Informed Consent

Immune Mechanisms of Vitamin D in a Randomized Controlled Trial to Reduce Chronic Pain after Burn

NCT number NCT05619289
Document Date 09/17/2024

University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: __9-17-2024___
IRB Study # 22-1310
Title of Study: Immune mechanisms of Vitamin D in a randomized controlled trial to reduce chronic pain after burn
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CONCISE SUMMARY

The purpose of this study is to assess the feasibility of administering Vitamin D to reduce pain severity in patients hospitalized for major thermal burn injury. This study will also investigate mechanisms by which Vitamin D reduces pain severity in the aftermath of burn injury. The information we learn by doing this study may help us to develop some target treatments for chronic pain development after burn injury.

This is a double-blind, placebo-controlled, randomized study. “Double-blind” means that neither you nor the study staff will know who is receiving Vitamin D and who is receiving a placebo (an inactive substance containing no study drug also administered orally). “Randomized” means that the group you will be placed in is decided by change from a computer, like flipping a coin, with a 50% chance that you will receive Vitamin D.

Participants in this study will have a blood sample collected, as well as a vitamin D finger prick test, after enrollment, and again 6 weeks after initial injury. Blood samples will be analyzed for immune mechanisms in the aftermath of burn injury. Participants will also be asked to complete questionnaires at four separate time points: at enrollment, at 6 weeks after injury, and 3 and 6 months after injury. Participation is complete once the 6-month assessment has been completed.

Risks of taking the blood sample are discomfort and/or bruising; infection, excess bleeding, clotting, or fainting are also possible. If you are interested in learning more about this study, please continue to read below.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?
The purpose of this study is to assess the feasibility of administering Vitamin D to reduce pain severity in patients hospitalized for major thermal burn injury. We will measure the ability of Vitamin D administration to generate sustained increases in whole-blood Vitamin D concentrations, between baseline and 6 weeks. The ultimate goal is to observe the relations of immune factors and chronic pain after burn injury.

You are being asked to be in the study because you have experienced a major burn injury that may need tissue grafting.

Are there any reasons you should not be in this study?
You should not be in this study if:

- You cannot speak or read English
- You do not have a telephone to receive text messages or follow-up phone calls
- You do not have a functioning email address to receive secure emails from the REDCap database for survey invitations
- You are not willing to provide blood samples
- You have a substantial additional injury, such as a long bone fracture
- You are a prisoner
- Your burn care requires an escharotomy or fasciotomy
- You have a chronic skin disorder characterized by substantial pruritus
- You have acute psychosis, thoughts of suicide, or harming others (homicide)
- You are pregnant, breastfeeding, or plan to become pregnant while taking part in this study
- You have a disorder of pain processing or diminished capacity to perceive pain
- You are sedated or require a breathing tube.

How many people will take part in this study?
Approximately 40 people at this institution will take part in this study.

How long will your part in this study last?
After enrollment, we will follow-up with you approximately 6 weeks after your burn injury and will arrange to have your blood drawn at that time in the on-campus clinic, which will take about 20-30 minutes. We will also email and/or call you at 3 months and 6 months for follow-up. Stored specimens will be stored for an indefinite length of time for future specimen analysis.

What will happen if you take part in the study?
It is important for you to know that your choice to participate in this study will in no way affect your normal course of treatment during your hospitalization. This study is interventional in nature and will involve you taking a single dose of 6 capsules of Vitamin D or placebo. If you agree to participate in the study, we would ask you to participate in the activities listed below. These activities are divided into two periods: initial day 1 evaluation (today), and evaluations after hospital discharge (email and clinic).

Today:

- Your interview today will last about an hour. This interview will assess symptoms (including pain symptoms related to your wound) since your burn injury, your health before your burn (including smoking and use of alcohol and other drugs, if applicable), mental health information, and any other information you would like to share about your experience. You may choose to not answer an interview question, for any reason.
- We would also record information about your burn injury and hospital treatment from your patient record. This information would include information about the medications and other treatments you receive during hospitalization and at discharge. We would also record demographic information such as your date of birth and gender.
- We would take a blood sample (2 tablespoons of blood total, no more than 30 ml). These blood samples would be used to look for genes, other components of your body's cells (RNA, immune cells), fats, and Vitamin D levels that may be associated with the recovery process after burn injury. You will not be given any information about the results of any blood testing related to this study. The results would not be useful to you or your doctors. We will also do a vitamin D finger prick test to test your baseline vitamin D level.
- You will be randomized to receive either one dose of 6 capsules of Vitamin D or a placebo. You will take 6 capsules at one time. A placebo is an inactive substance containing no study drug. The choice of who gets Vitamin D and who gets placebo will be made randomly, like tossing a coin. Neither you nor the study team members will know which one you are getting. If you are discharged before the pharmacy can prepare the study drug, study personnel will mail the study medication to the address you have provided. Please note: Study drug must be mailed to a physical mailing address; it cannot be mailed to a P.O. box. You will be asked to take the study medication upon receipt, and no later than 1 week from the date of your burn injury. Study personnel will call you to collect information about the date, time, and number of capsules taken. You will be

provided with a postage-paid envelope to return your empty medication bottle to the study site.

Evaluations after Hospital Discharge: Weekly through 6 weeks, 3 months, and 6 months after burn injury

- Weeks 2-5:
  - We will follow up via email with links to electronic surveys administered within REDCap. These will be brief surveys to assess pain and any changes to your health. These assessments should take less than 10 minutes to complete.
- 6 weeks:
  - We will follow-up via email with links to electronic surveys that are administered within REDCap. These surveys will assess outcomes related to your burn injury. You may choose to not answer an interview question, for any reason. We may call you if we are unable to reach you via email. Each of these assessments would take about 30 minutes. Each survey would assess your current symptoms (including pain symptoms), your current health (including smoking and use of alcohol and other drugs, if applicable), your sleep, your metal health, and any other information you would like to share about your experience.
  - At the 6-week time point, we would have you return to the on-campus clinic to take blood samples (2 tablespoons of blood total, no more than 30ml). These blood samples would be used to look for genes, other components of your body's cells (RNA, immune cells), fats, and Vitamin D levels that may be associated with wound healing and the recovery process after burn injury. You will not be given any information about the results of any blood testing related to this study. Another vitamin D finger prick test will be done to compare to your baseline value.
- 3 months
  - We will follow-up via email with links to electronic surveys that are administered within REDCap as detailed above.
- 6 months
  - We will follow-up via email with links to electronic surveys that are administered within REDCap as detailed above.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?

Vitamin D:

The risks of taking Vitamin D are rare and mild. However, side effects from over supplementation of Vitamin D may include headache, loss of appetite, dry mouth, metallic taste, and nausea/vomiting. To minimize risks, you will not be enrolled if

you are taking Vitamin D supplements in excess of 800 IU daily, or if your vitamin D test results are greater than or equal to 100 ng/mL

Interviews:
You may face some sensitive questions in your telephone/follow-up interview. These questions may cause you to experience some unpleasant or stressful feelings. However, we have taken measures to make this process as comfortable for you as possible. If there are any particular questions that you do not want to answer, you do not have to, and you may stop any interview at any time. We will be collecting data about your injury and your overall health; every attempt will be made to protect this information.

Confidentiality:
There is a very small risk of a breach of confidentiality during this study. This risk will be minimized by keeping your information on a secure database (REDCap), training of research personnel involved in the study, and we will deidentify your personal information on blood samples.

Blood draws:
When blood samples are taken, you could feel lightheaded. Bruising or bleeding and slight pain can occur at the site of the needle insertion. This usually is a temporary discomfort. When possible, the blood samples for this study will be taken at the time that blood samples are already going to be taken for your clinical care. Rarely, infection may also occur around the area of needle insertion.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Pregnancy tests will be done on all females who might be able to get pregnant at the start of the study. If this has not already been performed as a standard of care test ordered by your doctors at the time that we approach you for participation, the test will be paid for by the research team and will be of no cost to you.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?
Records of your participation in this study will be secured in the data coordinating center. No subjects will be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could

be reviewed by representatives of the University, research sponsors, or government agencies for purposes such as quality control or safety.

A Federal law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?

You will receive $35 for today's enrollment assessment and $45 for the blood sample collection. At 6 weeks, you will receive $35 after the completion of the 6-week assessment and $45 for the clinic blood sample collection. At the 3- and 6-month time points, you will receive $45 after the completion of each assessment. If there are no missed visits (including the 5, brief, weekly surveys), you will receive a completion bonus of $50. In total, there is up to $300 available in payment for completion of study activities. You will receive gift cards as the method of payment. The payment schedule is detailed in the table below:

Visit	Compensation	Location
Enrollment	$35	On-site
+ Blood Sample	$45	On-site
6-week Follow-up	$35	On-site/Questionnaire may be completed online
+ Blood Sample	$45	On-site
3-month Follow-up	$45	Remote Questionnaire
6-month Follow-up	$45	Remote Questionnaire
Total	**$250**	
Completion Bonus	$50	No missed visits (including weekly surveys)
Total	**$300**	

In order to process payments, the University may share certain identifiable information about you, such as name and contact information, with third parties that the University retains to process payments on its behalf. If you do not want to agree with sharing your information with these third parties, then you will be unable to receive payment/compensation for participating in the study.

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

Will it cost you anything to be in this study?

It will not cost you anything to be in this study.

Who is sponsoring this study?

This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

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 website at any time.

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent

_____
Signature of Witness, if applicable: e.g. literacy issues, visually impaired, physically unable to sign, witness/interpreter for non-English speaking participants using the short form)

_____
Date

_____
Printed Name of Witness