

The efficacy, accuracy and complications of corticosteroid injections of the knee joint

James G. McGarry · Zubin J. Daruwalla

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Abstract

Purpose Corticosteroid knee injections are being increasingly used in the conservative management of knee osteoarthritis. The procedure is usually performed in secondary care by orthopaedic surgeons and rheumatologists, but as the role of general practitioners in chronic disease management expands, joint injections are now frequently being performed in primary care. It is commonly perceived amongst clinicians that the benefits of corticosteroid knee joint injections in treating symptomatic knee osteoarthritis significantly outweigh the risks of complications.

Methods The evidence in the literature for the benefits, accuracy, safety and complications of corticosteroid knee injections in osteoarthritis is reviewed. The perception that serious complications are rare is addressed, and the incidence of infectious complications is estimated.

Results and conclusions Short-term symptomatic relief is the only evidence-based benefit of corticosteroid injection of an osteoarthritic knee. Accurate intra-articular placement is not achieved in up to 20% of injections and varies considerably with the anatomical approach used. There is no evidence that a medial approach is more accurate. The incidence of serious infectious complications following knee joint injections ranges widely, and may be as high as 1 in 3,000 and potentially far higher in high-risk patients for whom specialist management is advised.

Keywords Knee · Osteoarthritis · Joint injections · Corticosteroids · Complications · Infection

Introduction

Corticosteroid knee injections are being increasingly used in the conservative management of knee osteoarthritis [4]. The procedure is usually performed in secondary care by orthopaedic surgeons and rheumatologists (and trainees in either specialty), but as the role of general practitioners in chronic disease management expands, joint injections are now frequently being performed in primary care. Serious but avoidable complications of a simple corticosteroid knee joint injection can result in significant morbidity as is well documented in case reports in the literature. In the case of infectious complications this can be extremely costly, resulting in prolonged hospital stay for lengthy courses of antibiotics and even the need for surgical intervention. It is widely perceived, however, that such serious complications from corticosteroid knee joint injections are rare, and that their benefits in treating symptomatic knee osteoarthritis significantly outweigh any associated risks.

In this review of the literature, the evidence for the benefits of corticosteroid joint injections in knee osteoarthritis is discussed, along with the various factors that may influence their efficacy, including the accuracy of intra-articular needle placement. Regarding the potential complications of knee joint injections, the perception amongst clinicians that the incidence of infectious complications is extremely low is addressed, and an attempt is made to quantify the incidence of infectious complications based on reports in the literature. The wide range of other local and systemic complications that can occur following knee joint injections are also reviewed. Recommendations are made regarding which patients are at higher risk of infectious complications and should, therefore, be managed by experienced specialists who can best appreciate the risks

J. G. McGarry (✉) · Z. J. Daruwalla
Department of Orthopaedic Surgery, Adelaide and Meath
Hospital incorporating the National Children's Hospital
(AMNCH), Tallaght, Dublin 24, Republic of Ireland
e-mail: mcgarryj@tcd.ie

versus benefits for each individual patient, and minimize the risk of serious complications.

Evidence for the benefits of corticosteroid joint injections in osteoarthritis

The Cochrane collaboration conducted a systematic review in 2006 of 28 RCTs investigating the efficacy and safety of corticosteroid joint injections in knee osteoarthritis (OA) [4]. The review confirmed the short-term benefits of corticosteroid joint injections, which were more effective than placebo or hyaluronic acid (HA) with respect to pain relief for up to 3 weeks. However, longer-term benefits (from 4 weeks on) of corticosteroids are questionable as corticosteroids were not statistically proven to be as effective with respect to function and pain relief as HA. Since this Cochrane meta-analysis, in 2009 Bannuru et al. published a systematic review and meta-analysis yielding similar conclusions; that corticosteroids provide symptomatic relief of pain for up to 4 weeks, but that HA is superior longer term [3]. Hepper et al. also concluded in a systematic review that corticosteroid injections for knee OA yields clinical benefits only for 1 week and amounts to a short-term treatment of a chronic problem [27].

Factors influencing the efficacy and safety of knee joint injections

In the literature, three publications have suggested that correct intra-articular placement may not be entirely necessary for clinical benefit. In a double-blind randomized control trial by Sambrook et al., it was concluded that peripatellar injection (infiltration of corticosteroid into soft tissues around the patella) may be just as effective as intra-articular injection [43]. In a study by Jones et al., more than half of the extra-articular injections (which represent one-third of the overall) did still yield some clinical benefit [30]. This is perhaps why the improved accuracy with use of US-guidance (relative to clinical judgement, 82.6 vs. 66.3%) does not necessarily translate to a better clinical outcome [15]. However, the majority of authors agree that accurate intra-articular needle placement will both maximize efficacy and minimize procedure-related complications. Several have aimed to evaluate this accuracy by fluoroscopic imaging and have shown that more than 20% of injections are in fact not intra-articular [7, 30]. In the study involving 109 patients by Jones et al., up to one-third of knee and ankle injections were confirmed radiographically as extra-articular (and aspiration of fluid was not a sensitive predictor of intra-articular placement) [30]. The use of US-guidance could clearly improve the percentage

of injections achieving correct intra-articular placement, as reported by Balint et al. who found that success of joint fluid aspiration increased from 32 to 97% with US-guidance [2]. However, Hall and Buchbinder question the cost-effectiveness of routine dependence on US-guidance and whether this would translate to better clinical outcomes [26].

Other simple techniques to improve the accuracy of needle placement have, therefore, been developed. A trial was conducted into a backflow technique, which involves repositioning the needle until a free backflow of injected lidocaine occurs. In 32 of 33 cases, the technique was accurate [33]. Others have recommended injection of a small amount of air to facilitate subsequent confirmation of intra-articular placement: Bliddal et al. report that in 51 of 56 cases correct placement was verified by a sharply defined shadow in the suprapatellar pouch on subsequent radiographs [7]; and Glattes et al. confirmed correct intra-articular placement by a 'squishing' sound (sensitivity of 85%, specificity 100%) [22].

There does not appear to be any evidence that the widely used medial approach is the most accurate or effective anatomical approach in achieving intra-articular needle placement. For example, in a prospective study of 240 patients, three different anatomical approaches (anterolateral, anteromedial and lateral mid-patellar) were investigated [29]. All knee injections were performed by one orthopaedic surgeon, and positioning of the needle tip in the intra-articular space (and not anterior fat pad or subsynovial tissues) was confirmed by fluoroscopic imaging. Anterolateral and anteromedial approaches (with the knee flexed) had an accuracy of 71 and 75%, respectively, whilst the lateral mid-patellar portal (with knee extension) had an accuracy of 93% [29]. Esenyel et al. conducted a comparison of four different injection sites in cadavers [16]. They found that accuracy was lowest with a medial mid-patellar approach (56%), and highest with an anterolateral approach (85%, $P < 0.001$). In the review article by Hall and Buchbinder, it was concluded that standard landmarks are suitable for most patients, but they advise the use of ultrasound guidance to maximize efficacy in technically difficult knee injections, such as in obese patients [26].

Performing knee joint injections under aseptic conditions is of utmost importance in minimizing infectious complications. However, in the literature there appears to be wide variation in the degree of precautions used. In a survey by Charalambous et al., only 32.5% of respondents always used sterile gloves, only 16.3% used sterile towels to isolate the injection site and 8.9% did not change needles between drawing the steroid and injection [9] (for standard guidelines on aseptic technique see Neustadt [35]).

Complications that can arise from corticosteroid knee joint injections

It is broadly perceived amongst clinicians that complications following joint injection are indeed rare, the most serious being joint infection which can have a mortality of up to 11% [41]. For example, Farooq and Devitt report a survey of orthopaedic surgeons throughout Ireland and the UK, aiming to quantify the perceived risk of infection following a joint injection [17]. Half of 853 surgeons perceived the risk of infection as 1 in 1,000 injections, and 33% perceived the risk as even lower at 1 in 10,000. Furthermore, a survey of 32 rheumatologists estimated the risk of bacterial arthritis to be as low as ~4.6 in 100,000 injections [38]. In a survey of 100 surgeons, 100 rheumatologists and 50 general practitioners conducted by Charalambous et al., 12.6% of those surveyed had ever encountered septic arthritis (which presumably represents only a percentage of overall bacterial infection) following joint injection, which according to the authors makes it a rare complication [9].

But is the actual risk of bacterial infection due to corticosteroid knee injections as low as is perceived? In the literature there have been several case reports describing bacterial infection and septic arthritis, but not many publications aiming to quantify rates of bacterial infection (and most of these were published more than 20 years ago). Reported rates of infection range from 1 in 3,000 [19], 1 in 10,000 [18], and 1 in 50,000 [24]. Despite this variability, a rate of 1 in 16,000 (taken from a 1979 Rheumatology textbook [34] is frequently cited in the literature. However, Von Essen and Savolainen reviewed 443 cases of bacterial arthritis post-joint injection and concluded that this figure of 1 in 16,000 in fact under-estimates the risk of bacterial infection [47]. Regarding septic arthritis alone (which presumably represents a proportion of bacterial infection), a very low incidence throughout Iceland of 9.0 per 100,000 during 2002 has been reported [20]. However, interestingly Ostensson and Geborek report a potentially much higher frequency of septic arthritis of ~1 per 2,000 injections in rheumatoid patients who had undergone cytotoxic immunosuppressive treatment and received a joint injection within the previous 3 months [37]. Perhaps an alternative risk-benefit appraisal may be appropriate in immunosuppressed patients before offering intra-articular joint injection.

In a randomized trial in 90 patients who were administering a peri-articular injection of steroids following a uni-condylar knee arthroplasty, Pang et al. [39] report a benefit with respect to post-operative pain and joint movement at 3 months, without any increased incidence of joint infection at 2 years. However, in a recent randomized control trial by Christensen et al. investigating the post-operative benefits of periarticular corticosteroid knee joint injections following total knee arthroplasty in 76 patients,

it could not be ruled out that the corticosteroid joint injections were a causative factor in the development of a severe infection in the prosthetic joint of one patient (the only proven benefit was shorter hospital stay, with no effect on post-operative pain relief, motion or function) [13]. Also, Papavasiliou et al. report that of 144 patients who had undergone total knee replacements, 3 patients developed deep infections, all of whom received pre-prosthetic intra-articular injections [40]. Clearly it is possible that pre- and peri-operative corticosteroid joint injections are indeed associated with a higher incidence of postoperative infectious complications in prosthetic joints and caution is advised. Whether clinicians are aware of this potentially higher risk of infection in these high-risk groups has not been addressed in any publications or surveys to date.

In the literature there are several case reports documenting other local and systemic complications (besides infectious) from corticosteroid injections of the knee. Local complications include self-limiting post-injection flare [42], skin atrophy [8], tendinopathy [6], increased risk of patellar tendon rupture [11], albigans arthritis [14], asymptomatic hydroxyapatite calcifications [21], tendon and fascial ruptures in treatment of athletic injuries [36], Nicolau syndrome [12] and saphenous neuropathy in an obese patient where anatomy was likely obscured [28]. In the literature there were no reports of haemorrhage as a recognized complication of joint injection. Thumboo and O'Duffy published a prospective study on 15 patients, 4 weeks following joint injections on standard doses of warfarin [45]. None were complicated by swelling or haemorrhage. In the absence of more substantial evidence it may not be necessary to stop essential anticoagulants prior to injection.

Systemic complications reported include sudden loss of vision [1], osteonecrosis [31], adrenal suppression [25] and transient hyperglycaemia [5, 25]. Joint injections of hyaluronic acid (HA) have been shown to cause mild transient pain and swelling in up to 20% of patients [48] and granulomatous synovial inflammation [10], which likely involve an inflammatory reaction to HA as opposed to arising from technical factors related to injection administration. The majority of the above systemic and local complications are isolated case reports and therefore can be considered very rare, but nevertheless highlight the importance of an aseptic technique, accurate intra-articular needle placement and awareness of the possible systemic effects when injecting corticosteroids locally.

High-risk patients for whom specialist management is advised

Of 251 general practitioners in a region in the UK, 66.4% have performed joint injections but over half of all

injections are by just 15.6% [32]. Similarly in Northern Ireland it has been reported that 5% of 300 general practitioners perform the majority of primary care injections [23]. In both studies, the majority of general practitioners performing injections regularly had adequate prior hospital training in a related specialty (orthopaedics, sports medicine or rheumatology), which is reassuring with regard to reducing post-injection complications. Nevertheless, in the interests of maximizing both efficacy and safety there are certain patients for whom treatment by experienced specialists is more advisable:

1. In severe osteoarthritis, injection by specialists may result in more successful and safer intra-articular placement. For example, Toda and Tsukimura report that an anteromedial approach with simultaneous ankle traction and 30 degrees of knee flexion is significantly more accurate than either a seated anteromedial approach or a lateral patellar approach in the most severe grade of osteoarthritis (100% accuracy vs. 55 and 55%) [46]. Schumacher and Chen also recommend an anterior approach with knee flexion to elevate the patella and facilitate entry into the joint space in patients with osteophytes or knee flexion contractures [44].
2. Considering the potentially far higher rate of infection in patients who later required knee arthroplasty [40], it is imperative that specialist opinion is sought prior to joint injection for any patient for whom joint replacement may be required in the near future. A safe time interval after which any increased risk (if a patient were to undergo joint arthroplasty) returns to baseline is not known, and since symptomatic relief in severe osteoarthritis whilst awaiting elective arthroplasty is a common indication for corticosteroid joint injections, it is crucial to determine whether the short-term benefits outweigh any increased risks of infection following eventual arthroplasty.
3. A higher incidence of infection in rheumatoid patients who received immunosuppressive therapy in the past year [37] should prompt caution and specialist referral for such patients as an alternative risk–benefit analysis

may be appropriate. This high-risk group should include any immunocompromised or diabetic patients.

4. In technically difficult cases, such as in obese patients or in those patients with severe knee osteoarthritis, the administration of knee joint injections is best performed by specialists who can utilize various anatomical approaches in achieving intra-articular needle placement, who frequently perform complex injections and have access to US-guidance.

Conclusions

Short-term symptomatic relief is the only evidence-based benefit to corticosteroid injection of an osteoarthritic knee. Long-term benefit beyond 4 weeks is not proven. The incidence of infectious complications of joint injections is not well documented, and may range from 1 in 3,000 to 1 in 50,000. Bacterial infection and other serious local and systemic complications are correctly perceived amongst clinicians as being rare, but infectious complications in higher risk patients may be far more common. This higher risk group includes those patients who have undergone immunosuppressive therapy, immunocompromised patients and those who have or may have in the near future a prosthetic joint. Surveys of clinician's perceptions have not reflected this important fact to date.

Regarding intra-articular placement of knee joint injections, accurate placement is not achieved in up to 20% of injections. Simple techniques to confirm needle tip positioning by backflow of injected lidocaine or by injection of a small amount of air with subsequent radiographic confirmation can significantly improve accuracy. US can also improve this accuracy but its routine use may not be cost-effective and should be reserved for technically difficult cases. There is no evidence available that the commonly used medial approach is the most accurate anatomical approach.

Whilst the majority of joint injections in primary care are safely performed by general practitioners who have prior hospital training in related specialties, based on the

Table 1 Recommendations arising from a review of the literature

Short-term symptomatic relief is the only evidence-based benefit of corticosteroid injection of an osteoarthritic knee

The incidence of infectious complications following knee joint injections ranges from 1 in 3,000 to 1 in 50,000 but may be far higher in immunosuppressed patients

To minimize potentially serious complications, specialist referral is advised for technically difficult cases (e.g. in obese patients where anatomical landmarks are not palpable), in severe osteoarthritis and in immunosuppressed patients

Accurate intra-articular placement is not achieved in up to 20% of injections and varies considerably with the anatomical approach used. There is no evidence that a medial approach is more accurate

Further research is required to determine whether there is a higher risk of infection in patients with prosthetic knees who received prior corticosteroid joint injections

review of the literature there are certain patients for whom treatment by experienced specialists is best advised to maximize efficacy and minimize the risk of complications. These include patients with severe osteoarthritis (OA) who have or may require joint prostheses in the short term, high-risk patients including those who have received immunosuppressive therapy, immunocompromised or diabetic patients and in technically difficult cases where anatomical landmarks are not easily palpable, for example in the obese. For a summary of main points, refer to Table 1.

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