MANUAL AND MANIPULATIVE THERAPY IN ADDITION TO REHABILITATION FOR OSTEOARTHRITIS OF THE KNEE: ASSESSOR-BLIND RANDOMIZED PILOT TRIAL

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ABSTRACT

Objectives: The purpose of this study was to examine the methodological integrity, sample size requirements, and short-term preliminary clinical outcomes of manual and manipulative therapy (MMT) in addition to a rehabilitation program for symptomatic knee osteoarthritis (OA).

Methods: This was a pilot study of an assessor-blinded, randomized, parallel-group trial in 2 independent university-based outpatient clinics. Participants with knee OA were randomized to 3 groups: 6 MMT sessions alone, training in rehabilitation followed by a home rehabilitation program alone, or MMT plus the same rehabilitation program, respectively. Six MMT treatment sessions (provided by a chiropractic intern under supervision or by an experienced chiropractor) were provided to participants over the 4-week treatment period. The primary outcome was a description of the research methodology and sample size estimation for a confirmatory study. The secondary outcome was the short-term preliminary clinical outcomes. Data were collected at baseline and 5 weeks using the Western Ontario and McMasters Osteoarthritis Index questionnaire, goniometry for knee flexion/extension, and the McMaster Overall Therapy Effectiveness inventory. Analysis of variance was used to compare differences between groups.

Results: Eighty-three patients were randomly allocated to 1 of the 3 groups (27, 28, and 28, respectively). Despite 5 dropouts, the data from 78 participants were available for analysis with 10% of scores missing. A minimum of 462 patients is required for a confirmatory 3-arm trial including the respective interventions, accounting for cluster effects and a 20% dropout rate. Statistically significant and clinically meaningful changes in scores from baseline to week 5 were found for all groups for the Western Ontario and McMasters Osteoarthritis Index ($P \leq .008$), with a greater change in scores for MMT and MMT plus rehabilitation. Between-group comparison did not reveal statistically significant differences between group scores at week 5 for any of the outcome measures ($P \geq .46$).

Conclusions: This pilot trial suggests that a confirmatory trial is feasible. There were significant changes in scores from baseline to week 5 across all groups, suggesting that all 3 treatment approaches may be of benefit to patients with mild-to-moderate knee OA, justifying a confirmatory trial to compare these interventions. (J Manipulative Physiol Ther 2015;38:1-21.e2)

Key Indexing Terms: *Pilot Projects; Osteoarthritis; Knee; Musculoskeletal Manipulations; Rehabilitation*

Osteoarthritis (OA) is the most common form of chronic arthritis, with radiologic evidence of joint degeneration in more than 50% of people older than 65 years, with a propensity for symptomatic OA to occur in women.[1,2] The knee joint is one of the most commonly affected by OA, leading to a burden on the

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individual and the community through reduced quality of life, diminished capacity for employment, and an increase in health care costs.[3] With an aging population globally, the problem of OA of the knee will likely worsen, which has prompted the development of clinical practice guidelines that now recommend treatment at an early stage of the disease, using health promotion/exercise to reduce progression, and optimization of both pharmacologic and nonpharmacologic treatment.[4]

For mild to moderate OA, clinical practice guidelines promote a multimodal treatment approach that includes drug therapy and nonpharmacologic treatment, such as patient education, exercise, and weight optimization.[5] Physical therapies, such as manual and manipulative therapy (MMT), are also emerging as a viable treatment option,[6–8] particularly in combination with other interventions like exercise,[9] health promotion, and simple analgesia.[10] Manual and manipulative therapy can offer positive outcomes for knee OA[8,11,12] but needs to be explored further within the context of multimodal care.

Combining treatments to form a package of care for a specific disorder implies the delivery of a complex intervention, the outcome of which may be confounded by internal and external factors.[13] Therefore, the trials testing complex interventions require modeling or piloting prior to a confirmatory trial with a view to optimize the research design and determine feasibility.[14–16]

The purpose of this trial was to conduct an external pilot trial and compare MMT, a rehabilitation program, and the combination of MMT plus the rehabilitation program for mild to moderate OA of the knee. The primary outcome was to assess the design integrity, with a view to provide a critique of the research design, offer design recommendations, and provide a sample size estimate for a larger confirmatory trial. The secondary outcome was to gain insight into preliminary clinical outcomes. The research hypothesis was that the 3 treatment approaches would show significant change in scores from baseline to week 5 and that there would be a significant difference between treatment groups. To achieve the primary end-point, the following objectives were covered by descriptive analysis of (*a*) patient recruitment, enrollment, and allocation; (*b*) data collection and patient retention; (*c*) acceptability of interventions; and (*d*) sample size calculations.

Methods

Trial Design and Changes to the Methods After Commencement

This study was initially designed as an assessor-blind, parallel-group clinical trial with 1-, 3-, and 6-month follow-up. However, toward the latter part of this study, access to funding became more difficult, which impacted recruitment and data collection. The authors realized that a pilot study was needed to inform the design of future trials to account for financial and recruitment problems. Therefore, this trial is presented as a 2-center, assessor-blind, parallel-group short-term clinical trial with balanced randomization (1:1). The results and recommendations of this pilot trial may be considered a template for a fully-powered confirmatory trial. The study protocol was not updated as regularly as was desired on ClinicalTrials.gov. However, third-party access resulted in premature cancellation/closure of the study on the website. The recommendation for future trials is to limit third-party access to the protocol on ClinicalTrials.gov and to ensure regular updating, to facilitate transparency in the conduct of the trial. This project received approval from the relevant institutional review board of Cleveland Chiropractic College (IRB No. 08132010) and the Research Ethics Committee of Durban University of Technology. The trial was registered with Clinical.Trials.gov (NCT01188837).

Evaluation of the Research Integrity and Methodological Rigor

The primary outcomes of this study included the following: patient recruitment, enrollment, and allocation; data collection and patient retention; acceptability of interventions; sample size calculations; and research design alternative. Sample size calculations were performed and reported using the data from this external pilot trial. Initial calculations were based on the *F* test (analysis of covariance [ANCOVA]) for fixed effects, main effects, and interaction effects at a 95% level of confidence to achieve statistical Power of 80% (using G* Power software, www.psycho.uni-dusseldorf.de, Dusseldorf, Germany) taking into account the effect size, the number of groups, the number of covariates, and the degrees of freedom for the outcome measure (Western Ontario and McMasters Osteoarthritis Index [WOMAC]). For research design alternative, multisite or cluster randomized trials as a potential research design were discussed. Accordingly, a sample size estimate is offered with this design in mind.

Selection Criteria

Inclusion Criteria. All eligible participants had a diagnosis of mild-moderate knee OA based on the diagnostic criteria of the American College of Rheumatology and the Kellgren-Lawrence grade for knee OA, suitable grades for this study being grades 0 to 3.[17,18] This diagnosis was reached after assessment by the lead clinician and radiographic investigation of each eligible participant. The radiographs were read and interpreted by a Diplomate in Chiropractic Radiology who was blind to the study criteria, data, and randomization.

Inclusion and exclusion criteria are in Figure 1.

Setting, Practitioners, and Participants

This study was implemented across 2 chiropractic university-based outpatient teaching clinics, 1 in the city of