

Intra-articular corticosteroid injection for osteoarthritis

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Intra-articular corticosteroid injection

Intra-articular injection of corticosteroid is an effective, safe and rewarding procedure. Osteoarthritis (OA) is a condition that only affects joints so it seems logical to target therapy directly to the joint and thus, bypass the potential side effects of systemic administration. Following the first report of the use of intra-articular corticosteroid in 1951 by Hollander *et al.* [1], the procedure has become popular with both clinicians and patients [2]. Injection of long-acting insoluble corticosteroids into the knee produces rapid improvement in symptoms and can be repeated with predictable benefit in suitable patients [3–8].

Sites other than the knee

The knee is by far the most common site requiring injection for OA, although other joints such as the hip and thumb base (first carpo–metacarpal joint [CMCJ]) can also be successfully injected [9–13]. Although the only randomized controlled trial (RCT) for thumb-base injection versus placebo was negative, it was insufficiently powered [14], and injection of the first CMCJ for OA remains a popular treatment for patients with pain that is resistant to other measures. In one RCT, a single corticosteroid injection was demonstrated to be superior to three, weekly injections of hyaluronan for first CMCJ OA [15], although both were effective. Ultrasound or other imaging guidance is now preferred for some joints, especially in the hip [13], but this is not necessary for injection of the large and readily accessible knee joint, which requires only a good technique and knowledge of basic anatomy. Although studies have demonstrated that the accuracy of knee injection is not as good as most clinicians would hope (approximately a 70% success rate) [16–17], image guidance is unnecessary in the vast majority of cases, especially when synovial fluid is obtained

(confirming accurate placement) and the practitioner is experienced [16]. Having said this, there is increasing evidence that ultrasound guidance improves clinical outcome and an increasing number of rheumatologists are now utilizing this technique [18].

Efficacy

Intra-articular corticosteroid injection is quick and simple to carry out and in RCTs it has a large effect size (ES) of 1.27 at 7 days post-injection for pain relief against placebo for knee OA [10]. It produces relatively rapid relief of severe pain within a few hours or days. Although this benefit is relatively short lasting, in RCTs (1–4 weeks), individual patients may derive benefit for 2–3 months or longer. When used with other treatments, this relatively large ES is likely to improve confidence in, and adherence to, other treatments including core nonpharmacological interventions. For these reasons, the UK regulatory body, NICE, recommends intra-articular corticosteroid injection as a useful adjunct to core treatment for the relief of moderate-to-severe pain in OA patients [10]. Many guidelines suggest that patients having a 'flare', or those with a joint effusion, may particularly benefit from a steroid injection, which seems logical for a drug with a potent anti-inflammatory effect. However, there is little objective evidence that the presence of clinically assessed joint inflammation is a predictor of clinical outcome, although the presence of an effusion may improve the accuracy of injection, which itself is a predictor of response [8,16]. Although not all patients respond, it is a rewarding procedure for the vast majority who do. It may even work well for patients with advanced radiographic change. Some patients receive three-monthly injections as an integral part of their management plan, providing excellent supplemental symptom relief [19]. In addition, the predictable benefit can be used to an advantage for special events,



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such as family weddings, celebrations or holidays, by delivering an injection just prior to the event. Some patients with advanced OA and significant comorbidity prefer to have repeat injections, supplemented with other pharmacological and nonpharmacological measures, rather than proceed to knee replacement.

Evidence-based practice

The philosophy of evidence-based (EB) clinical practice is to make rational clinical decisions in the light of available evidence and to integrate the best research evidence with clinical expertise and patient values [20]. The three main forms of evidence for clinical management are:

- Research – mainly RCTs for efficacy and observational studies for safety;
- Expert practitioner experience, opinion and common sense;
- Patient acceptability, experience and opinion.

Perhaps surprisingly for such a highly recommended treatment, the research evidence for intra-articular corticosteroid is relatively limited and many studies are old and therefore of low quality when formally scored [4–7]. This probably reflects the fact that the other two EB components (patient and expert experience and opinion) are so overwhelmingly supportive that there is no perceived need for further large well-conducted trials. However, additional research evidence might be helpful in identifying simple predictors of response since currently, this remains inconclusive [3,8]. In RCTs, disease duration, radiographic scores, inflammatory markers and signs of inflammation have not been demonstrated to correlate with the efficacy of intra-articular corticosteroids [3,8].

Nonspecific effects of treatment

A recently published systematic review and meta-analysis of placebo response in OA RCTs confirmed the appreciable ES of ‘placebo’ on pain relief [21] and identified some of the factors that may determine the size of this effect. The route of delivery of a treatment has a large impact on placebo ES, and in this meta-analysis, the highest placebo ES was seen with intra-articular injections. Furthermore, this ES was even higher when serial rather than single injections were given. This was highlighted by RCTs of serial injections of hyaluronan, which have only modest benefit at best when the substantial nonspecific effect of repeated injections is subtracted [22]. Interestingly, planned serial corticosteroid

injections also produce added benefit over single injections with no specific arrangement for future repetition. It is therefore apparent that there is a high expectancy and certain ‘magic’ associated with the intra-articular route (FIGURE 1). Although ‘placebo response’ is often regarded as a nuisance for assessing treatment benefits in RCTs, it has been suggested that practitioners should maximize the nonspecific benefits of treatment for conditions such as OA, in which the ES of placebo (just one form of ‘contextual’ or ‘meaning’ response) is clearly greater than the specific effect of any of its treatments [23]. The best ways to do this are by making a thorough patient assessment, listening to and addressing patient concerns, seeing the patient again to determine the outcome and re-enforcing positive messages [23].

“Commonly used preparations for intra-articular injection are the longer acting hydrophobic steroids...”

Practical points

An aseptic technique and use of sterile equipment is mandatory. Gloves should be worn to protect the operator but need not be sterile if a no touch technique is used [24,25]. Simple swabbing with alcohol is as effective as chlorhexidine in killing skin flora [26]. For knee injection, the patient should be positioned on a couch with the injection area supported sufficiently so that the muscles can comfortably relax. For apparently ‘dry’ knees and those with only small fluid collections, a medial approach may be preferred. For this, the site of entry is just below the midpoint of the patella and the needle is aimed directly under the patella. Synovial fluid may be aspirated after as little as 1 cm of penetration and deep introduction of the needle is not usually required. Pressure can be applied with the other hand to the lateral aspect of the knee to encourage fluid over to the medial side. A superolateral approach is commonly used for large effusions that distend the suprapatellar pouch. Aspiration of synovial fluid may improve the outcome in patients with knee effusion who are treated with intra-articular steroid [27]. However, it is advantageous not to aspirate to complete dryness, as leaving a little fluid may reduce the risk of needle displacement when the syringe barrels are being changed. This is important since there may be uncertainty regarding injection placement in the absence of withdrawn fluid [8,16]. Correct placement is further supported by lack of resistance to the injection. Commonly used preparations

for intra-articular injection are the longer acting hydrophobic steroids such as methylprednisolone acetate and triamcinolone hexacetonide.

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 “Intra-articular corticosteroid is an excellent and safe treatment for patients with knee OA.”

Safety & aftercare

Provided that sterile equipment and a sensible, aseptic approach are used, knee injection is a very safe procedure. For the patient, the procedure should be no worse an experience than venepuncture. After needle withdrawal, the puncture site should be pressed with a cotton wool ball until local skin bleeding has stopped. Patients on anticoagulation treatment can be safely injected provided the international normalized ratio (INR) is within the therapeutic range, appropriate care is taken and pressure is maintained a little longer on the puncture site. The procedure is relatively quick and any discomfort should be short lived. The toxicity of steroid injection is low but patients should be warned about facial flushing (12%), post-injection flare (15%) and sepsis (estimated at a < 1:78,000 risk) [2]. Although the risk of infection is extremely small [28,29], individual cases continue to be reported, so it is best to warn the patient of this remote possibility. Prosthetic joints should not be injected without consulting an orthopedic specialist. Subcutaneous atrophy is more of a concern with periarticular injections [30], but a small area of skin depression or depigmentation may occur due to steroid leaking back at the injection site, especially if a fluorinated steroid (triamcinolone) is used. It is generally proposed that the frequency of injections should be no more than three monthly, although there is no conclusive evidence of any detrimental effect on cartilage or bone from steroid injection in patients with arthritis. There are some theoretical concerns from animal experiments, but a large case series of long-term follow-up of children with juvenile idiopathic arthritis, who had received multiple injections, failed to demonstrate any adverse effect on the joint [31,32]. Raynauld *et al.* demonstrated that there were no deleterious effects from three monthly steroid injections for knee OA in a 2-year RCT, only clinical benefits [19].

There is some evidence of systemic absorption following intra-articular steroid injection, but this is unlikely to be clinically important in the large majority of cases [33–35]. The patient may be told that a small amount of the injection is



Figure 1. There is a high expectancy of benefit from intra-articular injection and this contextual response can be used advantageously.

absorbed into the system but that this is unlikely to have any significant effects. Some advocate bed rest or reduced activity for 12–24 h following injection into a large weight-bearing joint in order to improve therapeutic benefit, as injected material leaves the joint more rapidly with use of the joint. However, the two main studies of post-injection rest show conflicting results and so the issue is unresolved [36–38]. Nevertheless, the constraints on bed capacity in most rheumatology services result in the pragmatic advice for patients to simply avoid undue activity for the first 24 h following the injection. Some rheumatologists provide written information for the patient but often this will not be read and understood until after the injection so the discussion with the patient remains important.

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Conclusion

Intra-articular corticosteroid is an excellent and safe treatment for patients with knee OA. It should be offered to individual patients where appropriate, to supplement core nonpharmacological measures as part of a package of care. The contextual response to injection therapy is substantial and this can help to optimize the other benefits of management.

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