

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	COMPARING TWO DRY NEEDLING INTERVENTIONS FOR PLANTAR HEEL PAIN: A RANDOMIZED CONTROLLED TRIAL
AUTHORS	Al-Boloushi, Zaid; Gómez-Trullén, Eva Maria; Arian, Mohammad; Fernández, Daniel; Herrero, Pablo; Bellosta-López, Pablo

VERSION 1 - REVIEW

REVIEWER	Uselli Federico Humanitas San Pio X Hospital - Foot and Ankle Division - Milano, Italia
REVIEW RETURNED	25-Mar-2020

GENERAL COMMENTS	<p>Dear authors, I appreciated the topic studied and the structure of your work with randomization of the two samples. I appreciated your conclusions and I think needling could be a valid, although slightly invasive treatment for plantar heel pain with myofascial trigger points. There are few things to review in my opinion.</p> <p>In the Introduction, many acronyms are used without explanation, moreover in general the acronyms used in your paper are excessive and sometimes make reading difficult. I therefore suggest reducing the number of acronyms.</p> <p>The article is very detailed and well structured, however in the Results there are too many statistical values reported in brackets, which once again make reading difficult. I suggest to report only the statistical validity of your results in the text and possibly provide more statistical details within a table.</p> <p>Except for these small corrections, your paper certainly deserves its publication both for the subject matter and for the effort made.</p>
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REVIEWER	riccardo d'ambrosi IRCCS Istituto Ortopedico Galeazzi Milan Italy
REVIEW RETURNED	25-Mar-2020

GENERAL COMMENTS	abstract:add mean age of the patients add p-value in results
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	<p>introduction Introduction is overall too long. should be about one page. Start directly with the topic of the manuscript hypothesis and aim are ok</p> <p>design is ok</p> <p>Methods Inclusion and exclusion criteria are not clear only one scale for foot scores? not necessary to explain all the scores.</p> <p>statistical analysis correlations are missing</p> <p>results results are the worst section of the paper. please re-assess completely. is impossible to read.</p> <p>discusson please don't repeat results in discussion which are the clinical implications of the study?</p> <p>conclusions too long</p>
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REVIEWER	Efthymios Iliopoulos Brighton & Sussex University Hospitals, NHS Trust United Kingdom
REVIEW RETURNED	26-Mar-2020

GENERAL COMMENTS	<p>The authors present a prospective randomised trial, comparing two dry needling interventions to patients with plantar heel pain. The primary outcome measure did not illuminate any statistically significant differences between the two study groups, but there were some differences in the secondary outcome measures during different follow-up time periods.</p> <p>This was an interesting well designed study. I feel that the presentation of the study in this manuscript can be enhanced and there are some issues that have to be addressed by the authors. Please see my comments in the word document below.</p> <p>Title: The title should contain the information that the plantar heel pain examined is caused by myofascial trigger points.</p> <p>Abstract:</p> <ul style="list-style-type: none"> - In the participants section the average age of the cohort should be stated. - The interventions section should be rephrased, in order to avoid confusion, i.e. 'Two study groups randomly formed, both of them received stretching protocol exercises. The first study group received' - On the outcome measures section, the authors mention that the primary measure was the FHSQ, but later in the text the authors mention that the primary measure was the Foot Pain domain of the FHSQ. This should be mentioned in the abstract. - The authors are repeating the time periods of the follow-ups
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	<p>for each outcome measure. This should be rephrased in order to avoid the repetitions.</p> <ul style="list-style-type: none"> - On line 64 there is a typographic mistake. The 'cm' should be removed. - In the conclusion the statement that there were no significant differences between groups, is not accurate, as there are some statistically significant differences in the text. These should be at least mentioned here as well. <p>Article summary: In the article summary section the authors have added bullet points for the strengths and limitations of the study, not a summary of the article. This section should be changed.</p> <p>Introduction: Line 89: The first phrase should be changed as it is confusing for the reader. Possibly rephrase to: 'Plantar heel pain (PHP) is very common pathology in the foot...' Line 92: The word 'from' should be added. 'population may suffer from this condition' Line 93: Please rephrase - Plantar heel pain is caused by various pathologies such as... Line 97: Remove the word 'proper' and change the word 'difficult' to 'challenging' At the end of the introduction's first paragraph the authors explaining well the PNE technique, but the previous section should be rephrased, as it is confusing for the reader. Maybe a fragmentation to more paragraphs can be useful.</p> <p>Methods: At the participants section there is a very large paragraph describing the inclusion criteria, the exclusion criteria and the power analysis. It would be easier to reads if it was fragmented in three separate paragraphs. Line 136: please rephrase Line 140: 'according to the Kuwaiti law', what is this phrase referring to? Lines 137-145. This is a very long sentence, makes it difficult to follow. Please rephrase. Line 164: Please replace the word 'eligibility criteria' to 'inclusion criteria' Line 173: Please replace the word 'dosage' with the word 'frequency' Lines 186-187: Please rephrase: The patient's position (supine, ...) was depending on each muscle examined, and was the same... Lines 189-192: Was only one physiotherapist participated in the study or multiple? Were they blinded for the intervention? Line 228: please remove the words 'after randomization' Line 228: gender etc. can be labelled as demographic & disease data. Line 254: The phrase 'by intention to treat, carrying the lost values forward, does not make sense. Please rephrase.</p> <p>Results: The drop rate of the study is quite high and definitively higher than the authors expected. According to the power analysis mentioned in the methods section the study should have at least 39 patients enrolled in each of the study groups. In the flow-chat it is mentioned that only 37 patients finished the treatment in the PNE group, which is lower than the minimum needed one. Furthermore, only 30 patients from that group completed the final follow-up. The authors should have added more patients in the groups initially, in order to overcome this very high drop rate during the treatment. It is worth to mention that the drop rate of the follow-ups is what expected for such study.</p>
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	<p>My suggestion is that the authors should at least check the power level of the study as it stands now, and if under-powered, this should be clearly stated in the manuscript, or enrol more patients if possible.</p> <p>The presentation of the results is adequate, but the authors have found two statistically significant differences between the two groups on the secondary measures. This should be more clearly stated in the manuscript as it is an important finding.</p> <p>Line 278: Please add the word 'groups' at the end of the sentence.</p> <p>Discussion:</p> <p>The discussion should start with the most important finding of the present study in order to give emphasis and illuminate the main findings of the study.</p> <p>Line 349: There should be a typographic mistake on the VAS values, as the VAS range from 0 to 10.</p> <p>Line 353: Please rephrase, this sentence is very difficult to understand.</p> <p>Line 361: please add the word 'the' in 'Regarding the quality of life,...)</p> <p>Line 372-373: The authors mention the side effects hematoma and bruising, but this is not mentioned in the results section. Were such side effects present in this study?</p> <p>Line 377: The authors mention that because they found 118 patients with MTrPs, this is a common cause of heel pain. This cannot be derived from this study, as we do not know how many patients had heel pain but not MTrPs.</p> <p>Conclusions:</p> <p>The conclusion is quite well written. It is worth to mention that the authors illuminate the differences between groups in the different time point. This should be the case for the conclusion in the abstract, as at the moment ends with the statement that there were no differences between groups.</p> <p>Tables:</p> <p>Table 1: It is difficult to understand what exactly the musculoskeletal medication is, please add some examples.</p> <p>Table 3: Please make more clear which of the p values are within and between groups.</p> <p>It would be better for better understanding of the results to add 2-3 graphs. Demonstrating how the results changing during the different time periods.</p> <p>CONSORT List appropriately reported.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Usuelli Federico

Institution and Country: Humanitas San Pio X Hospital - Foot and Ankle Division - Milano, Italia

Please state any competing interests or state 'None declared': None to declare

Please leave your comments for the authors below Dear authors, I appreciated the topic studied and the structure of your work with randomization of the two samples. I appreciated your conclusions and I think needling could be a valid, although slightly invasive treatment for plantar heel pain with myofascial trigger points. There are few things to review in my opinion.

In the Introduction, many acronyms are used without explanation, moreover in general the acronyms used in your paper are excessive and sometimes make reading difficult. I therefore suggest reducing the number of acronyms.

We have substantially reduced the number of acronyms used throughout the text, we hope that this enhances the readability of the paper. We have left MTrPs which is a commonly used acronym in this field, as well as PHP. We now spell out dry needling and percutaneous needle electrolysis.

The article is very detailed and well structured, however in the Results there are too many statistical values reported in brackets, which once again make reading difficult. I suggest to report only the statistical validity of your results in the text and possibly provide more statistical details within a table. Considering also the editor's suggestions, we have rewritten the results section, grouping all secondary measurements into the same paragraph as the results were all similar. We have reduced the statistical information in the results section to facilitate reading.

Except for these small corrections, your paper certainly deserves its publication both for the subject matter and for the effort made.

We thank the reviewer for this comment.

Reviewer: 2

Reviewer Name: riccardo d'ambrosi

Institution and Country: IRCCS Istituto Ortopedico Galeazzi Milan Italy Please state any competing interests or state 'None declared': none

Please leave your comments for the authors below abstract: add mean age of the patients add p-value in results

We have added mean age in the abstract and p-values in results.

Introduction

Introduction is overall too long. should be about one page. Start directly with the topic of the manuscript hypothesis and aim are ok

Bearing in mind also the suggestions made by the other reviewers, we have decided to rewrite part of introduction and we have shortened it a bit, making a few changes to improve reading.

design is ok

Methods

Inclusion and exclusion criteria are not clear only one scale for foot scores?

not necessary to explain all the scores.

Regarding inclusion criteria we followed similar inclusion criteria as other published studies, however, we avoided to include more conditions for including patients as we needed a big sample (i.e defining a foot pain threshold to be included in the study). After including patients, we performed many foot measurements, however, we only considered these as assessment and not for inclusion to avoid the risk of not reaching the required sample. Besides, these inclusion and exclusion criteria were peer reviewed in the protocol published at <https://joser-online.biomedcentral.com/articles/10.1186/s13018-019-1066-4>

statistical analysis

correlations are missing

Due to the limits in the manuscript and the objectives of this study, any correlations or regression analysis are secondary and should be considered for other studies. This was not considered in the protocol approved and published as an objective therefore, because of these two reasons we have

not included such analysis. We have improved tables 3 and 4 with the mean differences for every moment from baseline.

results

results are the worst section of the paper. please re-assess completely. is impossible to read. We have rewritten this section completely grouping some of the results.

discusson

please don't repeat results in discussion which are the clinical implications of the study?

We removed repeated results as much as possible and added possible explanations for the difference of results with other studies and clinical implications, as suggested by other reviewers.

conclusions

too long

We have grouped conclusions according to the results.

Reviewer: 3 **Please see attached review in pdf format for this reviewer's full comments** Reviewer Name: Efthymios Iliopoulos Institution and Country: Brighton & Sussex University Hospitals, NHS Trust United Kingdom Please state any competing interests or state 'None declared': None declared.

Please leave your comments for the authors below The authors present a prospective randomised trial, comparing two dry needling interventions to patients with plantar heel pain. The primary outcome measure did not illuminate any statistically significant differences between the two study groups, but there were some differences in the secondary outcome measures during different follow-up time periods.

This was an interesting well designed study. I feel that the presentation of the study in this manuscript can be enhanced and there are some issues that have to be addressed by the authors. Please see my comments in the word document below.

Title:

The title should contain the information that the plantar heel pain examined is caused by myofascial trigger points.

We think that it is better to maintain the title as it is, as it was registered with this title in clinicaltrials.gov and also published as a protocol with the same title. We think that it is clear in the abstract and it is recommended to avoid making further changes to registered protocols.

Abstract:

- In the participants section the average age of the cohort should be stated.

We have added this information.

- The interventions section should be rephrased, in order to avoid confusion, i.e. 'Two study groups randomly formed, both of them received stretching protocol exercises. The first study group received'

We have added this at the beginning of the intervention section to make this clearer.

- On the outcome measures section, the authors mention that the primary measure was the FHSQ, but later in the text the authors mention that the primary measure was the Foot Pain domain of the FHSQ. This should be mentioned in the abstract.

FHSQ does not give a global score. The results are divided by subdomains. The sample size calculation was made according the primary outcome, which was Foot Pain domain, so we corrected this in the abstract too, to make it coherent with primary measure reported and sample size calculation.

- The authors are repeating the time periods of the follow-ups for each outcome measure. This

should be rephrased in order to avoid the repetitions.

We have rephrased the results and discussion sections to avoid repetitions and improve reading.

- On line 64 there is a typographic mistake. The 'cm' should be removed.

We have corrected this.

- In the conclusion the statement that there were no significant differences between groups, is not accurate, as there are some statistically significant differences in the text. These should be at least mentioned here as well.

We realize that the conclusions were very similar to the results, therefore, we took conclusions from the rewritten section in the main manuscript and adapted it.

Article summary:

In the article summary section the authors have added bullet points for the strengths and limitations of the study, not a summary of the article. This section should be changed.

We have kept this after checking the author guidelines, which state "An Article Summary, placed after the abstract, consisting of the heading 'Strengths and limitations of this study', and containing up to five short bullet points, no longer than one sentence each, that relate specifically to the methods"

Introduction:

Line 89: The first phrase should be changed as it is confusing for the reader. Possibly rephrase to: 'Plantar heel pain (PHP) is very common pathology in the foot...'

Thank you, we have rewritten this.

Line 92: The word 'from' should be added. 'population may suffer from this condition'

Corrected.

Line 93: Please rephrase - Plantar heel pain is caused by various pathologies such as...

Corrected.

Line 97: Remove the word 'proper' and change the word 'difficult' to 'challenging'

Corrected.

At the end of the introduction's first paragraph the authors explaining well the PNE technique, but the previous section should be rephrased, as it is confusing for the reader. Maybe a fragmentation to more paragraphs can be useful.

We have moved the sentence "The identification of the main cause of pain can be challenging as this is often multifactorial,³⁰ and despite its prevalence, the etiology of PHP is not well understood.^{24, 25} The presence of myofascial trigger points (MTrPs) within the muscles of the foot and lower leg may play an important role in people in PHP,³⁸ an implicit assumption underlying many recent studies.^{12, 15, 16, 29} In addition, there is a lack of consensus regarding the ideal management approach for PHP.^{10, 32, 37}" This is now placed earlier in the text, as it was more related with the first paragraph

Methods:

At the participants section there is a very large paragraph describing the inclusion criteria, the exclusion criteria and the power analysis. It would be easier to reads if it was fragmented in three separate paragraphs.

Corrected.

Line 136: please rephrase

We have rewritten this.

Line 140: 'according to the Kuwaiti law', what is this phrase referring to?

We have rewritten this to explain it better.

Lines 137-145. This is a very long sentence, makes it difficult to follow. Please rephrase.

We have rewritten this sentence assigning each criterion to a number.

Line 164: Please replace the word 'eligibility criteria' to 'inclusion criteria'

Corrected.

Line 173: Please replace the word 'dosage' with the word 'frequency'

Corrected.

Lines 186-187: Please rephrase: The patient's position (supine, ...) was depending on each muscle examined, and was the same...

Corrected.

Lines 189-192: Was only one physiotherapist participated in the study or multiple? Were they blinded for the intervention?

One physiotherapist treated patients (ZA). We have inserted the initials to show that there was only one physiotherapist. Another physiotherapist made the assessments (MA), we have also included these initials. Only the assessor was blinded, as the physiotherapist treating patients knew each group, and therefore to provide treatment and maintain blinding was not possible. In the assessment section this is described as follows "An independent assessor (MA) blinded to treatment group allocation conducted all assessments at baseline, and at the 4, 8, 12, 26 and 52-week follow-up. Demographic and disease data were collected at baseline."

Line 228: please remove the words 'after randomization'

Corrected.

Line 228: gender etc. can be labelled as demographic & disease data.

Corrected.

Line 254: The phrase 'by intention to treat, carrying the lost values forward, does not make sense. Please rephrase.

We have rewritten this phrase to explain it better, with the last observation carried forward, which was the procedure used for missing values.

Results:

The drop rate of the study is quite high and definitively higher than the authors expected. According to the power analysis mentioned in the methods section the study should have at least 39 patients enrolled in each of the study groups. In the flow-chart it is mentioned that only 37 patients finished the treatment in the PNE group, which is lower than the minimum needed one. Furthermore, only 30 patients from that group completed the final follow-up. The authors should have added more patients in the groups initially, in order to overcome this very high drop rate during the treatment. It is worth to mention that the drop rate of the follow-ups is what expected for such study. My suggestion is that the authors should at least check the power level of the study as it stands now, and if under-powered, this should be clearly stated in the manuscript, or enrol more patients if possible.

The sample-size calculation initially estimated that 39 participants per group would provide 80% power to detect a minimally important difference of 13 points in the pain domain of the Foot Health Status Questionnaire FHSQ with a standard deviation of 20 points and an alpha risk at 0.05. As the reviewer comments, we detected a higher number of drop-outs than expected and we recalculated drop-out rate with the initial drop-out rate for the first patients and recruited more patients. The power is correct until the 8-week measurement where 78 patients were evaluated, and may have affected the following measurements. However, we analyzed by intention to treat so the number of patients analyzed were 102, with no risk of low power. However, this methodology can be more conservative so we also conducted a per protocol analysis without any differences. We have included a paragraph to explain these and the possible clinical implications in the discussion section. Both ITT analysis and drop-outs, could have led to not detecting the treatment effect, more markedly in the PNE group, so we have discussed this in clinical implications.

The presentation of the results is adequate, but the authors have found two statistically significant differences between the two groups on the secondary measures. This should be more clearly stated in the manuscript as it is an important finding.

We have rewritten the conclusions.

Line 278: Please add the word 'groups' at the end of the sentence.

Corrected

Discussion:

The discussion should start with the most important finding of the present study in order to give emphasis and illuminate the main findings of the study.

We have removed the first paragraph as it was not a proper discussion and more like introduction.

Line 349: There should be a typographic mistake on the VAS values, as the VAS range from 0 to 10. It is not an error, but as the other study reported on a 100 scale we converted our 10 to 100 to make them comparable. We have deleted this part as requested by other reviewer as it was duplicating results and made the discussion too long.

Line 353: Please rephrase, this sentence is very difficult to understand.

As recommended also by another reviewer, we have now rewritten this sentence.

Line 361: please add the word 'the' in 'Regarding the quality of life,...')

Corrected.

Line 372-373: The authors mention the side effects hematoma and bruising, but this is not mentioned in the results section. Were such side effects present in this study?

Yes, there were some common side effects like hematoma. It was an error as we had copied the text from the protocol. We have corrected this in the results sections indicating some mild adverse effects.

Line 377: The authors mention that because they found 118 patients with MTrPs, this is a common cause of heel pain. This cannot be derived from this study, as we do not know how many patients had heel pain but not MTrPs.

We agree, we have removed this sentence.

Conclusions:

The conclusion is quite well written. It is worth to mention that the authors illuminate the differences between groups in the different time point. This should be the case for the conclusion in the abstract, as at the moment ends with the statement that there were no differences between groups.

We have rewritten part of the conclusion as requested by other reviewer and we have revised the differences between groups to be sure that they were well reported. We have changed the conclusions in the abstract according to the new conclusions section.

Tables:

Table 1: It is difficult to understand what exactly the musculoskeletal medication is, please add some examples.

We have checked the official categories and the proper name should be neuromodulators or antiepileptic medication such as Lyrica or Cymbalta, therefore we have changed this in the text, although without adding examples, in order to be homogenous with the rest of categories as we think it is more clearly understood now.

Table 3: Please make more clear which of the p values are within and between groups.

It would be better for better understanding of the results to add 2-3 graphs. Demonstrating how the results changing during the different time periods.

CONSORT List appropriately reported.

We have added new columns to tables 3 and 4 to show the changes between baseline and the different measurement times. As the number of figures/tables is limited we have decided to improve data in the tables and maintain data there because although figures are more graphic we would be losing data and we think that it is important that both the mean (SD) and mean change (95% CI) appear as data and not a graphic. We have also detailed this further in the headings to differentiate intra and inter-groups

VERSION 2 – REVIEW

REVIEWER	riccardo d'ambrosi italy
REVIEW RETURNED	05-May-2020

GENERAL COMMENTS	authors answered in full to all reviewers queries
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REVIEWER	Efthymios Iliopoulos Brighton & Sussex University Hospitals
REVIEW RETURNED	12-May-2020

GENERAL COMMENTS	<p>The authors have made a significant effort to improve the manuscript. The manuscript has been enhanced significantly and the authors have clarified adequately the points made by the reviewers. Following are some minor comments for the revised manuscript.</p> <p>Abstract Avoid the repetition of the time points the primary and the secondary measures collected.</p> <p>Even though in the main text you have mentioned the differences found between the two groups, this is not shown in the abstract. Please amend the results and the conclusion of the abstract.</p> <p>Article summary The points of the article summary refer to the strengths and limitations of the study, please amend this section to depict the article's summary as a whole.</p> <p>Main text Line 249: No patients were involved. What does this statement mean? The study subjects are patients so to what this statement refers to?</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer (attached pdf)

Abstract: Avoid the repetition of the time points the primary and the secondary measures collected.
Corrected

Even though in the main text you have mentioned the differences found between the two groups, this is not shown in the abstract. Please amend the results and the conclusion of the abstract.

After reviewing the abstract we found that differences between groups were included in the results, but not in the conclusion, so we added it to the conclusion also.

“Both percutaneous needle electrolysis and dry needling were effective for plantar heel pain management, reducing mean and maximum pain since the first treatment session, with long lasting effects (52 weeks) and significant differences between groups in the case of Quality of Life at 52 weeks in favor of the percutaneous needle electrolysis group.”

Article summary

The points of the article summary refer to the strengths and limitations of the study, please amend this section to depict the article's summary as a whole. We have followed the editor's requests on this section, including two more points, but maintaining the strengths and limitations as requested in the Journal guidelines: “An Article Summary, placed after the abstract, consisting of the heading ‘Strengths and limitations of this study’, and containing up to five short bullet points, no longer than one sentence each, that relate specifically to the methods.” As a result of this, we have included these two additional points:

- This is a single center trial and results may not be generalizable.

- Due to the large number of drop-outs, our study had the limitation of being underpowered to report a difference between the two groups.

Main text

Line 249: No patients were involved. What does this statement mean? The study subjects are patients so to what this statement refers to?

This refers to patient involvement in decisions, so we have detailed this a bit more. This is a specific request from BMJ Open Journal (see explanation of patient involvement at <https://blogs.bmj.com/bmjopen/2018/03/23/new-requirements-for-patient-and-public-involvement-statements-in-bmj-open/>)

We included: No patients were involved in the design, recruitment or conduction of this study and the burden of the intervention was not assessed by patients themselves neither.