Study Protocol

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Home-based exercise programmes for individuals with intermittent claudication: A protocol for an updated systematic review and meta-analysis

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Abstract

Background: The aim of this updated review is to consider the evidence base for the effectiveness of home-based exercise programmes as a treatment option for improving walking distance in patients with intermittent claudication.

Methods: The Medline, EMBASE, CINAHL, PEDro and Cochrane CENTRAL databases will be searched for terms including 'intermittent claudication', 'peripheral arterial disease', 'home-based exercise' and 'home-based walking'. No date restrictions will be used but only articles in the English language will be included. Both randomised and non-randomised trials of home-based exercise programmes versus a comparator arm will be included, and a meta-analysis using only the randomised controlled trials will be attempted if the assumptions of heterogeneity are met. Data extraction will include study details, sample description, intervention description, length of follow-up and outcomes measures. The primary outcome measure is objectively measured maximal walking distance or time, with secondary outcome measures including pain-free walking distance or time, changes in physical activity and quality of life. We will also provide a narrative description of the effective components of a home-based exercise intervention which can aid future recommendations.

Conclusion: Overall, this proposed review and meta-analysis aims provide a comprehensive and complete overview of the evidence base for home-based exercise programmes, which can aid clinicians in the management of their patients.

Keywords

Intermittent claudication, peripheral arterial disease, exercise, home-based, walking, community

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Introduction and rationale

Peripheral arterial disease (PAD) is categorised by stenotic or occlusive atherosclerotic lesions in the arteries that supply the legs, limiting blood flow.[1] The incidence of PAD increases with advancing age and large-scale global estimates demonstrate that it affects 1 in 10 over the age of 70 years and 1 in 6 over the age of 80 years.[2] The main symptomatic manifestation of PAD is intermittent claudication (IC), which is a reproducible ambulatory lower limb muscle pain, relieved by rest, that occurs due to an oxygen supply and demand imbalance.[3,4]

IC can impede daily activities, functional capacity and quality of life (QoL) while also carrying an increased mortality risk.[3–7] These impediments can cause a cycle of disability; as pain increases with walking, patients walk for shorter distances, leading to muscle atrophy and a further reduced walking capacity.[8]

First-line treatment for IC is a supervised exercise programme (SEP) which ideally includes 2 h of supervised exercise per week for 12 weeks, whereby patients are encouraged

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to walk to the point of maximal pain.[9] There is overwhelming evidence that exercise programmes are of significant benefit for improving walking time and distance in those with IC, as demonstrated in a recent Cochrane review.[10] This benefit is obtainable from low or higher intensity supervised walking or differing modes of exercise (e.g. cycling).[11,12]

Despite its benefits, a recent systematic review found that approximately 1 in 3 IC patients screened were suitable and willing to join a SEP, suggesting it is underutilised.[13] Furthermore, research has shown that not all NHS Vascular units have access to a SEP.[14] Consequently, there has been an increased interest in home-based exercise programmes (HEPs). A recent Cochrane review in 2018 considered supervised exercise versus home-based exercise versus walking advice for IC which demonstrated that HEPs were inferior to SEPs for improving walking distance at 3 months.[15] The HEP group also did not show significant improvements in maximum walking distance (MWD) when compared to the walking advice group. However, the differences in increased MWD elicited by the SEP group was 210 m versus the walking advice group, but lower at 120 m versus the HEP group, suggesting HEPs may be more beneficial than walking advice.[15] Another systematic review published in 2013 demonstrated that there was low quality, preliminary evidence that HEPs can provide an improvement in walking capacity and QoL in IC patients.[16] However, the evidence also suggests that these improvements may be inferior to those seen with SEPs. The review concluded that more robust trials are required to build the evidence base for HEPs in patients with IC, which should have prompted further research.[16] Therefore, this protocol, written in accordance with PRISMA-P guidelines,[17] proposes to update the previous systematic review. The aim of this updated review is to consider the effectiveness of HEPs as a treatment option for improving walking distance or time in patients with IC.

Our proposed review differs to the aforementioned Cochrane review as this only included studies that had a SEP as one comparator arm, whereas we will include studies that compare a HEP with any comparator arm, such as walking advice and a no exercise control, rather than a SEP. In addition, we will consider changes in physical activity as an outcome measure and identify the components of an effective intervention to help provide guidance on an effective HEP programme that can be used in practice. Finally, the search for the Cochrane review was concluded in December 2016, meaning that any articles published after this date will not be encompassed in their results.

Methods

Search strategy and inclusion criteria

Prospective non-randomised and randomised controlled trials (RCTs) that consider the effect of a home-based exercise regimen versus a comparator arm (SEP, exercise advice or no exercise control) on walking distance or time for patients with IC will be included. In contrast to the previous review, in order to maximise data, studies that include other PAD subgroups (i.e. asymptomatic or atypical leg pain) in addition to IC will be included, only if the data on the IC subgroup can be obtained. Other PAD subgroups will not be included as SEPs are only currently recommended for the treatment of IC, with HEPs being a potential alternative.

The HEP intervention will include structured advice to increase physical activity by guiding patients in terms of frequency, intensity and/or duration rather than basic advice 'to go home and walk'. Patients may be monitored via use of pedometers, accelerometers, physical activity monitors, exercise diaries or any combination thereof. Encouragement can also be provided by regular supportive interactions, such as telephone calls or visits either at home or at the research centre. However, in line with previous research, active monitoring for HEPs will be limited to a maximum of two interactions per week.[18] For comparator arms, SEPs will be defined as any actively supervised exercise regime for the treatment of IC regardless of the duration, frequency or intensity of the programme. The exercise advice group will be defined as patients who are encouraged to walk more at home, without receiving specific recommendations for an exercise regimen. The no exercise control group will consist of those who either receive no exercise-specific advice or are told to maintain their usual physical activity levels.

The original search strategy searched four databases for terms including 'peripheral arterial disease' [AND] 'self-management' [AND] 'exercise' and yielded 311 results. The proposed search will build on this and include five databases (CINAHL, PEDro, Medline, EMBASE and Cochrane CENTRAL) and a wider range of search terms (draft search included in Supplemental Appendix 1). Although it was included in the previous review, the PsychINFO database will not be searched as it was not considered an appropriate for the context of the current review. In addition, trial registers such as clinicaltrials.gov and the web of science conference proceedings will be searched and authors of any relevant protocols and conference abstracts will be contacted to obtain study outcome reports where possible. As the proposed search differs from that of the original review, no date restrictions will be applied to ensure that any studies not encompassed in the previous search will be retrieved and only studies published in the English language will be included.

Data management, selection and collection process

Titles and abstracts identified by the database search will be interrogated for potential eligibility by two independent reviewers. The full-text of these potentially eligible studies will be obtained and further interrogated for inclusion. Reference lists of any screened full-texts will also be hand

searched for other relevant papers. Any disagreement between the two reviewers in terms of inclusion will be resolved by consensus with a third.

Data extraction will then be performed by two reviewers using a standardised form, which will then be inputted and managed using a Microsoft Excel database (Microsoft, 2010, Redmond, WA, USA). Data regarding search hits, duplicates and included and excluded (with explanation) studies will also be recorded in the database to allow creation of the PRISMA flow diagram.[19] Data extraction will include study characteristics (country, design and appropriate information to assess the quality of the study), sample size and description, a description of the intervention and control conditions, outcome measures, length of follow-up and main findings related to outcome measures (sample data extraction sheet shown in Supplemental Appendix 2).

Outcome measures

The primary outcome will be objectively measured (via either treadmill or corridor-based tests) MWD or maximum walking time (MWT). Secondary outcomes measures (where reported) will be objectively measured pain-free walking distance (PFWD) or pain-free walking time (PFWT), health-related QoL, assessed using validated disease specific or generic scales such as the short-form 36 (SF-36) and changes in physical activity, either objectively measured or self-reported. PFWD/PFWT will be defined as the time or distance where the patient first experiences leg pain during the walking test and MWD/MWT will be defined as the time or distance at which the patient can no longer continue walking due to maximal pain. These outcomes have been selected as the previous review demonstrated that there was low-level evidence to suggest that HEPs can improve walking capacity and QoL in patients with IC, while physical activity has also been selected to establish any potential lifestyle changes as a result of the HEP.

Risk of bias and rating the quality of evidence

Risk of bias in individual studies will be assessed using the Cochrane collaboration tool which includes six domains.[20] Information will be extracted from each study and a judgement made for each domain that will be either 'high risk', 'low risk' or 'unclear risk' if sufficient detail is not provided. In the case of 'unclear risk' study, authors will be contacted for more information. A justification statement will be given for each risk domain, describing the methods utilised in each study, using verbatim quotes where possible as recommended in the Cochrane handbook.[20] Two independent reviewers will assess the risk of bias and discuss any disagreements. Consensus with a third reviewer will be sought should an agreement not be reached.

Quality of evidence will be assessed by two independent reviewers using the GRADE approach.[21] Initial assessment will be made based on design and will then be revised (upgraded or downgraded) based on the following criteria: risk of bias, inconsistency, indirectness, imprecision and publication bias.[21] Quality level is then categorised based on this revision as high (very confident that the true effect lies close that of the estimate of effect), moderate (true effect is likely to be close to the estimate of the effect, but may be substantially different), low (true effect may be substantially different from the estimate of effect) and very low (true effect is likely to be substantially different from the estimate of effect).[21]

Data analysis and synthesis

To increase the scope of this systematic review, both RCTs and non-RCTs will be included and a narrative synthesis of non-RCTs produced. In an attempt to overcome the heterogeneity that previously precluded it, we propose to undertake a meta-analysis using only the included RCTs. Meta-analysis will be performed using Review Manager 5 (RevMan 2014), to produce forest plots with an overall effect estimate and associated 95% confidence intervals. An element of heterogeneity is likely across studies due to possible differences in the types of interventions and outcomes reported.[22] Substantial heterogeneity will be considered present if the I^2 is $>50\%$ and the p value for the Chi^2 test is <0.10. Should substantial heterogeneity not be present, data will be pooled and a meta-analysis performed using a fixed-effects model. However, if substantial heterogeneity is found, this will be evaluated based on the cause and one of two courses of action will be taken. Should it be felt that the heterogeneity is unexplained, a meta-analysis will be performed using a random-effects model as this considers heterogeneity in the effect estimate.[22] It does not however remove it and the heterogeneity will be considered during interpretation of results. Furthermore, should meta-analysis be deemed appropriate, the robustness of the findings will be determined via sensitivity analysis. For this, we will alter the dataset by removing RCTs of lower quality based on the risk of bias assessment and repeating the analysis.[23] If the analysis is robust, the change in outcomes should be minimal.[23]

However, should heterogeneity be caused by an identifiable reason, such as clear differences between interventions, data will not be pooled for meta-analysis as this may provide misleading results.[22] In this case, as with the previous review, a narrative approach will be used and between-group effect sizes for MWD or MWT calculated.[16]

Results will be presented as a head-to-head analysis of the effectiveness of HEPs versus each comparator arm. It is therefore anticipated that results will be presented as HEPs versus SEPs, HEPs versus exercise advice and HEPs versus no exercise control. In addition, should adequate data be available, subgroup analysis of HEPs will be performed on the basis of monitoring, gender, comorbidities (such as diabetes and coronary heart disease) and disease severity

(categorised by ankle brachial pressure index or Rutherford/Fontaine classification). This will allow us to identify the effect of these factors on outcomes follow HEPs.

We will also provide a narrative description of the components of effective HEP interventions, such as the volume of exercise or the use of dietary and lifestyle advice and psychological components. Effective HEP interventions will be identified as those that induce a significantly greater change ($p \leq 0.05$) for at least one outcome, when compared with the exercise advice or no exercise control comparator groups. For trials comparing SEP and HEP, without a third no exercise control or exercise advice comparator group, the HEP intervention will be considered effective if it induces a significant positive change from baseline ($p \leq 0.05$).

Discussion and conclusion

This article proposes an update of a 2013 systematic review which considered the role of HEPs for patients with IC. The previous review should have prompted further research by suggesting more robust trials are needed to build an appropriate evidence base for HEPs in IC.[16] This renewed evidence base was evaluated in an updated Cochrane review which demonstrated that HEPs were markedly inferior to SEPs for improvements in MWD and PFWD at 3 months.[15] Our proposed review differs from this Cochrane update as it will include, rather than exclude, studies that use a no exercise control group, thus evaluating the benefit of HEPs versus control. Although guidelines do recommend walking advice in the treatment of PAD, meaning studies including no exercise advice may not exist, a preliminary search has revealed at least two potentially eligible articles that include groups of this nature.

There are possible limitations that may occur within the proposed review. The original review published in 2013 noted that heterogeneity precluded meta-analysis, which may be the case for the proposed review. Although we will still include both randomised and non-randomised trials to enhance the scope of this review, we aim to overcome the problem of heterogeneity by only including RCTs in the proposed meta-analysis.

In addition, as further research was only prompted by the previous review in 2013, it is possible that some trials are still ongoing or data are yet to be published. Although we hope to minimise this possibility by searching clinical trial registers and contacting authors for study outcomes where possible, we cannot eradicate it as some trials may not be registered.

Overall, this proposed review seeks to consider the renewed evidence base for the effectiveness of HEPs as an alternative treatment option for IC, by performing an update of a previous review and furthering it by performing a meta-analysis of the included RCTs, based on heterogeneity. The inclusion of both randomised and non-randomised trials, while also performing a meta-analysis of RCTs, will provide a comprehensive and complete overview of the evidence base for HEPs, which can aid clinicians in the management of their patients. In addition, by outlining the effective components of an intervention, this review can aid exercise professionals to design and implement a structured, evidence-based HEP for those IC patients unable to attend SEP.

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Supplemental material

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