



Q/How do hyaluronic acid and corticosteroid injections compare for knee OA relief?

EVIDENCE-BASED ANSWER

A | **INCONSISTENT EVIDENCE** shows a small amount of pain relief early (one week to 3 months) with corticosteroid (CS) injections and an equally small improvement in pain relief and function later (3 to 12 months) with hyaluronic acid (HA) injections (strength of recommendation [SOR]: **B**, meta-analysis of a randomized

controlled trial [RCT] and inconsistent RCTs).

Guidelines state that CS injections can be considered for symptomatic knee osteoarthritis (OA), but that insufficient evidence exists to recommend HA injections (SOR: **B**, evidence-based guidelines).

Evidence summary

A 2015 network meta-analysis of 137 RCTs with 33,243 patients (ages 45-76 years) with knee OA compared the effectiveness of a variety of treatments including intra-articular CS and HA.¹ At 3 months, the effect on pain was not significantly different between the CS and HA groups (12 trials; effect size [ES]=0.02; 95% confidence interval [CI], -0.12 to 0.17). However, a small but significant improvement in function was noted (scoring system not defined) at 3 months favoring HA (ES=0.24; 95% CI, 0.06-0.43; number of trials not specified).

At 3 and 6 months, HA improves pain, but not function, more than CS

Another meta-analysis published in 2015 examined the effectiveness of intra-articular CS and HA in 7 RCTs with 583 patients with knee OA.² All 7 trials were included in the network meta-analysis and discussed separately to evaluate different time points.

Pain at one month wasn't significantly different using a visual analog score (VAS) of one to 100 (4 trials; 245 patients; mean difference [MD]=1.66 points; 95% CI, -0.90 to 4.23). At 3 and 6 months, the HA group reported significantly reduced pain compared with

the CS group (3 months: 3 trials; 320 patients; MD=12.58 points; 95% CI, -17.76 to -7.40; 6 months: 5 trials; 411 patients; MD=9.01 points; 95% CI, -12.62 to -5.40). There were no significant differences in function outcomes (Index of severity for OA of the knee by Lequesne et al; The Knee Society Clinical Rating System), maximum flexion, or adverse events.

Triamcinolone improves pain, function, but not for long

A 2016 double-blind RCT of 110 patients with knee OA compared intra-articular HA and triamcinolone, assessing pain and function at intervals between 24 hours and 6 months.³ Patients in the HA group received a single injection of 6 mL hylan G-F 20 (Synvisc); patients in the CS group received 1 mL of triamcinolone acetone 40 mg and 5 mL of 1% lidocaine with epinephrine.

The CS group reported significantly less pain (VAS score 1 to 100) at 24 hours than the HA group (24 points vs 36 points; $P=.002$); relief lasted as long as one week (14 points vs 23 points; $P=.018$). After the first week, no difference was seen in pain between groups for as long as 6 months.

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Corey Lyon, DO;
Emily Spencer, MD;
Jack Spittler, MD
University of Colorado
Family Medicine Residency,
Denver

Kristen Desanto, MSLS,
MS, RD, AHIP
University of Colorado
Health Sciences Library,
Aurora

DEPUTY EDITOR

Rick Guthmann, MD,
MPH
Advocate Illinois Masonic
Family Medicine Residency,
Chicago

Function, assessed by a modified Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC 1 to 100; higher score indicates worse pain, stiffness, and function) showed a significant improvement with CS at 2 weeks (25 points vs 31 points; $P=.03$), but no difference at any other time point up to 6 months.

HA (mostly) improves pain, function more than betamethasone

A 2015 RCT of 200 patients with knee OA compared the effectiveness of intra-articular HA and betamethasone.⁴ Evaluators were blinded and assessments were made at 3, 6, 9, and 12 months. The HA group received 2.5 mL of 1% HA (Suprahyal); the CS group received betamethasone dipropionate 5 mg plus betamethasone sodium phosphate 2 mg in 1 mL.

The CS group had significantly less pain (VAS 1 to 10) at 3 months compared with the HA group (2.2 points vs 3.1 points; $P=.004$), but the HA group had less pain at all other time points (6 months: 3.9 points vs 2.4 points; $P=.0001$; 9 months: 5.5 points vs 3.6 points; $P=.0001$; 12 months: 6 points vs 4.1 points; $P=.0001$).

The WOMAC function subscores (0 to 68; lower indicates more function) were significantly better at all follow-up points in the HA group compared with the CS group (3 months: 19 vs 25; $P=.0001$; 6 months: 17 vs 29; $P=.0001$; 9 months: 25 vs 42; $P=.0001$; 12 months: 28 vs 42; $P=.0001$).⁴

Recommendations

The American Academy of Orthopaedic Surgeons 2013 work group couldn't recommend for or against using intra-articular CS for patients with symptomatic knee OA based on inconclusive evidence.⁵ They also couldn't recommend using HA (SOR: strong).

The National Institute for Health and Care Excellence (NICE) stated in 2008 that intra-articular CS injections should be considered as an adjunct to core treatments for the relief of moderate to severe pain in people with OA.⁶ In 2014, NICE recommended against offering intra-articular HA injections for managing OA.

The US Veterans Administration and Department of Defense have issued guidelines stating that clinicians may consider intra-articular CS injections for patients with symptomatic knee OA (US Preventive Services Task Force [USPSTF] Grade B).⁷ They report insufficient evidence to recommend for or against the use of intra-articular HA with the caveat that HA may be considered for patients who don't respond adequately to nonpharmacologic measures and who have an inadequate response, intolerable adverse events, or contraindications to other pharmacologic therapies (USPSTF Grade I). **JFP**

References

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Inconsistent evidence shows a small amount of pain relief at one week to 3 months with corticosteroid injections.