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Acupuncture and other physical treatments for the relief of pain due to osteoarthritis of the knee: network meta-analysis☆

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SUMMARY

Objective: To compare the effectiveness of acupuncture with other relevant physical treatments for alleviating pain due to knee osteoarthritis.
Design: Systematic review with network meta-analysis, to allow comparison of treatments within a coherent framework. Comprehensive searches were undertaken up to January 2013 to identify randomised controlled trials in patients with osteoarthritis of the knee, which reported pain.
Results: Of 156 eligible studies, 114 trials (covering 22 treatments and 9,709 patients) provided data suitable for analysis. Most trials studied short-term effects and many were classed as being of poor quality with high risk of bias, commonly associated with lack of blinding (which was sometimes impossible to achieve). End of treatment results showed that eight interventions: interferential therapy, acupuncture, TENS, pulsed electrical stimulation, balneotherapy, aerobic exercise, sham acupuncture, and muscle-strengthening exercise produced a statistically significant reduction in pain when compared with standard care. In a sensitivity analysis of satisfactory and good quality studies, most studies were of acupuncture (11 trials) or muscle-strengthening exercise (9 trials); both interventions were statistically significantly better than standard care, with acupuncture being statistically significantly better than muscle-strengthening exercise (standardised mean difference: 0.49, 95% credible interval 0.00–0.98).
Conclusions: As a summary of the current available research, the network meta-analysis results indicate that acupuncture can be considered as one of the more effective physical treatments for alleviating osteoarthritis knee pain in the short-term. However, much of the evidence in this area of research is of poor quality, meaning there is uncertainty about the efficacy of many physical treatments.

Introduction

The objective of treating osteoarthritis of the knee is usually the alleviation of pain and improving quality of life. Failure to control pain may result in reduced mobility and reduced participation in daily activities, which may further exacerbate symptoms. The regular use of pharmacological agents for pain may be associated with significant side effects (such as gastrointestinal bleeding)[1], and many patients want non-pharmacological treatments for pain relief[2,3]. Effective alternatives to pharmacological pain relief are therefore desirable.

Five guidelines (ACR[4], AAOS[5], OARSI[6], EULAR[7], and NICE[8]) have evaluated treatment effects on key outcomes of knee osteoarthritis (including pain, function, and disability). All recommend treatment with muscle-strengthening and aerobic exercise, education, weight loss (if required), and, where necessary, paracetamol and/or topical NSAIDs; when these are ineffective, a choice of one or more options from a range of pharmacological and non-pharmacological treatments is sometimes recommended, including transcutaneous electrical nerve stimulation (TENS), thermal (heat/cooling) treatments, insoles, and braces. The OARSI guideline recommended using acupuncture, AAOS found the acupuncture evidence to be inconclusive, and the ACR conditionally recommended acupuncture only for patients with moderate-to-severe pain who are unable or unwilling to undergo total knee arthroplasty. EULAR and NICE did

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not recommend use of acupuncture; one of the reasons for the commissioning of this review – as part of a programme of projects on acupuncture and chronic pain, funded by the National Institute for Health Research (NIHR) under its Programme Grant for Applied Research Programme – was the uncertainty within the NICE decision-making process with regard to the level of evidence on acupuncture for osteoarthritis relative to other physical treatments. The rationale for this systematic review was to compare acupuncture with available alternative physical treatments that might be prescribed by a GP, or used by a physiotherapist, since uncertainty exists regarding which treatments are best.

Although numerous reviews have evaluated individual types of physical treatment, few randomised trials have directly compared these treatments. One way to overcome this limitation is to use network meta-analysis, which allows assessment of relative efficacy when direct treatment comparisons are insufficient or unavailable. In the context of the present review it should enable all relevant physical treatments to be compared with each other. The purpose of this systematic review, therefore, was to conduct a comprehensive synthesis using network meta-analysis methods in order to compare the effectiveness of acupuncture with other relevant physical treatments for alleviating pain due to osteoarthritis of the knee.

Methods

A systematic review was conducted following the general principles outlined in the Centre for Reviews and Dissemination (CRD) Guidance[9] and the PRISMA statement[10]. This paper reports an update of a systematic review and network meta-analysis conducted in 2011, which is available on the CRD website[11].

Literature search

A range of resources was searched for published and unpublished studies, grey literature, and on-going research (see eMethods 1). We searched 17 electronic databases from inception to January 2013, without language restrictions. A combination of relevant free text terms, synonyms and subject headings relating to osteoarthritis of the knee and named physical treatments were included in the strategy. Bibliographies of relevant reviews and guidelines were also checked, and Internet searches were made of websites relating to osteoarthritis.

Study selection and intervention definitions

Two reviewers independently screened all abstracts and full papers, with disagreements resolved by discussion, or a third reviewer. We included randomised controlled trials (RCTs) assessing pain (as a primary or secondary outcome) in adults with knee osteoarthritis (with a population mean age of $\geq$55 years). Eligible treatments were any of the following: acupuncture, balneotherapy, braces, aerobic exercise, muscle-strengthening exercise, heat treatment, ice/cooling treatment, insoles, interferential therapy, laser/light therapy, manual therapy, neuromuscular electrical stimulation (NMES), pulsed electrical stimulation (PES), pulsed electromagnetic fields (PEMF), static magnets, Tai Chi, TENS, and weight loss. The following were excluded: predominantly home-based and unsupervised exercise interventions, surgical interventions, pharmaceutical interventions, interventions which combined two or more physical treatments, and studies comparing only different regimens/durations/modalities of the same intervention. Populations with varus/valgus malalignment were excluded as were studies which did not report data in a format suitable for network meta-analysis (see Outcomes section).

We classified adjunctive components of the experimental interventions into five categories, based on what was reported in the trials: 'treatment as usual', 'treatment as usual' plus specified home exercise or education, 'treatment as usual' plus specified (trial-specific) analgesics, no medication, and no medication plus specified home exercise or education. Eligible comparators included any form of standard/usual care or waiting list control (which could incorporate analgesics, education, and exercise advice) all of which we called 'standard care'. Placebo interventions, no intervention, and sham acupuncture were also eligible. Sham acupuncture was treated as a separate comparator because of evidence suggesting it is more active than an inert 'placebo'[12,13]. All pain scales were eligible.

Assessment of trial quality and data extraction

Trial quality was assessed using an adaptation of a checklist (14 questions) from a previous review by CRD[14]. Using an algorithm, studies were then graded as excellent, good, satisfactory or poor, and also given an assessment based on the Cochrane risk of bias tool[15] [see eTables I(a and b)]. Data extraction and quality assessments were performed by one reviewer and independently checked by a second. Disagreements were resolved by discussion or a third reviewer.

Outcomes and data transformations

WOMAC pain (using a VAS or Likert scale) was the preferred pain measure. When studies did not measure WOMAC pain, another pain scale was included in the analysis with prioritisation of scales made on a clinical, or prevalence, basis (further details in the 2011 report)[11]. Hedges-g standardised mean differences (SMDs) were calculated for the meta-analyses (studies reporting medians could not be analysed). Results for different doses/regimens of the same type of treatment within a study were pooled. In an initial analysis only final values were used. However, we included more studies by calculating final values for trials reporting change from baseline data, provided trial baseline data together with variance estimates (e.g., standard deviations) were also reported. In order to present more clinically meaningful results, we present both SMDs, and SMDs converted to the WOMAC pain VAS 0-100 scale.

Synthesis

A network meta-analysis draws on both direct evidence (treatments compared in the same trial) and indirect evidence (different treatments studied in separate trials, but compared when they use a common comparator), with the benefit of randomisation in each study retained. For indirect and direct evidence to be consistent, population and intervention characteristics must be similar across comparisons[16–21]. Inconsistency between direct and indirect evidence was assessed using the node-splitting method[17,22]. The SMD was assumed to be normally distributed and a random effects network meta-analysis model was selected since clinical and methodological heterogeneity within treatments appeared likely[23]. Analyses were conducted using WinBUGS software (version 1.4). Further method detail can be found in eMethods 2.

We conducted analyses with interventions categorised both with, and without, any adjunct treatments. Furthermore, in order to attempt to assess both the immediacy and durability of effects, we planned analyses for three time points: end of treatment (our primary time point) as defined in the studies; 3 months from the start of treatment (the time point closest to 3 months from the start