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REVIEW

Injectable corticosteroids in treatment of arthritis of the knee

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ABSTRACT: Injection of corticosteroid preparations for the local treatment of musculoskeletal disorders affecting the knee, such as osteoarthritis and rheumatoid arthritis, has been used widely since the 1950s. This local therapy minimizes systemic toxicity and can result in rapid improvement in symptoms, most often as an adjunctive therapy for acute or severe symptom flares. The evidence assessing safety and efficacy is reviewed and analyzed. Intra-articular knee injection technique is described and is a procedure that is easy to learn and can be performed quickly in an office or hospital setting.

Corticosteroid injections with long-lasting crystalline suspensions (depot formulations) have been widely used to treat arthritis and other painful musculoskeletal conditions since the 1950s.[1] Their continuing use can be attributed to their safety record and the prompt, often substantial relief that they can provide patients. For patients with arthritis who fail to gain adequate relief from oral medications and nonpharmacologic treatments, intra-articular corticosteroid injections are one of the few alternative nonsurgical adjunctive therapies available.[2-4]

This review examines the safety and efficacy of intra-articular corticosteroid use in the treatment of conditions affecting the knee and reviews guidelines and techniques for corticosteroid injections.

Safety of intra-articular corticosteroid therapy

Intra-articular corticosteroid injections have demonstrated an excellent safety record over many years and are described by the American College of Rheumatology (ACR) as "safe and effective when administered by an experienced physician."[5] As with any pharmacologic agent, however, corticosteroids do have side effects, and treatment should only be given in the setting of an appropriate, documented indication. Most clinicians recommend at least 3 months between injections, largely out of concern for the potential effects of corticosteroids on joint structure (see below), but data supporting this specific interval are lacking.[6-8]

Table 1 lists potential side effects of intra-articular corticosteroid therapy, with methods to minimize them. Local reactions to intra-articular corticosteroids range from common, usually mild, side effects, such as postinjection flares, to serious but rare complications, such as septic arthritis or skin or fat atrophy.[9] Postinjection flares occur in about 2% to 6% of patients[8,10] and are believed to result from chemical synovitis in response to the injected crystals.[7,11] These flares are typically managed by analgesic therapy or ice packs[9] or occasional re-aspiration of the fluid. Joint infection is an extremely rare complication. Incidences from 1 in 3000 to 1 in 50 000 have been reported.[12] Symptoms of infection usually occur 3 to 4 days after injection, whereas postinjection flares are usually observed within the first 24 hours. Subcutaneous lipoatrophy was the only significant complication observed in a prospective study of intra- and

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Table 1 Potential side effects of intra-articular corticosteroid treatment (and methods that may decrease their incidence)[8,9,48,57]

Systemic effects (avoid high doses and multiple simultaneous injections, utilize accurate injection techniques)
Tendon weakening/rupture, fat atrophy, muscle wasting, skin pigment changes (avoid misdirected injections)
Septic arthritis (use aseptic technique, withhold therapy in at-risk patients)
Nerve and blood vessel damage (utilize accurate injection techniques)
Postinjection symptom flare/synovitis (avoid same preparation for future injections)
Flushing (avoid high doses)
Anaphylaxis (take careful drug allergy history)
Steroid arthropathy (avoid high doses and overly frequent injections)

periarticular injections of methylprednisolone acetate, affecting 4 of 672 patients (0.6%).[13] This complication may be more common with less soluble agents, such as the triamcinolone compounds.[8]

A major concern involving intra-articular corticosteroid use is joint degradation, either as a catabolic effect of the agent or from increased use of a less painful but still diseased joint. Studies in rabbits found that intra-articular corticosteroids caused degeneration in mature cartilage cells (chondrocytes),[14] but this has not been supported by studies in primates.[15] Transient effects on bone formation have been observed in humans, but no net effects on bone resorption were detected.[16] No evidence of increased loss of joint space was observed in patients receiving triamcinolone acetonide injections every 3 months for up to 2 years for osteoarthritis of the knee,[17] and frequent injection of rheumatoid joints was not associated with a higher frequency of joint replacement surgery.[18] In 21 children receiving intra-articular corticosteroid injections into the knee (n = 18), ankle (n = 2), or elbow (n = 1), no effect on cartilage integrity or inhibition of statural growth was observed during a 13-month study.[19] A retrospective review of radiographs of 76 injected joints of children with chronic arthritis found joint changes compatible with the underlying disease, with the possible exception of the hip.[20]

Systemic effects after intra-articular corticosteroids are uncommon. Flushing may be observed a few hours after injection.[8] The absence of net impact on bone resorption in humans suggests that corticosteroid-induced osteoporosis is not a major concern in patients receiving reasonable numbers of corticosteroid injections.[16] Myopathy, although occurring with systemic therapy, has not been seen with local injections.[21] Although corticosteroids can occasionally affect glucose control, a small study in which diabetic patients received soft tissue injections of methylprednisolone acetate did not detect a significant effect on blood glucose levels.[22]

Use and efficacy of intra-articular corticosteroid therapy for conditions affecting the knee

Corticosteroid injections have been used successfully in a number of conditions, with osteoarthritis the most common and best studied. Surveys have indicated that approximately 90% of orthopedists and 95% of rheumatologists employ such therapies,[23,24]and ACR recommendations for the management of rheumatoid arthritis and osteoarthritis of the knee support their use.[5,25] The following sections review current data concerning the efficacy of intra-articular corticosteroids in conditions affecting the knee.

Osteoarthritis

Probably the most common use for intra-articular corticosteroid injections into the knee is the treatment of osteoarthritis. For painful and swollen joints, arthrocentesis followed by intra-articular glucocorticoid injection can be an effective way to decrease pain and allow exercise that can increase quadriceps strength.[25] Although typically used as an adjunctive treatment to systemic analgesic therapy and physical measures, corticosteroid injection is also an appropriate monotherapy in selected patients according to the ACR recommendations for treatment of osteoarthritis of the knee.[25] The short-term effects (1-4 weeks) of injected corticosteroids relative to placebo for osteoarthritis of the knee have been shown.[26,27] A long-term effect is more difficult to demonstrate.

About three-fourths of treated patients with osteoarthritis of the knee experience a positive response to intra-articular corticosteroid injection.[28] Factors that affect this response remain unclear,[29] although one report found that patients with clinical evidence of effusion and those who had synovial fluid successfully aspirated at the time of injection showed greater improvements,[28] and another found that men experienced a more significant benefit than women.[30] Use of intra-articular corticosteroids plus joint lavage may have some short-term additive effect.[27,31]

Two recent meta-analyses[32,33] examined the efficacy of intra-articular corticosteroids in osteoarthritis of the knee. The meta-analysis by Arroll and Goodyear-Smith[32] involved 10 placebo-controlled, randomized trials. Pooled data from 6 studies that examined improvement in symptoms at 2 weeks indicated that corticosteroid injection was significantly more effective than placebo ($P = 0.00001$).[32]

Pooled data from the two meta-analyses[32,33] found a significant effect on pain in favor of corticosteroid treatment