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ABSTRACT

Objective: To assess the effects of mobilisation with movement (MWM) on pain, range of motion (ROM) and disability in the management of shoulder musculoskeletal disorders.

Methods: Six databases PubMed (MEDLINE), CINAHL, SPORTDiscus, PEDro, Cochrane library, and Scopus were searched for randomized control trials (RCTs). The ROB 2 tool was used to determine risk-of-bias and the quality of the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Meta-analyses were performed for the sub-category of frozen shoulder and shoulder pain with movement dysfunction to evaluate the effect of MWM in isolation or in addition to exercise therapy and /or electrotherapy when compared with either no treatment, exercise therapy, electrotherapy alone or other types of manual therapy

Results: Out of twenty-five studies, twenty-one were included in 8 separate meta-analyses for pain, ROM, and disability in the 2 sub-categories of shoulder disorders. For frozen shoulder, the addition of MWM significantly improved pain (SMD -1.23, 95% CI -1.96, -0.51, $I^2=89\%$), flexion ROM (MD -11.73, 95% CI -17.83, -5.64, $I^2=82\%$), abduction ROM (mean difference -13.14, 95% CI -19.42, -6.87, $I^2=85\%$) and disability (SMD -1.50, 95% CI (-2.30, -0.7, $I^2=89\%$). For shoulder pain with movement dysfunction the addition of MWM significantly improved pain (SMD -1.07, 95% CI -1.87, -0.26, $I^2=86\%$), flexion ROM (mean difference -18.48, 95% CI -32.43, -4.54, $I^2=90\%$), abduction ROM (MD -32.46, 95% CI -69.76, 4.84, $I^2=97\%$) and disability (SMD -0.88, 95% CI -2.18, 0.43, $I^2=92\%$). The majority of studies were found to have a high risk of bias. Where appropriate, the clinical significance of the pooled differences was compared against Minimal Clinically Important Difference values.

Discussion: MWM in addition to other forms of physiotherapy is associated with improved pain, mobility and function in patients with a range of shoulder musculoskeletal disorders including frozen shoulder. The effects were clinically meaningful for flexion and abduction ROM. However these findings need to be interpreted with caution due to the high levels of heterogeneity among included studies and inclusion of studies with a high risk of bias. The reasons for high levels of heterogeneity and risk of bias are explored.

Level of Evidence: Treatment, level 1a.

Keywords: Mulligan's mobilisation with movement, manual therapy, systematic review, shoulder dysfunction

Introduction

Demand for effective conservative management of shoulder conditions reflects its prevalence as the third most common musculoskeletal (MSK) condition seen in United Kingdom (UK)(1) with one year prevalence among a global survey reported to be between 4.7 to 46.7%(2). Clinicians may be challenged by the scope of possible structural diagnoses, the changing nomenclature used to describe the experience of pain, distress and loss of function, and the application of recommended management strategies(3).

Current guidelines for the conservative management of shoulder conditions include exercise, patient education, manual therapy, activity modification, non-steroidal anti-inflammatory drugs, and corticosteroid injections(4,5). The hierarchy in the priority of these strategies suggests exercise as the first in line for management(6). Multi-modal care has also been promoted(7), as have strong recommendations for exercise combined with manual therapy in a recent literature review(6).

The application of effective manual therapy is ambiguous due to the variety of techniques, dosage, duration of affect, progressions and rational for its usage (6). In systematic reviews, all varieties of manual therapy are synthesised(6–9) which often does not allow discrimination between techniques or help guide clinicians. Mobilisation with movement (MWM) is one specific form of manual therapy gaining increasing popularity with a number of studies showing treatment benefit for a range of shoulder conditions(9–12). MWM involves the application of sustained gliding force (passive mobilization component) with a concurrent active movement performed by the patient (active movement component). The application of MWM, when precisely indicated, has beneficial effects on painful movement and thereby function is immediately improved. Thus MWM can be distinguished from passive, practitioner-applied manual therapy which is based on a test-treat-retest model of application(13). The immediate symptom modification feature of MWM may allow greater clarity to allow clinicians to discriminate between manual therapy selections.

Previous systematic reviews evaluating the effectiveness of MWM lack the precise work on shoulder (14,15), and excluded many studies focused on a shoulder specific population(16). Although a recent systematic review for shoulder conditions has been undertaken(17), the current review is indicated as the previous work lacked robustness due to, identification and exclusion of studies selected, the presence of new studies since its release, and no pre-registration of its proposal. Therefore, we undertook a systematic review with meta-analysis

to determine the additional benefits of MWM when compared to other non-surgical forms of management, including other forms of manual therapy, electrotherapy, placebo, sham, or no treatment for shoulder musculoskeletal disorders in 2 categories; frozen shoulder or shoulder pain with movement dysfunction. Frozen shoulder is a readily identifiable syndrome, but the diagnosis of other shoulder specific disorders is problematic. Hence, we chose to separate frozen shoulder from other unknown shoulder disorders.

METHODS

This review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The systematic review was prospectively registered on PROSPERO: CRD42020210618.

Data sources and searches

The following databases were searched: PubMed (MEDLINE), CINAHL, SPORTDiscus, PEDro, Cochrane library, and Scopus, from inception to January 2021 (appendix 1).

Appropriate search and MeSH terms were adapted and applied to each database. To supplement the initial database searches, a manual search of the references listed in identified systematic reviews was also conducted.

Eligibility criteria

We included randomised controlled trials (RCTs) and randomised cross-over studies evaluating the effects of MWM or self-MWM on shoulder condition, either alone or in combination with other interventions. The comparator group comprised no intervention, any other form of conservative intervention including “wait and see”, usual care, standard care, sham, or placebo but not including MWM intervention. Studies were considered if they included adults aged 18 years and above of either gender and used outcome measures of pain severity, range of motion (ROM), and disability scores.

Studies were excluded if the full text was not available and if the language was not English. Duplicate studies identified as a result of searching multiple databases were removed using EndNoteX8 software. The titles and abstracts were screened by two assessors independently (KS and GM), according to predetermined eligibility criteria. Full text articles were assessed and, if there was uncertainty over the inclusion of a study, a third reviewer (SR) was consulted until consensus was reached.

Quality assessment and data extraction

Each study’s risk of bias was assessed using the ROB 2.0 tool(18). This tool evaluates the risk of bias across five domains; the randomisation process, deviations from intended

interventions, missing outcome data, measurement of outcomes, and selection of reported results. The tool includes algorithms that map responses to signalling questions onto a proposed risk-of-bias judgement for each domain, leading reviewers to make a judgement of 'Low risk of bias', 'Some concerns', or 'High risk of bias' both for each domain and as an overall risk-of-bias judgement for each study. Two reviewers (KS, GM) independently performed risk of bias assessments on all studies and any discrepancies were resolved by consensus discussion.

The approach proposed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group for rating the quality of the best available evidence and developing health care recommendations(19) was used to rate the quality of the evidence and grade the certainty of outcomes in the meta-analysis. Using the GRADE approach, the quality of evidence was rated independently by two reviewers (KS and GM) according to four levels ranging from high to very low (Box 1).

Box 1: Quality of evidence ratings using the GRADE approach

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Two independent reviewers extracted data using a data extraction form. Other review members were consulted if necessary. If all information was not readily available in the studies, numerical data was requested from author groups.

Data synthesis

A narrative synthesis of aggregate data was provided within the review by describing the population characteristics, methodology and results of included studies.

The trials were compared for homogeneity through visual examination (Table 1 and 2). If trials were sufficiently homogenous and could be grouped according to outcome measures i.e. range of motion, pain, and disability scores, a meta-analysis was performed to provide a quantitative synthesis of aggregate data from the included studies. If only one study was available in the grouping, meta-analysis could not be performed and the statistics from that single study were reported. Review Manager 5.3 (Cochrane Collaboration) software was used for the statistical analysis. If all included trials used the same outcome measure, a summary of intervention effects was reported as a weighted mean difference with 95% confidence intervals and p value. If the included trials used different outcome measures, a summary of intervention effects was reported as a standardised mean difference with 95% confidence intervals and p value. A fixed-effect model was used when there was no evidence of heterogeneity between studies, otherwise, a random-effects model was applied. Clinical variation and heterogeneity between studies was examined and evaluated using Q statistic and I² tests. Forest plots were used to illustrate the outcomes of meta-analysis. The I² statistic, an expression of inconsistency of studies' results, describes the percentage of variation across studies because of heterogeneity rather than by chance. A high value of I² (>50%) and P < .05 indicate statistically significant heterogeneity among the studies for an outcome. The reasons for high heterogeneity were explored. The interpretation for trivial, small, medium, and large effect sizes (≤ 0.2 trivial effect, 0.2–0.49 small effect; 0.5–0.79 medium effect; ≥ 0.8 , large effect) were chosen(20).

RESULTS

Results of the Literature Search

A literature search was conducted in 6 databases from inception to January 2021 and identified a total of 1956 studies (Appendix 1). After removing duplicates 1620 studies remained for title and abstract screening. 17 additional studies were identified through hand searching reference lists. Thus the title and abstract of 1637 studies were screened. From these, 31 potentially eligible studies for full-text assessment were identified, and 25 (10–12,21–42) studies were included based on the inclusion and exclusion criteria (Figure 1).

Insert Figure 1 here

The characteristics of included studies are summarised in Table 1 (frozen shoulder sub-category) and Table 2 (shoulder pain and movement dysfunction sub-category).

Qualitative synthesis

All included studies were RCT's. Two of the RCT's were a crossover design (26,40) and two were pilot studies(10,28). Only six studies were registered with a clinical trial registry(10,12,24,26,36,38). In the evaluated studies there were a total 1014 participants. Fourteen studies evaluated 665 patients with frozen shoulder and 11 studies evaluated 349 patients with shoulder pain and movement dysfunction. Among the frozen shoulder sub-category, all studies except two(11,34) evaluated MWM in combination with exercise therapy. MWM was compared with other manual therapy techniques including Maitland mobilisation (7 studies) and Kaltenborn mobilisation (2 studies). All studies included patients with unilateral stage-II frozen shoulder except 3 studies, where the stage of frozen shoulder was not reported(25,27,41). Three studies included patients with frozen shoulder who had a history of diabetes mellitus(21,35,42). In the shoulder pain and movement dysfunction sub-category, three studies evaluated MWM in isolation which was compared with a sham intervention(12,26,40). In 7 studies, MWM was used in conjunction with electrotherapeutic modalities such as the heat therapy, cryotherapy, therapeutic ultrasound and transcutaneous electrical nerve stimulation (TENS). There was wide variability in the MWM treatment dosage such as the number of treatment sessions utilised during the study period which ranged from a minimum of 3 sessions to a maximum of 24 sessions. MWM intervention was applied for a minimum of 1 week and a maximum of 2 months and only three studies followed patients over a longer time course, with a maximum of 3 months follow-up(10,11,35). None of the studies followed the Mulligan Concept treatment guidelines of only applying MWM in patients who had a beneficial effect following a trial MWM. The most commonly reported MWM technique was a postero-lateral glide combined with active arm elevation. Only two studies evaluated an inferior glide which was combined with movement of hand behind back(23,36). One study evaluated scapulothoracic MWM in a weight bearing position(39).

Insert Table 1 and 2 here

Risk of bias assessment

The results of the risk of bias assessment are seen in Figure 2. Of the 25 studies assessed, three were rated as an overall risk of bias of 'low risk', four were rated as 'some concerns' and 18 were rated as having 'high risk'. The most common methodological problems in the included studies resulting in a high risk of bias were a lack of concealed allocation (14

studies) and failure to blind outcome assessors (13 studies). As most studies were not registered prospectively there was often no study protocol, leading to a decision of ‘some concerns’ for domain two and domain five for most studies.

Insert Figure 2 here

Meta-analysis

Meta-analysis was carried out on the results from 21 studies using the post intervention scores for experimental and control groups. For studies comparing MWM with more than one control group, control groups were combined into a single group. Analysed studies displayed high levels of heterogeneity ($I^2 > 75\%$), hence the results are presented based on the random effects model. Meta-analysis was not possible in four studies for the following reasons: mean values and SD were not reported(10,28); or inadequate data was available(31,37). Authors of studies with missing data were contacted but no response was received except for Romero et al(10) where data was not available.

Meta-analyses were performed for the sub-category of frozen shoulder (12 studies available) and for the sub-category shoulder pain with movement dysfunction (9 studies available) to assess the immediate effects of MWM on pain, flexion and abduction ROM, as well as disability up to 2 months post intervention. For both sub-categories, meta-analyses were performed to evaluate the effect of MWM, either in addition to exercise therapy and/or electrotherapy or MWM alone (experimental group) when compared to either exercise therapy and electrotherapy alone or other type of manual therapy (control group). The random effects model was chosen as a conservative measure to account for heterogeneity among included studies. Standardized Mean Differences (SMD) with 95% confidence intervals (CIs) were calculated for pain and disability. Mean Differences (MD) with 95% confidence intervals (CIs) were calculated separately for flexion and abduction ROM.

Frozen shoulder

Pooled data from eight studies with 345 participants were combined for analysis of the effects of MWM on pain. Statistically significant improvement was present post intervention favouring MWM (SMD [95% CI]: -1.23 [-1.96, -0.51] $Z = 3.35$ ($P = 0.0008$) with high levels of heterogeneity ($I^2 = 89\%$) (Figure 3 A). Pooled data from nine studies with 430 participants were grouped for analysis of the effects of MWM on flexion ROM. Statistically significant improvement was present post intervention favouring MWM (mean difference [95% CI]: -11.73 [-17.83, -5.64] $Z = 3.77$ ($P = 0.0002$) with high levels of heterogeneity ($I^2 = 82\%$)

(Figure 3 B). Pooled data from nine studies with 465 participants were grouped for analysis of the effects of MWM on abduction ROM. Statistically significant improvement was present post intervention favouring MWM (mean difference [95% CI]: -13.14 [-19.42, -6.87] $Z = 4.10$ ($P < 0.0001$) with high levels of heterogeneity ($I^2 = 85\%$) (Figure 3 C). Pooled data from eight studies with 305 participants were grouped for analysis of the effects of MWM on disability. Statistically significant improvement was present post intervention favouring MWM (SMD [95% CI]: -1.50 [-2.30, -0.71] $Z = 3.69$ ($P = 0.0002$) with high levels of heterogeneity ($I^2 = 89\%$) (Figure 3 D).

Insert Figure 3 here

Shoulder pain with movement dysfunction

Pooled data from seven studies with 228 participants were grouped for analysis of the effects of MWM on pain. Statistically significant improvement was present post intervention favouring MWM (SMD [95% CI]: -1.07 [-1.87, -0.26] $Z = 2.61$ ($P = 0.009$) with high levels of heterogeneity ($I^2 = 86\%$) (Figure 4 A). Pooled data from seven studies with 173 participants were grouped for analysis of the effects of MWM on flexion ROM. Statistically significant improvement was present post intervention favouring MWM (mean difference [95% CI]: -18.48 [-32.43, -4.54] $Z = 2.60$ ($P = 0.009$) with high levels of heterogeneity ($I^2 = 90\%$) (Figure 4 B). Pooled data from five studies with 151 participants were grouped for analysis of the effects of MWM on abduction ROM. Statistically significant improvement was present post intervention favouring MWM (mean difference [95% CI]: -32.46 [-69.76, 4.84] $Z = 1.71$ ($P = 0.09$) with high levels of heterogeneity ($I^2 = 97\%$) (Figure 4 C). Pooled data from five studies with 155 participants were grouped for analysis of the effects of MWM on disability. Statistically significant improvement was present post intervention favouring MWM (SMD [95% CI]: -0.88 [-2.18, 0.43] $Z = 1.32$ ($P = 0.19$) with high levels of heterogeneity ($I^2 = 92\%$) (Figure 4 D). Improvement in shoulder flexion and abduction ROM in both sub-categories is clinically relevant, as improvement was greater than the reported MDC of 11° for patients with shoulder pathologies(43).

Insert Figure 4 here

GRADE analysis for frozen shoulder sub-category

For the frozen shoulder sub-group, the certainty of the effect estimate was rated as very low for all four variables analysed in the meta-analysis (Table 3). For the shoulder pain with

movement dysfunction sub-group, the certainty of the effect estimate was rated as very low for all four variables analysed in the meta-analysis (Table 4).

Insert table 3 and 4 here

Discussion

The objective of this systematic review and meta-analysis was to determine the additional benefits of MWM in terms of pain, flexion and abduction ROM, as well as disability when compared to other non-surgical forms of management, including other forms of manual therapy, electrotherapy, placebo, sham, or no treatment for shoulder musculoskeletal disorders in 2 categories; frozen shoulder or shoulder pain with movement dysfunction.

Findings

Our results indicate important benefits of MWM for all variables in each category, although caution is required in interpretation due to high levels of heterogeneity and risk of bias.

This is the first systematic review with meta-analysis to evaluate the clinical effectiveness of MWM in isolation or in addition to other physiotherapeutic modalities on pain, ROM and disability for commonly encountered shoulder conditions in clinical practice. The only other systematic review of MWM for shoulder did not include meta-analysis. Most of the included studies in our review evaluated MWM techniques designed to increase shoulder flexion and abduction ROM, thus studies that evaluated these movements were considered for meta-analysis. MWM demonstrated statistically significant and clinically relevant benefits in patients with stage II frozen shoulder when compared to exercise, passive manual therapy or electrotherapy. Similarly, for patients with shoulder pain and movement dysfunction, MWM demonstrated statistically significant and clinically relevant benefits when compared to exercise alone, electrotherapy or sham interventions. In addition to ROM, MWM conferred a statistically significant improvement in pain intensity over a control condition in both frozen shoulder and shoulder pain and movement dysfunction sub-categories.

The SMD score was -1.23 (95% CI -1.96, -0.51) in patients with frozen shoulder, and -1.07 (95% CI -1.87, -0.26) in patients with shoulder pain and movement dysfunction.

Improvement in pain was statistically significant and favoured MWM even when the control group included other passive joint mobilisation techniques or sham interventions. This would suggest that pain relief with MWM may be attributed more to neurophysiological effects

rather than biomechanical effects of stretching local articular structures(44) since MWM is applied with minimal force, being always pain-free.

In patients with frozen shoulder, flexion ROM improved significantly more following MWM than the control condition (including Maitland, Kaltenborn, and Spencer techniques among others shown in Table 1) with mean difference of -11.73 (95% CI -17.83, -5.64). For abduction, the mean difference was -13.14 (95% CI -19.42, -6.87). In patients with shoulder pain and movement dysfunction the mean difference in flexion and abduction ROM was -18.48 (95% CI -32.43, -4.54) and -32.46 (95% CI -69.76, 4.84) respectively. These effects were not only statistically significant, but also clinically relevant as the improvements in ROM were greater than the MCID of 11° for these 2 measures(43). Similar to pain, improvement in ROM was statistically significant even when the control group included other passive joint mobilisation techniques. MWM is likely to involve less force than other forms of manual therapy. Again this suggests that improvements in ROM after MWM may be related to neurophysiological effects rather than a mechanical influence on capsular and ligamentous extensibility.

Disability improved significantly more following MWM than the control condition (Table 1) with a SMD of -1.50 (95% CI -2.30, -0.71) and SMD of -0.88 (95% CI -2.18, 0.43) in the category's frozen shoulder and shoulder pain and movement dysfunction respectively. Direct comparisons with the MCID are not possible due to the standardization of the disability measures used in the studies included in meta-analysis. The effect sizes for all outcomes were large (> 0.8) for both sub-categories(20). However, the studies included in meta-analysis displayed high levels of heterogeneity ($I^2 > 75\%$), and the GRADE certainty of effect estimate was rated as very low for all variables in both categories, challenging the strength of these results(45). Pain relief and clinically relevant improvement in shoulder ROM may allow patients to exercises more effectively during their rehabilitation and could explain the significant improvement seen in disability.

The results are in accordance with previous systematic reviews reporting on the efficacy of MWM for peripheral joint disorders including the shoulder, in terms of pain(16,17,46) and ROM(14,16,17). However, there was disagreement with respect to disability. Our analysis compared MWM to any other intervention including sham as well as other forms of manual therapy. A previous review of MWM for peripheral joints found no effect on disability when

comparing MWM with other forms of manual therapy(46). In any case, both reviews found high levels of heterogeneity, so we should be cautious about the results.

Heterogeneity displayed in the results of included trials could be explained by the choice of outcomes. It follows that the outcome measure of ROM is very valid for a patient with significant functional stiffness seen in a type II frozen shoulder, but would be of little value in a patient presenting with subacromial pain syndrome, where pain intensity with load, disability or other measures are more meaningful(47).

Divergent methods of application of MWM are also suggested in accounting for heterogeneity in results. It is recommended MWM is both an assessment tool and treatment artefact. Its use as a treatment should only follow when an immediate positive modification to a patient's affected movement or function occurs(47,48). If a trial MWM proves ineffective, varying the weight-bearing status of the patient using different functional positions, or trialling the use of other forms of MWM are attempted until all avenues are exhausted. The studies found applied RCT and RCT crossover models, assessing standardised adjuncts alone, which lack the finesse to adopt the above guideline. This can be viewed as antithetical to the clinical setting. Interestingly, RCT's evaluating the effects of MWM for lumbar radiculopathy(49) and post ankle sprain(50) using the advised guidelines have been undertaken. In Nguyen's work, despite the fact that there was an overall 84% positive response rate to MWM for ankle sprain, not all patients responded to the first applied MWM technique. The authors postulate this to be a likely outcome in the shoulder, where MWM's for the scapulothoracic joint, glenohumeral joint, acromioclavicular joint, and spine can be attempted. It is suggested that each patient may require a different approach that is clinically reasoned, patient-centred, and modifiable to achieve the best outcome for the patient(51). This resonates with guidelines emphasising the importance of individualised care within a holistic package of multi-modal management in musculoskeletal conditions(4,6), and is useful to the clinician as it represents a truer reflection of the treatment interaction.

Strength and limitations

A strength of this systematic review is that more studies were included than a recent systematic review with similar inclusion criteria evaluating the effect of MWM on shoulder conditions(17). The additional studies were identified by searching reference lists and non-indexed journals. Additionally our review provides statistical pooling of data through meta-analysis, which is generally considered to be more precise(52). In addition the GRADE

approach was used to assess the quality of results. A weakness of this review is that most of the included studies only evaluated the effects of MWM post intervention, thus it was not possible to report on the long-term effects. Included studies demonstrated significant clinical, methodological, and statistical heterogeneity and most of the included studies showed high risk of bias due to their methodological weaknesses; hence improvements observed in all outcomes cannot be solely attributed to MWM intervention and caution is required when considering the results.

Future research scope

The authors recommend future studies follow a more pragmatic clinically-reasoned and patient-centred approach to the use of the MWM with long-term follow up. More detailed description of the MWM technique used in clinical trials, and effects of trial MWM's with details of positive responders is advised. Progression of MWM to include greater load, potentially with over-pressure, should be considered, as should the use of self-MWM and the application of tape, especially within the context of effective patient communication, building patient resilience and providing self-management strategies. As found with exercise in the management of shoulder conditions, the type, dosage, duration and application of manual therapy in shoulder conditions is ambiguous(6). By distinguishing between passive manual therapy and MWM, clinicians may be aided in their selection and application of techniques, whereas synthesising data for manual therapy as a whole is likely to only give insight into the impact of physical touch in the therapeutic relationship. The authors recommend future systematic reviews into shoulder manual therapy make this division.

Conclusion

This systematic review revealed that MWM in isolation or in addition to exercise therapy and /or electrotherapy is superior in improving pain, ROM, and disability in patients with shoulder dysfunction when compared with either exercise therapy and electrotherapy alone or other type of manual therapy. However the evidence is of low quality owing to high levels of heterogeneity among included studies and inclusion of studies with high risk of bias.

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