Feasibility of Bisphosphonate Use on Sleeve Gastrectomy Associated Bone Loss: Healthy Body, Healthy Bones Trial

NCT04279392

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ADULT CONSENT - CLINICAL BIOMEDICAL

Title of this Research Study

Feasibility of Bisphosphonate Use on Sleeve Gastrectomy Associated Bone Loss: Healthy Body, Healthy Bones Trial

Invitation and Summary

You are invited to take part in this research study. Participation in this research study is voluntary. You do not have to take part.

Here is a summary of the purpose, methods, risks, benefits, and alternatives, to help you decide whether or not to take part in the research.

Weight-loss surgery is positive in many ways. It helps reduce obesity and obesity-related diseases. However, weight-loss surgery is known to have negative consequences on our bones. When our bones become unhealthy, we have an increased risk of breaking a bone.

The purpose of this study is to see if a bone protecting medicine can help stop the bone loss that happens after weight-loss surgery.

The study includes an assessment of your bones, diet, and physical health before your surgery and at 9 months after surgery. Six weeks after surgery you will receive an intravenous (IV) infusion of an active or inactive medication. An IV is a way to deliver fluids or medicine directly into your body through a vein. You will be randomly assigned to either the active intervention group or the non-active intervention group. You do not get to pick the group you are in. There is a 50% chance you will be placed in the active intervention group and a 50% chance you will be placed in the non-active intervention group. Both groups will receive an infusion, but one infusion delivers the intervention we are testing and one does not. The active intervention is a bone medicine called zoledronic acid, which is a medicine used to treat poor bone health. Because this study is "blinded" you are not told your group until the final study visit.

When you enroll in this study you will have a bone scan of your spine, hip, knee, and arm, and a CT scan of your spine and hip. These are scans that help us measure the health of your bones. You will also have blood drawn to measure factors that tell us about the health of your bones. You will complete questionnaires, complete physical function assessments, and receive calcium and vitamin D supplements. The study will supply calcium to meet your daily needs. You will also receive vitamin D. The

amount of vitamin D supplements you receive will depend on your vitamin D labs. These supplements will be provided before your surgery.

You will be provided with a bariatric vitamin for use following your surgical operation. You will continue on calcium supplements throughout the 9-month study period. At the study completion visit at 9-months after your operation, you will have your second bone scan and CT scan and complete all study questionnaires and physical function tests. If you want, you can find out to which group you were assigned at this time.

There are risks associated with this study. The most important and likely risks come from the active intervention, which is a bone medicine called zoledronic acid. The bone medicine sometimes causes joint pain, muscle pain, headaches, and flu-like symptoms. There are other risks from the bone scans as well, such as radiation exposure. The risks will be described in greater detail later in the consent form. We take every action we can to make sure you are safe and the risks are low.

The possible benefits of being in this study are that you may be able to prevent bone loss after your weight-loss surgery, if you are randomized to the active intervention.

The alternatives to participating in this study are to not participate. Zoledronic acid can be prescribed by your doctor if they are concerned about your bone health. Vitamin D, calcium and a bariatric vitamin are available over the counter. You could also participate in a bone-loading exercise program that includes weight-lifting, and/or jumping exercises.

Why are you being asked to be in this research study?

You are invited to participate because:

- You are 19 years of age or older
- You are planning a sleeve gastrectomy procedure at Nebraska Medicine
- If you are a woman, you are postmenopausal, or if you are pre-menopausal, you are incapable of childbearing or have a documented non-hormonal intrauterine device
- You are less than 350 pounds

What is the reason for doing this research study?

Adults who undergo bariatric surgery are at risk for developing low bone mass and higher risk of breaking bones in the future. This research is trying to see if an osteoporosis medicine is effective in reducing bone loss and the risk of breaking

bones following bariatric surgery.

All medicines and imaging tests in this study are FDA approved.

What will be done during this research study?
You have also received a timeline of events in this study to go along with the written descriptions below.

Enrollment Visit:
After the consent process you will complete several surveys. You will complete The National Osteoporosis Foundation Calcium Intake Estimate, which estimates the calcium in your diet**.** You will complete a physical activity survey called the Human Activity Profile (HAP), and a survey about your knee pain and function called the Knee Injury and Osteoarthritis Outcome Score (KOOS) at this visit. You will have two tubes (about 4 teaspoons) of blood drawn so we can measure factors which indicate how your bones are functioning. If you are a female less than 60, you will have an additional 2 teaspoons of blood drawn so we can also do a test to confirm you are in menopause. You will be asked to complete a hand grip test, sit and stand in a chair five times in a row, and walk 13 feet to evaluate your strength and walking function. Study personal will access your health record to get details about your surgery, other medical conditions, and medications you are taking.

The enrollment visit should take about 1 hour in total. Study personnel will contact you via phone or email following the visit to schedule the remaining research visits.

Bone Scans (Imaging Visit 1): The first imaging visit will take place at the Nebraska Medicine Village Pointe Location, before your surgery date. You will be measured on a standard scale for weight. You will also have your waist circumference measured by study personnel. You will have a DXA scan of your hips, lumbar spine, arm and knee. This scan also provides information about your body composition. You will also have a CT scan of your lumbar spine and hip which tells us about your muscles and bones. Based on results the vitamin D levels in your blood, you will be prescribed vitamin D supplements. You will be given 1200 mg calcium per day and will receive a 9-month supply of the Bariatric ProCare vitamin along with instructions on how to take them following surgery. If you choose, research staff will send DXA bone scan results to your provider.

This visit will take place before your bariatric operation and should take approximately 2.5 hours including driving time. You will be compensated for this visit.

Intervention/Infusion visit: You will return 6 weeks following your surgery for the intervention/infusion visit. We will do our best to schedule this visit with your bariatric surgery 6-week follow-up visit.

The intervention/infusion visit will take place at the Nebraska Medicine Campus. You will first receive a blood draw when you arrive for your regularly scheduled 6-week follow up visit with your bariatric physician. Following your bariatric visit, you will go to the UNMC Clinical Research Center. At the Clinical Research Center, you will have your infusion. Based on which group you were assigned, you will receive either non-active saline intervention (placebo) or active intervention (zoledronic acid) intravenous (IV) infusion. An IV infusion is a method of delivering fluids or medicine directly into a vein. The infusion will take place over a minimum of 15 minutes, and we will ask you to remain in the Clinical Research Center for an additional 15 minutes following the infusion. Study personnel will ask you about side-effects you experience after the infusion**.** You will be provided with a take-home sheet detailing common and/or expected reactions to the intervention, with instructions about how to manage them.

The intervention/infusion visit will take approximately 3 hours in total. You will be compensated for this visit.

24 Hour Check in: You will be contacted (via text, email or phone) following the infusion to collect and address any adverse events/reactions/concerns you may have.

2 Month Check in:
You will be contacted (via text, email or phone) following the infusion to collect and address any adverse events/reactions/concerns you may have.

Bone Scans (Imaging Visit 2): The final imaging visit will take place at the Nebraska Medicine Village Pointe location, 9-months after your surgery date, and serves as the completion of the study. The study completion visit is very similar to the first imaging visit before your surgery**.** At this visit you will have your weight, and waist circumference measured. You will have a second DXA scan, CT scan and 4 teaspoons of blood drawn**.** You will complete the physical function tests (hand grip test, sit and stand in a chair five times in a row, and walk 13 feet), and all study questionnaires again. Since you will no longer receive study supplied calcium and vitamin D supplements, research staff will review the recommended amounts of calcium and vitamin D and bariatric vitamin supplementation for you to purchase and

continue taking. We will also provide information about how to take care of your bones. You can find out the group to which you were assigned if you wish.

We will call after your visit to review the bone scan results will with you.

The 9-month visit will take approximately two hours. You will be compensated for this visit.

What are the possible risks of being in this research study?

Zoledronic Acid (Active-intervention): The most commonly reported adverse effects of Zoledronic acid are fever (8.7%-17.9%), joint pain (17.9%-23.8%), high blood pressure (6.8%-12.7%), muscle pain (4.9%-11.7%), and headache (3.9%-12.4%). There are other rare, but serious side effects including renal impairment (kidney problems), kidney failure, severe bone, muscle and joint pain, injection site reactions (allergic reactions), anaphylaxis (severe allergic reaction), atrial fibrillation (heart condition) and osteonecrosis of the jaw (bone breakdown).

Placebo (non-active intervention): The placebo medication used in this study (saline), has no known side effects. However, if you are not randomized to the active medication group, it is possible that you will not maintain the quality and strength of your bones over the study period.

Bone Scans (DXA and CT): This research study involves exposure to radiation that is not necessary for your medical care and is for research purposes only.

DXA: There are risks associated with radiation from DXA bone density testing. DXAs are safe, non-invasive and painless. Subjects will have two DXA scans (pre-op and 9 months post-op).

CT Scan: A CT scan is non-invasive and relatively painless. Risks associated with radiation from CT scan testing are more significant than DXA. CTs are safe, non-invasive and painless; however, they deliver a larger dose of ionizing radiation than traditional X-rays.

Radiation Safety: This research study involves exposure to radiation. Please note that this study involves radiation exposure that is not necessary for your medical care and is for research purposes only. The total amount of radiation (2400 millirems) you will receive from participating in this study is about 48% of what radiation workers (for example, x-ray technicians) are allowed to receive annually. The risk is comparable to the risk of working in a "safe" industry, such as office work. Scientists disagree on

the exact risk of radiation doses at these levels. One possible effect could be a very slight increase in cancer risk. The increase with this amount of radiation is less than 1 in 25,000 (much less than 1/100th of a percent). This additional risk is too small to be measured and is generally regarded as insignificant.

Please tell your doctor if you have taken part in other research studies or received any medical care that used radiation (for example, any x-rays or nuclear medicine scans). This way we can make sure that you will not receive too much radiation.

Peripheral intravenous (IV) placement: Risks associated with placement of an IV include discomfort, redness at IV site, bruising, IV fluid leaking into the surrounding tissues, air introduced into the vein, and phlebitis (inflammation of the vein).

Please tell the researchers if you have taken part in other research studies or received any medical care that used radiation (for example, any x-rays or nuclear medicine scans). This way we can make sure that you will not receive too much radiation.

Calcium and Vitamin D usage: Vitamin D supplements are relatively safe. Too much calcium can be harmful. Stomach upset, constipation, and kidney stones have occurred with high intakes of calcium; however, our study uses the recommended dose of calcium. You are encouraged to drink at least 8 glasses of water a day while you are taking calcium and vitamin D supplements. You should not take additional supplements of calcium and vitamin D supplements above those prescribed for the study.

Blood Draw: Risks associated with drawing blood are minimal, with the most common being bruising and discomfort at the blood draw site. Sometimes, people become dizzy, lightheaded, or feel faint during or after a blood draw. A rare complication is infection at the venous access site.

It is possible that other rare side effects could occur which are not described in this consent form. It is also possible that you could have a side effect that has not occurred before. There is always a risk of other side effects that we cannot predict. You will be asked to inform the research staff about all medications, vitamins, and supplements you take, and medical conditions. This may help avoid side effects, interactions, and other risks.

What are the possible benefits to you?

If you agree to take part in the study, you may or may not experience direct benefit.

The possible benefits of participating in this study may include a reduction in bone loss during the study period, which may be critical in reducing long-term fracture risk in bariatric surgery patients. As everyone may respond differently to therapy, there is no way to know in advance if this study will be beneficial in each individual case.

What are the possible benefits to other people?
We hope the information learned from this study could be used in developing a recommended protocol for patients who undergo bariatric surgery to maintain their bone health after bariatric surgery.

What are the alternatives to being in this research study?
The alternative to participating in this study is to not participate in this study, and receive standard of care, which is a recommendation from the healthcare provider to take a bariatric vitamin**.** Bariatric vitamins, Vitamin D, and Calcium are each available over the counter. Zoledronic Acid can be prescribed off study, if there is concern for bone loss. An additional alternative is to participate in a bone-loading exercise program, which might include weight lifting and jumping exercises.This study will provide the subject with the standard of care, and will provide education on bone preserving strategies.

Alternatives for increasing bone health include participation in a weight-bearing and weight lifting exercise program, and medication. We encourage you to discuss options with your healthcare provider.

Instead of being in this research study, you can choose not to participate.

What will being in this research study cost you?
There is no cost to you to be in this research study.

Will you be paid for being in this research study?
You will be paid to be in this research study. You will receive nominal monetary compensation for your time and expenses associated with study visits and time to administer treatments. Compensation is as follows:

$50 for Imaging and blood collection Visit 1.
$75 for the Infusion and Blood collection Visit.
$50 for Imaging Visit 2.

Payment will be in the form of Visa gift cards. You will also receive all study lab tests, bone scans, and vitamin and mineral supplementation (calcium, vitamin D and

bariatric vitamins) at no additional cost to you.

Who is paying for this research?
This research is being paid for by grant funds from the Society of Endoscopic and Gastrointestinal Surgeons (SAGES) and the Nebraska Medicine Research Support Fund.

What should you do if you are injured or have a medical problem during this research study?
Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at The Nebraska Medical Center. If there is not sufficient time, you should seek care from a local health care provider.

Treatment and Compensation for Injury: If you are experiencing a medical emergency, please call 9-1-1. UNMC/Nebraska Medicine has no plans to pay for any required treatment or provide other compensation. Agreeing to this does not mean you have given up any of your legal rights.

How will information about you be protected?
You have rights regarding the protection and privacy of your medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include your medical record number, address, birth date, medical history, the results of physical exams, blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your research and medical records will be maintained in a secure manner.

Who will have access to information about you?
By signing this consent form, you are allowing the research team to have access to your PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at UNMC/Nebraska Medicine.

Your PHI will be used only for the purpose(s) described in the section "What is the reason for doing this research study?"

You are also allowing the research team to share your PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that your information may be shared with these groups:
    - The HHS Office for Human Research Protections (OHRP)
    - The Food and Drug Administration (FDA)
- The HIPAA Privacy Rule requires the following groups to protect your PHI:
    - Researchers at UNMC/Nebraska Medicine involved in the study
    - Your health insurance company

You are authorizing us to use and disclose your PHI for as long as the research study is being conducted. You may cancel your authorization for further collection of PHI for use in this research at any time by contacting the principal investigator in writing. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, you will no longer be able to participate in this research.

How will results of the research be made available to you during and after the study is finished?
Information obtained in the course of the research that will not be shared with you is which group you are assigned to, the active medication group or the inactive medication group. By signing this authorization, you are temporarily giving up your right to see this research-related information while the research is going on. You will be able to see this information if you wish after the research is completed.

What will happen if you decide not to be in this research study?
You can decide not to be in this research study. Deciding not to be in this research will not affect your medical care or your relationship with the investigator or the Institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

What will happen if you decide to stop participating once you start?
You can stop participating in this research (withdraw) at any time by contacting the Principal Investigator or any of the research staff. Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or this institution. You will not lose any benefits to which you are entitled. For your safety, please talk to the research team before you stop taking any study drugs or stop other related procedures. They will advise you how to withdraw safely. If you withdraw you may be asked to undergo some additional tests. You do NOT have to agree to do these tests.

You may be taken off the study if you do not follow instructions of the investigator or the research team.

You may also be taken off the study if

- You have a major surgical complication during or after your surgery including an anastomotic leak
- You develop a diagnosis of osteoporosis
- Your kidneys begin to function improperly
- You are found to be pre-menopausal
- You are prescribed a medication which affects bones
- Your physician feels it is unsafe for you to continue in this trial

Will you be given any important information during the study?
You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want to continue being in the study.

What should you do if you have any questions about the study?
You have been given a copy of "*What Do I Need to Know Before Being in a Research Study?*" If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

What are your rights as a research participant?
You have rights as a research subject. These rights have been explained in this consent form and in The Rights of Research Subjects that you have been given. If you have any questions concerning your rights, or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
  - Telephone: (402) 559-6463
  - Email: IRBORA@unmc.edu
  - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
  - Telephone: (402) 559-6941
  - Email: unmcrsa@unmc.edu

Documentation of informed consent

You are freely making a decision whether to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.
- You have decided to be in the research study.
- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Subject _____
Date _____

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the subject. In my judgment, the subject possesses the legal capacity to give informed consent to participate in this research and is voluntarily and knowingly giving informed consent to participate.

Signature of Person obtaining consent _____
Date _____

Authorized Study Personnel

Principal

* Bilek, Laura
phone: 402-559-6923
alt #: 402-559-2470
degree: PT, PhD

Secondary

* Kothari, Vishal
phone: 402-559-6592
alt #: 402-559-6592
degree: MD

Lead Coordinator

Flores, Laura
alt email: 575-621-7708

phone: 402-559-6923
alt #: 402-552-6444
degree: Medical Student

What Do I Need To Know Before Being In A Research Study?

You have been invited to be in a **research study**. Research studies are also called "clinical trials" or "protocols." **Research** is an organized plan designed to get new knowledge about a disease or the normal function of the body. The people who are in the research are called **research subjects**. The **investigator** is the person who is running the research study. You will get information from the investigator and the research team, and then you will be asked to give your **consent** to be in the research.

This sheet will help you think of questions to ask the investigator or his/her staff. You should know all these answers before you decide about being in the research.

What is the **purpose** of the research? Why is the investigator doing the research?

What are the **risks** of the research? What bad things could happen?

What are the possible **benefits** of the research? How might this help me?

How is this research different than the care or treatment I would get if I wasn t in the research? Are there other treatments I could get?

Does **everyone** in this research study get the same treatment?

Will being in the research **cost** me anything extra?

Do I have to be in this research study? Will the doctor still take care of me if I say **no**?

Can I **stop** being in the research once I ve started? How?

Who will look at my **records**?

How do I reach the investigator if I have more **questions**?

Who do I call if I have questions about being a **research subject**?

Make sure all your questions are answered before you decide whether or not to be in this research.

Academic Research & Services Building 3000 / 987830 Nebraska Medical Center / Omaha NE 68198-7830
402-559-6463 / FAX 402-559-3300 / Email: irbora@unmc.edu / http://www.unmc.edu/irb

THE RIGHTS OF RESEARCH SUBJECTS
AS A RESEARCH SUBJECT YOU HAVE THE RIGHT

to be told everything you need to know about the research before you are asked to decide whether or not to take part in the research study. The research will be explained to you in a way that assures you understand enough to decide whether or not to take part.

to freely decide whether or not to take part in the research.

to decide not to be in the research, or to stop participating in the research at any time. This will not affect your medical care or your relationship with the investigator or the Nebraska Medical Center. Your doctor will still take care of you.

to ask questions about the research at any time. The investigator will answer your questions honestly and completely.

to know that your safety and welfare will always come first. The investigator will display the highest possible degree of skill and care throughout this research. Any risks or discomforts will be minimized as much as possible.

to privacy and confidentiality. The investigator will treat information about you carefully, and will respect your privacy.

... to keep all the legal rights you have now. You are not giving up any of your legal rights by taking part in this research study.

to be treated with dignity and respect at all times

The Institutional Review Board is responsible for assuring that your rights and welfare are protected. If you have any questions about your rights, contact the Institutional Review Board at (402) 559-6463.