Transcutaneous Electrical Nerve Stimulation of Penile Nerves for Treatment of Delayed Ejaculation

Study Protocol

NCT04115540

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Scientific Protocol

1) **Name of study**

Transcutaneous electrical stimulation of the penile nerves for delayed ejaculation

2) **PI and other key investigators or key study personnel**

Michael Eisenberg (PI) and Michelle Ferrari

3) **Specific source of institutional funding (account number)**

No institutional funding

4) **List of sources from whom you are seeking funds (or have sought funding) for this project**

Urology Department, Stanford University School of Medicine

5) **Specific aims and basic hypothesis including an explicit primary hypothesis or goal**

The aim of this clinical trial is to test the safety and feasibility of using transcutaneous electrical nerve stimulation of the penile nerves to reduce ejaculatory latency in men with delayed ejaculation. We hypothesize that this type of stimulation, either before or during sexual activity, will reduce ejaculatory latency time.

6) **General background (2 page maximum including published preclinical and animal data supporting basic hypothesis, if relevant)**

Delayed ejaculation (DE) is a condition in which men suffer a delay of intravaginal ejaculatory latency time (IELT) of more than 21-23 minutes.[1] Due to variations in definition and inherent difficulty in characterizing the prevalence of the condition, the epidemiology is varied. However, the prevalence ranges in the literature from about 1-4% with the true incidence believed to be higher.[1,2] Current treatment for DE is either counseling or off label pharmaceuticals. Counseling generally involves addressing a known underlying psychogenic cause and can involve such interventions as cognitive behavioral therapy, sex therapy, or psychotherapy.[3] However, these techniques can offer be time consuming and their efficacy varies greatly. Off label medications are the only current pharmacotherapy available for the treatment of DE. Various medications have been used off-label such as ephedrine, bupropion, and oxytocin. While some of these medications improve IELT, they remain cumbersome as they are daily medications and have potential serious adverse side effects.[2,3]

There are currently no devices on the market for treatment of DE, however the anatomy of the penis allows for potential intervention. The main nerves to the penis branch off the pudendal nerve and provided sensory innervation allowing for stimulation and therefore are a potential target for treatment of DE. We therefore hypothesize that transcutaneous electrical stimulation of the nerves of the penis, either before or during sexual activity, may improve IELT. While there have been no animal or human studies in the literature looking at DE specifically, transcutaneous stimulation of branches of the pudendal nerve to treat a variety of urologic conditions has been done in the past. Laessoe et al demonstrated that transcutaneous vibratory stimulation of the penis can induce ejaculation as well as reduce detrusor overactivity within the bladder while Sonksen et al showed that perineal transcutaneous electrical stimulation can treat stress urinary incontinence.[4,5] Transcutaneous penile nerve stimulation through vibration was shown in 66 patients with spinal cord injury to be successful in inducing ejaculation.[6] Finally, Fode et al found in post-prostatectomy patients that transcutaneous penile nerve stimulation with vibration may be helpful in improving erectile function.[7] While none of these studies examined DE specifically, they do demonstrated that transcutaneous stimulation of the penile nerves, or more proximal branches, can lead to observable effects within the structures they innervate which can be applied in treatment of DE.

7) **Preliminary unpublished data (1 page maximum)**

We performed a pilot study using a transcutaneous electric nerve stimulator (TENS 7000) with TENS pads applied directly to the penis in men with delayed orgasm. The study enrolled 14 men who wore the device during intercourse, before intercourse, and daily in serial fashion for 6 weeks each. Men completed validated questionnaires regarding sexual function as well as questions regarding device use/comfort. Approximately 40% of men reported subjective improvement with mean scores on intercourse and overall satisfaction showing increases. However, 64% of men reported problems with using the TENS pads on the penis which limited use.

Using the feedback, we designed a unique wearable to continue this project based. The device use similar technology to other devices available online for neurostimulation of the penis. The device is connected to the TENS unit leads and uses conductive rubber to apply current directly to the skin. Instead of TENS pads there are two sets of conductive rubber tubes which pass current to stimulate penile nerves. The devices uses an elastic system to fit securely on the penis and deliver TENS stimulation. Men are provided guidance to use a similar range of stimulation parameters (e.g. Amplitude, voltage, frequency, pattern) to the TENS pad pilot study. The size of the device will prevent most men from using the device during intercourse. Rather the device will be used either before sex or daily (2 arms to the next proposed pilot study).

8) **Experimental design and data analysis, including inclusion and exclusion criteria, statistical basis for the number of subjects to be enrolled, the statistical plan for analyzing at least the primary hypothesis, matrix showing procedure plan for each study visit, data safety monitoring plan (4 pages maximum)**

We will be conducting a small clinical trial to test the safety and feasibility of a currently commercially available transcutaneous electrical nerve stimulator (TENS 7000) for treatment of delayed ejaculation.

This will involve enrollment of up to 12 men with a diagnosis delayed ejaculation. This number was chosen as the purpose of the study is to test the safety and feasibility of transcutaneous electrical stimulation of the penile nerves. Once an initial trial has been conducted, it would be expanded to more individuals for more robust statistical analysis. Our inclusion criteria are: men >18 years old and sexually active. Our exclusion criteria are: men <18 years old, not sexually active.

Due to the trial size (up to 12 men) to test safety and feasibility, we will not be able to perform a full statistical analysis but will rather be able to have men fill out a validated questionnaire on sexual function which encompasses questions that assess ejaculation.

Subjects will be contacted via chart review at Stanford Healthcare as the single site involved in the study (phone script has been included in the IRB protocol). Many have already expressed willingness to participate including men who were enrolled in the original pilot study. Willing individuals will present to the urology clinic at Stanford at an assigned date and time. They will then be interviewed in a private clinic room with one of the trial staff. This interview will consist of outlining the study purpose and protocol, reviewing the consent form, and teaching on use of the device. After this is done, if they are interested in proceeding, they can sign the consent form and take it home to consider it more. Contact numbers will be provided at that visit. We will also provide them with a link to the Qualtrics survey to take before proceeding. After this visit, no further in person visits will be required. If they have any questions, they will be able to call the number provided. If they experience any adverse events, they will be instructed to contact us immediately.

Use of the device will be explained at their one and only in person clinic visit. They will be provided with a transcutaneous electrical nerve stimulator (TENS 7000) and shown how to use it as well as the range of settings for the its use in DE. They will be showed how to apply the device to the penis. Participants will be able to use the device prior to sexual activity (immediately before sexual encounter for 10 minutes or daily for up to 14 days prior) to "prime" their system or during sexual activity. Each participant will use the device these three separate ways for 6 weeks each (total of 12 weeks of use).

Participants will have 12 weeks to use the device with follow up at each 6 week point filling out a the same questionnaire via Qualtrics they filling out prior to beginning the study to quantify sexual and ejaculatory function.

The primary outcome is subjective improvement in the participants perception of their DE. Secondary outcomes will be assessed via the validated questionnaire International Index of Erectile Function (IIEF) which contains questions pertaining to ejaculation and sexual satisfaction.

Data for this project will be stored within a password protected file on an encrypted laptop approved by Stanford IT. Identifiers will be MRN and study ID. This document will only be available to the researchers on the IRB. Once all data has been collected and study is finished, this document will be deidentified by removing the MRN and study ID.

9) **Significance (1 paragraph or less)**

This study is significant as it has the potential to show proof of concept for a device to treatment delayed ejaculation, which currently has no device or medication approved for it.

10) **Key references**

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4. Læssøe L, Sønksen J, Bagi P, et al. Effects of ejaculation by penile vibratory stimulation on bladder capacity in men with spinal cord lesions. *J Urol*. 2003;169(6):2216-2219. doi:10.1097/01.ju.0000058770.15127.d6
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6. Sønksen J, Biering-Sørensen F, Kristensen JK. Ejaculation induced by penile vibratory stimulation in men with spinal cord injuries. The importance of the vibratory amplitude. *Paraplegia*. 1994;32(10):651-660. doi:10.1038/sc.1994.105
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