can be felt. After all vascular tests have been completed you will go to the tilt table lab with the study staff. An intravenous (IV) catheter will be placed in your arm so that we can administer normal saline continuously. This is part of the normal procedure during all tilt tests in case you were to need medicine for excessive nausea. Your heart rate and blood pressure will be monitored as you are placed on a mechanical table, tilt table, a table that will tilt you upward to an almost standing position. The position accomplished by the tilt table procedure mimics daily life stressors which may induce orthostatic intolerance.

You will have approximately 2.5 tablespoons of blood drawn before the tilt table begins and 2.5 tablespoons drawn during the tilt table. You blood will be drawn from the IV catheter.

Once your blood is drawn and the results are obtained and reviewed by the study doctor, the blood will be discarded. Some of the results from your blood samples may aid the doctor in prescribing specific treatment. Some of the results will be collected for research purposes only. The results of the tests performed with your blood will be made available to you upon request. Some of the results will not be put in your medical record.

The results of your blood samples will be used for research and is also a part of your general standard of care.

At the end of visit 1, the study staff will give you a bottle of over the counter Vitamin D and instruction about how to take it. You will be instructed of the daily dosage based on your vitamin D level and consultation and with your physician. You will take the recommended dosage for at

least 2 months and then return for your final research visit.

We will ask you to fast, not eat food or drink any beverage, at least 2 hours after a light meal consisting of toast and juice prior to the visit.

The same tests and procedures will be repeated at visit 2.

How long will I be in this study?

This study will involve 2 separate visits at Wake Forest Baptist Health Center which will be two and a half hours each and will be scheduled at least 2 months apart.

If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

Are there any benefits is in this research study?

We hope that the supplementation of vitamin D will improve your symptoms. We hope the information learned from this study will help us to identify a better treatment for you. We also hope that the information gathered from this study will help other people in the future.

Are there any risks to this research study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the procedures we are studying include:

- The risks of taking vitamin D is the potential of vitamin D toxicity usually caused by a person taking megadoses of vitamin D. Toxicity could result in excess calcium in your blood, poor appetite, nausea, vomiting, weakness, frequent urination and kidney problems.

- You may feel anxious while having the tilt table test.

- You may experience dizziness or light headedness during the vascular tests and should inform the study staff if this occurs.

- You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions.

- Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

- There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Reproductive Risks and other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential

What other choices are there?
You do not have to be in this study to receive treatment. You should talk to your doctor about all of the choices you have. Instead of being in this study, you could follow what treatment regimen your doctor suggests.

Will information about me be kept private?

In this research study, any new information we collect about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** medical history, physical exam, vital signs, current medications, and nausea profile and anxiety questionnaires.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it might no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Hossam Shaltout that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Hossam Shaltout, PhD

[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in a special section of your medical record. This part of the medical record will only be available to people involved in the research study or persons treating you at this Medical Center. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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 Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

The data for this study will be kept private and confidential to the extent allowed by federal and state law.

Are there any costs or payments for being in this research study?

You will be paid $50 for all completed study visits. If you withdraw from the study for any reason before completion, you will be paid $25 for each completed study visit. To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

There are no costs to you for taking part in this study. All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

Will your research records be confidential?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law. However, there is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

What if I becomes injured or ill during the study?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for his/her care. This is because the insurer is required by law to

report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

What are my rights as a research study volunteer?
Your participation in this study is completely voluntary. You may choose not to take part in this study, choose not to answer specific questions, or leave the study at any time. There will be no penalty or loss of benefits to which you are entitled if you choose not to give your permission to take part or you withdraw from the study. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your medical best interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

Who can I talk to if I have questions?
For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Hossam Shaltout at [redacted] or [redacted] for after hours.
The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a signed copy of this consent form.

What does my signature on this consent form mean?
Your signature on this form means that:

- You understand the information given to you in this form
- You have been able to ask the researcher questions and state any concerns
- The researcher has responded to your questions and concerns
- You believe you understand the research study and the potential benefits and risks that are involved.
- You understand that even if you give your permission, you may choose not to take part in the study.

Statement of Consent

I give my voluntary permission to take part in this study. I will be given a copy of this consent document for my records.

Signature of Participant_____ Date: ___/___/___Time:___:___ am pm

Printed Name of Participant:_____

Statement of Person Obtaining Informed Consent

I have carefully explained to the participant being asked to take part in the study what will happen to you.

I certify that when this person signs this form, to the best of my knowledge, he or she understands the purpose, procedures, potential benefits, and potential risks of his or her participation.

I also certify that he or she:

- Speaks the language used to explain this research
- Reads well enough to understand this form or, if not, this person is able to hear and understand when the form is read to him or her
- Does not have any problems that could make it hard to understand what it means for him or her to take part in this research.

Signature of Person Obtaining Consent:_____ Date:___/___/___ Time:___:___am/ pm

Printed Name of Person Obtaining Consent:_____