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Conservative treatment of acute knee osteoarthritis: A review of the Cochrane Library

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ABSTRACT

Objective: To analyze conservative treatment of knee pain in patients with osteoarthritis.

Methods: A Cochrane Library search related to knee osteoarthritis was analyzed. Five main strategies for the conservative treatment of knee osteoarthritis have been reviewed: medical treatment, physical medicine and rehabilitation, intra-articular injections, and acupuncture.

Results: Regarding medical treatment, non-steroidal antiinflammatory drugs (ibuprofen, diclofenac, arthrotec, celecoxib, naproxen, rofecoxib) were superior to acetaminophen. The benefits of tramadol or tramadol/paracetamol, non-tramadol opioids, glucosamine, diacerein, and doxycycline were small. Herbal topical treatment with preparations from medical plants seemed to improve pain. Concerning oral herbal therapy, Piascidine ad extracts of *Boswellia serrata* had a short-term effect on osteoarthritis symptoms. Regarding physical medicine and rehabilitation, there was limited evidence that a brace had additional beneficial effect compared with medical treatment alone. Land-based therapeutic exercise and aquatic exercise had at least a small short term benefit. Therapeutic ultrasound may be beneficial (low quality of evidence). The effectiveness of transcutaneous electrostimulation for pain relief has not been demonstrated. Electrical stimulation therapy may provide significant improvements. Regarding intra-articular injections, viscosupplementation seemed to be an effective treatment for pain relief in the short-term (months). The short-term (weeks) benefit of intra-articular corticosteroids in the management of knee osteoarthritis has been demonstrated. The benefits of acupuncture were small. Self-management education programs resulted in no or small benefits on pain relief.

Conclusions: Five main strategies for the conservative treatment of knee osteoarthritis exist that must be used before indicating surgical treatment: medical treatment, physical medicine and rehabilitation, intra-articular injections, acupuncture, and self-management education programs.

1. Introduction

Osteoarthritis (OA) is a frequent cause of knee pain. There are a number of conservative treatments of knee OA that must be used before indicating surgical treatment. The purpose of this review was to analyze the existing conservative strategies for the treatment of pain related to knee OA.

2. Materials and methods

Cochrane Library systematic reviews related to the conservative treatment of knee OA were searched. There are five main strategies for the conservative treatment of knee OA: medical treatment, physical medicine and rehabilitation, intra-articular injections, acupuncture, and self-management education programs.

3. Results

3.1. Medical treatment

3.1.1. Acetaminophen

Published guidelines and expert opinion were divided over the relative role of acetaminophen (also called paracetamol or Tylenol) and non-steroidal anti-inflammatory drugs (NSAIDs) as first-line

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pharmacologic therapy of OA. The comparative safety of acetaminophen and NSAIDs is also important to consider. In a systematic review Towheed *et al.*^[11] assessed the efficacy and safety of acetaminophen versus placebo and versus NSAIDs (ibuprofen, diclofenac, arthrotec, celecoxib, naproxen, rofecoxib) for treating knee OA. The evidence to date suggested that NSAIDs were superior to acetaminophen for improving knee and hip pain in people with knee OA. The size of the treatment effect was modest, and the median trial duration was only six weeks, therefore, additional considerations need to be factored in when making the decision between using acetaminophen or NSAIDs. In knee OA subjects with moderate-to-severe levels of pain, NSAIDs appear to be more effective than acetaminophen.

3.1.2. Tramadol

Tramadol is increasingly used for the treatment of OA because, in contrast to NSAIDs, tramadol does not produce gastrointestinal bleeding or renal problems, and does not affect articular cartilage. Cepeda *et al.*^[12] sought to determine the analgesic effectiveness, the effect on physical function, the duration of benefit and the safety of oral tramadol in people with OA. Tramadol or tramadol/paracetamol decreased pain intensity, produced symptom relief and improved function, but these benefits were small. Adverse events, although reversible and not life threatening, often caused participants to stop taking the medication and could limit tramadol or tramadol plus paracetamol usefulness.

3.1.3. Oral or transdermal opioids

Opioids may be a viable treatment option if patients with knee OA suffer from severe pain or if other analgesics are contraindicated. However, the evidence about their effectiveness and safety is contradictory. Nüesch *et al.*^[13] tried to determine the effects on pain and function and the safety of oral or transdermal opioids as compared with placebo or no intervention in patients with knee OA. The small to moderate beneficial effects of non-tramadol opioids were outweighed by large increases in the risk of adverse events. Non-tramadol opioids should therefore not be routinely used, even if osteoarthritic pain is severe.

3.1.4. Glucosamine

Towheed *et al.*^[4] reviewed all randomized controlled trials, evaluating the effectiveness and toxicity of glucosamine in OA. The Western Ontario and McMaster Universities Arthritis Index outcomes of pain, stiffness and function did not show a superiority of glucosamine over placebo. Glucosamine was as safe as placebo.

3.1.5. Diacerein

Diacerein acts differently from traditional NSAIDs which inhibit prostaglandin synthesis, leading to adverse gastrointestinal effects. It has been proposed that diacerein acts as a slow-acting, symptom-modifying and perhaps disease-structure modifying drug for OA. Fidelix *et al.*^[15] reported that pain reduction with diacerein treatment was minimal. In fact, in Europe the use of diacerein has been not recommended.

3.1.6. Doxycycline

Pre-clinical data suggested that doxycycline might act as a disease-modifying agent for the treatment of knee OA, with the potential to slow cartilage degeneration. Da Costa *et al.*^[6] have found that the benefit of doxycycline was minimal to non-existent.

3.1.7. Chondroitin

Singh *et al.*^[7] have reported that in the short-term chondroitin (alone or combined with glucosamine) was better than placebo regarding the improvement of pain.

3.1.8. Topical and oral herbal therapy

Regarding topical treatment with preparations from medical plants, Cameron *et al.*^[8] have reported that Amica gel and Comfrey gel seemed to improve pain. Concerning oral herbal therapy, Piascidine ad extracts of *Boswellia serrata* had a short-term effect on OA symptoms^[9].

3.2. Physical medicine and rehabilitation

3.2.1. Braces and orthoses

Patients with knee OA can be treated with a brace or orthosis (shoe insole). The main purpose of these aids is to reduce pain. Duivenvoorden *et al.*^[10] have reported that the benefits of braces and orthoses for treating knee OA have not been shown.

3.2.2. Exercise

Fransen *et al.*^[11] reported that land-based therapeutic exercise was beneficial for people with knee OA in terms of reducing joint pain for at least 2–6 months.

Regarding the intensity of exercise Brosseau *et al.*^[12] evaluated the effectiveness of therapeutic exercise of differing intensities on objective and subjective measures of disease activity in people with knee OA. Both high intensity and low intensity aerobic exercise appeared to be equally effective in improving a patient's functional status, gait, pain and aerobic capacity for people with knee OA. Further research involving a greater number of subjects, and a larger number of studies involving a control group were needed to further substantiate these results.

Clinical experience indicated that aquatic exercise may have advantages for OA patients. Bartels *et al.*^[13] found that aquatic exercise appeared to have some beneficial short-term effects for patients with knee OA while no long-term effects have been documented. Based on this, one may consider using aquatic exercise as the first part of a longer exercise program for OA patients. The controlled and randomized studies in this area are still too few to give further recommendations on how to apply the therapy, and studies of clearly defined patient groups with long-term outcomes are needed to decide on the further use of this therapy in the treatment of OA.

Regnaux *et al.*^[14] made a comparison between high-intensity and low-intensity exercise programs. In the short-term no differences were found regarding the improvement of pain and physical function.

3.2.3. Therapeutic ultrasound

Therapeutic ultrasound is one of several physical therapy modalities suggested for the management of pain and loss of function due to OA. Rutjes *et al.*^[15] compared therapeutic ultrasound with sham or no specific intervention in terms of effects on pain and function safety outcomes in patients with knee OA. In contrast to the previous version of this review, their results suggested that therapeutic ultrasound may be beneficial for patients with knee OA. Because of the low quality of the evidence, we are uncertain about the magnitude of the effects on pain relief and function, however. Therapeutic ultrasound is widely used for its potential benefits on both knee pain and

function, which may be clinically relevant. Appropriately designed trials of adequate power are therefore warranted.

3.2.4. Transcutaneous electrical nerve stimulation

Rutjes *et al.*^[16] did not demonstrate the effectiveness of transcutaneous electrical nerve stimulation for pain relief.

3.2.5. Electromagnetic fields

Li *et al.*^[17] assessed the effectiveness of pulsed electric stimulation for the treatment of knee OA and the most effective and efficient method of applying an electromagnetic field, through pulsed electromagnetic fields or electric stimulation, as well as the consideration of length of treatment, dosage, and the frequency of the applications. Current evidence suggested that electromagnetic field treatment may result in moderate pain relief in patients with knee OA.

3.3. Intra-articular injections

3.3.1. Viscosupplementation

Bellamy *et al.*^[18] assessed the effects of viscosupplementation in the treatment of knee OA. They found that viscosupplementation was an effective treatment for knee OA with beneficial effects: on pain, function and patient global assessment, and at different post injection periods but especially at the 5–13 week post injection period. Overall, the aforementioned report supported the use of the hyaluronic acid in the treatment of knee OA.

3.3.2. Intra-articular injections of corticosteroids

Jüni *et al.*^[19] evaluated the efficacy and safety of intra-articular corticosteroids in treatment of knee OA. The report could not confirm whether this treatment is effective after 1–6 weeks.

3.4. Acupuncture

Manheimer *et al.*^[20] assessed the effects of acupuncture for treating knee OA. Sham-controlled trials showed statistically significant benefits. However, these benefits are small, do not meet our pre-defined thresholds for clinical relevance, and are probably due at least partially to placebo effects from incomplete blinding. Waiting list-controlled trials of acupuncture for peripheral joint OA suggested statistically significant and clinically relevant benefits, much of which may be due to expectation or placebo effects.

3.5. Self-management

Self-management education programs try to teach patients how to take an active role regarding their behavior modification. Kroon *et al.*^[21] reported that this treatment resulted in no or small benefits on pain relief.

4. Discussion

In this review, the conservative treatment of knee pain in patients with OA is analyzed^[1–21]. The Cochrane Library search performed has shown five main strategies for the conservative treatment of knee OA: medical treatment, physical medicine and rehabilitation, intra-articular injections, acupuncture, and self-management education programs.

Medical treatment has a great importance^[1–9]. NSAIDs have shown to be superior to acetaminophen. The benefits found of tramadol or tramadol/paracetamol, non-tramadol opioids, glucosamine, diacerine, and doxycycline are small. An improvement in the intensity of pain has been found with herbal topical treatment with preparations from medical plants. Oral herbal therapy, with Piascledine (an herbal supplement that contains extracts of soybean and avocado, 300 mg daily) and extracts of *Boswellia serrata* has a short-term effect on OA symptoms.

Regarding physical medicine and rehabilitation^[10–17], therapeutic ultrasound may have some beneficial effects. Electrical stimulation therapy may improve symptoms. Intra-articular injections of corticosteroids relieve pain for weeks, while intra-articular injections of hyaluronic acid (viscosupplementation) relieve pain for months^[18,19]. The benefits of acupuncture seem to be small^[20]. Self-management education programs have no benefits or small benefits on pain relief^[21].

Five main strategies for the conservative treatment of knee OA exist: medical treatment, physical medicine and rehabilitation, intra-articular injections, acupuncture and self-management education programs. These methods must be used before indicating surgical treatment.

Conflict of interest statement

The author reports no conflict of interest.

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