A Pilot Study of the Safety and Feasibility of Transcutaneous Electrical Nerve Stimulation (TENS) for Chronic Ocular Pain

NCT05531643

February 2, 2024

Participant Name: _____ Date: _____ SSN: _____

Title of Study: A pilot study of the safety and feasibility of transcutaneous electrical nerve stimulation (TENS) for chronic ocular pain

Principal Investigator: Elizabeth R. Felix, PhD. VA Facility: Miami VA Hospital

WHAT IS THE STUDY ABOUT AND WHY ARE WE DOING IT?

We are asking you to choose whether to volunteer or not for a research study funded by the Department of Veterans Affairs about how transcutaneous electrical nerve stimulation (TENS) affects eye pain. TENS consists of the use of mild electric current produced by a device applied to your skin which may help reduce pain. We want to see if TENS delivered to the area around the eyes may be helpful for eye pain. This initial information is to give you key points to help you decide whether to participate in this study. We have included detailed information after this section. Taking part in this study is completely voluntary.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

The purpose of this research is to collect information on the safety, effectiveness, and side effects of Cefaly®, a transcutaneous electrical nerve stimulation (TENS) device approved by the Food and Drug Administration (FDA) for migraines. We want to test whether this TENS device can reduce or lessen chronic eye pain. If you fully qualify for this study, your participation in this research will last about **12 months.** This is a randomized study with two groups. One group will receive treatment with active electrical stimulation (Cefaly® TENS device) and the other group will receive low levels of stimulation that we do not think will be effective.

There will be **4 in-person visits and several brief phone interviews**. During the **first visit**, we will give you all the details of the study and have you sign an informed consent form if you agree to participate. You will then fill out questionnaires, undergo an eye exam and a sensitivity test. The first visit is expected to take about 1.5 hours. Based on the first visit, we will see if you qualify to continue for the rest of the study.

The **second visit** will last approximately 3 hours. During this visit you will complete questionnaires and we will test your sensitivity to nonpainful and painful stimuli and perform the first session with the TENS device.

You will then go home with the device and be required to self-administer treatment at least 3 times per week for 6 months. We will call you periodically to ask about side effects, number of TENS sessions per week, and eye pain severity.

Visits 3 and 4 will be at three and six months after TENS initiation, and include questionnaires, an eye exam and sensitivity tests. After the 6-month period, you will be made aware of which treatment group you belong to. Those who got the low levels of stimulation will be prescribed an active treatment device if they would like. We will then call you monthly to ask you about your eye pain until the end of your study participation (months 7-12). You do not need to return the device once the study concludes.

The Miami VA Healthcare System will screen approximately 100 participants (including veterans and non-veterans from Bascom Palmer Eye Institute), with a target enrollment of 50 participants in the TENS trial.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

TENS has helped some people in reducing their eye pain, but a scientific study has not yet been done on this. This study will provide useful information about the safety, effectiveness, and side effects of TENS for eye pain across a number of people. *For a complete description of benefits, refer to the Research Details.*

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You will not be allowed to participate in this study if you have use any of the following devices or conditions: pacemaker, cardioverter defibrillator, neuro-stimulation (brain or spinal cord), bone growth stimulations, indwelling blood pressure monitors, or epilepsy. You may decide not to participate because of the long participation time (total of 12 months). Also, there is no guarantee that TENS will help reduce your eye pain. *For a complete description of procedures and risks, refer to the Research Details section.*

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits, or rights you would normally have if you chose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Anat Galor, MD and Elizabeth Felix, PhD of the Miami VA If you have questions, suggestions, or concerns regarding this study or if you want to withdraw from the study please contact:

Dr. Anat Galor: [redacted]

Dr. Elizabeth Felix: [redacted]

Participant Name: _____ Date: _____ SSN: _____

Title of Study: A pilot study of the safety and feasibility of transcutaneous electrical nerve stimulation (TENS) for chronic ocular pain

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RESEARCH DETAILS

WHAT IS THE PURPOSE OF THIS STUDY?

By doing this study we hope to find out whether Cefaly®, a transcutaneous electrical nerve stimulation (TENS) device cleared by the FDA for migraines, is safe and effective for reducing chronic eye pain.

You are being asked to participate in the study because you have at least moderately severe chronic eye pain, often described as "burning," "dry," and "aching." If you decide to be in this study, you will be one of about 100 people in this study.

HOW LONG WILL I BE IN THE STUDY?

This study is expected to take approximately two years at the Miami VA Healthcare System. Your individual participation in the project will take 12 months, including 4 in-clinic visits and periodic brief phone interviews. We expect to enroll 50 participants in the complete TENS trial.

WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

If you decide to take part, your participation should be completely voluntary, you will not receive any penalties or loss of benefits if you decide to discontinue your participation at any stage of the study. This is a randomized, double-blinded study with two possible groups. One group will receive active electrical stimulation from a Cefaly® device placed on an electrode on your forehead for 20 minutes, and the other group will receive very low levels of electrical stimulation from an identically looking Cefaly® device ("sham" TENS) placed on the forehead for 20 minutes. You'll have a 66% chance of being assigned to the active group, and 33% chance of being assigned to the sham group. Neither you nor the research team will know which group you've been assigned to. After the 6-month treatment period, you will be made aware of which treatment group you belong to. Those in the active treatment group will keep their TENS device. Those in the sham device group will be prescribed an active treatment device at this time, if they want. We will then call you monthly to ask you about your eye pain until the end of your study participation (months 7-12). You may keep the device once the study concludes.

WHAT IS EXPECTED IF I TAKE PART IN THIS STUDY?

If you decide to participate, you will have:

1st in-clinic visit at the Miami VA Hospital: about 1.5 hours

- You will be asked to provide information about your medical history
  - History of epilepsy, pacemakers, trauma and/or skin infection on the forehead and are currently pregnant.
  - If you have any of the conditions mentioned above, you will not be able to participate as it might be unsafe for you to receive TENS treatments.
- You will fill out questionnaires about dry eye symptoms, eye pain severity and impact of symptoms on daily activities.
  - If, for any reason, you wish not to answer specific questions or you wish to terminate the session, you will be able to do so.

- You will undergo testing of your corneal sensitivity.
  - A research device that delivers air puffs at different speeds to the surface of the eye will be used.
- You will undergo an eye examination to evaluate tear function and quantity
  - A paper strip will be placed on the lower lid edge of each eye, and you'll be asked to close your eyes for 5 minutes to measure the amount of tears produced.
  - A small quantity of fluorescein dye will be placed in the lower lid of each eye, and you'll be asked to blink and refrain for a few seconds to observe tear function.
  - You'll be asked to grade your ocular pain on a 0-10 scale and the research team will repeat the same question 30 seconds after placing a numbing drop in each eye.

Once all the tests and questionnaires are completed, the research team will decide if you are a candidate for the TENS trial. A person not involved directly with the study (the study statistician) will assign you by chance to one of the two groups. Neither you nor the other research team members will know which group you were assigned to until the study is completed.

2nd in-clinic visit: about 3 hours

The second visit will occur after the screening visit (1st visit), and only for those who qualify to be in the full study. This visit will last approximately 3 hours.

- You will undergo testing of your corneal sensitivity
  - A research device that delivers air at different speeds to the surface of the eye will be used.
- You will undergo testing for cutaneous (skin) sensitivity
  - We will test your skin sensitivity to vibration and heat on your forehead and forearm.
  - For vibration we will measure the amount of stimulation needed for you to feel the vibratory stimuli.
  - For heat, we will measure the temperature that causes you to feel slight pain. We will also ask you to rate how much pain you feel at different temperatures.
- We will perform a demonstration and give you instructions on how to properly use and activate the Cefaly® device.
  - You will then be required to apply and activate the device by yourself, as a study staff member evaluates your performance to make sure you will be able to do this at home on your own.
  - Once the research team confirms you feel comfortable using Cefaly® we will continue with the first 20-minute application of the device while you are in the lab.
- We will ask you about your pain and any side effects after the TENS application.
  - The presence and severity of side-effects and ocular pain will be asked at 5-, 30-, 60-, and 120-minutes post-TENS.
- We will ask you whether you think you got the active or sham TENS treatment.
- You will undergo repeat testing of ocular and cutaneous sensitivity.
  - The measures described above will be re-assessed with the same methods to obtain a comparison before *vs.* after TENS.

- After the initial in-lab trial of TENS, you will be sent home with the device and instructed to use it 3 times a week (or more, if you choose to) for 6 months. Each at-home session will consist of a 20-minute stimulation period.

Interview phone calls every two weeks for the 6-month in-home treatment period: about 10 minutes

- A member of the research team will call you to ask you about the number of times a week you've used Cefaly®, any side effects you experienced, and the level of your ocular pain severity during the past week.

3rd in-clinic visit scheduled at 3 months after visit 2: about 1.5 hours

- We will perform an ocular examination (as described above).
- We will repeat the ocular and cutaneous sensitivity testing (as described above).
- We will ask you how many times a week you have been using the TENS device, any side effects you have been having, and we will ask you to guess whether you have the sham or active TENS treatment.
- You will complete a questionnaire about your eye pain symptoms
- You will need to bring your Cefaly® device with you to this visit. A member of the research team will download the information collected by the device to see how many times and how long you have used the device.

4th in-clinic visit scheduled at 6 months: about 1.5 hours

- The same procedures performed during the 3rd in-clinic visit will take place again during the 4th in-clinic visit.
- We will inform you which treatment group you belong to. If you are part of the sham group, you will be prescribed a new active treatment device if you would like.

Monthly calls: about 10 minutes

- For the remaining months (7-12 months), we will call you once per month to ask questions about side effects, ocular pain symptoms, and whether you have continued to use the TENS device.

During the entire research study, Dr. Galor, Dr. Felix, or any member of the study team will be available to answer any questions you might have. We will also monitor your symptoms, side effects, alert you of any problem encountered, and act accordingly in any emergency. Risks and discomforts are explained in the next section.

Once the research study has concluded the research team will publicly publish the results on clinicaltrials.gov.

<u>Participant expectations and responsibilities:</u>

- Use the TENS device (Cefaly®) at least 3 times a week for 20 minutes during 6-months.
- The maximum use for the device is **ONE** daily 20-minute session during 6 months even if pain persists.

- Inform the research staff as soon as possible if you're having any problems with the device.
- Contact the research study team if you wish to leave the study at any time. You will not face any penalties or loss of benefits for doing so.
- Keep your study appointments. If you miss an appointment, please contact the investigator or research staff to reschedule.
- Tell the investigator or research staff if you believe you might be pregnant.
- Keep the study device in a safe place for your use only and away from children.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.
- While participating in this research study, do not take part in any other research project without approval from the investigators. Taking part in other research studies without first discussing it with the investigators of this study may might invalidate the results of this study, as well as that of the other studies.
- You do not need to return the device to the research team once the study has ended.

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

Any procedure has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed.

1. Filling out questionnaires:

These pose no physical risk. However, there is a potential for emotional distress as you reflect on the severity of your pain and the impact it has on your life. The likelihood of this risk is low, and the severity is expected to be mild with only temporary impact. If, for any reason, you wish not to answer specific questions or wish to terminate the session, you will be able to do so.

2. Ocular examination:

Use of numbing drops and fluorescein dye can cause short-term discomfort, but this is rare.

3. Assessment of pain thresholds:

Ocular sensitivity is measured by delivering an air puff to the cornea. Cutaneous sensitivity is measured via a contact thermode delivering heat stimuli to the skin of the forehead and forearm. There is no risk of damage to the cornea or skin with testing, as the devices have intensity and duration limits based on safety cut-offs. Subjects do experience brief unpleasant sensations, and occasionally redness of the skin, due to the nature of the testing. The risk of experiencing unpleasantness is high, though it is not a serious risk as the severity of the unpleasantness is mild and short-lived.

4. Transcutaneous Electrical Nerve Stimulation (TENS)

There are certain side effects of TENS: the possibility that TENS would increase headache or ocular pain; skin irritation due to the adhesive used on the electrode; unpleasant sensation with higher intensity of electrical stimulation. These side-effects occur infrequently, are usually mild, and are temporary once TENS is stopped.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks related to usual care provided by your doctor are not related to this study. You should talk with your health care providers if you have any questions about the risks related to your usual care.

Photographs, audiotaping, or videotaping

The study team has explained that by signing this Informed Consent Document, you voluntarily authorize pictures and/or voice recording(s) to be taken of you by the study staff while you are participating in this study. You also authorize disclosure of the picture and/or voice recording for the following purposes:

-Publications and presentations (your identity will never be disclosed).

-As a personal guide ensuring the correct placement and use of the Cefaly® device.

You will not receive any royalty, fee, or other compensation for such use. If you refuse to grant consent, there will be no effect on any VA benefits to which you may be entitled. You may, at any time, exercise the right to cease being filmed, photographed, or recorded, and may withdraw your consent for up to a reasonable time before the picture, video or voice recording is used.

If you wish to allow the research team to take your photographs and or videos, please sign here:

Signature: _____ Date: _____

Inclusion of Women of Childbearing Potential

The safe use of Cefaly® in pregnant women and nursing mothers has not been established. Consequently, there may be risks to you (or to your embryo or fetus) if you are or may become pregnant that are unknown. Women of childbearing potential enrolling in this study must (i) have been using a birth control measure (an intrauterine device (IUD), birth control pills, a condom, diaphragm, or abstinence) for the previous three months, (ii) must have a negative pregnancy test, and (iii) must agree to continue to use a birth control measure for the duration of the study. If, while participating in the study, you suspect you have become pregnant, please contact the study physician immediately. Women are of childbearing potential unless they have been surgically sterilized (for example tubal ligation or hysterectomy) or are post-menopausal, that is, no menstrual period for more than 6 months. Nursing mothers may not participate in this study.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

We do not know if you will get any benefits from taking part in this research study. However, possible benefits may include:

- Reduction in chronic eye pain
- Provide a possible treatment option for eye pain.
- Improve function and quality of life in patients suffering from chronic ocular pain.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

If you choose not to be in this study, you will continue to receive usual treatment from your medical provider at the eye clinic. Treatment options can include the use of drops, oral medications, or participation in other research studies if you decide to be a part of those in the future.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

All private information and biospecimens collected will be de-identified, every subject will be assigned a study identification ID number in the format ###-AAA. The number code will be assigned consecutively, and the three-letter code will be an identifier for research purposes, it will not include the participants initials.

Your name and other personal identifiable information will not be released to other parties unless you give us specific written permission to do so. You will be told and given in writing any new information that might affect your decision to be in the study. You may ask any questions you want about the study, and we will try to answer them.

We will mitigate risks to confidentiality and data security by keeping all sensitive information behind locked doors, in locked filing cabinets. Electronic files with any potential identifiers will be password protected on computers that require login credentials from authorized users.

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 website at any time.

WHAT IS THE COST TO ME IF I TAKE PART IN THIS STUDY?

You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

You will receive a total of $350 as a direct deposit to your bank account if you assist all the in-clinic visits. You will receive the amount listed after you complete each visit. All participants will complete the 1st Visit, but only some will qualify to complete the rest of the study. If you do not qualify for the full study, you will be paid for the 1st visit only.
If you wish to withdraw from the study, you will only receive compensation for the visits completed at the time.
1st Visit screening (1. 5 hours): $50
2nd visit-TENS trial (3 hours): $100
3rd visit at 3 months (2 hours): $100
4th visit at 6 months (2 hours: $100
In addition, participants who complete all in-person visits and participate in 90% of the phone interviews will receive an extra $100.

Total possible payment is $450.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

The VA will provide treatment for research related injury in accordance with applicable federal regulations (38 CFR 17.85). An injury is considered study-related if it is caused by study activities that are different from the treatment you would have received if you were not in the study. The VA will not voluntarily pay medical treatment of other injuries or illnesses or any other type of compensation. You do not; however, give up your right to pursue this or other compensation by signing this consent or by being in the study.

If you should have a medical concern or get hurt or sick because of taking part in this study, call:

DURING THE DAY:

Dr. Anat Galor, at [redacted] and Dr. Elizabeth Felix at [redacted]

AFTER HOURS:
Dr. Anat Galor at [redacted] and Dr. Elizabeth Felix [redacted]

Emergency and ongoing medical treatment will be provided as needed.

DO I HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You can refuse to be in the study or stop being in the study at any time. If you do refuse or discontinue participation, there will be no penalty or loss of benefits. The care you are entitled to at the VA will not be affected. You may call the Chief of Medical Administration Service or his representative at 305-575-7000, extension 3051, or you can call the Patient Advocate's Office at (305) 575-3392. You may also call these numbers to verify that this is a valid study. There is not adverse consequence to withdrawal the study.

The research team may continue to review the data already collected for the study but cannot collect further information, except from public records, such as survival data.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION (Include if applicable)

The study investigator may decide to terminate your participation if:

1. The research team thinks continuing in the study will harm you.
2. If you do not cooperate or if you repeatedly fail to show up for scheduled study visits and phone calls.
3. If you develop any of the conditions that are unsafe for Cefaly device use, including but not limited to: pregnancy, epilepsy, pacemaker placement, skin lesion on forehead.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

If you have any questions, concerns, or would like to obtain information or seek input about the study and cannot contact the research study team or would prefer to speak with an individual who is unaffiliated with the research study, you may call the IRB office at 305-575-7000 x 4278 or the Patient Advocate's Office at (305) 575-3392.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

If new information regarding the safety profile and effectiveness of Cefaly device is obtained during this study we will provide it to you, allowing you to decide if you would like to continue in this study.

FUTURE USE OF DATA AND RE-CONTACT

Your de-identified data may be used for future analysis and studies. All electronic data will be stored on devices approved by the Veterans Administration. Any hard copies will be kept locked in a file cabinet in a locked office only accessible to the research staff. Research staff and their collaborators can access the de-identified data as appropriate for their role, as approved by the principal investigator.

If you wish to allow the research team to use your de-identified data for future analysis and research studies, please sign here:

Signature: _____ Date: _____

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr. Felix and/or the research staff has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it. A copy of this signed consent will also be put in your medical record.

Participant Name: _____ Date: _____ SSN: _____

Title of Study: A pilot study of the safety and feasibility of transcutaneous electrical nerve stimulation (TENS) for chronic ocular pain

Principal Investigator: Elizabeth R. Felix, PhD. VA Facility: Miami VA Hospital

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name (Please Print)	_____ Participant's Signature	_____ Date