NOTICE: This document contains comments from the reviewers and editors generated during peer review of the initial manuscript submission and sent to the author via email.

Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
RE: Manuscript Number ONG-21-603

Transcutaneous electrical nerve stimulation for pain management during aspiration abortion up to 83-days gestation

Dear Dr. Lerma:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by May 03, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

This is a well conducted and written study comparing IV sedation to TENS for people undergoing aspiration abortion. It certainly adds to our understanding of how to manage pain during an aspiration abortion. I do have a few comments that I feel would make the paper stronger.

I had never heard of TENS before reading this paper. I learned that it is over the counter in the discussion. Please consider a more robust discussion of TENS in the intro and help the reader understand what TENS is and why the authors felt this study was needed (I'm so glad it was done, but I didn't arrive at that conclusion until the discussion).

Abstract - clear and concise

Intro
Lines 97-98 "Oral sedation and IV sedation, with paracervical block, are not equivalent, with 98 those having IV sedation reporting clinically significantly less pain." Reads awkwardly. I had to read it twice. Consider rephrasing.

Lines 112-114—I appreciate the context of TENS for hscope. I think a more robust explanation of how it is used for other outpatient procedures is warranted however. Was it just the hscope study that made the authors design this trial? After reading the discussion, I learned that TENS has been used for med ab patients, consider including this information in the intro.

Methods
Lines 154-161: how did the authors develop this protocol for adjusting the TENS? Does it follow standardized guidelines for the device? My expectation is that the audience will have no familiarity with TENS, so some explanation about what standard use of TENS is would be helpful.

Results
Clear and easy to follow.

Discussion
Line 344: here is would be nice to understand what usually happens after a patient gets TENS. Is there any minimal observation time for TENS? Would the only observation needed be for the abortion procedure itself?
Line 352: consider changing to "our study generalizable to a US population"
Reviewer #2:

Introduction:
the authors state previously TENS has not been studied in first trimester abortion, however, the following study did evaluate this question, though intervention was after the procedure: (Platon B, Andrél P, Raner C, Rudolph M, Dvoretsky A, Mannheimer C. High-frequency, high-intensity transcutaneous electrical nerve stimulation as treatment of pain after surgical abortion. Pain. 2010 Jan;148(1):114-119. doi: 10.1016/j.pain.2009.10.023. Epub 2009 Dec 2. PMID: 19959293. RCT, post-op pain relief following first trimester abortion); this study should be included in the introduction/discussion, as it supports this manuscript's assertion

otherwise, the introduction is well written, concise, and supports the need for the current study

Methods:
methodology is generally well written, however, I question that utility of blinding the patients if one of the arms is a sedative, i.e. the patient receiving the sedative would realize either during/after the procedure that they were in fact sedated, vs the patients not in the sedative group would similarly realize that they are not sedated, how do the authors account for this type of bias, i don't think this really diminishes the results, i just think it is not possible to truly blind a patient if one arm is placebo and one arm is a drug that impacts cognition, thus i do not think you can realistically call this a blinded study, since the investigators were also unblinded unless level of sedation was monitored in both groups and were similar; additionally in the results 80% of patients knew which arm they were in, which again, argues against the fact that this was a blinded study, while the intention maybe was to have participants blinded

line 195: has pain at the time of aspiration been reported as the worst pain related to this procedure? if so, please provide citation;

Results:
line 286-287: in the manuscript the authors state the in the intention to treat analysis the TENS VAS scores for block, dilation and aspiration have a statistically significant difference compared to IV sedation, however, the reverse appears to be true, the per protocol table shows TENS patient pain to be significantly higher at multiple instances compared to IV; and ITE analysis reveals that only dilation and baseline pain are significantly different; additionally i am confused about how the TENS group pain scores indeed are higher in the ITE than the per protocol group with IV sedation scores remaining the same, but are no longer statistically significant; this does not seem to make sense

Discussion:
line 330-339: do the authors have an explanation for why pain scores were under-predicted by the providers? even the patient anticipated pain scores were higher. If the study was designed using anticipated or actual pain scores in the study, would the sample size to demonstrate non-inferiority be different?

line 347: again, I question whether the patients were truly blinded if the vast majority were aware of what group they were in

the overall conclusion that TENS is non-inferior to IV sedation: while this is true strictly speaking for aspiration in both the ITE and per-protocol analyses patients in the TENS group experienced more pain during parts of the procedure compared to the IV sedation group, and one might argue that overall it is inferior for controlling pain, especially if conclusion is based on the per protocol analysis; I might re-state your conclusion as the following "TENS was found to be non-inferior compared IV sedation for pain experienced with aspiration, but was found to have significantly higher pain scores compared to IV for other portions of the procedure"

Reviewer #3:

General overview
Manuscript # ONG-21-603 reviews a randomized controlled trial that aims to evaluate the effectiveness of TENS for early surgical abortion pain management in comparison to standard intravenous sedation. The investigators demonstrated that TENS might be a useful alternative to IV sedation, when either are combined with paracervical block. After a careful and unbiased analysis of the results, I believe their conclusion that TENS is "non-inferior" to IV sedation is an exaggeration.

The study is randomized appropriately, and both groups apparently begin the study with similar prognoses for achieving the predesigned outcomes. Statistical methods seem appropriate. Clinicians and research personnel were not blinded to group allocation, and 80% of the subjects in both groups were able to accurately determine the group to which they were assigned. What effect this condition may have had on the results is uncertain.

The manuscript is well organized, easy to follow, and mostly well-written. The Discussion section contains sentence fragments, run-on sentences, phrases with vague meaning, and unnecessary adjectives. It requires substantial revision to maintain adherence to acceptable technical writing principles.

Specific questions/comments
I disagree with the conclusion that the study established noninferiority between TENS and IV sedation for the following reasons:

1. 9 of 55 subjects in the TENS group (17%) required rescue treatment with IV sedation, presumably because TENS was not effective for them. These subjects would have had a powerful influence on the results, but they were not counted in the per protocol analysis, and in the Intention to Treat analysis, their response was probably influenced more by IV sedation than TENS.
2. These 9 subjects were completely omitted from the "Likelihood to recommend" analysis because, for some reason, the outcome was measured only by per protocol groups, not intention to treat. Even without their inclusion, the difference nearly reached statistical significance, in favor of IV sedation.
3. Significantly improved pain control was found in the IV sedation group with speculum insertion, tenaculum placement, paracervical block, and cervical dilation. These are important steps of the abortion procedure.

Why were the outcomes in Table 3 analyzed only by per protocol and not intention to treat?

Did the 9 subjects from the TENS group who required crossover treatment continue to receive electrical stimulation in addition to IV sedation? Did they all receive both midazolam and fentanyl? If not, how was the determination made of which drugs to administer?

Overall acceptability of the pain management method should be a primary outcome measure, measured as a categorical variable (acceptable vs. not acceptable), and analyzed based on "Intention to Treat" groups.

In the Discussion, the authors illustrate conditions such as lack of clinician blinding and subject impairment, that may have biased the study in favor of IV sedation, yet no conditions were noted that may have biased the results in the other direction. My impression would be that the lack of blinding would be just as likely to tilt results in either direction, possibly based on the preconceived biases of the clinicians and study personnel. I am also not aware of any good argument that recent receipt of IV opiates or benzodiazepines would make anyone more likely to "over rate" their pain experience.

STATISTICS EDITOR COMMENTS:

General and lines 60-61 and 157-162: How can the participants be blinded to treatment, in that they were able to feel the effect of the TENS and gave feedback to the staff as to the level required? Does not seem to qualify as a blinded protocol, although the groups were randomized.

Fig 1: Need to analyze results from the ITT groups and then for the PP groups.

Fig 2: The primary outcome should first be shown for the ITT analysis, not the PP analysis.

lines 195-198: The primary outcome was pain evaluation at the rime of aspiration, all other times are secondary. Should clearly separate the primary from all secondary outcomes.

Table 1: Since there were from 46 to 55 in each column, the %s should be rounded to nearest integer %, not cited to 0.1% precision.

Table 2: Need to clearly separate the primary from secondary outcomes and the primary outcome should be in format of non-inferiority.
EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
   A. OPT-IN: Yes, please publish my point-by-point response letter.
   B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page. Each of your coauthors received an email from the system, titled "Please verify your authorship for a submission to Obstetrics & Gynecology." Each author should complete the eCTA if they have no yet done so.

3. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

4. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the article (after the References section).

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.
7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal’s electronic author form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.

9. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

12. ACOG is moving toward discontinuing the use of "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

13. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test...
more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1").

14. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

15. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found at the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top).

16. Figure 1: Please upload as a figure file on Editorial Manager.
Figure 2: Please add tick marks along the x-axis. Please upload as a figure file on Editorial Manager.
Figure 3: Please upload as a figure file on Editorial Manager.

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

17. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at https://wkauthorservices.editage.com/open-access/hybrid.html.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.
You will be receiving an Open Access Publication Charge letter from the Journal's Publisher, Wolters Kluwer, and instructions on how to submit any open access charges. The email will be from publicationservices@copyright.com with the subject line 'Please Submit Your Open Access Article Publication Charge(s)'. Please complete payment of the Open Access charges within 48 hours of receipt.

***

If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision’s cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and

* A point-by-point response to each of the received comments in this letter. Do not omit your responses to the Editorial Office or Editors’ comments.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by May 03, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
John O. Schorge, MD
Associate Editor, Gynecology

2019 IMPACT FACTOR: 5.524
2019 IMPACT FACTOR RANKING: 6th out of 82 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.