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Invited Review

Evidence-Based Review of Nonsurgical Treatments for Knee and Hip Osteoarthritis

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Abstract

Knee and hip osteoarthritis (OA) are highly prevalent joint diseases that lead to chronic pain, disability, and increased mortality. In this review, we provide a summary of nonsurgical treatments available for knee and hip OA that have evidence to support their use. We also provide a summary of the treatments available for knee and hip OA that do not have sufficient evidence to support their use. Treatments covered in this review include pharmacologic and nonpharmacologic modalities.

Keywords: Hip, knee, osteoarthritis, treatment

Introduction

Osteoarthritis (OA), also referred to as degenerative arthritis, is a common form of joint disease. Osteoarthritis typically affects the knee, hip, hand, and spine, involving a single joint site or multiple sites. The global burden of OA is massive. The prevalence of symptomatic knee OA among those ≥60 years is roughly 12%.[1] The prevalence of symptomatic hip OA is approximately 4.2%.[2] With the aging of the population and the high burden of overweight/obesity, the two major risk factors, it is not surprising that the prevalence of knee and hip OA is increasing. OA is more common in women than in men. Joint trauma is another risk factor for OA, particularly in younger adults. The impact of OA on morbidity and mortality is substantial.[3] In fact, knee OA is a leading cause of mobility-disability worldwide.[3] Patients with knee and hip OA are less active and have a greater risk of mortality.[4]

Osteoarthritis is a whole-joint disease. Articular cartilage loss is the hallmark, but synovitis, subchondral bone sclerosis, and osteophytes are other pathologic features of OA. Radiographic features of OA include joint space narrowing (reflecting cartilage loss), juxtaarticular bone sclerosis, and osteophyte formation.[5] Additionally, advanced imaging such as ultrasound[6] or magnetic resonance imaging (MRI) can detect synovitis and intra-articular soft tissue derangements, such as meniscal or ligamentous injury, both pathologies implicated as sources of pain in OA.[7] Pain, generally associated with joint use, is the cardinal clinical feature of OA. Weakness of muscles supporting the joint is often present and contributes to the reduced physical function and disability associated with knee and hip OA.[8,9] Instability or "buckling" of the knees is a common presentation of knee OA, which is related to muscle weakness and/or internal derangement (e.g., anterior cruciate ligament tear).[10]

Understanding the source of pain and instability helps to identify the treatments for OA. This review summarizes the evidence-based nonsurgical treatments currently available for knee and hip OA. The need for evidence-based treatment is key given the high prevalence of OA to allow for safe and effective treatment in keeping with the well-being of the patients.

Search Strategy and Selection Criteria

References for this review were identified through searches of PubMed with the search terms "Osteoarthritis," "Knee," "Hip," "Prevalence," "Ultrasound," "Magnetic resonance imaging," "Pain," "Buckling," "Synovitis," "Bone marrow lesion," "Treatment," "Guidelines," "Nonsteroidal anti-inflammatory drugs," "Topical," "Intra-articular," "Glucocorticoids," "Steroids," "Hyaluronic acid," "Duloxetine," "Tramadol," Opioids," "Hydroxychloroquine," "Methotrexate," "Anti-TNF," "Biologics," "Radiofrequency ablation," "Prolotherapy," "Stem cells," "Exercise," "Aerobic," "Resistance," "Balance," "Aquatic," "Brace," "Orthoses," "Kinesiotaping."

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Treatment Strategies

Overarching Goals of Treatment

There are no disease-modifying pharmacotherapies available to halt the progression or reverse the changes of OA in a joint. Thus, the goal of treatment is to provide symptomatic relief, preserve physical function, and prevent disability. The approach to treatment of OA, in principle, is similar for all joints but is primarily based on knee OA, for which most evidence exists.

Treatment Targets

While some people with radiographic evidence of OA in their joints may not have pain, most patients do report some degree of pain from OA.[11] In the early stages, pain may be intermittent and limited to joint use, but later in the disease course, pain may become persistent. To treat OA pain effectively, we need to understand the sources of pain. Studies utilizing imaging at different intervals have identified joint structures that correlate with pain. For example, a longitudinal study using MR imaging of the knees identified the presence of synovitis, knee effusion, and bone marrow edema to correlate with knee pain in OA.[12] This is relevant to the management of OA because traditionally, OA is considered a degenerative joint disease with "wear and tear." Of note, MR imaging is useful in understanding the pain sources in OA, but MR imaging is not recommended in clinical practice to ascertain these pathologies, nor are they helpful in guiding treatment. Another open-label trial demonstrated that synovial volume was associated with pain and shrank in response to steroid injection[13] further demonstrating the role of synovitis in OA pain. Similarly, another study, utilizing data from a large osteoarthritis cohort, examined and determined that subchondral bone marrow lesion volume is associated with weight-bearing pain.[14]

Histologic evidence also corroborates the presence of synovitis in the majority of cases of OA, suggesting a role, not only as a source of pain but also an important role potentially in the pathogenic mechanism.[15] Therefore, synovitis is considered a treatment target. The bone marrow edema refers to transient lesions in the subarticular bone as a consequence of microtrauma. Therefore, avoiding trauma and adopting joint protective strategies would be helpful for pain management in OA. In addition, structures surrounding the joint (e.g., bursae) can be sources of pain in knee and hip OA.

Main Points

- Osteoarthritis of the knee and hip is common joint disease that pain and difficulty walking.
- No treatment is available at this time that can cure osteoarthritis. Therefore the goal of treatment for knee and hip osteoarthritis is to improve pain and ability to function in daily life.
- Education, exercise and braces are important components of treatment of osteoarthritis.
- Medications known as non-steroidal anti-inflammatory drugs or NSAIDS are commonly used to treat pain and inflammation.
- Steroid injections also help with pain relief.

Treatments with Evidence for Use in Knee and Hip Osteoarthritis

In recent years, guidelines for the management of OA have been promulgated by many societies, including the European Alliance of Associations for Rheumatology (EULAR),[16] the National Institute for Health and Clinical Excellence (NICE),[17] the Osteoarthritis Research Society International (OARSI)[18] and the American College of Rheumatology (ACR).[19] Compared to the previous versions of treatment guidelines, recent or updated versions emphasize the importance of a multi-modal approach, combining physical and pharmacologic strategies.[19,20] We provide below a summary of recommendations for knee and hip OA management, nonpharmacologic and pharmacologic, that have been proposed by more than one society and supported by strong evidence. We also provide a summary of treatments not supported by evidence and those that should be avoided due to potential adverse effects.

Nonpharmacologic Treatments for Knee and Hip Osteoarthritis

Education, exercise, and orthosis/assistive devices for mobility are essential components of the multimodality approach to managing knee and hip OA. We describe each one of these strategies below.

Patient Education: Engaging patients and partnering with them through education and shared decision-making is an important component of OA management. Patients often refer to the term "arthritis" for any joint-related symptoms. Therefore, they need to be educated about the difference between OA vs. inflammatory arthritis. This helps with setting goals and expectations, and even with treatment, for e.g. that they may not be completely pain-free. While most of the evidence pertaining to education in OA management is in conjunction with exercise intervention, a systematic review that included studies on education by itself or in combination with other modalities found a positive impact in older adults (>50 years) on pain and function in knee and hip OA.[21]

Exercise and Weight Loss: A large body of evidence supports the important role of exercise in knee and hip OA.[22] There are many types of exercise, and each has its own importance.[23] Resistance or strengthening exercises are essential for maintaining muscle support across joint lines. Strengthening of hip abductors and knee extensors is especially beneficial for hip and knee OA, respectively. Aerobic exercise is helpful for weight loss and maintaining endurance. Neuromuscular exercise (e.g., NEMEX) helps with balance training.[24] Aquatic exercises have the advantage of offering aerobic exercise in a low-impact environment, which is helpful for those with knee and hip OA with pain on weight bearing. Tai chi is a form of mind and body exercise that reduces pain in knee OA.[25] However, the exercise recommendation is general and standardized to fit all, as we are not at a stage where personalized exercise prescriptions with dose and duration can be provided to individual patients.

Orthoses and Assistive Devices: Unloader braces for tibiofemoral OA are recommended,[26] although the evidence for patellofemoral OA is not as strong. These braces, when fitted properly, divert weight-bearing loads from diseased to non-disease regions of the joint and can reduce pain.[26] They may also provide welcomed stability. A cane is strongly recommended, providing assistance with ambulation for those with knee and hip OA, for pain, instability, and muscle weakness.[27] Older adults with mobility impairments may use a walker for balance and support.

Pharmacologic Agents

Drugs that target inflammation are utilized in oral, topical, or intraarticular forms for OA pain management. Also utilized for treatment are drugs that provide pure analgesia without any effect on underlying pathology, as described below:

Systemic and Topical Nonsteroidal Anti-inflammatory Drugs (NSAIDs): the most commonly used class of drugs for OA is NSAIDs. Their anti-inflammatory effect is through

blockade of the prostaglandin pathway. Many trials have indicated a positive response to systemic NSAIDs for OA.[28] However, NSAIDs have a multitude of adverse effects, including renal, gastrointestinal (GI), and cardiovascular. Some NSAIDs have a lower cardiovascular risk than others. The cyclooxygenase 2 (COX-2) inhibitors were developed to have minimal GI side effects. A large trial (PRECISION) compared the efficacy of the COX-2 inhibitor with 2 other nonspecific NSAIDs (ibuprofen and naproxen) and found that the GI side effects were lower in celecoxib and the cardiovascular and renal adverse effects were safer for celecoxib than one or both comparators.[29] In light of their adverse effects, it is recommended that NSAID use for OA be limited to the short term and at an anti-inflammatory dose. Systemic absorption is low for topical NSAIDs. The systemic concentration was reported to be 5-17 times lower in topical diclofenac compared with oral diclofenac.[30]

Topical NSAIDs work through local absorption through the skin into the joint tissue of superficial joints, such as knees and hands. Their efficacy for deeper joints, such as the hip, has not been established. In comparison to systemic NSAIDs, the efficacy of topical NSAIDs is lower, but due to their better safety profile, it is advisable to try topical NSAIDs as a first line for knee OA, especially for older adults.[31] The adverse effects of topical NSAIDs are limited to cutaneous local irritation.

Acetaminophen or Paracetamol: In trials, the effect size for acetaminophen/paracetamol is small, but it may be considered for patients with comorbidities that preclude the use of NSAIDs. In vitro studies have demonstrated the COX-2-blocking property of acetaminophen[28,32] but its anti-inflammatory effect in patients has not been demonstrated. Monitoring of hepatic function is recommended, especially if the cumulative dose of acetaminophen exceeds 3 g/day.

Tramadol and Opioid Analgesics: These are discouraged for use as first-line agents, yet there are some patients who may benefit from pure analgesia. The analgesic effect of tramadol is through a dual mechanism—central processing of pain through blockade of neurotransmitters and weak blockade of μ-opioid receptors, but efficacy is low.[33] A recent large study showed increased mortality associated with the use of tramadol compared to NSAIDs, therefore raising concern regarding safety.[34]

Intra-Articular Corticosteroids: There is strong evidence to support the efficacy of intra-articular corticosteroids for short-term pain relief with intra-articular (IA) corticosteroids.[35] Corticosteroid injections provide anti-inflammatory effects through local drug delivery. There is systemic absorption for 24-36 hours post-injection. However, IA steroid injection is a safe office procedure that can be performed at the bedside for the knee joint; ultrasound guidance is preferred for hip injection.[36] The risk of bleeding or infection is rare with proper procedural protocol. No specific formulation is preferred. A recent large trial suggested the possibility of IA steroid-induced cartilage loss,[37] but subsequent large-scale studies have shown that patients treated with steroid injections are at no higher risk of progression or knee replacement than patients not so treated.[38]

Other: While there are no direct head-to-head comparisons, in a network meta-analysis, topical NSAIDs and capsaicin were noted to be equally efficacious in prior studies.[39] The challenges of capsaicin are the possibility of eye contamination and the poor efficacy of deeper joints, such as the hip.

Treatments that Lack Sufficient Evidence for Use in Knee and Hip Osteoarthritis

Nonpharmacologic Treatments: There are several other physical modalities being used in practice that do not have strong evidence to support their use. Kinesiotaping may be helpful in knee OA.[40] The hip joint is too deep to benefit from it. The mechanism of kinesiotaping is to lift the skin and soft tissue so that the nociceptors are offloaded while allowing a range of movement across the joint. Taping may also provide enhanced proprioceptive input, which has been reported to be impaired in persons with OA. The jury is still out on the type of shoe or lateral/medial wedge.[41] Similarly, while acupuncture is popular among patients due to its relative safety, the results are controversial in their support for knee/hip OA pain.[42,43] Pain societies have described radiofrequency ablation as a potentially useful tool for pain relief for knee and hip pain, but there is limited data to support its more widespread use.[44] Transcutaneous electrical nerve stimulation (aka TENS) units have been used for back pain, but evidence is scant to support their use in knee or hip OA pain.

Pharmacologic Treatments: Duloxetine has shown evidence for providing pain relief in knee OA patients in prior trials.[45,46] The mechanism is unclear, but possibly through central pain processing. However, a recent cluster randomized trial demonstrated no benefit for knee and hip OA, which likely suggests a lack of efficacy.[47] While synovitis is a potentially important target for treatment, disease-modifying treatments that are useful in controlling synovitis in rheumatoid arthritis and other inflammatory arthritis are not helpful for OA.[48] Due to the potential for serious adverse effects of immunomodulating therapies, their use in OA is strongly discouraged. Similarly, while subarticular bone is involved in OA, bone-modulating therapies have not been shown to benefit OA pain or pathology.[49] Despite the potent anti-inflammatory effect, systemic steroids have not shown any evidence for knee or hip OA for pain or function, even though there is some evidence to suggest improvement in pain and function in hand OA with 6 weeks of prednisone 10 mg/day.[50] Based on the fact that the viscosity of the knee joint fluid that provides lubrication for movement is reduced in OA and that hyaluronic acid is one of the components of the knee synovial fluid that provides viscosity, hyaluronic acid injections are used for OA pain. Unfortunately, a large number of published and unpublished trials raise concern for the lack of efficacy of hyaluronic

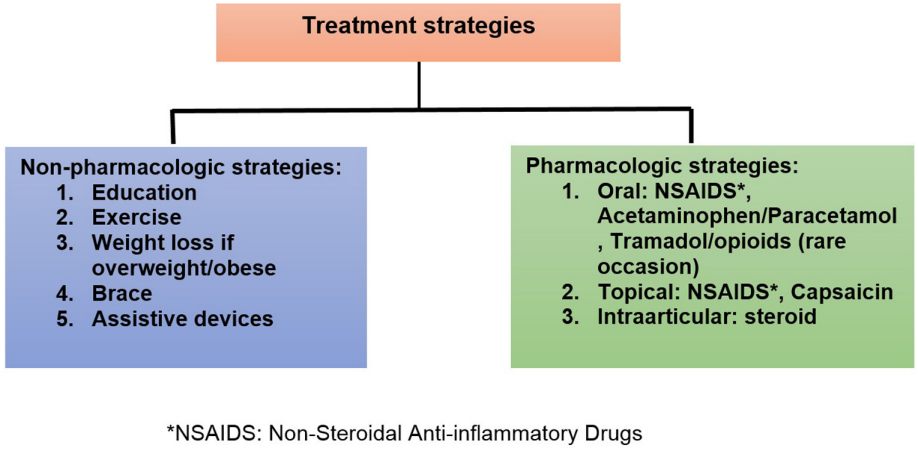

Figure 1. Treatment strategies for osteoarthritis of knee and hip.

acid preparations for OA symptoms.[51] There is no evidence to support the use of supplements such as glucosamine, chondroitin, and vitamin D for OA.

Other: The evidence is even poorer for therapies such as prolotherapy and stem cell transplant; therefore, it is important for rheumatologists to recommend against such therapies.

Conclusion

The goal of the treatment for knee and hip OA is to minimize pain and maximize function. Patient education is key to goal-setting. Treatments for which there is definite evidence to support their use in knee and hip OA are exercise and braces for nonpharmacologic strategies and NSAIDs (systemic and topical), acetaminophen, and intra-articular corticosteroids for pharmacologic options (Figure 1). The emphasis should be on a multimodal approach to managing patients and taking into account their individual preferences and needs.

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