IRB Number: Pro00111100
NCT05472740
Study Title: Transcutaneous electric nerve stimulation for analgesia during outpatient endometrial biopsy: a randomized controlled trial (TENS RCT)
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Study Location: Duke University
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Abstract

Our planned study aims to evaluate the efficacy of transcutaneous electrical nerve stimulation for analgesia at the time of outpatient endometrial biopsy.

We will conduct a double-blind, placebo-controlled randomized controlled trial. We will recruit patients over 18 years of age who are undergoing an outpatient endometrial biopsy at Duke gynecologic oncology and general gynecology clinics. After informed consent, participants will be randomized to either the active TENS arm or the placebo TENS arm. They will obtain a pre-procedural survey to collect demographic and personal information as well as a post-procedural survey to assess for post-procedural symptoms, acceptability and tolerability. Pain at the time of endometrial biopsy will be collected across discrete time intervals using a visual analogue scale (VAS).

We hope to recruit 160 participants for this trial and we plan to analyze pain scores between the control and treatment groups as our primary study objective. Risks will be minimal given that TENS is accepted as a safe, over-the-counter non-pharmacologic analgesia method.

Design and Procedures

Patient selection

We will conduct a double-blind, placebo-controlled randomized controlled trial. We will recruit patients over 18 years of age who are undergoing an outpatient endometrial biopsy at Duke gynecologic oncology and general gynecology clinics. Our exclusion criteria include age younger than 18 years, unable to follow study instructions and/or independently adjust TENS settings, cutaneous damage at the TENS application site, any electronic implanted device, inability to understand or declines to sign the informed consent form, and previous personal experience using a TENS unit. We also will not enroll patients who are undergoing a concurrent procedure at the time of biopsy (ie. they're having a biopsy and an IUD placed). Pregnant women will be excluded from the study as a part of the standard of care before having an endometrial biopsy, therefore a pregnancy test may be done for reproductive-aged women. Endometrial biopsy is used to detect endometrial hyperplasia and cancer, however we expect fewer than 15% of patients to be diagnosed with endometrial cancer.

Spanish-speaking Participants Long form translation

The study consent form has been translated into Spanish by Communication Access Partners, Inc DBA Language Resources, a translation company based in Greensboro, NC. The Spanish version of the long consent form can be found in the consent form section of this protocol. The back translation (Spanish into English) and translation certificates can be found in the Other Protocol Documents section. The certified medical Spanish interpreter in clinic will present the consent form to the patient with a study team member present. They will translate any questions the patient has for the study team member into English, and then they will translate the study team responses back into Spanish for the patient. If the patient agrees to participate, they will sign the consent form as will the study team member. The study team member will document the translator's name and that the Spanish version of the consent

was presented to the patient by the translator in the consent documentation note in Epic. Spanish-speaking patients will have survey questions interpreted by the medical Spanish interpreter; our surveys will not be interpreted into Spanish prior. The interpreter will interpret and accompany Spanish-speaking patients throughout the entire procedure.

Short form translation

Spanish-speaking patients may also be included using a certified medical Spanish interpreter and a bilingual adult witness using a short-form Spanish consent. Spanish-speaking patients will have survey questions interpreted by the medical Spanish interpreter; our surveys will not be interpreted into Spanish prior. The interpreter will interpret and accompany Spanish-speaking patients throughout the entire procedure. The bilingual adult witness may be a clinician, if needed. The clinician will not be affiliated with this study and will not be on KP.

Given that many endometrial biopsies will be determined as part of the workup during a visit for abnormal uterine bleeding, eligible patients will be introduced the study at the time of determination for an endometrial biopsy. Participants will have the entirety of time from introduction of study to starting the procedure to decide whether to enroll, and can withdraw from the study at any time.

After informed consent, participants will be randomized to either the active TENS arm or the placebo TENS arm. Randomization will occur in Redcap using a schema provided by the statistician. Participant demographics and clinical information will be collected on a standardized survey in RedCap including self- reported age, race, ethnicity, level of education, history of previous endometrial biopsy, medical history, daily narcotic, or anxiolytic use. Pre-procedural anxiety will be assessed via a 100 mm visual analogue scale with 0 mm being “no anxiety at all” and 100 being “the most anxious I have ever been”.

As there is no standard analgesia option, patients may be offered pain medication prior to the procedure such as ibuprofen. While this would not be a contraindication to enrollment, we anticipate adequate block randomization for this to normalize in both groups, and we will note what form of analgesia was used during our statistical analysis. We believe there is an important value to allow providers to continue their normal standard of care options.

Intervention

Participants will be randomly assigned either to the active TENS group or the placebo TENS group via the Redcap randomiziation tool. We will attempt to blind both the patient and the provider to the intervention. The clinical research coordinator helping with placement, teaching, and operation of the TENS unit will not be blinded. Clinical coordinators will read from a prepared script that will be the same for the placebo and intervention arms. A Spanish-speaking patient will have the script interpreted to them by a certified medical Spanish interpreter. A TENS 7000 that is FDA-approved will be used for this project. TENS units will be placed parallel to the vertebral column at the T-10-L1 and S2-S4 levels as done in previous studies.

Prior to applying the TENS pads to the patient, the study coordinators will ensure the TENS unit has been set to the determined, standardized frequency. The patient will be able to adjust the intensity.

All subjects will have four TENS pads placed on their backs. Those in the active TENS group will have all four electrodes connected to all four pads by the study coordinator. Those in placebo TENS group will have

only two electrodes (one electrode from each wire) connected to two pads. The remaining two electrodes (one from each wire) will be covered with a tight-fitting cap. The subjects can still turn on and adjust the device, just as they would if they were in the active TENS group.

The TENS will be initially turned onto a low frequency by the clinical coordinator. This will be standardized for all patients. The patient will then be told to individually adjust the intensity to each patient's maximum sensory level, or when they feel a strong tingling sensation that is not painful. Patients will be told to maintain the stimulation at the maximum non-painful level and to increase the intensity if they are experiencing pain during the procedure. The TENS will start 5 minutes prior to the procedure and continue until 5 minutes after the completion of the procedure. The provider will be blinded to the patients' group allocations as they will enter the room after initiation of TENS.

Outcome Measures

The primary outcome will be pain at the time of endometrial biopsy; we hypothesize that participants in the active TENS group will have reduced pain scores compared to placebo group. Pain scores will be collected using a 0-100 mm visual analogue scale (VAS) with 0 mm being "no pain" and 100 mm being "worst pain imaginable" during the procedure to be collected by the clinical coordinator. VAS scores will also be collected at the following discrete times: speculum placement, tenaculum placement, immediately after biopsy, removal of speculum, 5 minutes after biopsy and 15 minutes after biopsy.

Patients and providers will fill out a post-evaluation survey including post-procedural symptoms and questions to assess tolerability and acceptability of the biopsy procedure. Secondary outcomes include pain scores at other intervals throughout the procedure, satisfaction with the biopsy, and whether certain factors (anxiety level at the time of biopsy, medication use, sociodemographic factors) are correlated with higher pain scores. Patients will also be asked if they thought they were in the placebo group or the treatment group, and whether they would choose the same pain control if they had to have another EMB. Providers will be asked to evaluate ease of procedure on a 100 mm scale and to estimate perceived pain during the procedure on a 100 mm VAS scale. All information will be collected in RedCap.

Duke Raleigh/Macon Pond (Duke Women's Cancer Care Raleigh)

Patients will also be enrolled and will receive treatment at the Duke Raleigh Macon Pond location (Duke Women's Cancer Care Raleigh). The study's research coordinators will perform all study-related duties and do not anticipate needing the assistance of the Duke Raleigh clinical research team.

Adverse Events/Safety Reporting

The study team will maintain an adverse event log to track any adverse incidents and will also report these to the IRB for record-keeping purposes. Specifically, the study team with look for cases of post-procedural syncope, heavy bleeding, or reaction to TENS unit for a week following the biopsy; any subject will be offered study withdrawal. Any need for hospitalization or death that is probably study related will be immediately reported to the IRB as a UPIRTSO; we expect none of these cases to be study-related. The PI will review and assess frequency, severity and relevancy to the study of all AEs on an ongoing basis throughout the duration of the trial. Tri-monthly reviews by the PI will be completed as a more comprehensive review to look for AE trends.

Study Duration

We estimate we will stop enrolling new participants in October 2023 or if we reach 160 consents, whichever comes first.