Transcutaneous electrical nerve stimulation (TENS) for pain control during first trimester abortion: A blinded randomized controlled trial

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Abstract
Surgical abortion remains the most common outpatient gynecologic procedure in the world and most commonly occurs in the first-trimester. This procedure has been found, repeatedly, to be highly safe and efficacious. Globally, access to abortion is largely determined by a number of extraneous circumstances. In the United States, among these determinants are political, geographical, social, and clinical factors. Clinical factors, including access to pain control, can contribute to abortion access. A recent National Abortion Federation provider survey documented that 54% of respondents prefer the use of local anesthesia with additional IV sedation, deep sedation, or general anesthesia. A disadvantage to receiving these types of sedation is the inability for patients to drive home themselves, which can be a barrier to receiving care. Investing in expanding modalities of pain control could lead to expanded access to abortion. A previous abortion trial comparing TENS to IV sedation found similar postoperative pain scores with a significantly shorter recovery time in the TENS group, however, they did not evaluate intraoperative pain scores. Our team conducted a randomized controlled trial comparing TENS to IV sedation (in conjunction with local anesthesia) for first-trimester surgical abortion and found that TENS had non-inferior pain scores to IV sedation and was considered an acceptable modality for pain control among participants. In this proposed study, our primary outcome will be reported pain using a Visual Analogue Scale (VAS) during cervical dilation. Secondary outcomes will include VAS scores at other time points, satisfaction, and time spent in recovery.

Specific aims
Through this double blinded randomized controlled trial, we hope to demonstrate evidence that Transcutaneous electrical nerve-stimulation (TENS) is an acceptable, non-invasive alternative pain control option for people undergoing surgical abortion in the first-trimester who would otherwise only be using local anesthesia. Ultimately, we hope to identify a pain control strategy that is inexpensive and free of anesthesia risks in effort to break down barriers to abortion care, particularly in low-resource settings, where access to pain control medications is limited.

Rationale
Worldwide, in 2010-2014, 25% of all pregnancies ended in abortion making surgical abortion one of the most common gynecologic procedures. Globally, access to abortion is largely determined by a number of extraneous circumstances. In the United States, among these determinants are political, geographical, social, and clinical factors. Clinical factors, including access to pain control, can contribute to abortion access. A recent National Abortion Federation provider survey documented that 54% of respondents prefer the use of local anesthesia with IV mild, moderation or deep sedation, or general anesthesia. A disadvantage to receiving these types of IV sedation is the inability for patients to drive home themselves, which is a barrier to receiving care that will only worsen as people will be expected to travel farther for abortion. Investing in expanding modalities of pain control could lead to expanded access to abortion in addition to improved experience for patient.

Transcutaneous electrical nerve-stimulation (TENS) is a nonpharmacologic means of pain control that delivers electrical currents through the skin and reduces pain by peripheral and central mechanisms. TENS activates descending inhibitory systems in the central nervous system to reduce sensitivity to pain (hypoalgesia). Previous TENS research identifies intensity as a critical factor in efficacy. High intensity is associated with better pain control, as higher pulses activate deeper tissue afferents. TENS has been researched as pain control in a number of different settings, including cancer pain, lower back pain, labor, and a range of

gynecologic procedures and disorders. There is insufficient evidence to make broad conclusions regarding the efficacy of TENS for pain control in the majority of settings.

A recent study examined the use of TENS for pain relief during office hysteroscopy (rigid). [redacted] found that high intensity TENS was associated with a clinically significant reduction in VAS pain scores in comparison to placebo. While hysteroscopy differs procedurally from first-trimester surgical abortions, we are motivated by the efficacy of TENS in the setting of hysteroscopy, as the timing for greatest pain reported with surgical abortion is when instruments enter the uterus.

Previous research of TENS use for pain control in abortion care show TENS to be effective for pain associated with medication abortion, uterine aspiration, and postoperative pain. Compared to IV sedation, pain control in the TENS group was non-inferior for reducing aspiration pain with first trimester aspiration abortion. Both groups reported a pain level of greater than 6cm on a 10cm visual analogue scale (VAS), where 10cm was labeled as "worst pain imaginable". In a postoperative setting, Platon found that participants using TENS reported pain relief levels greater or equal to 3cm on a VAS. TENS subjects spent significantly less time to recover.

Although TENS may be non-inferior to IV sedation for pain control, IV sedation is not always an option in an outpatient setting and may act as a barrier for patients who do not have a ride home after the procedure. In such cases, alternatives modalities for pain control include ibuprofen and a paracervical block. If effective, TENS would provide a useful non-pharmacologic adjunct to the current standard and improve pain management for patients undergoing aspiration abortion in the first trimester.

We propose a double blinded, randomized controlled trial that studies the effect of adding TENS to the standard ibuprofen plus lidocaine paracervical block for pain control. We hope to identify a means of non-pharmacologic pain control for first-trimester surgical abortion that is inexpensive, noninvasive, accessible, free of side effects, safe from complications, and easy to use.

Research design and methods

Design: Parallel, double-blinded, randomized, controlled superiority trial

Enrollment/procedure visit:

Patients presenting to Stanford Gynecology Clinic for first trimester surgical abortion (gestational age < 12 weeks), who plan to have ibuprofen and local anesthesia, will be approached for enrollment. If participants agree to be blinded and randomized, they will be assigned a study ID. The patient will be block randomized to one of two study groups following consent: 1) Active TENS or 2) Sham TENS. Demographic data will be collected.

For participants randomized to the experimental group (TENS), care will be provided to the following protocol:

- A baseline and anticipated pain score will be collected using a Visual Analog Scale (VAS) pain assessment tool on a 0-100 mm scale (0 being no pain, 100 being worst pain imaginable) by a research coordinator.
- The patient will receive pre-procedure medications (promethazine, ibuprofen, azithromycin) per standard protocols.
- Prior to the procedure, the patient will have two sets of two self-adhesive electrodes placed parallel to the spinal cord at the T-10-L1 and S2-S4 levels for TENS administration.
    - Non-blinded study coordinator will turn on the TENS unit 5 minutes prior to the procedure and monitor stimulating frequency level (80-100Hz and pulse duration of 400 microseconds; intensity or frequency will be monitored to be administered to a non-painful level). The study coordinator will use a script with all patients to ensure provider blinding between participants.
- The procedure will commence and various VAS pain scores will be collected at the completion of each of the following steps:

    - Speculum placement (time recorded)
    - Tenaculum placement
    - Paracervical black administration
    - Cervical dilation (collected after largest dilator passed)
    - Uterine evacuation
    - Speculum removal (time recorded)
- TENS unit will be turned off and electrodes removed.
- Overall VAS pain score will be collected.

For participants randomized to the control group (sham TENS), care will be provided to the following protocol:

- A baseline and anticipated pain score will be collected using a Visual Analog Scale (VAS) pain assessment tool on a 0-100 mm scale (0 being no pain, 100 being worst pain imaginable) by a research coordinator.
- The patient will receive pre-procedure medications (promethazine, ibuprofen, azithromycin) per standard protocols.
- Prior to the procedure, the patient will have two sets of two self-adhesive electrodes placed parallel to the spinal cord at the T-10-L1 and S2-S4 levels.
    - Non-blinded study coordinator will turn on the TENS unit and connect the patient to the unit; however, the unit will not be delivering electrical stimulation. The study coordinator will use a script with all patients to ensure provider blinding between participants.
- The procedure will commence and various VAS pain scores will be collected at the completion of each of the following steps:
    - Speculum placement (time recorded)
    - Tenaculum placement
    - Paracervical black administration
    - Cervical dilation (collected after largest dilator passed)
    - Uterine evacuation
    - Speculum removal (time recorded)
- TENS electrodes removed.
- Overall VAS pain score will be collected.

All groups:

- Post-procedure satisfaction questions will be administered to participants on a 0-100mm VAS (0 being “very dissatisfied” and 100 being “very satisfied”).
- Participants will rate their likelihood to recommend the pain control methodology to friends (0 being “very unlikely” and 100 being “very likely”)
- Post-procedure provider questions will be administered.
    - Ease of procedure, VAS score will be collected (0 being “very easy” and 100 being “very difficult”). Blinding assessment questions will collect which intervention both the provider and participant believed the participant had been randomized to.
- Side effects and adverse events will be documented.
- Time spent in recovery before being discharged will be documented.

<u>TENS Administration Protocol</u>

The TENS unit to be used in this study is a TENS 7000 (ROSCOE Medical). TENS will be emitted asymmetric, biphasic square waveform at consistent pulse rate of 90 Hz and a width of 300 microseconds.

In the active TENS group, the TENS therapy will be initiated five minutes before starting the procedure and during the entirety of the procedure, until speculum removal.

<u>Pre-Procedure Testing for TENS Group</u>

1. Have the patient, with gown open to the back, sit upright on the exam table.

2. Place two self-adhesive electrodes parallel to the spinal cord at T10-L1 and S2-S4 levels.
3. Without having connected lead wire to electrodes or TENS unit, turn on the power of TENS 7000 unit, ensuring to not go above level 1 while adjusting settings.
4. Adjusting MODE
a. Push MODE button once until Normal setting has been selected.
5. Adjusting Width, Rate and Time
a. Push SET once to adjust Width. Use the up and down buttons until Width is set to 300 μs.
b. Push SET twice to adjust Rate. Use the up and down buttons until Rate is set to 100 Hz.
c. Push SET three times to adjust Time. Use the up and down buttons until the time is set to 60 minutes.
6. Maintaining the level of the TENS unit at level 1, connect the lead wire to the TENS unit and to the electrodes.
7. Ask patient if they are able to feel any tingling sensation while at level 1.
8. Instruct patient that you will be increasing the intensity until they are able to feel an uncomfortable, but not painful, tingling, pins and needles sensation. State that you will go slowly and that they should state when they begin to feel any kind of sensation. Reiterate that the sensation should not be painful.
9. Begin increasing intensity and record level at which patient begins to feel sensation and when it is at appropriate “slightly uncomfortable but not painful” stage.
10. Shut off unit, disconnect lead wires, and prepare for procedure.

The TENS device’s intensity (amplitude) will be individually adjusted to each participant’s maximum sensory level (strongest reported tingling feeling without pain and with no muscle contractions). Patients will be counseled on the importance of maintaining the simulation at a maximum non-painful level. The TENS unit’s output intensity will be increased during the treatment every time the patient indicates they accommodated to the TENS stimulus.

Procedure TENS Administration for TENS Group
1. Once patient is prepared for procedure increase intensity to the setting recorded from Step 9.
2. Ensure patient is comfortable with setting and instruct them that at any point during the procedure if they are feeling pain they can ask for you to increase the setting.
3. Signal to provider that you are ready for the procedure to begin.
4. Adjust setting as necessary throughout procedure, recording any adjustments you make in the Adjustment Log.
5. When the provider indicates that procedure is complete, notify the patient that you will be turning the TENS unit off. Turn off the unit, disconnect the lead wires, and remove the adhesive electrodes.

Procedure TENS Administration for Sham TENS with Standard Ibuprofen and lidocaine paracervical block Group
1. Once patient is prepared for procedure maintain blinding by telling the patient you are turning on the device (the device should not be fully connected to the TENS electrodes).
2. Ensure patient is comfortable and instruct them that at any point during the procedure if they are feeling pain they can ask for you to increase the setting.
3. Signal to provider that you are ready for the procedure to begin.
4. Adjust setting as necessary throughout procedure, recording any adjustments you make in the Adjustment Log.
5. When the provider indicates that procedure is complete, notify the patient that you will be turning the TENS unit off. Turn off the unit, disconnect the lead wires, and remove the adhesive electrodes.

Primary outcome:
- Procedural pain with cervical dilation as measured by VAS.

Secondary outcomes:
- Procedural pain at various time points:
    - Speculum placement

    - Tenaculum placement
    - Paracervical block administration
    - Uterine evacuation
    - Speculum removal
- Procedure time
- Provider perceived ease of procedure
- Participant satisfaction
- Complications
- Time spent in recovery
- Participant's perceived group allocation

Criteria for the selection of subjects:
Inclusion criteria:

- Presenting for surgical abortion
- Gestational age <12 weeks
- ≥18 years of age
- Agrees to be randomized

Exclusion criteria:

- < 18 years of age
- Fetal demise
- Pre-procedure use of misoprostol

Data Analysis:
Prior studies have established that a difference of 30% or 13mm to 20mm difference on the 100mm pain visual analog scale (VAS) is considered clinically significant. The standard deviation in such studies was 24mm. To detect at least a 15 mm mean difference on the 100 mm VAS with 80% power and a significance level of 0.05, a total of 82 participants are required. Adding 10% to compensate for potential participant drop out and protocol violation we will aim to recruit 90 total of participants (45 per group).

Demographic characteristics will be compared between the two groups with descriptive statistics, specifically Chi-square test or Student's t-test where appropriate. Mean VAS scores will be compared to be consistent with published literature on VAS results. A t-test will be used to evaluate the primary outcome of pain at the time of cervical dilation. Median scores will also be assessed, as the data are not likely to be normally distributed; Wilcoxon's two-sample test will be used. To assess the mean change in pain score during the procedure and mean difference at various time points between groups, a mixed effects model and a repeated-measures ANOVA will be used. Univariate and multivariate analyses will be performed to evaluate potential confounders and determine independent predictors of pain at the time of cervical dilation.

Study data will be collected and managed using REDCap (Research Electronic Data Capture) tools hosted at Stanford University. Statistical analyses will be performed with SPSS Version 23 (IBM, Armonk, NY, USA).

Links with other projects
This project is not currently linked with any other projects.

Impact statement
The potential impact of the proposed research is far-reaching and applicable to abortion care in high- and low-resource settings. Reducing pain with surgical abortion mitigates a significant barrier to abortion care. In our current political climate in the United States, we may observe more people than ever traveling across state lines to access abortion care. Ensuring those who do not have the means to pay the additional cost associated with IV sedation and those who must drive or transport themselves (by bus or other travel means)

have adequate pain control is important to ensuring quality abortion care. Across the globe, people continue to receive abortion care in low-resource clinics and hospitals, many without the option to provide IV sedation—due to cost, provider level, or access to medical supplies. TENS is a low-cost strategy that many contribute to ensuring access abortion under circumstances that are low-risk and comfortable.

Further, if TENS is found to be superior to ibuprofen and local anesthesia alone, IV sedation may be avoided —reducing a known complication risk associated with surgical abortion.