Author's response to reviews

Title: Electrical Stimulation for Chronic Non-specific Low Back Pain in a Working-Age Population: A 12-Week Double Blinded Randomized Controlled Trial

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Author's response to reviews: see over
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BMC Musculoskeletal Disorders,

On behalf of all of the authors of this submission, I am pleased to submit the manuscript “Electrical Stimulation for Chronic Non-specific Low Back Pain in a Working-Age Population: A 12-Week Double Blinded Randomized Controlled Trial” for consideration for publication. This is a study protocol of a three arm, 12-week, blinded, randomized controlled trial evaluating effectiveness of a h-wave transcutaneous electrical stimulation device as compared to both a traditional transcutaneous electrical stimulation device and a sham device for the treatment of moderate to severe chronic low back pain. We are anticipating publishing multiple original articles investigating factors related to these treatments as well as novel assessment methods for evaluation of chronic low back pain.

This is an industry sponsored trial, however the sponsor has not made decisions regarding study design and will not be involved in the execution or evaluation of the study.

Please thank the reviewers for their careful attention to our submission and their thoughtful suggestions. I have outlined my revisions and comments with the comments from reviewers below.

Major compulsory revisions:
1. Intervention time not clear. While it is clear from the manuscript that assessment will be conducted at enrollment and at week 1, 4, 8 and 12, it is not clear what the treatment period is? Agreed, treatment time is 12 weeks. I have made changes to both the abstract and the body of the text on page 8 and 9.
2. Page 6. In general the entire section on outcome measures is not clear and not sufficiently specific. (page 6-7). Thank you for this comment, we have tried to clarify the text, and included a table of outcomes to simplify these measures.

Thank you for your comments on clarifying the methods to allow for more transparency and replication of the study design. We have attempted to clarify the intervention and outcomes.

a. VAS score will refer to what period (day of assessment? overall period between assessments? etc.) Agreed that this is not clear, clarifying statements were made in the outcome section of the proposal.

b. It is stated that physical activity levels will be measured with accelerometers. When and for what period? Is it throughout the entire treatment period, a few hours, days before assessment time? The accelerometer measures will be continuous for the length of the study. The accelerometers we are using have a
40 day memory and battery life and are changed out at regular intervals. Clarifying Statements were made in the outcome section.

c. How is strength measured? Some details are provided on page 7, but these are not specific enough. For example what is meant by pushing and pulling strength test? Strength is measured using a load cell attached to a computer to measure forces exerted. This is part of the BTE EvalTech tool, which has its own standards and protocols for qualifying efforts. Clarifying Statements were made in the outcome section and the addition of a figure to demonstrate the testing maneuvers was added.

d. What is meant by the term "up to maximum baseline pain level"
"Up to maximum baseline pain level" was replaced with more specific information for each outcome measure. How is "duration of time standing comfortably" measured? They will stand quietly until uncomfortable? These are self-reported outcomes not measured outcomes, therefore subjective based upon participant reporting. Clarifying statements made in outcome section.

e. What walking endurance test is used? What is meant by duration and distance walking comfortably mean? Again they will self-report the estimated distance and duration they can walk until uncomfortable. Clarifying statements made in outcome section

f. More detail is necessary for describing the "standardized protocol on a BTE system" at least what functions are assessed. Details added to this paragraph on page 6.

h. The description does not seem consistent. Will all these tests be performed twice at each visit as implied by the sentence "assessments will be measured pre and post treatment at these visits? This does not seem quite feasible! Yes, many measures will be both pre and post treatment at the same visit for visits 1 and 2, where patients will be receiving treatment during their visit. One issue we want to address is short term efficacy of the devices. Clarifying comments made on page 7.

i. On page 7, it is stated that all measures will be assessed electronically or administered electronically. I assume that what is meant is using electronic equipment? How can these then be measured on week 8 on the phone? We changed the text to read "All measures will be assessed using computerized data collection methods at baseline and each follow-up, except at the 8-week follow-up where outcomes will be assessed over the phone." Otherwise all measures are collected via computer for complete data capture. Text to this extent has been added to the manuscript.

k. Details on validity and reliability of at least the major outcomes should be provided. This has been addressed, including references for primary outcome.

3. Page 8. What are the stimulation parameters used with the H-Wave, the pulse duration? and pulse frequency? What is meant by "patients will be required to reach near maximal intensity on low frequency" Is it maximally tolerated intensity, or maximal intensity offered by the device? Will the maximal intensity induce only
sensory stimulation, or muscle contractions and painful stimulation as well? The stimulation parameters in terms of pulse duration and frequency are proprietary for the manufacturer. Text has been added stating “H-Wave utilizes a bipolar exponentially decaying pulse with frequencies between 1-70Hz and a pulse duration of 5 milliseconds along with some other proprietary factors.” The maximal intensity offered by the device is the goal of the treatment intensity, however patients are instructed to achieve the highest intensity possible, and lower intensities are accepted if the patient cannot comfortably reach the maximal device intensity. The maximal intensity may in some patients induce transient muscular contractions. Patients are instructed not to increase the intensity to a painful level. Text to this effect has been added to the manuscript.

4. Page 8. More details are required to describe the TENS stimulation as well. How many channels/electrodes will be used. Where will they be placed. What is the pulse duration and waveform? Will subjects be encouraged to increase intensity to level of sensory, motor or painful stimulation?

Details regarding the location of pads, intensity and pulse duration have been clarified. Text has been added to clarify these points.

Minor Essential Revisions

Abstract

Abstract should include more details as to intervention – intervention parameters, number of visits and contact time. Thank you. We added text to address these shortcomings.

Introduction

1. Unique characteristics of the H-Wave device not well described (what pulse duration or frequency). Text has been added to address this shortcoming.

2. The rational for this comparison is not well substantiated. Unique characteristics of the H-Wave device noted are related primarily to changes in circulation and lymphatic system. How are changes in these systems expected to affect chronic pain syndrome. Excellent point, thank you. This has been addressed in the text.

3. More references should be included to substantiate various claims made both regarding the effect of TENS and H-Wave. This has been addressed in the text by adding references and text regarding the claims of efficacy.

Methods and Materials

Regarding use of pacemakers etc..It is stated that “patients will be dissuaded from using these devices if not actively using at the time of enrollment” – can't dissuade an individual from using a pacemaker if he needs one. Treatment should be terminated. Clarification made on page 4. Participants who have a pacemaker or other implanted device are excluded from the study. The devices discussed in “patients will be dissuaded from using these devices” refer to personal home based electrical stimulation devices not pacemakers etc.

Discretionary Revisions

Why used both the Oswestry Index and the Roland Morris Instrument? Both are
self reported questionnaires regarding function, measuring pretty much the same thing. While both measure the same domain, many articles used previously use only one or the other. We wanted to have an article that can be directly compared to multiple TENS RCTs regardless of the outcome that each article measured. In terms of cost, each metric only takes a few minutes for each participant to complete, particularly when it is computerized.

MCR1: In the introduction, a summarized literature review on the efficacy of electrotherapy is lacking. After reading your literature review, it should be clear to the reader that the research question you are asking is relevant (functional improvement induced by electrotherapy). We completely agree. We have clarified the study question in addition to improving the literature review and addressed this statement with additional text.

MCR2: The chapter ‘method’ is hard to follow. Perhaps assessments can be displaced in a chapter ‘procedure’ and the description of ‘objective measure’ in the chapter ‘outcome measure’. ‘Compliance’ and ‘discontinuation’ can be included in the chapter ‘outcome measures’ as ‘other measures’. In the same way, ‘usual care’, ‘rescue medication’, ‘interventions not allowed’ can be included in the chapter ‘intervention’ as ‘other interventions’. We believe that the bold elements are important for improving clarity and efficiently judging the quality of the trial. We wish to preserve the headings but have rearranged to improve flow and readability. These headings are selected based upon ACOEM Practice Guidelines and AGREE II scoring criteria.

MCR3: It would be interesting to add expected findings. We do not expect to find a difference in the two active treatment devices and language to that effect has been added.

Minor Essential Revisions
Abstract
MER 1: The number of subject is different in the text (38/32). Please check. Thank you for identifying that error. We have corrected it to 38.
MER 2: Expected findings can be displayed at the end of the abstract. Text has been added into the abstract stating the null hypothesis.

Introduction:
MER 3: (cf MCR1). Overall it’s difficult to understand why electrotherapy is interesting for chronic low back pain. Authors should probably explain what is the gain expected with electrotherapy (back pain, leg pain, function, activities). This is discussed on page 3, however we have expanded the text to address this comment.

MER 4: For the first paragraph, the reader suggests to keep only the last sentence (Despite the relative ….treat). The references are lacking in the second paragraph. We respectfully disagree with excluding sentences about burden and costs of LBP as those statements demonstrate the need for identifying efficacious treatments. Even if small gains are made in treatment efficacy, the
impacts are significant because of the large burden on society. Text to this effect have been added.

MER 5: The last sentence of the introduction should be introduced earlier to explain the goal of this trial. We respectfully disagree with the reviewer on this statement. We feel that the last paragraph of the introduction outlines the study purpose in most occasions. We have added text earlier in the introduction to address this comment and provide insights to the reader into the study purpose.

MER 6: The reader suggests recalling the recommendation those LBP patients must stay active and that electrotherapy fits with that specific goal. We are only recommending that patients stay active and electrotherapy treatment is very specific to that goal. If we can reduce pain and improve function, including activity, then patients will have better outcomes.

Method:

MER 7: All spinal surgery should be considered as exclusion criteria. We are excluding all significant spinal surgery, however if surgery was minor or remote, we do not want to exclude these participants. It is important to assess the efficacy of the treatments among the population of LBP patients. We will be reporting the number of surgeries in each group and assessing if this was a potential confounder.

MER 8: “Sham device…treatment”: if electrical current can be perceived by patients it cannot reasonably be considered as sham treatment. The reader suggests to argue this issue more. The authors should try to test their blinding effect after the experiment. Please check existing references for blinding effect in electrotherapy. Thank you for the suggestions. We will be assessing blinding by asking participants what treatment arm they believe they are in, which will be reported once the study is completed. There is no evidence that low levels of electrical current is clinically effective, however we wanted patients in this arm to believe they are receiving treatment and not drop out of the study. Text has been added to address this comment.

Outcome measures:

MER 9: The main criterion is ODI. The authors should better explain in the introduction why they use this criterion. We do not want to include outcome measures in the introduction; however we have added text in the outcome section to further justify the selection of the ODI as the primary outcome.

Assessments:

MER 11: “Comparable contact time will be used to minimize treatment bias”: like a case control study? between groups? The authors should explain this sentence. Our definition of contact time is time patients are with a provider or receiving treatment. This has been clarified in the text.

MER 12: The description of the objective measures can be included in ‘outcome measures’ or ‘materials’. For each measure, the authors can explain what kind of material is used, how the signal is processed, how the data are collected. In the previous chapter, the authors have already talked about timing assessment and questionnaires and the repetition is confusing. According to the reader, the
presentation in the abstract is clearer. (cf MCR 2). A table with the outcome measures and the assessments would be interesting. This has been added and addressed.

MER 13: For the accelerometer, more details are needed (recording time, analysis…) to explain how acceleration can provide information on physical activity. Accelerometers are the current gold standard for measuring ambulatory physical activity in research. They are widely used and have demonstrated validity. The original text included recording time and we added data regarding use. Additional text about validity has been added.

MER 14. A figure for the car pushing test would be interesting.

Treatment protocols. Thank you for the suggestion. A figure has been added.

MER 15: It could be interesting to know the current features of H Wave to compare with TENS. Text has been added stating “H-Wave utilizes a bipolar exponentially decaying pulse with frequencies between 1-70Hz and a pulse duration of 5 milliseconds along with some other proprietary factors.” Unfortunately, much of the device is proprietary.

Statistical analysis

MER 16. “Mlt is likely... groups”: please explain. Mlt is a typo and the M was deleted so that it now reads “It is likely...”

MER 17: Co variates appear here but are not described previously. Please check. Text has been added to the abstract and the statistical analysis sections to address this issue.

Discretionary Revisions

DR1/abstract: Assessments are displayed two times- Addressed in the text. Thank you

DR2/Introduction: ‘PENS’ is probably Peripheral ENS? Percutaneous electrical nerve stimulation, addressed in the text

DR 3/introduction: Why two references are situated at the bottom of page 4? These footnotes are not direct references but clarification of concepts noted above.


DR 5/ Assessment: OTC? PO QID? Addressed in the text.

DR 6/Statistical power: A reference seems to lack here (line 2). Addressed in the text.

DR 7/ Statistics: The ‘multiplicity’ should be replaced in the chapter ‘primary analysis’. Addressed in the text.

If you have any questions or need clarification of any aspects of our study, please do not hesitate to contact me at matt.thiese@hsc.utah.edu or 801.587.3322.

Thank you for your consideration of the submitted manuscript.

Respectfully,

[Signature]