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Clinical effectiveness of manipulation and mobilisation interventions for the treatment of non-specific neck pain: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Non-specific neck pain (NSNP) is a common musculoskeletal condition resulting in pain, physical limitations and associated functional disability. Current guidelines recommend manipulation and/or mobilisation as part of the multimodal management of NSNP. This study focuses on intervention at the articular level and aims to identify whether joint mobilisation or joint manipulation has a greater effect on function, range of movement or pain outcomes in the management of NSNP.

Methods and analysis A systematic review protocol has been designed and is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols. A targeted search strategy will enable searching of key databases from inception to 31 March 2020: CINAHL, PEDro, AMED, EMBASE, OVID, MEDLINE, Web of Science, PubMed and Google Scholar. Key journals will be searched using predefined keywords determined from preliminary scoping searches for randomised controlled trials of manipulation and mobilisation modalities for adults with NSNP in the absence of radiculopathy or whiplash, published in English. Grey literature and unpublished studies will also be searched. Studies will be screened by title and abstract and full text. Two independent reviewers will conduct the searches independently, extract data, assess risk of bias (Cochrane Risk of Bias Tool 2) and assess overall strength of evidence (Grading of Recommendations, Assessment, Development and Evaluation). Meta-analysis will be performed where individual studies measure comparable outcomes including performance-based outcome measures such as range of movement or patient reported outcome measures such as Neck Disability Index; and where interventions are comparable in their delivery such as number of oscillations and Maitland grading. Where not possible, data will be presented descriptively.

Ethics and dissemination This study does not require ethical approval. Findings will be submitted for publication to relevant peer-reviewed journals and will be presented at profession-specific conferences.

PROSPERO registration number CRD42020164457.

Strengths and limitations of this study

- This systematic review protocol has been designed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols and is registered on PROSPERO.
- The Cochrane Risk of Bias Tool 2 will be used to assess risk of bias of included trials by two reviewers.
- Grading of Recommendations, Development and Evaluation will be used to assess overall strength of evidence.
- By isolating the individual component that is, mobilisation and manipulation techniques from the multimodal treatment of non-specific neck pain, it is hoped that this review may reveal which technique yields the greatest change in outcomes.
- A potential limitation is that heterogeneity of interventions and outcomes may limit possible meta-analyses.

INTRODUCTION

Rationale

Neck pain is one of the biggest contributors to musculoskeletal disability, with a prevalence ranging between 16% and 75% worldwide,[1] impacting on the physical, social and psychological well-being of an individual, as well as imparting domestic and socioeconomic implications on society and business.[2] The global incidence of non-specific neck pain (NSNP) in the adult population is 4.9%, with the highest incidence in North America (mean 6.5%) followed by Western Europe (mean 6.3%).[3] Neck pain is the fourth greatest cause of global disability[4] and affects between 30% and 50% of adults in any given year.[5] Given the prevalence of neck pain, it is likely that most adults will experience neck pain at some point in their life.

NSNP is defined as pain or discomfort in and around the neck and shoulder girdle, with or without pain or sensory changes into the arms,[6] with or without the loss of cervical range of movement (ROM)[7] in the absence of infection, inflammatory or structural pathology (eg, fracture).[8] Although the specific aetiology of NSNP is not known, it is considered largely multifactorial in nature, with poor posture, occupational activity, sporting activities, depression and mechanical injuries such as strains being cited.[9] Based on the work of Kjaer *et al*,[10] current clinical guidelines for NSNP[11] recommend a multimodal approach to management including stretching, ROM exercises and manual therapy.

It is generally accepted that a multimodal approach is the most effective way of managing NSNP to include exercise, postural advice, manual therapy and acupuncture to name a few. There is little evidence about the efficacy of individual manual therapy interventions, and comparative clinical effectiveness in reducing pain and disability. Manual therapy interventions are used for people with NSNP with the aim of providing pain relief and restoring cervical ROM.[12] Commonly used techniques directed at the articular structures are mobilisations of varying amplitude and manipulation. Mobilisations are passive accessory oscillations applied to the vertebral joints along the plane of movement.[13] Manipulation has been defined as a high velocity, low amplitude, thrust manoeuvre applied in a perpendicular direction to the intended joint in order to engender movement at that joint, resulting in cavitation and surface separation of articular surfaces,[14] however there are studies which describe manipulation is other combinations of movement and direction of thrust.[15] The theory of surface separation has been demonstrated by computational vector analysis of forces software,[15] however there remains no evidence to show the real-time effects of joint separation, postulated to occur during manipulation.

Recent systematic reviews have identified that manipulation or mobilisation coupled with exercise is effective for the management of NSNP, but to date there is little evidence on the comparable effects of manipulation versus mobilisation.[16] Existing evidence of manual therapy compares manipulation to other inert modalities such as placebo and sham,[17] but few studies directly compare manual therapy modalities without additional interventions such as exercise. Current recommendations for manual therapy include thoracic and cervical manipulation or mobilisation,[10] however there is no consensus on which is most efficacious in treating NSNP. This information would be valuable to informing best multimodal intervention packages. This study therefore aims to identify whether joint mobilisation or joint manipulation has a greater effect on function, range of motion or pain outcomes in the management of NSNP.

Objectives

1. To evaluate the effectiveness of manipulation intervention for NSNP on function, ROM and pain outcome measures.
2. To evaluate the effectiveness of mobilisation intervention for NSNP on function, ROM and pain outcome measures.
3. To evaluate whether there is a difference in outcome between manipulation and mobilisation interventions for NSNP on function, ROM and pain outcome measures.

METHODS

Design

A systematic review and meta-analysis will be conducted in accordance to this predefined protocol that is reported according to the Preferred Reporting Items for Systematic Reviews and Meta Analyses Protocols (PRISMA-P) checklist. The systematic review will be reported in line with the PRISMA statement and flow diagram.[18]

Eligibility criteria

Studies selected for inclusion will meet the following PICOS criteria.[18] Studies not written in English will be excluded.

Population

Inclusion criteria: adults (>18 years) experiencing NSNP of any duration of symptoms, with or without loss of range of movement.[12]

Exclusion criteria: radiculopathy, whiplash, inflammatory arthropathy, history of cervical surgery, myelopathy or other red flag symptoms, interventions in addition to manipulation or mobilisation.

Intervention

Objective 1: eligible studies will describe manipulative techniques of the thoracic or cervical spine, where manipulation is specifically a high velocity, low amplitude manoeuvre directed at the spine, classified as grade V or a thrust technique.

Objective 2: eligible studies will describe mobilisation techniques that involve a localised passive force delivered to the joint at a specific vertebral level, classified as grades I–IV depending on their amplitude within the joint's normal physiological ROM.

Comparator

Comparator studies can include placebo, sham or inactive controls.

Outcome measures

Any continuous or dichotomous patient-reported or performance-based outcome measure evaluating function, range of movement and pain. Eligible outcome measures include, but are not limited to: Neck Disability Index (NDI); Neck Pain Questionnaire; quality of life scores such as SF-36, Neck Pain and Disability Scale or

Visual Analogue Scale pain score (or equivalent numeric rating scale) or ROM, which are validated, reliable and sensitive to change. Outcome measures will not be limited due to preliminary scoping searches showing few studies within the eligibility criteria.

Study design

Randomised controlled trials (RCTs), controlled clinical trials and cross-over trials will be eligible. Pilot and feasibility studies will not be included, where a feasibility study is defined as a preliminary study used to ascertain the best method by which a future study should take place, and a pilot study is defined as a small-scale study to test a research protocol, its data collection methods, sample, data handling tools, population and recruitment strategies in preparation for a larger scale study.[19]

Studies that directly compare manipulation or mobilisation will be included. Studies including other arms to trials such as acupuncture or exercise will be included where data are available per treatment arm. Studies with multiple arms will be considered if the interventions are in conjunction with the same additional modality, for example mobilisation plus exercise versus manipulation plus exercise, as long as the additional components are the same in terms of type and frequency.

Information sources

The search will use a sensitive subject and topic-based strategy from inception to 31 March 2020. Databases searched will be CINAHL, PEDro, AMED, EMBASE, OVID, MEDLINE, Web of Science, PubMed and Google Scholar. Manual searches of key journals for relevant articles, articles in press or published ahead of print will include Musculoskeletal Science & Practice, European Spine Journal, Journal of Orthopaedic & Sports Physical Therapy, Journal of Manual & Manipulative Physiotherapy, and Spine. Grey literature will be searched in Zetoc, Open Grey and British National Bibliography.

Search strategy

Searches will be performed independently by primary and secondary reviewers (EB and NJC, respectively), both practising musculoskeletal physiotherapists. Databases will be searched using keywords and combinations of predefined keywords and search strings, tailored to each database. An example search strategy is shown for MEDLINE in box 1. Keywords will be grouped together by category (outcome measure, dysfunction, design, intervention) using boolean operators AND/OR/NOT and combined across categories to increase the sensitivity of the search (box 1). Modifications of keywords will take place to account for alternative spellings and synonyms used interchangeably (ie, manipulation and "high velocity thrust" or HVT); keywords are detailed in table 1.

Study records

Data management

Records of selected studies will be managed in Microsoft Word for Mac (V.2018) and EndNote V.X9 (2018).

Box 1 Example of simple search of keywords in MEDLINE including search term combinations at lines 15, 28, 33, 47 and 48

Database: Ovid MEDLINE(R)<1946 to June Week 2 2020>

Search strategy:

1. neck pain.mp. or Neck Pain/ (10870)
2. cervicodynia.mp. (9)
3. cervical pain.mp. (850)
4. cervicalgia.mp. (113)
5. neck strain.mp. (43)
6. neck ache.mp. (26)
7. arthralgia.mp. or Arthralgia/ (13035)
8. myalgia.mp. or Myalgia/ (7409)
9. spondylosis.mp. or Spondylosis/ or Cervical Vertebrae/ (37321)
10. neck injury.mp. or Neck Injuries/ (5362)
11. neck dysfunction.mp. (81)
12. cervical spine.mp. (19137)
13. stiffness.mp. (54668)
14. neck disorder.mp. (31)
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 (127655)
16. neck disability index.mp. (1519)
17. neck disability questionnaire.mp. (3)
18. neck outcome score.mp. (4)
19. short form 36.mp. (8906)
20. outcome measure.mp. (54940)
21. disability.mp. (202611)
22. range of motion.mp. or "Range of Motion, Articular"/ (62641)
23. range of movement.mp. (2477)
24. VAS.mp. (41624)
25. Pain/ or Pain Measurement/ or visual analogue scale.mp. (205951)
26. NRS.mp. (5594)
27. Pain Measurement/ or numeric rating scale.mp. (86855)
28. 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 (529584)
29. controlled trial.mp. (533701)
30. crossover trial.mp. (5877)
31. clinical trial.mp. or Clinical Trial/ (683050)
32. randomi?ed controlled trial.mp. (525600)
33. 29 or 30 or 31 or 32 (937435)
34. Grade V.mp. (1210)
35. placebo.mp. (194046)
36. sham.mp. (75066)
37. manipulation.mp. or Manipulation, Orthopedic/ or Manipulation, Chiropractic/ or Manipulation, Spinal/ or Manipulation, Osteopathic/ (80610)
38. Thrust.mp. (3055)
39. high velocity.mp. (2698)
40. Manipulation, Orthopedic/ or Maitland.mp. or Physical Therapy Modalities/ or Musculoskeletal Manipulations/ (41727)
41. Musculoskeletal Manipulations/ or Mulligan.mp. (1883)
42. Physical Therapy Modalities/ or Physiotherapy.mp. (45827)
43. Osteopathic Medicine/ or osteopathy.mp. or Manipulation, Osteopathic/ (5172)
44. Manipulation, Chiropractic/ or Chiropractic/ or Chiropractic.mp. (5085)
45. adjustment.mp. (165339)
46. HVLA.mp. (77)
47. 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 (565851)
48. 15 and 28 and 33 and 47 (1284)

Table 1 Keywords used within search strategy

Outcome measure	Dysfunction	Design	Intervention
Neck disability index	Cervical pain	Controlled trial	Adjustment
Neck pain questionnaire	Cervicalgia	Crossover trial	Chiropractic
Neck outcome score	Cervical spine	Clinical trial	Grade V
Short form 36	Cervicodynia	Randomi?ed controlled trial	High velocity
Outcome measure	Neck strain		HVLA
Disability	Neck		Maitland
Range of motion	Neck pain		Manipulation
Range of movement	Neckache		Manual therapy
VAS	Arthralgia		Mobili?ation
Visual analogue scale	Myalgia		Mulligan
NRS	Spondylosis		Osteopathy
Numeric rating scale	Neck injury		Physiotherapy
	Neck dysfunction		Placebo
	Neck disorder		Sham
	Stiffness		Thrust

? denotes wildcard operator to account for variability in spelling, for example 'mobilisation' and 'mobilization'.

Selection process

Study selection will take place in two phases, (1) title and abstract and (2) full text, and will be performed by each reviewer independently against the inclusion and exclusion criteria. Titles and abstracts will be used to screen for suitability using a decision parameter of suitable/unsuitable/potentially eligible. Studies will be considered potentially eligible when on reviewing the abstract, it cannot be conclusively excluded. Full texts will be reviewed if suitability cannot be determined by the title and abstract alone, or in the case of disagreement. In the event of disagreement following discussion, a third reviewer (ABR) will have presiding decision. The study selection process will be reported in a PRISMA flow chart.[18]

Cohen's κ[20] will be used to assess the level of agreement between reviewers at both stages of the review process. For this review, Cohen's original description of significance follows where κ≤0.2 will be considered no agreement, 0.21–0.59 is weak, 0.6–0.79 is moderate and over 0.8 is considered strong agreement.

Data collection process

Data will be extracted independently by EB and NJC. Data will be extracted using the Cochrane 'data collection forms for intervention reviews: RCTs and non-RCTs' tool.[21] The tool will be initially piloted using five randomly selected studies and edited where necessary. The Template for Intervention Description and Replication (TIDieR) checklist will be used to describe the interventions reported in each included study.[22] Interventions will be tabulated and pooled by intervention type.

Table 2 Table of data items extracted from included studies

Content	Data items
General study information	Author, year of publication, journal
Study characteristics	Sample size, study design, randomisation description
Participant Information	Age, gender, chronicity of symptoms
Performance-based outcome measure	eg, Cervical range of motion, muscle power
Patient-reported outcome measure	eg, Neck Disability Index, Neck Pain Questionnaire
Results	Mean and SD of outcome measures

Data items

Data to be extracted from included studies are summarised in table 2. Where data are missing from studies, authors will be contacted for clarification and completeness. Where possible, data regarding adverse events will be extracted; although from the preliminary scoping searches, this is anticipated to be minimal.

Risk of bias in individual studies

Risk of bias (ROB) will be assessed using the Cochrane Risk of Bias V.2 (CROB2) tool[23] for each included study by the reviewers (EB, NJC). CROB2 has been selected as it is suitable to any type of randomised trial, and is considered comprehensive enough to be sensitive to all ROB, including selective reporting bias and bias arising from missing data; which other ROB tools are less sensitive to.[24] ROB will be tabulated following an initial pilot on the same five randomly selected studies for piloting data extraction. The CROB2 tool considers random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases, and will be used for each outcome measure in and across studies. ROB will be determined as high, uncertain or low.[25]

Data synthesis

The findings of the included studies will be synthesised and tabulated separately for manipulation techniques (objective 1) and mobilisation techniques (objective 2) by study characteristics, results and ROB. Details of interventions will be tabulated using selected components of the TIDier checklist.[24] TIDier ensures completeness

in the reporting of interventions and ensures detailed descriptions of the interventions under review.[22]

Meta-analysis will take place when outcomes and/or interventions are heterogeneically low (I^2 <50%). A random effects model will be used if there is clinical homogeneity, similarities between individuals, interventions and outcomes,[26] and the statistical heterogeneity, the assessment of whether genuine differences exist between results[27] is low. Interventions will be assessed for heterogeneity between studies with respect to modality, grading (ie, Maitland I–V), frequency and dosage. This will be determined from the recommendations from the Cochrane Handbook for Systematic Reviews of Interventions using I^2, where 0%–40% is low, 30%–60% is moderate 50%–90% is substantial and 75%–100% is considerable heterogeneity.[28] Continuous data will be quantitatively synthesised using standardised differences of mean (95% CI).[29] Dichotomous data will be analysed with risk ratios with 95% CI.[30] Based on preliminary literature searches, it is anticipated that outcomes retrieved will allow for meta-analysis based on the following characteristics:

- Study design.
- Patient-reported outcome measure (specifically NDI).
- Performance-based outcome measure (specifically cervical ROM).
- Chronicity.
- Intervention type.

Where meta-analysis is not possible, a narrative synthesis will be presented, describing the types or study, variations within interventions, study design, outcome measures, comparability and comments about the study's overall quality. Groups of studies which are deemed to be heterogeneous will undergo narrative synthesis for interventions and comparator and outcome measured. Where narrative synthesis is undertaken, descriptions of variations within interventions, study design, outcome measures, populations, overall comparability and comments about the study's overall quality will be reported as well as extraneous variable which might affect the overall outcome.[31]

Meta-biases

To address potential reporting and publication biases, grey literature and conference proceedings will be searched to identify unpublished studies. Studies will be reviewed for reporting bias to ensure that all planned outcomes identified in the protocol for reporting were actually reported; they will be presented narratively and assessed against their protocol, where available, to ensure that all data have been reported. Results will be tabulated, describing the study design, sample, intervention, outcome measure and will be commented on regarding their quality.

Confidence in cumulative evidence

The strength of the overall body of evidence will be assessed using GRADE (Grading of Recommendations, Assessment, Development and Evaluation) to provide a transparent and systematic method of presenting evidence.[32] This approach includes the domains of ROB, imprecision (95% CI around the best estimate of absolute effect), inconsistency (applicability of intervention outcomes in a population of interest) and publication bias (consideration of missing or excluded data).[33] GRADE considers all factors which will contribute to the quality of the results, the evidence for the outcomes and the magnitude of the effect size. It ensures clarity in presenting the results and a systematic process to data review. The GRADE domains will be assessed to yield an arbitrary score of very low, low, medium or high and can be used to directly evaluate the methodological quality of studies included;[34] and will demonstrate that the quality of evidence retrieved reflects the extent to which there is confidence that the point estimate is correct. GRADE will be used to determine the overall quality of evidence, and will be determined not serious (no change in quality) serious and very serious, which will in turn downgrade the quality to evidence levels 1 and 2, respectively with no change for not serious ROB.[21]

DISCUSSION

Although current guidelines[11] advocate a multimodal approach including manipulation and mobilisation for managing NSNP, there is a paucity of evidence of what specific intervention of manual therapy is most beneficial. By isolating the individual components within the multimodal treatment of NSNP, it is hoped that this review may reveal which manual therapy technique yields the greatest change in pain, function and disability outcomes. If effectiveness of each intervention is clear, this will inform selection of individual components of a multimodal intervention. Furthermore, there is no evidence of how best to deliver manual therapy in terms of frequency and dosage to optimise treatment outcomes in order to bring about a more expedient and complete resolution of symptoms and disability. Although this is not a primary focus of this review, preliminary data to inform a future study may be obtained. Furthermore, the added complexity of using mobilisations as a therapeutic intervention is that techniques are often delivered as a series of repeated movements within the patients' normal physiological range of motion classified as grades I–IV. Variability within 'dosage' delivered and grade of intervention may influence outcomes.

This review intends to analyse the difference, if any, between manipulation and mobilisations and intends to inform our understanding of what type of manual therapy may be most effective within the multimodal management of NSNP. Due to the incidence of NSNP in the general population and the cost burden to the economy, it is hoped that this review may inform best practice in implementing patient care and inform future comparator studies and clinical trials of manual therapy in order to deliver efficient, effective patient care.

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