A systematic review of injectable corticosteroid for osteoarthritis of the first metatarsophalangeal joint

Ian Reilly (ianreilly@nhs.net)
Northamptonshire Healthcare Foundation NHS Trust  https://orcid.org/0000-0002-2786-5739

Gillian Bromley
Northamptonshire Healthcare Foundation NHS Trust  https://orcid.org/0000-0001-8973-0584

George Flanagan
Northamptonshire Healthcare Foundation NHS Trust  https://orcid.org/0000-0002-5166-7580

Systematic Review

Keywords: Steroid injection, first metatarsophalangeal joint, osteoarthritis, hallux rigidus, systematic review

DOI: https://doi.org/10.21203/rs.3.rs-105785/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Intra articular steroid injection is a common treatment modality for relief of pain and inflammation associated with degenerative joint disease. Use of injectable steroid preparations is widely accepted as safe and effective for the treatment of osteoarthritis of the first metatarsophalangeal joint. Despite the frequency of use, literature specific to pathology of the first metatarsophalangeal joint is sparse. The aim of this systematic review was to determine if good quality research exists to enable clinicians to adopt an evidenced based approach to corticosteroid injection of the first metatarsophalangeal joint. Despite the frequency of use, this review found no high quality studies that support the use of intra articular corticosteroid injection of the first metatarsophalangeal joint in osteoarthritis.

Background

The use of injectable corticosteroid as part of a treatment strategy for painful joints is a common treatment modality. In degenerative disease the intended aim is to reduce the pain and inflammation associated with osteoarthritis (OA) as well as improve joint function [1]. The use of intra-articular (IA) corticosteroid injections (CSIs) for the treatment of OA is supported by guidelines provided by the United Kingdom (UK) National Institute for Health and Care Excellence (NICE) in patients who experience joint pain that is not adequately controlled by oral and/or topical options or where such treatment is contraindicated [2]. The basis for this guidance is largely derived from conclusions drawn from research into the efficacy of IA CSI's at the knee and shoulder [3,4]: data from these studies has been extrapolated and applied to other synovial joints such as the first metatarsophalangeal joint (1st MPJ).

Osteoarthritis is the leading cause of disability in adults worldwide and results in significant morbidity [5]. Joints in the foot are often affected by this condition with the 1st MPJ being most commonly affected pedal joint [6]. Symptomatic 1st MPJ OA affects approximately 10% of the adult population and the prevalence increases with age - as do comorbidities amongst sufferers – with the result that reduced pharmacological treatment options available for pain relief in these patients [7]. Symptoms arising from OA are notoriously difficult to manage with oral analgesics alone: this ultimately results in a significant burden on primary care services [8]. This provides the niche for IA CSI, i.e. where other conservative treatment has failed, is contraindicated or where there is a desire or requirement to postpone the need for surgical intervention. Unmanaged foot pain is an independent risk factor for depression and falls in adults [9,10,11].

The authors are experienced injectors and are active in teaching CSI techniques to under- and post-graduate students. Anecdotally we find that 80-90% of patients experience improvement following IA CSI for 1st MPJ OA but the extent and duration of that improvement varies. The variability in outcomes following CSI for 1st MPJ OA raises numerous questions: to what extent is pain reduced? Is joint function improved? Which patients are most likely to benefit from this treatment? What is the frequency with which corticosteroid should be administered and whether the use of ultrasound guided injections improves treatment outcomes [12,13,14]. Furthermore, there has been debate surrounding whether a steroid based solution when combined with local analgesia may even be chondrotoxic [15]. A Cochrane Review from 2010 [16] concerned with identifying optimal treatment modalities for 1st MPJ OA found low level evidence for physical therapy only. A systematic literature review was therefore undertaken (as part of a larger body of work being undertaken by the lead author) in order to identify randomised trials that had used IA CSI for OA of the 1st MPJ.

Methods

The research question is: is the use of corticosteroid injections for osteoarthritis of the first metatarsophalangeal joint in adults a safe and effective method of reducing pain and improving joint function?

In order to ensure a systematic review, minimise the risk of bias and provide transparency for replication of the process, a predetermined research methodology protocol was used, based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [17]. This was registered with PROSPERO. (Trial registration number: CRD42019135950. Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019135950).
Selection criteria

Inclusion

Pre-determined inclusion and exclusion criteria were used. Only systematic reviews, randomised controlled trials (RCTs), quasi randomised trials and controlled clinical trials were considered for inclusion as they form the hierarchy of evidence and are most likely to provide a robust evidence base suitable for informing clinical practice [18]. Those papers found were then screened for the following criteria:

- Trials in which an IA CSI into the 1st MPJ used for the treatment of OA in adults,
- Diagnosis and grading of OA in participants could be achieved via clinical examination and/or via radiological means [19],
- Any gender or ethnicity was considered.

In order to be able to determine the efficacy of treatment, trials were required to have provided quantitative or qualitative measures both pre- and post-intervention in order to be able to ascertain the mean differences relating to pain and/or joint function outcomes.

Exclusion

Trials in which intradermal, subcutaneous, intramuscular or extracapsular corticosteroid injections were performed were excluded, as were not trials that tested the efficacy of IA CSIs for conditions other than for OA, or tested CSIs at joints other than the 1st MPJ. Due to the high risk of bias, cohort and case studies, articles based on expert opinion, retrospective studies and narrative-based literature reviews were excluded [18].

Search strategy and data sources

To answer the research question a keyword search of six electronic databases (AMED, CINAHL, EMBASE, MEDLINE, PUBMED, and COCHRANE) up to February 2020 was undertaken by graduate research podiatrist (GB) to identify clinical trials that had tested the efficacy of IA CSI for the treatment of 1st MPJ OA.

AMED (1985 to 05.02.2020)
CINAHL (1982 to 05.02.2020)
EMBASE (1974 to 05.02.2020)
MEDLINE (1950 to 05.02.2020)
PUBMED (1966 to 05.02.2020)
COCHRANE (1966 to 05.02.2020)

No date or language restrictions were applied. Reference lists were reviewed, and key author searches were made to reduce the risk of any pertinent literature being missed. A list of keywords and results yielded are provided in table 1.

Table 1: Search terminology and results yielded by database
| #  | Database | Search term                                  | Results |
|----|----------|----------------------------------------------|---------|
| 1  | AMED     | (osteoarthritis).ti,ab                       | 2945    |
| 2  | AMED     | (hallux).ti,ab                               | 1252    |
| 3  | AMED     | (metatarsophalangeal).ti,ab                  | 771     |
| 4  | AMED     | (injection).ti,ab                            | 2035    |
| 5  | AMED     | (steroid).ti,ab                              | 454     |
| 6  | AMED     | (hallux limitus).ti,ab                       | 62      |
| 7  | AMED     | (hallux rigidus).ti,ab                       | 178     |
| 8  | AMED     | (1 AND 2)                                    | 35      |
| 9  | AMED     | (1 AND 3)                                    | 37      |
| 10 | AMED     | (6 OR 7 OR 8 OR 9)                           | 272     |
| 11 | AMED     | (4 AND 10)                                   | 5       |
| 23 | CINAHL   | (osteoarthritis).ti,ab                       | 21838   |
| 24 | CINAHL   | (hallux).ti,ab                               | 2033    |
| 25 | CINAHL   | (metatarsophalangeal).ti,ab                  | 1197    |
| 26 | CINAHL   | (injection).ti,ab                            | 43132   |
| 27 | CINAHL   | (steroid).ti,ab                              | 15241   |
| 28 | CINAHL   | (hallux limitus).ti,ab                       | 100     |
| 29 | CINAHL   | (hallux rigidus).ti,ab                       | 319     |
| 30 | CINAHL   | (23 AND 24)                                  | 63      |
| 31 | CINAHL   | (23 AND 25)                                  | 82      |
| 32 | CINAHL   | (28 OR 29 OR 30 OR 31)                      | 472     |
| 33 | CINAHL   | (26 AND 32)                                  | 13      |
| 34 | EMBASE   | (osteoarthritis).ti,ab                       | 79498   |
| 35 | EMBASE   | (hallux).ti,ab                               | 5812    |
| 36 | EMBASE   | (metatarsophalangeal).ti,ab                  | 3924    |
| 37 | EMBASE   | (injection).ti,ab                            | 581417  |
| 38 | EMBASE   | (steroid).ti,ab                              | 163137  |
| 39 | EMBASE   | (hallux limitus).ti,ab                       | 153     |
| 40 | EMBASE   | (hallux rigidus).ti,ab                       | 664     |
| 41 | EMBASE   | (34 AND 35)                                  | 183     |
| 42 | EMBASE   | (34 AND 36)                                  | 258     |
| 43 | EMBASE   | (39 OR 40 OR 41 OR 42)                      | 1068    |
| 44 | EMBASE   | (37 AND 43)                                  | 21      |
| 45 | EMBASE   | (38 AND 43)                                  | 12      |
| 46 | CINAHL   | (27 AND 32)                                  | 5       |
| 48 | AMED     | (5 AND 10)                                   | 4       |
| 49 | Medline  | (osteoarthritis).ti,ab                       | 54837   |
Risk of bias

In order to assess their validity, RCTs were reviewed using the Critical Appraisal Skills Programme (CASP) checklist [20], which uses six quality assessments of studies and considers the risk of (selection, performance, detection, attrition and reporting) bias. Systematic reviews were appraised using a Centre for Evidence-Based Medicine (CEBM) appraisal tool for systematic reviews [21] which uses six quality assessments to determine validity of reviews based on methodological design. Each quality assessment for data was awarded a 'low', 'high' or 'unclear' risk of bias. Two reviewers independently (GB, GF) appraised the studies and results were collated. If there was disparity between results, a discussion was to be raised. If consensus could not be achieved the senior author (INR - a consultant podiatric surgeon with a special interest in injection therapy) was appointed to make the final decision. Evidence from the identified literature was considered and an appropriate weighting awarded based on the quality of evidence they provided.

Initial inter-rater results following an appraisal of studies was 84% consistent between two reviewers. Following a discussion regarding the variation in quality assessment, 100% consensus between reviewers was achieved. Evidence from the identified literature was considered and an appropriate weighting awarded based on the quality of evidence they provided. Themes regarding joint pain, function and the safety of CSIs are discussed. Due to only one RCT being identified for inclusion, no meta-analysis was possible.
Data extraction

Data was extracted from research that fulfilled the inclusion criteria by using a pre-determined list of parameters to determine the efficacy of the intervention and validity of methods used for testing. These parameters considered: the design of study, sample size, demographics, diagnostic criteria used, disease severity, intervention tested (type, dosage, method of administration), outcomes, follow up and results. Reported adverse effects (type, duration and severity) were recorded to determine the safety of the intervention. Data from these themes was entered into a spreadsheet to be used for discussion.

Results

A search of electronic databases identified 111 studies for possible inclusion. Sixty-four duplicates were excluded and 47 titles and abstracts were assessed. Titles and abstracts were assessed independently (GB and GF) and evaluated against the aims of this study and its predetermined selection criteria. Full text articles believed to be appropriate were accessed and further assessed for relevance against the predetermined inclusion criteria. If there was a difference in opinion as to whether an article should be included for review, a discussion was raised between the two main authors and if it was not possible to reach a consensus then the senior author was given the final vote on selection. 36 articles were rejected and 11 full text articles were retrieved for assessment against the selection criteria (figure 1). One RCT and one systematic review were identified for inclusion in this review.

Randomised controlled trials

One single blinded randomised trial that compared the efficacy of a single dose of intra articular triamcinolone acetonide (TA) with sodium hyaluronate (SH) delivered without image guidance for mild symptomatic hallux rigidus in thirty-seven adults was identified for inclusion [22] – see table 2. The title of the paper was misleading (sodium hyaluronate in the treatment of hallux rigidus. A single blind randomized study) in that its use of CSI was not mentioned.

Table 2. Quality assessment of randomised controlled trials (CASP checklist)

| Pons et al. 2007 [22] |
|------------------------|
| Quality Assessment:    |
| Result: Bias Risk:     |
| Quality score:         |
| Did the trial ask a clearly focused question? | Yes | Screening question | 2/2 |
| Was the assignment of patients randomised? | Unclear | Selection bias | 1/2 |
| Were all the patients who entered the trial properly accounted for at its conclusion? | Yes | Attrition bias, reporting bias | 2/2 |
| Were patients, health care workers and study personnel ‘blind’ to treatment? | No | Performance bias, detection bias | 0/2 |
| Were the groups similar at the start of the trial? | Unclear | Selection bias | 1/2 |
| Aside from the experimental intervention, were the groups treated equally? | Yes | Performance bias | 2/2 |

Changes in joint pain and function

A reduction in mean visual analogue scale (VAS) pain scores at rest or on palpation was observed in both treatment groups. Mean VAS scores (n/100 mm) reduced at baseline from 58.7 mm to 34.1 mm in the TA group. A significant decrease in dorsiflexion or plantarflexion VAS pain scores was also observed in both groups: mean VAS scores decreased from 64.2 mm to 41.6 mm in the TA group. TH demonstrated reduced improvement in VAS pain scores on walking 20 metres compared to SH. Recipients of TA were reported to have a mean improvement in hallux function of 4.1 on the American Orthopaedic Foot and Ankle Society Score (AOFAS) for
hallux evaluation. Overall, TA was found to be inferior in terms of the number positive responders to treatment, pain reduction and improvement in hallux function when compared to those treated with SH. Benefits were reported as relatively short lasting in both arms of the trial: 52.9% in the TA group and 46.6% in the SH group progressed to surgery within 12 months.

The mean quality score for the RCT reviewed was 66% demonstrating limited methodological quality and potential bias. In this trial there was no attempt to blind investigators involved in data collection and evaluation of outcome measures. The trial had a small sample size with a significant female gender bias and all participants had mild joint disease potentially limiting the application of conclusions drawn from this to other patient populations. However, the most significant limitation with this trial was that interventions were administered to participants with 1st MPJ OA and hallux valgus with no sub group analysis provided according to condition. This caused the paper to be rejected from the 2015 Cochrane review [16]. Given that the underlying pathophysiology of these distinct conditions differs, it is reasonable to expect that treatment outcomes relating to joint pain and function following an IA SCI may vary between recipients with different conditions. Furthermore, the proportion of recipients reported to have progressed to surgery may have been skewed given that the usual treatment for hallux valgus is surgical correction of the deformity. From this trial it was not possible to determine the efficacy of corticosteroids as an intervention to treat osteoarthritis at the 1st MPJ.

Adverse effects

Similarly, the lack of blinding in data collection and evaluation of adverse effects associated with the interventions administered poses a significant bias risk. Due to the lack of sub group analysis it was not possible to determine whether the frequency or type of adverse effects differed by condition. Data relating to adverse effects was collected by non-blinded investigators post intervention, were mild and arose in just 5% of recipients; no serious adverse effects were reported.

Systematic reviews

A recent review [14] that set out to provide comprehensive list of evidence-based recommendations regarding conservative treatment modalities for 1st MPJ OA included a review of injection therapy. Authors of the review found ‘fair evidence’ to support the use of IA CSIs to treat 1st MPJ OA. However, the methodology was neither systematic nor comprehensive: only a single database was searched for clinical trials and the risk of pertinent literature having been missed was high. The author’s recommendations were made based on an appraisal system [23] that allocates a level of evidence for an intervention based solely on the design of studies identified; it does not consider the methodological quality of trials or risk of bias. Rama [24] pointed out that this system is a derivative of the levels of evidence system [25] and cautioned regarding the limitations of this style of review. He highlighted the need to not generalise evidence in order to avoid misleading conclusions being drawn.

The injection therapy trials identified in this review lacked heterogeneity in terms of solutions tested and design of trials. In spite of this, the authors grouped six trials relating to injection therapy together for data analysis and a collective level of evidence was allocated to injection therapy as a whole. Since this review did not consider the risk of bias and validity or clinical significance of outcomes from trials it identified, and failed to use a systematic methodology the study was excluded from this review as it was deemed to provide a summary of interventions for healthcare professionals only [24].

This review identified one systematic review that considered the efficacy of any treatment modality, including but not limited to injection therapy, for 1st MPJ OA [16]. The 2010 systematic review (see table 3) was a comprehensive piece of research with high quality methodology and low risk of bias. It identified one low quality study with a high risk of bias to support the use of physical therapy to reduce the pain of osteoarthritis at the big toe joint. It found no evidence to support the efficacy of corticosteroid injections for hallux rigidus (see note above re Pons et al, 2007).
Table 3. Quality assessment of systematic reviews (CEBM framework)

| Zammit et al. 2010 [16] |
|-------------------------|
| **Quality Assessment:** |
| Result:                |
| Quality Score:         |
| What question did the systematic review address? | Which interventions are optimal for treating osteoarthritis of the big toe? | 2/2 |
| Is it unlikely that important, relevant studies were missed? | Yes | 2/2 |
| Were the criteria used to select articles for inclusion appropriate? | Yes | 2/2 |
| Were the included studies sufficiently valid for the type of question asked? | No, identified a lack of available evidence and high risk of bias. | 0/2 |
| Were the results similar from study to study? | One study identified for inclusion only. | 0/2 |

**Discussion**

Originally suggested by Cotterill in 1887 [26], hallux rigidus / limitus (1st MPJ OA) are terms used to describe arthritic changes at the 1st MPJ. Many theories regarding the aetiology of 1st MPJ OA have been postulated. Traditionally, osteoarthritis was viewed simply as a degenerative condition characterised by the degeneration of joint cartilage over time that resulted in progressive pain, stiffness and loss of joint function. However, a greater understanding of the pathophysiology of osteoarthritis indicates that symptoms arising from the disease are caused by the body’s attempt to repair damaged cartilage and that it is this process of repair and remodelling that results in abnormal bone growth and inflammation that involves the entire joint [16].

In a review of 114 patients it was found that irrespective of age, females are twice as likely to develop 1st MPJ OA [27]. A positive family history is strongly associated with bilateral joint disease, whereas unilateral joint involvement is often precipitated by trauma and does not routinely progress to involve both feet. Little consensus exists between studies regarding other possible causes although Coughlin and Shumas [27] discuss pes planus, Achilles tendon contracture, hallux valgus, hallux valgus interphalangeus, a flat metatarsal head, metatarsus adductus, a long first metatarsal, metatarsus primus elevatus, and first ray hypermobility in the development of this condition. Furthermore, a number of recent retrospective studies that have considered the natural course of 1st MPJ OA suggest that progression of the disease is far more variable than previously thought and that for many it may follow a more benign course with symptoms that can be adequately managed with conservative treatment methods such as physical, mechanical or pharmacological therapy [28]. It is therefore increasingly important for clinicians to understand when to administer IA CSIs and which patients would derive the greatest benefit from treatment.

Corticosteroid is a synthetic version of the endogenous hormone glucocorticoid found in vertebrates that is produced in the adrenal gland cortex. Amongst its other functions in the cardiovascular, metabolic and nervous systems; glucocorticoids provide a feedback mechanism within the immune system to reduce inflammation. Synthetic corticosteroids administered orally or via injection can be exploited to mimic this action and can be used to suppress unwanted, immune mediated inflammatory responses caused by many disease processes including osteoarthritis. Corticosteroids act to reduce inflammation and suppress the immune response at various levels:

- Leucocytes and monocytes transform into macrophages, a larger and more bactericidal cell that release lysosomal enzyme that ushers in further inflammatory processes. By suppressing the adhesion of leucocytes, the formation of macrophages is reduced which inhibits the release of lysosomal enzyme and leads to a reduction in further inflammation [29].
- Lymphocytes aid in activation of T cells and macrophages that have been produced causing rapid division and cytokine secretion. Cytokines are associated with both the initial activation and ongoing sensitization of the nociceptive receptors on sensory neurons.
perceived as chronic pain mediators. By reducing the effect of lymphocytes by depleting the amount of T cells and secretion of cytokines pain is reduced [30].

- Cytokines are also responsible for releasing eicosanoid, a signalling molecule that stimulates other inflammatory mediators including histamine and prostaglandins. Both histamine and prostaglandins cause vasodilation of the surrounding blood vessels. This vasodilation leads to increased swelling and also contributes to the sensitisation of nerves resulting in pain perception. By reducing vasodilation and stimulation of pain receptors swelling and pain are reduced [31].

This systematic review was conducted in order to assess the effectiveness and safety of intra articular corticosteroid injection as a treatment modality for 1\textsuperscript{st} MPJ OA. A thorough and systematic literature search was completed in order to identify pertinent literature on the subject area and forty-seven studies were identified for possible inclusion. After exclusions were applied from the selection criteria to ensure that the correct condition, joint and treatment were being considered 11 pieces of literature remained of which two have been considered in detail. The remaining literature was mainly comprised of studies that provide low level evidence such as narrative reviews, retrospective case studies or non-controlled clinical trials.

One single blind randomized trial that compared the efficacy of a single corticosteroid injection with hyaluronate was identified [22]. A critical appraisal of this trial found it to have a high risk of bias. Furthermore, the solutions administered to participants were for two distinct conditions, hallux valgus and hallux rigidus and no details for sub group analysis were provided. It was therefore not possible to determine what influence this may have had on the outcome measures relating to pain reduction and improved joint function for hallux rigidus. From this trial it was not possible to determine with any level of certainty or specificity the efficacy of corticosteroids as an intervention to treat osteoarthritis at the hallux.

CSIs are generally considered safe drugs with steroid are being the most commonly reported adverse event though rare complications that may arise following administration of intra articular steroid including anaphylaxis, disturbance of menstrual pattern and avascular necrosis [32]. Data relating to adverse effects was collected by Pons et al post intervention were mild, and arose in just 5% of recipients. It was not possible to determine the quality of reporting of adverse effects in this trial or whether adverse effects arose in hallux valgus and/or hallux rigidus joints. However, the reported rate of adverse effects is homogenous with the 6% rate of mild adverse effects reported by following 1,708 steroid injections into both soft tissue and joints of the foot and ankle [33]. The most common side effect reported was a steroid ‘flare’, an acute inflammatory reaction to the steroid solution which made up 75% of the reported side effects. Vasovagal episodes, facial flushing, local skin reactions, short term paraesthesia and a temporary increase in blood glucose levels were also reported but were rare. No infections were reported by the study, a result consistent with the view that joint infection is a very rare complication resulting in septic arthritis. No adverse effects following the administration of 22 CSIs for hallux rigidus were noted by Grice et al [34] although they do report that the positive results (seen in 20 of the 22 patients) only lasted longer than three months in three of that cohort. At two years, two patients (9%) remained asymptomatic, but 12 patients (55%) had undergone surgery. Peterson and Hodler [35] and Kilmartin [36] also note that most adverse effects experienced following an intra articular joint injection of steroid are mild and transient and can be managed by the patient with self-care advice. These papers support the anecdotal view that in general, CSIs are safe and that adverse effects tend to be moderate and time-limited.

Numerous narrative reviews exist regarding treatments for hallux rigidus and include CSIs but provide no evidence-based recommendations for treatment. An exception to this was a comprehensive review [14], the aim of which was to provide evidence-based recommendations regarding conservative treatment modalities for hallux rigidus and included a review of injection therapy. Authors of the review based their recommendations on an established appraisal system [23] that allocates a level of evidence for an intervention based on the design of studies identified. Rama [24] pointed out that this system is a derivative of the widely established levels of evidence system [25] and cautioned regarding the limitations of this style of review. He highlighted the need to not generalize evidence in order to avoid misleading conclusions being drawn. King et al grouped six trials relating to injection therapy together for data analysis regardless of the fact that interventions and trial designs differed. A ‘collective’ level of evidence was allocated to injection therapy in general rather than by individual solutions. This led to skewed results given that the quality of trial design that had tested
hyaluronate was superior to other interventions such as corticosteroid. Given that this review did not use a methodology that considered the risk of bias, validity or clinical significance of results of trials this study was excluded from this review as it was deemed to provide a narrative review.

One systematic literature review that included an appraisal of the efficacy of corticosteroid injections for osteoarthritis at the big toe joint [16] was included in this review. The Cochrane review was well designed, well executed and found to have a low risk of bias. Zammit et al [16] did not identify any robust evidence to support the efficacy of corticosteroid injections for the treatment of hallux rigidus and made no recommendations regarding its safety due to the high risk of bias. This view is consistent with the findings of this review that found it was only possible to make generalisations relating to the safety of intra articular corticosteroid injections.

This review did not find evidence of sufficient quality to confirm whether intra articular corticosteroid injections are an effective intervention for the management of symptomatic osteoarthritis at the 1st MPJ. The current literature that exists was found to be of poor methodological design. In the only randomized controlled clinical trial that tested corticosteroid, it was found to be mildly inferior to hyaluronate in terms of pain reduction for patients with mild osteoarthritis [22]. However, in a robust randomised placebo controlled [38] trial of intra articular injections for osteoarthritis no benefit was derived from sodium hyaluronate vs saline placebo.

**Conclusion**

There are a number of narrative reviews concerned with the conservative and surgical treatment modalities that can be used to inform the management of symptomatic hallux rigidus. A number of case and retrospective [26,27] studies have evaluated the use of injectable corticosteroids in the foot or ankle but controlled clinical trials in this area are few.

Many interventions exist that are intended to reduce the symptoms associated with OA of the 1st MPJ. In spite of the lack of evidence to support their use, IA CSI remain popular amongst health care professionals and patients alike because they are quick and inexpensive to administer with the perception of rapid relief, minimal recovery time and few side effects [32]. In cases of mild osteoarthritis some retrospective studies indicate that CSIs may provide months and occasionally, years of relief for hallux rigidus [28]; a retrospective study by Smith et al in 2000 [37] found 75% of patients that had previously declined surgical treatment for symptomatic hallux rigidus were happy with this decision, had not experienced an increase in pain undergone despite degeneration of the joint, and were able to manage symptoms with stiff soled shoes and accommodative footwear. It is unclear whether progression to surgery has any association with the administration of intra articular corticosteroid but given the risk of chondrotoxicity [15] this warrants further investigation.

This review found no high quality evidence to support the use of IA CSI as an effective treatment modality for symptomatic 1st MPJ OA. Uncertainty regarding variables that may influence treatment outcomes such as concomitant footwear use [39] remains. Existing research that tested intra articular corticosteroid was found to be of poor methodological design with a high risk of bias. High quality, randomised, controlled clinical trials that test the efficacy of IA CSI are required. The severity of 1st MPJ OA amongst recipients in trials should be classified prior to intervention by clinical and radiological examination [19] and a sub group analysis of outcome measures provided according to disease severity. Further research to determine whether treatment outcomes are improved by the use of image guidance, extrapolation of side effects [40] and whether the use of IA CSI in 1st MPJ reduces surgical burden would be beneficial.

**Declarations**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All authors have no competing interests to declare. Organisation ethical approval was not required as the systematic review and did not include human subjects nor did it utilise personal or organisation information. All authors made substantial contributions to the works enclosed.
References

1. Lam A, Chan JJ, Surace M F. Hallux rigidus: how do I approach it? World Journal of Orthopaedics. 2017;8(5):364-371. doi: 10.5312/wjo.v8.i5.364.

2. National Institute of Health and Care Excellence (NICE). Osteoarthritis: care and management. Clinical Guideline [CG177] NICE (online). 2014. Available from: https://www.nice.org.uk/guidance/cg177 [Accessed 05.03.2020].

3. Juni P, Hari R, Rutjes AWS, Fischer R, Silletta MG, Reichenbach S, Costa BR. Intra-articular corticosteroid for knee osteoarthritis. Cochrane Database of Systematic Reviews. 2015. Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD005328.pub3/full [Accessed 05.03.2020].

4. Soh E, Li W, Ong K, Chen W, Bastida D. Image guided versus blind corticosteroid injections in adults with shoulder pain: a systematic review. BMC Musculoskeletal Disorders. 2011;12(137). doi: 10.1186/1471-2474-12-137.

5. Neogi T. The epidemiology and impact of pain in osteoarthritis. Osteoarthritis Cartilage. 2013;21(19):1145-1153. doi: 10.1016/j.joca.2013.03.018.

6. Gould, N, Schneider, W, Ashikaga, T. Epidemiological survey of foot problems in the continental United States: 1978-1979. Foot & Ankle. 1980;1(1):8-10. doi: 10.1177/107110078000100104.

7. Anderson MR, Ho BS, Baumhauer JF. Current concepts review: hallux rigidus. Foot and Ankle Orthopaedics. 2018;3(2):1-11. doi: 10.1177/2473011418764461.

8. Kingsbury S R, Conaghan PG. Current osteoarthritis treatment, prescribing influences and barriers to implementation in primary care. Primary Health Care Research & Development. 2012;13(4):373-381. doi: 10.1017/S1463423612000072.

9. Awale A, Dufour AB, Katz P, Menz HB, Hannan MT. Link between foot pain severity and depressive symptoms. Arthritis care & research. 2016;68(6): 871-876. doi: 10.1002/acr.22779.

10. Bergin SM, Munteanu SE, Zammit GV, Nikolopoulos N, Menz HB. Impact of first metatarsophalangeal joint osteoarthritis on health-related quality of life. Arthritis Care & Research. 2012;64(11):1691-1698. doi: 10.1002/acr.21729.

11. Van Saase JL, Romunde LK, Cats A, Vandenbrucke JP, Valkenburg HA. Epidemiology of osteoarthritis: Zoetermeer Survey. Comparison of radiological osteoarthritis in a Dutch population with that in 10 other populations. Annals of the Rheumatic Diseases. 1989;48(4):271-280. doi: 10.1136/ard.48.4.271.

12. Pekarek B, Osher L, Buck S, Bowen M. Intra-articular corticosteroid injections: A critical review with up-to-date findings. The Foot. 2011;21(2):68-70. doi: 10.1016/j.foot.2010.12.001.

13. Kunnasegaran R, Thevendran G. Hallux rigidus. Non operative treatment and orthotics. Foot and Ankle Clinics. 2015;20(3):1558-1934. doi: 10.1016/j.fcl.2015.04.003.

14. King CK, James Loh SY, Zheng Q, Mehta KV. Comprehensive review of non-operative management of hallux rigidus. Cureus. 2017 Jan;9(1). doi: 10.7759/cureus.987.

15. Farkas B, Kvell K, Czompoly T, Illes T, Bárdos T. Increased chondrocyte death after steroid and local anesthetic combination. Clinical Orthopaedics and Related Research®. 2010 Nov 1;468(11):3112-20. doi: 10.1007/s11999-010-1443-0.

16. Zammit GV, Menz HB, Munteanu SE, Landorf KB, Gilheany MF. Interventions for treating osteoarthritis of the big toe joint. Cochrane Database of Systematic Reviews. 2010. Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007809.pub2/media/CDSR/CD007809/CD007809_standard.pdf [Accessed 05.03.2020].

17. Moher D, Liberati A, Tetzlaff J, Altman DG, Prisma Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS med. 2009 Jul 21;6(7):e1000097. doi: 10.1371/journal.pmed.1000097.

18. Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. BMJ. 2005 Nov 3;331(7524):1064-5. doi: 10.1136/bmj.38636.593461.68.

19. Beeson P, Phillips C, Corr S, Ribbands W. Classification systems for hallux rigidus: a review of the literature. Foot & Ankle International. 2008 Apr;29(4):407-14. doi: 10.3113/FAI.2008.0407.

20. Critical Appraisal Skills Programme. CASP Randomised Controlled Clinical Trial Checklist. [online]. 2018. Available from: https://casp-uk.net/wp-content/uploads/2018/01/CASP-Randomised-Controlled-Trial-Checklist-2018.pdf [Accessed: 05.03.2020].

21. University of Oxford Systematic Review Critical Appraisal Sheet [online]. Oxford: Centre for Evidence Based Medicine. 2005. Available from: https://www.cebm.net/wp-content/uploads/2018/11/RCT.pdf [Accessed 05.03.2020].
22. Pons M, Alvarez F, Solana J, Viladot R, Varela L. Sodium hyaluronate in the treatment of hallux rigidus. A single-blind, randomized study. Foot & Ankle International. 2007 Jan;28(1):38-42. doi: 10.3113/FAl.2007.0007.

23. Wright JG, Einhorn TA, Heckman JD. Grades of recommendation. JBJS. 2005 Sep 1;87(9):1909-10. doi: 10.2106/JBJS.8709.edit.

24. Rama KR. Grades of Recommendation. JBJS. 2006;68(2):451. doi: 10.2106/00004623-200602000-00037.

25. University of Oxford Levels of Evidence 1 [online]. Oxford: Centre for Evidence Based Medicine. 2009. Available from: https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/ [Accessed 05.03.2020].

26. Cotterill JM. Stiffness of the great toe in adolescents. BMJ. 1887 May 28;1(1378):1158. doi: 10.1136/bmj.1.1378.1158.

27. Coughlin MJ, Shurnas PS. Hallux rigidus: grading and long-term results of operative treatment. JBJS. 2003;85(11):2072-88. PMID: 14630834.

28. Grady JF, Axe TM, Zager EJ, Sheldon LA. A retrospective analysis of 772 patients with hallux limitus. Journal of the American Podiatric Medical Association. 2002 Feb;92(2):102-8. doi: 10.7547/87507315-92-2-102.

29. Rhen T, Cidlowski JA. Antiinflammatory action of glucocorticoids - new mechanisms for old drugs. New England Journal of Medicine. 2005 Oct 20;353(16):1711-23. doi: 10.1056/NEJMra050541.

30. Li YS, Luo W, Zhu SA, Lei GH. T cells in osteoarthritis: alterations and beyond. Frontiers in immunology. 2017 Mar 30;8:356. doi: 10.3389/fimmu.2017.00356.

31. Cole BJ, Schumacher Jr RH. Injectable corticosteroids in modern practice. JAAOS-Journal of the American Academy of Orthopaedic Surgeons. 2005 Jan 1;13(1):37-46. doi: 10.5435/00124635-200501000-00006.

32. Corticosteroid injections. Reilly I, in Foot and Ankle Injection Techniques: A Practical Guide. Metcalfe SA, Reilly I. Churchill Livingstone, England. ISBN: 9780702031076.

33. Anderson SE, Lubberts B, Strong AD, Guss D, Johnson AH, DiGiovanni CW. Adverse events and their risk factors following intra-articular corticosteroid injections of the ankle or subtalar joint. Foot & Ankle International. 2019 Jun;40(6):622-8. doi: 10.1177/1071100719835759.

34. Grice J, Marsland D, Smith G, Calder J. Efficacy of foot and ankle corticosteroid injections. Foot & ankle international. 2017 Jan;38(1):8-13. doi: 10.1177/1071100716670160.

35. Peterson C, Hodler J. Adverse events from diagnostic and therapeutic joint injections: a literature review. Skeletal Radiology. 2011 Jan;40(1):5-12. doi: 10.1007/s00256-009-0839-y.

36. Kilmartin TE. Corticosteroid injection therapy in Podiatry. Podiatry Now. 2017;20(2), CPD pullout.

37. Smith RW, Katchis SD, Ayson LC. Outcomes in hallux rigidus patients treated nonoperatively: a long-term follow-up study. Foot & Ankle International. 2000 Nov;21(11):906-13. doi: 10.1177/10711007002110103.

38. Munteanu, S, Menz, H, Zammit, G, Landorf, K, Handley, C, ElZarka, A, DeLuca, J. Efficacy of intra-articular hyaluronan (Synvisc®) for the treatment of osteoarthritis affecting the first metatarsophalangeal joint of the foot (hallux limitus): study protocol for a randomised placebo controlled trial. J Foot Ankle Res. 2009;2(2). doi: 10.1186/1757-1146-2-2.

39. Frecklington M, Dalbeth N, McNair P, Gow P, Williams A, Carroll M, Rome K. Footwear interventions for foot pain, function, impairment and disability for people with foot and ankle arthritis: a literature review. In Seminars in arthritis and rheumatism 2018 Jun 1 (Vol. 47, No. 6, pp. 814-824). WB Saunders. doi: 10.1016/j.semarthrit.2017.10.017.

40. Kompel A, Roemer F, Murakami A, Diaz L, Crema M, Guermaz, A. Intra-articular corticosteroid injections in the hip and knee: Perhaps not as safe as we thought? Radiology. 2019;293(3). doi: 10.1148/radiol.2019190341.