Reviewer’s report

Title: A comparison of isometric, isotonic concentric and isotonic eccentric exercises in the physiotherapy management of subacromial pain syndrome/rotator cuff tendinopathy: study protocol for a pilot randomised controlled trial.

Version: 0 Date: 15 Feb 2017

Reviewer: Gregory Parkin-Smith

Reviewer’s report:

PAFS-D-17-00006

Comparison of isotonic (concentric and eccentric) and isometric exercises in the treatment of patients diagnosed with rotator cuff tendinopathy/subacromial pain syndrome: feasibility study protocol for a randomised controlled trial.

Rita Kinsella, BSc (Hons), MMACP; Sallie M Cowan, PhD, Grad Dip (Manip Physiotherapy); Lyn Watson, Grad Dip (Manip Physiotherapy); Tania Pizzari, PhD

Pilot and Feasibility Studies

Review of Paper

Abstract

A well-written abstract that contains the needed information to inform the reader about the intended pilot study, the main goals being (a) determining the feasibility of a future trial and (b) treatment effects.

The following are suggestions to improve the Abstract:

* Line 38: the authors state the study is to determine "feasibility" but it is unclear what "feasibility" is or how it is define. A sentence here on indeed how feasibility is measured/determined would be useful to inform the reader;

* Line 41: the authors indicate that this pilot study will determine the "treatment effects". Pilot studies are not fully powered to determine treatment outcomes or effects, and inferential statistics should be used with great caution. I understand that the authors wish to explore possible outcomes, but should clearly understand the limitation of pilot studies and that one cannot draw definitive conclusions from pilot study outcomes. Rather state that the analysis will offer insights into possible outcomes and guide the design of future studies. A very useful reference to read related to this is:


* Line 44: the sample size of 36 is indicted. I assume that this sample size was estimated using some list of criteria, or was it arbitrary? Note that performing inferential statistics on a total sample size of 36 (12 per group over 3 groups) very unlikely to offer meaningful results, so the authors should consider outcomes with great caution and should not be the focus of this pilot study;

* Line 51: the authors state the outcome measures being used. It would be useful for the authors to divide the outcome measures into primary outcome measures and secondary outcome measures, based on the clinical importance or clinical relevance of each outcome measure. This pilot study would then focus on using the primary outcome measures to inform the design of a future study and the data from these primary outcome measures could be used to estimate or calculate the sample size needed for a future definitive study (based on calculated effect size). I am assuming that sample size estimates will be discussed in the body of the paper;

* Line 56: Key words. Limit to 5 key words. Also, I did a key words search using Mesh Heading on PubMed, but the key words provided do not seem to match with Mesh Headings. It is best practice to choose keywords that are also mesh Heading or some type in the main databases. For example, the term "subacromial pain syndrome" may be replaced with a Mesh Term that is the same thing (from PubMed) -

*Shoulder Impingement Syndromes

*Rotator Cuff Impingement Syndrome

*Rotator Cuff Impingement

*Impingement, Rotator Cuff

*Impingements, Rotator Cuff

*Rotator Cuff Impingements

*Coracohumeral Impingement Syndrome

*Impingement, Posterosuperior Glenoid

*Impingements, Posterosuperior Glenoid
*Posterosuperior Glenoid Impingements*

Background & Aims

* The authors offer a convincing literature review in support of the pilot trial, and common sense tells us that isometric exercises would be useful in patients where their shoulder pain would prohibit full range-of-motion exercises;

* Line 96: I can't help but feel that high-load isometric exercises may lead to tearing of relevant rotator cuff muscles. How would this risk be reduced or mitigated? A brief sentence here would be informative;

* Line 108 and line 111: the authors again use the terms "feasibility" and "treatment effects. What is mean by "feasibility" and what are the criteria to determine feasibility? This is critically important to elucidate at this point in the paper. There are many aspects that would either make a study "feasible" or "unfeasible" e.g. resources, access to patients, staffing, and funding is probably the most important. These aspects of feasibility need to be offered and described in this paper;

* Line 115 and line 119: the author's state hypotheses, which implies that this pilot study intends to perform hypothesis testing using inferential statistics. I am not opposed to a degree of statistical testing in pilot studies with a view to offer insights into outcomes, but formal inferential statistics to determine outcomes should be avoided, as explained by Lancaster et al. (reference earlier). The sample size and poor Power of this pilot study would exclude the ability to offer meaningful and valid outcomes. This paper should be tempered by focusing the aims at feasibility and less so at hypothesis testing/treatment outcomes;

* The last section of the Background, lines 108 to 120, should be re-written with the view to provide the Aims and Objectives:

  o Primary Aim....

  o Secondary Aim...

  o To achieve these aims the objectives are to: Objective 1.... Objective 2.... And so on

* I note that there is no aim to examine, explore or evaluate the research design and process e.g. evaluation of the randomisation process, flow of patients, staff acceptance of the research design and process, and so forth. These elements are critical to the feasibility and design of a definitive study, particularly a RCT, and should thus receive attention in the write-up of a pilot study or a pilot study protocol;

Methodology
The description of the study is good and registered with ANZCTR.

Line 138: the authors offer a rationale that a minimum of 30 subjects per group would be required for a definitive, fully powered RCT. Although this estimate is based on a published trial, the sample size is very low and, in my view, unlikely to offer robust data for a full-scale RCT as suggested. Calculated sample sizes for musculoskeletal disorder RCT are usually underestimated and a sample size per group of around 120 is more likely to offer valid and reliable data in a definitive clinical trial. The minimum sample per group in a decent pilot trial is generally considered to be 30 /group, so the authors need to think carefully about the sample size per group chosen for their study (at 12 per group). Julious et al (2005) offers justification for a sample size per group as low as 12, but this is within the context of highly controlled laboratory or pharmaceutical settings, and does not account for the variance found in real-life clinical practice (Julious, Steven A. "Sample size of 12 per group rule of thumb for a pilot study." Pharm Stat 4, no. 4 (2005): 287-291). If the authors are going to stick to their stated sample size then a stronger argument is needed to support the sample size, particularly since a great deal of the inferences will be drawn from hypothesis test and outcomes. Amorin-Woods et al. (2016) paper offers a good approach to pilot study design (Lyndon G. Amorin-Woods, Lee Nedkoff, Gregory F. Parkin-Smith, and Colleen Fisher. "The Design of a Practice-based Study of Attendees at Chiropractic Offices in Western Australia." (2015).

The authors provide a good set of inclusion and exclusion criteria;

Line 156: an exclusion criteria is GHL and/or AC joint moderate-severe degeneration, which is quite sensible, but I do think that all participants would need a recent x-ray (if they do not have one) to determine the extent of degeneration. This would ensure consistency and reliability on the recruitment process;

Line 164: the authors indicate that inclusion/exclusion would be primarily based on clinical decision-making. Of course, clinical decision-making is essential in reaching any diagnosis, but for a study to be replicated and the process to be reliable, it is better to have a clear decision-making process. In this regard, a decision-making algorithm that guide diagnosis and inclusion would be useful for this pilot trial. This tried algorithm could then be used as reliable method of decision-making in a future definitive study. Such an algorithm would be appreciated by participating practitioners/clinicians;

The description of patients and recruitment is good. Any particular active recruitment or advertising planned?

Line 198: the authors offer the criteria for feasibility in this section, which appear sensible - (a) ease of recruitment (b) adherence to treatment, (c) non-compliance/drop-out, and (d) adverse events. These are entirely appropriate, but there is very little justification or expansion on these feasibility criteria in the paper. The authors should offer some benchmark or threshold levels for each criterion, which in turn would inform the authors/reader if a future study is indeed feasible. For example, what does "ease of recruiting mean" - 1 recruit per day? 10 per fortnight? To what degree do the participants need to be non-adherent before they are excluded? What adverse events would exclude them from the study, or is this about serious
adverse events? The devil is in the detail here, which I turn will inform the authors if a future definitive trial is feasible, more so than the treatment outcomes themselves;

* The secondary outcomes are well written and clear. There is a major focus on clinical outcomes, but I am still sceptical due to the sample size of 12 per group, which is small. Is this pilot study an "external" or an "internal" pilot study? If it is planned as an internal pilot study, the study may be able to just continue on and recruit a few more patients per group, say up to 20 per group, as part of the pilot component;

* The treatment intervention are described clearly and this section is good, since it spells out clearly what is to happen at each treatment/intervention session. The number of supervised sessions and home-exercise sessions are reasonable and are sufficient to produce a possible treatment effect;

* Line 290: the authors indicate that manual therapies may be included in treatment, but not always. Manual therapies, such as joint mobilisation, soft-tissue work/stretching, trigger point therapy and joint manipulation, may all have a therapeutic effect and thus confound the outcomes and negatively influence decision-making as to whether the isometric exercise specifically and discretely is having any meaningful effect. I would exclude any kind of manual therapy in the study as part of treatment - if manual therapy is included in some way, it changes the whole focus of the study and the study aims, so should not be included;

* Line 305: the level of significance is stated as p<0.5. Is this correct? Usually, the level of significance is <0.05 and the way it is written is "level of significance of p<0.05" or "α=0.05". A p-value of <0.5 is very high and may not be very meaningful - that said even p=0.1 is sometimes reasonable;

* Line 305: there is not much detail here regarding the anticipated statistical analysis. Please elaborate more on aspects such as: what type of data is expected, who will the data be organised and tabulated, who will do the statistical analysis, why is the proposed analysis and statistics chosen, how will the results be interpreted, will there be consensus agreement related to the results/outcomes?

* I note there is no mention of sample size calculations or estimated in the methods section for a definitive study. This is a critical component to a pilot study and the methods that are anticipated to be used to calculate the sample size of a future definitive study should be provided. A great deal is published on sample size estimated/calculations, but at least a brief description and anticipated calculations should be offered in this paper.

Overall, a well-written paper that contains the main elements of a pilot study. However, the authors need to expand on various aspects, as described previously, to make it a robust and meaningful pilot study.

**Level of interest**

Please indicate how interesting you found the manuscript:
An article of importance in its field

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license ([http://creativecommons.org/licenses/by/4.0/](http://creativecommons.org/licenses/by/4.0/)). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal