

The effect of hyaluronic acid injection compared to corticosteroids injection in hand osteoarthritis: a systematic review and meta-analysis of randomized control trials

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ABSTRACT

Background: Treatment of hand osteoarthritis (OA) often includes corticosteroid and hyaluronic acid (HA) injections. Some studies have reported better pain relief and improved function, whereas others have reported minimal long-term benefits. This study aimed to evaluate the effects of corticosteroids and HA injections on the management of hand OA.

Methods: PubMed, Embase, CENTRAL, and EBSCO Open Disk were searched from their inception to May 2024. Randomized controlled trials (RCTs) comparing intra-articular corticosteroid and HA injections in adults with hand OA were included. Data on demographics, interventions, and outcomes were extracted and the risk of bias was assessed using the Cochrane Risk of Bias 2. We performed a pairwise meta-analysis using a random-effects model to estimate the pooled effects of the included trials, that is, standardized mean differences (SMDs) with their corresponding 95% confidence intervals (CIs).

Results: Of 189 articles, three RCTs involving 180 participants (mean age, 62–62.9 years) were included. One RCT was identified through a database search, and two RCTs were identified through other searching techniques. The risk of bias was considered low in two trials and high in one trial. No significant difference in pain relief was found between the corticosteroid and HA treatments (SMD, 0.06; 95% CI, -0.23 to 0.35; $I^2=0.0\%$).

Conclusion: Corticosteroid and HA injections offered similar pain relief in patients with hand OA. Further long-term studies are necessary to evaluate the functional outcomes and potential side effects. However, this conclusion should be interpreted with caution due to the small sample size of the studies (PROSPERO registration number: CRD42024511411).

Keywords: Osteoarthritis; Hyaluronic Acid; Intra-Articular Injections; Pain; Treatment Outcome

Introduction

Osteoarthritis (OA) is a widespread and debilitating ailment that predominantly affects the elderly population, significantly

impairing daily functional activities and overall quality of life [1,2]. The administration of corticosteroids is a common pharmacological approach for managing hand OA [3], offering short-term pain relief through anti-inflammatory effects. However, concerns

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regarding potential cartilage degradation limit long-term application. Hyaluronic acid (HA) injections have been considered an alternative [4], aiming to improve synovial joint lubrication and restore the viscoelastic characteristics of synovial fluid, potentially facilitating extended symptom relief and functional enhancement. However, supporting evidence for HA in hand OA remains limited, despite some randomized trials demonstrating potential benefits.

Many previous studies on the effects of corticosteroids and HA in the treatment of knee joint OA may not be directly relevant to hand OA [4-7]. Unlike the joints of the hand, the knee joint is subjected to weight-bearing forces that may result in divergent treatment outcomes between these two manifestations of OA. The results suggest that HA relieved movement restriction, whereas corticosteroids mitigated pain in patients with no significant effect on joint stiffness. According to recommendations from the European Alliance of Associations for Rheumatology (EULAR), the American College of Rheumatology (ACR), and the Osteoarthritis Research Society International (OARSI), topical non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment for hand OA. If symptoms persist, oral NSAIDs should be considered, and in cases where intra-articular treatment is required, glucocorticoid injections are recommended [8,9]. However, evidence supporting their effectiveness in hand OA is limited, with mixed results from randomized controlled trials (RCTs), and most supportive data being derived from knee OA studies.

The effects of corticosteroids and HA on hand OA pain have been explored in various studies [5,10,11] and have yielded mixed results. Although corticosteroid injections may provide short-term pain relief, their long-term efficacy is uncertain and raises concerns about potential implications for joint integrity and

cartilage health; however, evidence on HA treatment is limited, with only a few studies suggesting its effectiveness compared to corticosteroids [10]. This lack of robust data highlights the need for focused research to determine the most effective treatments for hand OA. The objective of this study was to evaluate the comparative effects of HA and corticosteroids injection in managing hand OA. Given the differing mechanisms of action—anti-inflammatory for corticosteroids and viscoelastic restoration for HA—and the limited direct comparative evidence, this review focuses on RCTs that directly compare pain relief outcomes between the two treatments.

Methods

The report of this study followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [12]. The study protocol was registered on the PROSPERO (CRD42024511411).

Artificial intelligence (AI)-assisted language editing was performed using ChatGPT (version GPT-4; OpenAI). This tool has been used to improve grammar, syntax, and readability. The final manuscript has been authored, verified, and approved by our research team.

This study utilized data exclusively from previously published studies. As no new data were collected directly from human participants, Institutional Review Board (IRB) approval and informed consent were not required.

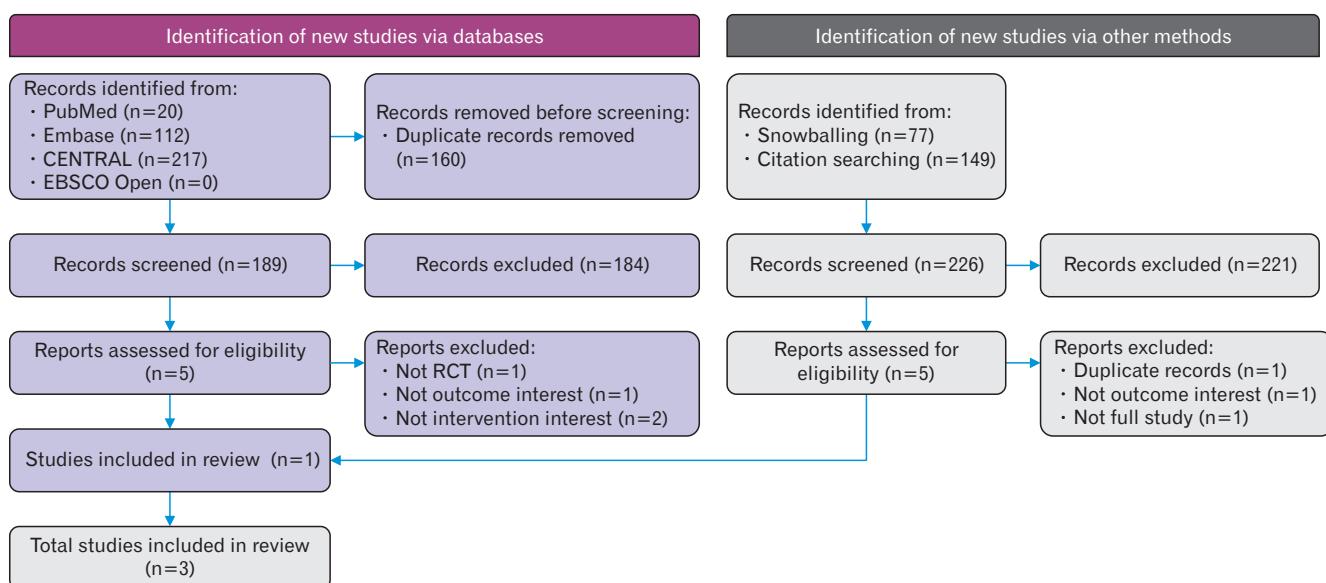


Figure 1. PRISMA flow diagram of study selection. CENTRAL, Cochrane Central Register of Controlled Trials; RCT, randomized controlled trial; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Search strategies and study selection

A systematic search was conducted from inception to May 2024 across the following databases: PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and EBSCO Open Dissertations. The complete search strategy is detailed in Supplement 1. Reference lists of the included papers and citation tracking were performed using Scopus.

We included RCTs without language restrictions that met the following inclusion criteria: (1) included adults with hand OA, including thumb-base OA, interphalangeal OA, and erosive OA, as determined by clinical diagnosis or fulfillment of the ACR of Rheumatology criteria for hand OA; (2) directly compared the effects of intra-articular corticosteroids and HA; and (3) reported pain outcomes. Studies involving participants with other diseases were eligible only if the data for those with hand OA were presented separately.

Two review authors (S.M. and N.S.) independently screened the titles and abstracts, followed by a full-text review. Disagreements between the authors were resolved through a consensus meeting, and in cases of non-consensus, a third reviewer (T.D.) made the final eligibility decision.

Data extraction

The following data were extracted from the included studies: demographics (age and sex), number of patients, definition/description of hand OA, intervention and comparator characteristics (dose, frequency, route of administration, and duration of intervention) outgrowth measures, time, points, and reported outcomes. One review author (S.M.) extracted data from each included study. A second review author (N.S.) verified extracted data.

Risk of bias assessment

Two authors (N.S. and S.M.) independently assessed the risk of bias in the included trials by using the Cochrane Risk of Bias 2 tool (RoB2) [13,14]. Overall judgment based on the five risk-of-bias domains was classified into three categories: high, some concern, and low. Disagreements between the reviewers were settled through discussion, and a consensus was reached with a third reviewer (T.D.). The results were visualized using Review Manager (RevMan) version 5.4 (The Cochrane Collaboration) [15].

Data analysis

The outcome of interest was pain relief. We performed a pairwise meta-analysis using a random-effects model to estimate the standardized mean differences (SMDs) was appropriate, as the included studies employed varying Visual Analog Scale scores (e.g., 0–10 and 0–100), necessitating standardization for meaning-

Table 1. Characteristic of included studies

Study author/ year	Total	Male	Mean age (y)	Country	Comparator	Intervention	Frequency of treatment (wk)	Duration of treatment (wk)	Time to evaluate outcome after treatment (wk)	Main outcome	Functional outcome
Stahl et al. [17] (2005)	42	6	62	Israel	Methylprednisolone acetate 40 mg	Sodium hyaluron 15 mg	Not show	4, 12, 24	Pain (VAS)	Grip and pinch strength (grip dynamometer)	
Bahadir et al. [19] (2009)	40	0	62.9	Turkey	Triamcinolone acetonide 20 mg	Sodium hyaluronate 5 mg	3 times at 1 week interval	4	4, 12, 24, 48	Pain (VAS)	Grip and pinch strength (grip dynamometer); hand function (DHI)
Monfort et al. [18] (2015)	88	11	62.8	Spain	Betamethasone 1.5 mg	Sodium hyaluronate 5 mg	3 times at 1 week interval	4	1, 2, 4, 12, 24	Pain (VAS)	Algo functional index for hand OA; SF-36 questionnaire (MCS-36, and PCS-36, respectively)

VAS, Visual Analog Scale; DHI, Duruoz Hand Index; OA, osteoarthritis; SF-36, 36-Item Short Form Health Survey; MCS-36, mental component summary of the SF-36, physical component summary of the SF-36.

ful comparison with the corresponding 95% confidence interval (CI). Statistical heterogeneity among the included trials was assessed using the chi-square test and I^2 [16]. We used the RevMan software for analysis.

Results

Search results

A total of 189 articles were identified through a bibliographic database search after the removal of duplicate records (Figure 1, Supplement 2). Of these, five full-text articles that passed the title/abstract screening were retrieved and reviewed for eligibility. One article was included after full-text review. Two additional RCTs were identified using other search techniques. Three trials were included in this meta-analysis [17-19].

Study characteristics

The studies of the three trials included in this analysis were conducted in Spain [18], Turkey [19], and Israel [17]. The duration of these studies varied from 6 to 12 months. The mean age of the participants across the studies ranged from 62 to 62.9 years. Collectively, 180 participants were involved in these studies, most of whom were female, as detailed in Table 1. All of these trials studied the treatment of hand OA with intra-articular injection therapy using radiographic evidence and the Eaton-Lister classification to confirm the diagnosis. The concentrations of intra-articular corticosteroid injections and intra-articular hyaluronate injections were used to compare betamethasone (1.5 mg) versus hyaluronate injections (5 mg), triamcinolone hexacetonide (20 mg) versus hyaluronate (5 mg), and methylprednisolone acetate (40 mg) versus hyaluronate injections (15 mg).

Quality of the included trials

According to the Cochrane Risk of Bias assessment version 2.0, the overall risk of bias of the two RCTs was judged as high [17,19]. The remaining trials were deemed to have a low risk of bias [18] (Figure 2).

Effect on pain

The results indicated no significant difference between the corticosteroid and HA groups, suggesting no clear evidence favoring one treatment over the other (SMD, 0.06; 95% CI, -0.23 to 0.35) without heterogeneity among the included trials ($I^2=0\%$) (Figure 3).

Functional hand outcomes

All studies reported functional hand outcomes, such as grip and pinch strength, but did not use consistent measurements to enable a meta-analysis. One study demonstrated that corticosteroid injections only improved grip strength, with no significant improvement in pinch measurements [17]. Similarly, another study found that patients treated with HA showed significantly greater differences in median functional index for hand OA

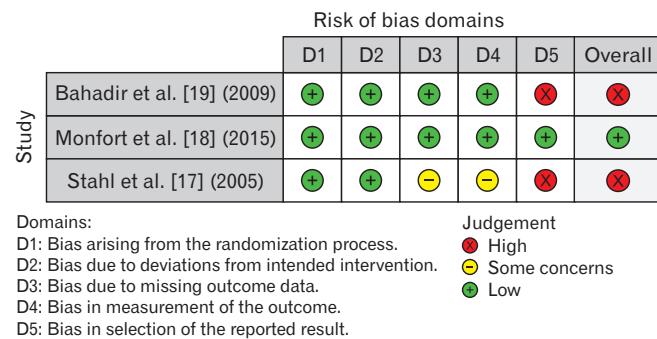


Figure 2. Risk of bias.

Hyaluronic acid vs. corticosteroids for pain reduction

Hyaluronic acid vs. corticosteroids

1.1 Pain reduction

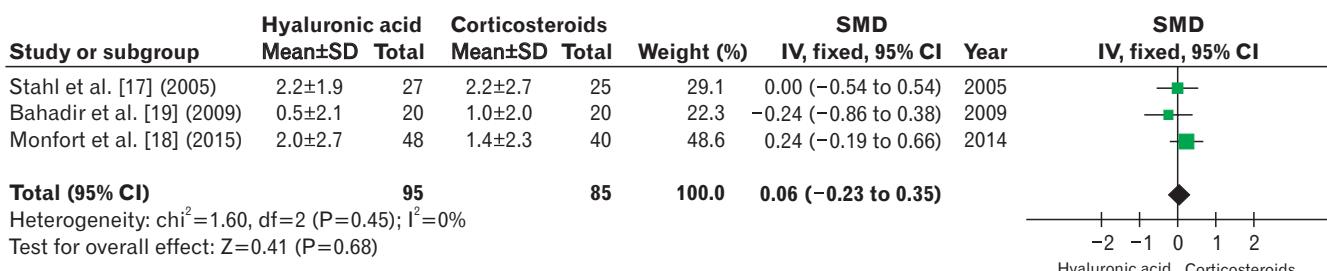


Figure 3. Comparison effect on pain. SD, standard deviation; SMD, standard mean difference; IV, inverse variance; CI, confidence interval; df, degrees of freedom.

scores between baseline and follow-up compared to those treated with betamethasone [18]. The last study by Bahadir et al. [19] showed that both steroid and HA treatments improved hand function based on the Duruoz Hand Index, no significant difference between the two groups was observed.

Discussion

This study specifically addressed hand OA, an area with limited existing research, and exclusively examined the effects of HA injections compared with corticosteroid injections. This approach provides a clearer understanding of the intervention outcomes of the two treatments. The pooled effect from the three included trials indicated that both corticosteroids and HA injections did not significantly differ considering their effects on pain reduction.

Our meta-analysis found no statistical heterogeneity, consistent with findings across the three trials. By excluding trials involving oral medications or other intra-articular substances such as prolotherapy, platelet-rich plasma, stem cells, infliximab, interferon, botulinum toxin, or normal saline, our study clearly evaluated the pain-reducing effects of HA and corticosteroid injections. Despite the superior ability of corticosteroids to reduce inflammation compared to HA, the findings indicated no significant difference in pain relief between the two interventions, regardless of their differing mechanisms of action. However, long-term follow-up after 6 months is recommended, focusing on pain reduction, hand function, and potential side effects.

A previous meta-analysis and RCT on thumb-based OA found no significant short-term pain reduction with corticosteroids and HA compared to placebo. It should be noted that platelet-rich plasma shows the potential for medium-term pain relief [20]. However, the efficacy of intra-articular interventions remains inconclusive compared with that of oral pharmacotherapy [21,22]. Additionally, the pain reduction mechanism may extend beyond pharmacotherapy, as evidence from studies has demonstrated the efficacy of placebo therapy compared with untreated control groups [23].

This study had several limitations. First, its highly specific design focused solely on comparing outcomes between HA and corticosteroids, without including comparisons with placebo or other types of medication [22]. Second, the findings were limited by the small number of studies available. However, this represents, to our best knowledge, the most comprehensive evidence gathered from a thorough and exhaustive search. Furthermore, the inability to compare other clinical outcomes, such as functional hand outcomes, is due to the use of various evaluation methods across different studies.

In conclusion, both corticosteroid and HA injections have demonstrated comparable efficacy in relieving pain associated with hand OA. However, the clinical significance of this finding remains inconclusive and should be interpreted with caution due

to the limited sample sizes of the included studies. These findings may inform clinical decision making among general practitioners, family medicine physicians, orthopedic surgeons, and rheumatologists involved in the management of hand OA. Future RCTs with larger sample sizes and longer follow-up periods are warranted to evaluate additional outcomes, including functional improvement, cost-effectiveness, and potential adverse effects, in order to better define the therapeutic role of these intra-articular interventions.

Article Information

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Data availability

Not applicable.

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Author contribution

Conceptualization: SM, NS. Data curation: SM, NS, KB. Formal analysis: NS, TD. Investigation: SM, NS. Methodology: TD. Resources: KB, TD. Software: KB, TD. Supervision: TD. Visualization: TD. Writing-original draft: SM, NS. Writing-review & editing: NS, TD, KB. Final approval of the manuscript: all authors.

Supplementary materials

Supplementary materials can be found via <https://doi.org/10.4082/kjfm.25.0125>. Supplement 1. Search strategies: from inception to 14 February 2024. Supplement 2. List of excluded articles and reasons for exclusion.

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