PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	PREDICTORS OF PAIN REDUCTION FOLLOWING MANUAL THERAPY IN PATIENTS WITH TEMPOROMANDIBULAR DISORDERS: A PROTOCOL FOR A PROSPECTIVE OBSERVATIONAL STUDY
AUTHORS	Asquini, Giacomo; Edoardo Bianchi, Andrea; Heneghan, Nicola R; Rushton, Alison B; Borromeo, Giulia; Locatelli, Matteo; Falla, Deborah;

VERSION 1 – REVIEW

REVIEWER	Mieszko Wieckiewicz Department of Experimental Dentistry, Wroclaw Medical University, Poland
REVIEW RETURNED	13-Jun-2019

GENERAL COMMENTS	Please follow my suggestions: 1. Abstract – you have to calrify it and define the aim of your paper (do the same at the end of introduction). 2. Line 100 – cite papers about prevalence of TMD not only from USA but from different parts of the world. You have to cite latest epidemiological articles. 3. Line 139 - You have to describe precisely what type of mouth appliance you are writing about? 4. Line 176 – Inclusion criterion no. 2, do you want to include all TMD or only a few disease entities? You have to precisely clarify it. TMD is a very wide and imprecise term. 5. Line 183 – Exclusion criterion no. 2 is imprecise. You have to precisely point out all conditions. 6. Line 194 – You wrote that expert dentist with >10 years' experience in the management of patients with TMD, will confirm the TMD diagnosis. You apply DC/TMD therefore you have to clarify how your examiner will be calibrate in DC/TMD. 7. Line 356 – you have to define the limitations of your study much more precisely. 8. Table 1 – I recommend to use another questionnaire to assess sleep quality. In my opinion Pittsburgh Sleep Quality Index (PSQI) is much more professional. Anxiety and depression have to be assess seprately with two different validated questionnaires. Classification of TMD has to be in accordance to DC/TMD taxonomy (Peck C. et al. Expanding the Taxonomy of the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), Journal of Oral Rehabilitation, 2014). Please don't use term parafunctions, I suggest to use term oral behaviours. To describe characteristic pain intensity and disability you have to use the latest version of GCPS (if you use DC/TMD then don't use questionnaires from RDC/TMD).

	In your protocol you have to apply only validated questionnaires. Please take a look at this useful link https://ubwp.buffalo.edu/rdc-tmdinternational/tmd-assessmentdiagnosis/dc-tmd/ You have to also reconsider VAS to assess pain intensity and morning pain intensity after sleeping. The modern science knows better tools to do it. General conclusion after reviewing your manuscript is that you have to very carefully reconsider applied questionnaires and once again think about your study protocol reliability.

REVIEWER	Bartosz Dalewski Pomeranian Medical University in Szczecin, Poland
REVIEW RETURNED	15-Jul-2019

GENERAL COMMENTS	The authors have put tremendous amount of work into preparation of this manuscript. It is well written and very clearly described but still just a study protocol. It is going to be very helpful for researchers undertaking the study, however, at this stage it does not bring anything new into the topic, as it does not scrutinise any data. I would be happy to review a version with results. P37L6 - Fig.1 Palpation test of lateral pterygoid area is a very contested thing as the muscle itself is barely accessible for finger palpation. According to Tanaka even inaccessible. For future purposes and to avoid potential criticism of some reviewers I suggest primarily using a load tests as described in P48L32. However, for scientific purposes comparison of two above factors might shed some new light onto entire issue, so palpation of a spot described at P37L6 could be described as control, or secondary but rather in this sequence (Bumann, Okeson, Rocabado).

REVIEWER	Ajith Polonowita Otago University, New Zealand
REVIEW RETURNED	16-Jul-2019

GENERAL COMMENTS	This will be an interesting study. Authors may want to consider the clinical effect of physical therapy ie local muscle therapy, placebo, neuromodulation ?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Mieszko Wieckiewicz

Institution and Country: Department of Experimental Dentistry, Wroclaw Medical University, Poland

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

Please leave your comments for the authors below

Abstract – you have to clarify it and define the aim of your paper (do the same at the end of introduction).

Thank you for this point, we have clearly defined the aim of our study in the abstract and at the end of the introduction.

Line 100 – cite papers about prevalence of TMD not only from USA but from different parts of the world. You have to cite latest epidemiological articles.

Thank you for this comment. We now cite additional and more recent epidemiological data.

Line 139 - You have to describe precisely what type of mouth appliance you are writing about?

We have added the type of mouth appliance used.

Line 176 – Inclusion criterion no. 2, do you want to include all TMD or only a few disease entities? You have to precisely clarify it. TMD is a very wide and imprecise term.

Thank you for this important point. We will include all patients that are identified according to the DC/TMD. We have modified criterion no.2: ”TMD diagnosis according the Diagnostic Criteria for TMDs (DC/TMD)”.

Line 183 – Exclusion criterion no. 2 is imprecise. You have to precisely point out all conditions.

Thank you for having noted this. We have added a list of specific conditions.

Line 194 – You wrote that expert dentist with >10 years’ experience in the management of patients with TMD, will confirm the TMD diagnosis. You apply DC/TMD therefore you have to clarify how your examiner will be calibrate in DC/TMD.

Thank you for this comment. We have clarified this in the text.

Line 356 – you have to define the limitations of your study much more precisely.

Thank you for this important point. We have expanded the possible limitations in this section.

Table 1:

- **I recommend to use another questionnaire to assess sleep quality. In my opinion Pittsburgh Sleep Quality Index (PSQI) is much more professional.**

Thank you for this suggestion. The Pittsburgh Sleep Quality Index (PSQI) is appropriate to assess sleep quality. However, we include a "sleep quality measure" because of its possible role among other factors in the transition from acute to chronic pain (Sayar et al., 2002). For this purpose, a non-specific scale [this scale - 11point [0-10] Numerical Rating Scales - owns moderate psychometric properties in fibromyalgia patients to assess current sleep quality with a symptom diary (Cappelleri et al., 2009)] could be enough. We therefore would prefer to retain or original measure of sleep quality.

- **Anxiety and depression have to be assess seprately with two different validated questionnaires.**

  Thank you for this comment. This scale assesses Depression and Anxiety separately and produces two different subscales [anxiety: HADS-A; depression: HADS-D] with 7 items and a total score from 0 to 21, with a higher score indicating elevated levels of anxiety and depression (Bjelland et al., 2002).

  HADS has been studied in different groups confirming adequate to excellent internal consistency of HADS-A [0.68-0.93] and HADS-D [0.67-0.90] (Bjelland et al., 2002). The HADS has excellent concurrent validity in comparison to other depression/anxiety scales (Bjelland et al., 2002).

- **Classification of TMD has to be in accordance to DC/TMD taxonomy (Peck C. et al. Expanding the Taxonomy of the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), Journal of Oral Rehabilitation, 2014).**

  Thank you for this comment. We have modified as you suggested.

- **Please don't use term parafunctions, I suggest to use term oral behaviours.**

  Thank you for this comment. We have modified as you suggested.

- **To describe characteristic pain intensity and disability you have to use the latest version of GCPS (if you use DC/TMD then don't use questionnaires from RDC/TMD).**

  Thank you for this comment. We have modified as you suggested.

- **In your protocol you have to apply only validated questionnaires. Please take a look at this useful link https://ubwp.buffalo.edu/rdc-tmdinternational/tmd-assessmentdiagnosis/dc-tmd/**

  Thank you for this helpful suggestion.

- **You have to also reconsider VAS to assess pain intensity and morning pain intensity after sleeping. The modern science knows better tools to do it.**

  Thank you for this point. We have now eliminated the candidate predictor "*Morning pain intensity after sleeping*" from the protocol.

General conclusion after reviewing your manuscript is that you have to very carefully reconsider applied questionnaires and once again think about your study protocol reliability.

Thank you agian for your comments and suggestions.

Reviewer: 2

Reviewer Name: Bartosz Dalewski

Institution and Country: Pomeranian Medical University in Szczecin, Poland

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

Please leave your comments for the authors below

The authors have put tremendous amount of work into preparation of this manuscript. It is well written and very clearly described but still just a study protocol. It is going to be very helpful for researchers undertaking the study, however, at this stage it does not bring anything new into the topic, as it does not scrutinise any data. I would be happy to review a version with results.

Thank you for this kind feedback, we are also very interested to see the results of the study.

P37L6 - Fig.1 Palpation test of lateral pterygoid area is a very contested thing as the muscle itself is barely accessible for finger palpation. According to Tanaka even inaccessible. For future purposes and to avoid potential criticism of some reviewers I suggest primarily using a load tests as described in P48L32. However, for scientific purposes comparison of two above factors might shed some new light onto entire issue, so palpation of a spot described at P37L6 could be described as control, or secondary but rather in this sequence (Bumann, Okeson, Rocabado).

Thank you for this important point. We have added more information about the the feasibility of the lateral pterygoid muscle palpation. In addition, we have decided that this parameter [pain at lateral pterygoid site from a load tests(<0,5 kg)] will not be considered alone but in combination with pain at other muscular sites.

Reviewer: 3

Reviewer Name: Ajith Polonowita

Institution and Country: Otago University, New Zealand

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

Please leave your comments for the authors below

This will be an interesting study. Authors may want to consider the clinical effect of physical therapy ie local muscle therapy, placebo, neuromodulation ?

> Thank you for your feedback. The aim of this study is to identify predictors associated with pain reduction in patients with TMD following manual therapy by analysing combination of patient-reported outcome measures and clinical tests. Such knowledge will support a more personalised management approach by facilitating clinical decision-making.

VERSION 2 – REVIEW

REVIEWER	Mieszko Wieckiewicz Wroclaw Medical University, Poland
REVIEW RETURNED	11-Oct-2019

GENERAL COMMENTS	I have concerns about abstract and conclusions. Presented abstract has to contain short background (introduction), aim of the study, material and methods and conclusions. At the end of the manuscript conclusions are not justified by the results (page 15). Therefore you have to rewrite this section according to this definition "When you write a paper, you always end by summing up your arguments and drawing a conclusion about what you've been writing about.". It's mean that you have to summing up your results but not present results again.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Mieszko Wieckiewicz
Institution and Country: Wroclaw Medical University, Poland Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below I have concerns about abstract and conclusions. Presented abstract has to contain short background (introduction), aim of the study, material and methods and conclusions.

Reply:
Since this is a protocol paper and not reporting the findings of the study yet, we have followed the appropriate headings for a protocol paper. When the results of the study are published the abstract will of course follow the more conventional abstract format including Background, Aims, Methods, Results, Discussion/Conclusion.

At the end of the manuscript conclusions are not justified by the results (page 15). Therefore you have to rewrite this section according to this definition "When you write a paper, you always end by summing up your arguments and drawing a conclusion about what you've been writing about.". It's mean that you have to summing up your results but not present results again.

Reply: This is a protocol paper, and as such, there are no results yet to report. We have revised the conclusion to specifically indicate that this is a protocol paper which describes what will be the first study to identify factors associated with pain reduction following manual therapy in patients with TMD. It is anticipated that the knowledge gained from the study described within this protocol, will facilitate clinical decision making for manual therapists managing patients with TMD.

We hope that we have now better clarified these concerns and thank you Reviewer again for the time spent reviewing our work.