A Comparative Study of the Efficacy of Intralesional Sodium Thiosulfate Versus Intralesional Normal Saline for the Treatment of Dystrophic and Idiopathic Calcinosis Cutis, A Double-Blind Randomized Placebo-Controlled Trial

NCT03639779

Date: May 21st, 2019

Title of Research Study: *A Comparative Study of the Efficacy of Intralesional Sodium Thiosulfate Versus Intralesional Normal Saline for the Treatment of Dystrophic and Idiopathic Calcinosis Cutis, A Double-Blind Randomized Placebo-Controlled Trial*

Informed Consent

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Co-Investigators: Naveed Sami M.D., Professor of Dermatology

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Investigational Site(s): UCF Health Clinic, 9975 Tavistock Lakes Blvd, Orlando, FL 32827, (407) 266-4900

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you have a current diagnosis of calcinosis cutis, at least 2 lesions of at least 2mm in size, and you have health insurance. You must be 18 years of age or older to participate in this study.

You cannot be in this study if: (1) you are allergic to sodium thiosulfate or its components, (2) you are unable to read and speak English, (3) you are pregnant or breast feeding, or (4) you are a prisoner.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team:

Dr. David Weinstein

Phone: (407) 266-4900

e-mail: david.weinstein@ucf.edu

Adam Foley, Medical Student, UCF College of Medicine

Phone: (850) 776-5528

e-mail: adamfoley7@knights.ucf.edu.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). You may talk to them at 407-823-2901or irb@ucf.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

Background and purpose: Calcinosis cutis is an uncommon dermatologic condition in which calcium deposits are formed in the skin. These deposits can be hard and painful and currently there is no standard treatment. Sodium thiosulfate is a medicine that is given intravenously (injected into the vein) for people who have cyanide poisoning. This same medicine has also been shown to help people who have renal failure and calcium in their skin. The purpose of this study is to determine the effectiveness of sodium thiosulfate when injected directly into the lesions of calcinosis cutis. A potential benefit is improvement of some of your lesions of calcinosis cutis.

How long will the research last?

We expect that you will be in this research study for 3 months, including three 90-minute appointments and one final 15-minute appointment, all at UCF Health.

How many people will be studied?

We expect about 10 people here will be in this research.

What happens if I say yes, I want to be in this research?

- Upon arrival at UCF Health, you will have time to read, ask questions and fill out this consent form before participation.
- If you are female, you may need to provide a urine sample for a pregnancy test to determine if you are eligible to participate in this research study. The reason for this is because one of the drugs you will receive as part of this study is sodium thiosulfate, and even though the dose is very small (maximum of 0.4ml of 40mg/ml of sodium thiosulfate), the effects of sodium thiosulfate on an embryo or fetus are not known. The urine pregnancy test must be negative for you to participate in the study. If you have an allergy to sodium thiosulfate or its components, you will not be allowed to participate in this study.
- If you are breastfeeding, you will not be allowed to participate in the study.
- After you consent to participation, 1 of your lesions of calcinosis cutis will be selected to be injected with sodium thiosulfate (0.1ml/cm2 of 40mg/ml sodium thiosulfate) and 1 other lesion will be injected with an inactive salt water treatments (0.1ml/cm2 of 0.9% sodium chloride). Before the injections, the lesions will be photographed and measured. The injections will be administered by Dr. David Weinstein. After the injections you will be asked to rate the pain of the injections. You will also be observed for 15-20 minutes post-treatment for any adverse effects. You will then have two more visits where you will receive an additional injection in the same lesions at each visit. You will then have a final visit to follow up on the final change, if any, in the lesions that were injected. Please see the timeline below:
    - Week 0 (Visit 1): 90 minutes
        - Consent
        - Screening
        - Selection and measurement of 2 lesions
        - Injection of lesions
        - Rating of pain of injections
    - 48 hours after injections:
        - You will receive a follow up phone call from Dr. Weinstein 48-hours after the injections to make sure you are doing well (5 minutes)
    - Week 4 (Visit 2): 90 minutes
        - Measurement of lesions
        - Injection of lesions
        - Rating of pain of injections
    - Week 8 (Visit 3): 90 minutes
        - Measurement of lesions
        - Injection of lesions
        - Rating of pain of injections
    - Week 12 (Visit 4): 15 minutes

- Measurement of lesions

- This study will require a total of 4 visits. Your responsibility is to remain truthful about all inquiries. You do not have to answer every question or complete every task. You will not lose any benefits if you skip questions or tasks.
- All visits will take place at the UCF Health clinic in Lake Nona located at 9975 Tavistock Lakes Blvd., Orlando, FL 32827.

The treatment each lesion will get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose which lesion receives which treatment you get. Each lesion will have an equal chance of being given each treatment. One lesion will receive the experimental treatment with sodium thiosulfate treatment and the other lesions will receive the inactive (salt water) treatment.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- ***Receive 3 sets of 2 injections (2 injections per visit)***
- ***Attend four in-clinic visits***
- ***Answer truthfully questionnaires given to you at your visits***
- ***Continue your current form of contraception for the duration of the study if you have the ability to become pregnant***

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate or not to participate.

Instead of being in this research study, your choices may include: continuing to receive your current care for calcinosis cutis with your rheumatologist or dermatologist.

The important risks and possible benefits of these alternatives include:

- No change or possible progression of your calcinosis cuts.

What happens if I say yes, but I change my mind later?

You can leave the research at any time. It will not be held against you.

You can withdraw from the study at any time during the study by contacting the principal investigator or co-investigators. If you decide to leave the research, no further data will be collected from you and you are free to leave. However, partial data already collected will be used for analysis. There will be no consequences for your choice to leave. If you decide to leave the study, contact the investigator so that the investigator can stop recording data from you.

Is there any way being in this study could be bad for me?

Risks: This study is considered more than minimal risk because of the injection you will receive, however there are no major anticipated risks associated with the study. Potential risks include:

- Discomfort and minimal pain upon injection and infiltration of sodium thiosulfate or normal saline.

- < 27% risk of nausea and vomiting
  - Note: this occurred when large volumes of the medicine were given intravenously for cyanide poisoning and has not yet been shown to occur when the medicine is injected into the skin
- < 2% Low risk of lowered blood pressure, headache, disorientation
  - Note: this occurred when large volumes of the medicine were given intravenously for cyanide poisoning and has not yet been shown to occur when the medicine is injected into the skin
- Negligible bleeding or bruising
- Risk of infection (<1%)

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

Note: DO NOT take part in this study if you are known to be allergic to sodium thiosulfate solution.

If you do suspect that you are having any adverse reaction, please contact Dr. David Weinstein. He can be reached via e-mail at david.weinstein@ucf.edu or (407)266-3627. If you need emergency care, call 911 or go to your nearest hospital or emergency room right away. It is important that you tell the doctors at the hospital or emergency room that you are participating in this research study. If possible, take a copy of this consent form with you when you go.

The procedures in this research are known to hurt a pregnancy or fetus in the following ways: Sodium Thiosulfate Injection is Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. Sodium Thiosulfate Injection should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

There are no reported epidemiological studies of congenital anomalies in infants born to women treated with sodium thiosulfate during pregnancy. In animal studies, there are no teratogenic effects in offspring of hamsters treated during pregnancy with sodium thiosulfate in doses similar to those given intravenously to treat cyanide poisoning in humans. Other studies suggest that treatment with sodium thiosulfate ameliorates the teratogenic effects of maternal cyanide poisoning in hamsters. In other studies, sodium thiosulfate was not embryotoxic or teratogenic in mice, rats, hamsters, or rabbits at maternal doses of up to 550, 400, 400 and 580 mg/kg/day, respectively.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include improvement of your lesions of calcinosis cutis treated. This improvement may only be temporary.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise

complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

The IRB may access your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, your name and contact information will be coded, and you will be given a unique identifier which will be stored in a separate folder in a locked drawer in a locked room at UCF Health. The data will be kept for a minimum of six years after the conclusion of the study (per UCF data retention policies). We will keep your name and other identifying information confidential.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Federal law provides additional protections of your medical records and related health information. These are described in an attached document.

Can I be removed from the research without my OK?

The person in charge of the research study can remove you from the research study without your approval. Possible reasons for removal include:

- Failure to follow instructions from staff
- Adverse reaction to one of the solutions
- The principal investigator ends the research study early

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

You will not be compensated for your time or traveling costs.

You will not be compensated for your time (approximately 5 hours) and will have to bear any transportation costs (gas, tolls, etc.). If your health insurance does not cover the costs for treatment related injury, you may be billed for the treatment.

If you need medical care because of taking part in this research study, contact the investigator and medical care will be made available. Generally, this care will be billed to you, your insurance, or other third party. UCF Health has no program to pay for medical care for research-related injury. In the event that you suffer a research-related injury, your medical expenses will be your responsibility or that of your third-party payer, although you are not precluded from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

If the treatment is effective you may request to have remaining lesions treated. However, this would not be covered by your insurance you would need to pay for it out of your own money.

You will be provided with a copy of this signed consent, in case you want to read it again.

You have to additionally sign the UCF Health HIPAA Authorization to start your participation in this study.

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	Date
Printed name of person witnessing consent process	