Randomized, Placebo-Controlled Study on the Efficacy of Transcutaneous Electrical Nerve Stimulation (TENS) for Pain Reduction during intrauterine device (IUD) Insertion in Outpatient Gynecology Offices

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Objective

To investigate the effectiveness of TENS in reducing pain during intrauterine device (IUD) insertion, compared to a placebo, in women seeking contraception or treatment of abnormal uterine bleeding.

Hypothesis

The TENS unit will reduce pain during IUD insertion compared to placebo, as measured by the VAS score

Background

There are limited options for pain management during outpatient gynecological procedures. Studies on cervical blocks, intrauterine anesthetic drug installations, or NSAIDS have had mixed results or lack of efficacy. Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological and non-invasive option for pain control. It works within minutes of application and there are no side effects or drug interactions. TENS is theorized to work for uterine pain in three different ways. The first theory is that pain signals from the uterus are blocked by activation of large nerve fibers which prevents the transmission of pain to the upper nervous system, thus reducing the perception of pain.1 The second theory is that the TENS stimulates beta endorphins secretion which alleviates pain.1 The third theory is that by creating a continuous cutaneous stimulation, TENS eliminates the response of small-diameter afferent fiber groups to perceive pain.2 Lastly, TENS can improve uterine blood circulation and therefore prevent ischemic pain.3,4

In a study that evaluated the efficacy of TENS for pain control during hysteroscopy, women with the TENS had less pain compared to the women in the control group and there were no difference in side effects.2 Another study on the use of TENS during hysteroscopy found that the women with the TENS had a decrease in pain scores during all points of the procedure compared to the control and placebo groups.5 Furthermore, patient satisfaction was also higher in the TENS group.5 In a study for efficacy for pain relief during endometrial biopsy, the women who received the TENS had less pain then the control group, especially post procedure.6

TENS is an untapped resource for IUD insertion. In my literature review I did not come across any studies or papers on the use of TENS for IUD insertion pain reduction.

Inclusion and Exclusion Criteria

	Inclusion Criteria
1.	Age 18-45 years old
2.	Individuals with a cervix and uterus
3.	Seeking intrauterine device (IUD) placement for contraception or management of abnormal uterine bleeding
4.	Meet medical eligibility for IUD placement (pregnancy does not meet medical eligibility)
5.	Ability to consent in English
6.	Ability to use the visual analogue scale (VAS)

	Exclusion Criteria
1.	Contraindications to IUD placement
2.	Use of analgesics within the last 4 hours prior to IUD placement
3.	Presence of a cardiac pacemaker
4.	Pregnancy
5.	Presence of an electronic device
6.	History of epilepsy

Number of Research Participants

We plan to enroll 60 patients, with 30 patients in each study arm.

Recruitment Methods

Subjects who are scheduled for an IUD insertion in any of the OB/GYN offices at UHCMC will be contacted via email or phone call regarding the study. OB/GYN providers at UHCMC can also contact the research team of a potential eligible patient so that the research team can contact the patient via an email or phone call. If patients meet study criteria, the study will be discussed with them and they will be invited to participate and contact information will be obtained for all consenting patients.

Setting

Recruitment will be conducted in person at any of the outpatient gynecology offices at UHCMC either by referral from a provider or the patient may be contacted via email or phone from a study investigator if that person is scheduled for an IUD insertion.

All IUD placements conducted for the research will take place at the Landerbrook office at 5850 Landerbrook drive, Mayfield Heights, Ohio; suite 300. Only Jean Marino APRN-CNP will be inserting the IUDs for the research project.

Consent Process

Study candidates will be screened as above. If a patient expresses interest in participation, a study investigator will provide a consent form for review either in person or via email. The investigator will then answer any questions prior to signing the consent form with the patient. A signed copy of the consent form will be copied and provided to the patient. The consent can be obtained prior to the scheduled IUD placement or immediately prior to the IUD insertion. All patients will be scheduled for the IUD placement at the Landerbrook office and future contact with study participants will be by phone or email, per each patient's preference.

Sharing of Results with Research Participants

☒ Results will **not** be shared with research participants
☒ Results will **not** be shared with research participants' doctors

Study Design

This will be a randomized, placebo-controlled study to investigate the effectiveness of TENS in reducing pain during intrauterine device (IUD) insertion, compared to a placebo, in women seeking contraception or treatment of abnormal uterine bleeding.

Eligible patients at any of the outpatient gynecology offices at UHCMC will be evaluated for inclusion/exclusion by review of their medical record or interview of the patient by the study investigators. The study will be discussed with the eligible patients; if they agree to participate, informed consent will be obtained. At this time, contact information will be obtained for all consenting patients. The IUD insertion may proceed at that time or the patient will be scheduled for a later date based on the patient's preference and availability of the provider inserting the IUD.

Inclusion criteria and desire for continued study participation will be verified prior to randomization. The following demographic questions will be obtained:

1. Age

2. BMI

3. Education level a. < high school b. high school degree or equivalent c. bachelor's degree or higher

4. Race

5. Number of vaginal deliveries

6. Time since last vaginal delivery

7. Number of cesarean sections

8. Number of operative vaginal deliveries

9. History of dysmenorrhea (rated: VAS scale)

10. Anticipated pain (rated: VAS scale)

11. History of central sensitization disorders

    a. Bladder pain

    b. Endometriosis

    c. Chronic pelvic pain

    d. Fibromyalgia

    e. POTS

    f. Chronic fatigue

    g. Chronic HA

    h. IBS

12. Current use of pain medications

13. Marijuana use to be answered by those 21 years old or older

    a. None

    b. Daily

    c. Weekly

    d. Monthly

    e. Rarely

    f. Not applicable, I am under 21 years old

A baseline REDCap questionnaire will be texted or emailed to confirmed study participants prior to participation. UH REDCap is a HIPAA-certified, secure, web-based data storage platform for research studies.

All patients will have the TENS unit applied: 2 pads from channel 1 will be at T10-L1 and the second set of pads will be from S2-S4; 5 minutes prior to the start of the procedure. Patients will then be randomized 1:1 ratio with half of the patients not having the TENS unit turned on and half will have the TENS unit turned on to a 80 hz preset frequency with 100 mA as the pulse width at normal mode.

Randomization will be performed using blocking with a block size of 10 and a 1:1 allocation ratio. The randomization sequence will be generated using a random number table.

After randomization, pain scale collected on laminated VAS with 6 rows at the following points:

1. Baseline

2. Speculum placement

3. Tenaculum placement

4. Uterine sound insertion

5. IUD placement and introducer removed

6. 5 minutes after placement

The response will be recorded by a study team member during the procedure and documented in RedCap immediately following the final data point 5 minutes after the procedure. After the response is documented in RedCap the data will be erased from the laminated card by the study team member.

The TENS unit will be removed 5 minutes after IUD placement. At that time the patient will be asked the following TENS Acceptability questions:

1. Did she like the TENS unit: y/n

2. Was the TENS unit painful: y/n

3. Would she recommend the TENS unit to a friend: y/n

This information will also be documented by the study team member in RedCap.

After the procedure, the provider will document:

1. Any complications from the TENS unit application:

2. Dilators used: y/n

3. Cervical block administered: y/n

4. Was the IUD placed: y/n

5. Complications from the IUD insertion:

Study Procedures

Recruitment of eligible patients will take place at any of the outpatient gynecology offices at UHCMC. The type of IUD inserted will be the patient's choice. After eligible participants have signed consent, the demographic questionnaire will be completed. All patients will have a TENS unit placed 5 minutes prior to IUD placement with half randomized to have it turned on. VAS scores will be obtained at 6 points during the procedure. VAS scale will be provided to the participant on a laminated page with marker. The patient will be notified at each of the 6 points and asked to rate her level of pain she is experiencing at that time. A study team member other than the PI will be present to record the response. The TENS unit will be removed 5 minutes after the IUD strings are trimmed. All IUDs will be placed by Jean Marino APRN-CNP. After the procedure, acceptability questions will be answered by the patient and Jean Marino will document provider questions which includes noting any complications from either the TENS unit or IUD placement and will follow standard procedure for medical care if either were to occur. Follow up after IUD placement will follow office protocol of 4-6 weeks with the provider of their choice and will not be considered part of the study. No additional inpatient or outpatient visits will be required as part of this study.

All of the IUDs are FDA-approved for contraception and/or abnormal uterine bleeding and carries minimal risk to patients. Patients will be encouraged to contact study investigators if they have any concerns about the IUD placement.

Source records include the individual patient electronic medical records in Epic and schedules for outpatient OB/GYN offices to look for patients scheduled to have an IUD.

Study Timeline

	Research-related study procedures that will be performed	Amount of time needed beyond what is normally needed
Eligible patients	Sign informed consent form	10 minutes
IUD insertion procedure	Verify inclusion and exclusion criteria and desire to participate in the study Complete questionnaire	30 minutes
Post IUD insertion	Complete acceptability questionnaire by the patient Complete provider questionnaire by Jean Marino	5 minutes

The study will open with IRB approval and when all of the supplies have arrived at the Landerbrook office. The study will close once we reach our goal of 60 patients who have completed the study. The participants will only be enrolled for the duration of the IUD insertion and completion of questions.

Data to be Collected for your study

The data collected for this study will be from the questionnaires detailed in the study procedures (questionnaires attached).

Data Analysis Plan

Outcome measures will be as follows:

Primary Outcome

- The TENS unit will reduce pain during IUD insertion compared to sham, as measured by the average VAS score.

Secondary Outcome

- The TENS unit will reduce pain at all other procedural points (excluding baseline) compared to placebo, as measured by the VAS score.

Assuming a two-sided alpha of 0.05, randomization of 30 participants per group provides a 90% power to detect a 20% between-group difference in VAS score.

Patients have the right to withdraw from the trial at any point. Other reasons a patient may be removed from the study after enrollment include:

- Exclusion criterion met or inclusion criteria not met after enrollment

Analysis of the study will be by intention to treat and thereby analyze all patients who undergo randomization, regardless of whether they complete the study. A per protocol analysis will also be done. The primary and secondary outcomes (VAS score) will be analyzed via ordinal regression, specifically the proportional odds model as implemented in the rms package for R. A two-sided alpha of 0.05 will be used to assess significance of the coefficient for the group difference in VAS score.

Risks to Research Participants

The risk with a TENs unit is minimal. It is a non-invasive method that has documented safety and efficacy in both labor and gynecology procedures. Possible risks include skin irritation and uncomfortable vibrations. Furthermore, asking the research questions will not prolong the IUD placement procedure.

Additionally, although the utmost care will be taken to ensure that participant information is recorded in REDCap, a HIPAA-certified, secure, web-based data storage platform for research studies, there is always the risk of a breach of confidentiality, meaning that information could be

accessed by unauthorized parties. This risk is very low, particularly given that the information maintained in REDCap cannot be used to identify participants personally.

Provisions to Protect the Privacy Interests of Research Participants

Study data will be collected and managed using the University Hospitals REDCap system, a HIPAAcertified, secure, web-based data storage platform for research studies. Identifiable information will be stored in a password-protected excel spreadsheet accessible only to study investigators. Finally, no personal identifiable information (PII) will be shared outside of University Hospitals and all nonidentifiable information will be pooled and released in aggregate in the final manuscript after statistical analysis is complete. Identifiers will be kept until completion of data analysis to allow for review of additional information that may become necessary during the statistical analysis phase.

After the completion of the statistical analysis phase and a sufficient length of time, the file containing the participating patients' PII will be deleted. Every attempt to obtain and maintain a complete and thorough record of data points will be made by study investigators. To protect patient privacy and maintain confidentiality, all medical information will be coded by a research record number, rather than by a participant's name or medical record number. No paper records will be kept, other than signed consent forms, which will be kept in a locked cabinet in a locked office.

Potential Benefit to Research Participants

This study may confer direct benefits to participants. Specifically, patients who have the active TENS unit may experience less pain with all points of the IUD placement. We hope that the information gleaned from this study will result in pain control options for future patients who desire an IUD placement.

Withdrawal of Research Participants

Participants may withdraw from the study at any time without stating a reason. There will be no consequences for withdrawal from the study before its completion.

Additionally, participants may be withdrawn from the study if they do not meet the criteria for participation or are unable to use the VAS scale during the IUD placement.

Alternatives to Participation

Participation in this study is voluntary. Participants can decline to participate or stop at any time without stating a reason. Non-enrollment or withdrawal from the study will not affect access to medical care to which patients would otherwise be entitled.

Costs to Research Participants

The cost of the IUD placement will be billed to their insurance. There will be no additional cost to be part of the research.

Research Participant Compensation

Participants in this study will receive a $25 gift card after the study procedure

Provisions to Monitor the Data to Ensure the Safety of Research Participants

The study investigators will review data for each patient entered into the REDCap system to confirm accuracy. The primary investigator will review the REDCap data set monthly to ensure completeness, accuracy, and adherence to the protocol. In addition, the study will be monitored by the UH Data Safety Monitoring Committee.

References

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