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Intra-articular Corticosteroids for Osteoarthritis of the Knee

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CLINICAL QUESTION Are intra-articular corticosteroids associated with improvement in pain and physical function compared with sham injection or no intervention in patients with knee osteoarthritis?

BOTTOM LINE Intra-articular corticosteroids may be associated with moderate improvement in pain and a small improvement in physical function up to 6 weeks after injection. However, the quality of the evidence is low.

Corticosteroids are potent anti-inflammatory agents with long-standing use in osteoarthritis treatment, but their effectiveness and safety are unclear. This article summarizes the results of a recent Cochrane review[1] that evaluated the association of intra-articular corticosteroids with benefits and harms compared with sham injection or no intervention in patients with knee osteoarthritis.

Editorial page 2607

Summary of Findings

Use of intra-articular corticosteroids was associated with a larger pain reduction than control (standardized mean difference [SMD], −0.40 [95% CI, −0.58 to −0.22]), which corresponds to a difference in pain scores of 1.0 cm on a 10-cm visual analog scale between corticosteroids and control. This effect size corresponds to a number needed to treat of 8 (95% CI, 6 to 13), meaning that for every 8 patients treated with corticosteroids rather than sham injection or no intervention, 1 patient will respond to treatment. The **Figure** shows random-effects meta-analyses by follow-up time and trial size.

Overall, corticosteroids were associated with a moderate benefit at 1 to 2 weeks after treatment (SMD, −0.48 [95% CI, −0.70 to −0.27]). The magnitude of this beneficial association decreased with increasing length of follow-up. There was no association of intra-articular steroids with benefit at 6-month follow-up (SMD, −0.07 [95% CI, −0.25 to 0.11]). When the meta-analysis was stratified by trial size, results from small trials were similar to the overall analysis. However, associations of intra-articular steroids with benefit were less strong in the 3 moderate to large trials that included 50 patients or more per trial group.

A test for interaction between trial size and treatment effect was positive (P = .01), suggesting small study effects. Findings were similar for physical function. Only 1 of these moderate to large trials that included a total of 100 patients reported adequate concealment of allocation, adequate measures to blind patients, and an intention-to-treat analysis.[2] This trial[2] included exercise therapy as a concomitant treatment in all patients, compared corticosteroid injection with sham injection, included only patients with local signs of inflammation, and used ultrasound guidance to ensure adequate intra-articular placement of needles when injecting a single dose of 40 mg of methylprednisolone acetate.

This trial did not find evidence that corticosteroids were associated with clinical benefits after follow-up of 2 weeks, 3 months, and 6 months.[2] The other 2 moderate to large trials compared corticosteroids plus viscosupplementation vs viscosupplementation only or corticosteroids plus joint lavage vs joint lavage only.[1]

Only 2 trials contributed to the random-effects meta-analyses of adverse events, withdrawal due to adverse events, and serious adverse events. There was no association of corticosteroids with adverse events; however, the 95% CIs were wide and could not exclude the possibility of harm. One small trial found no evidence that intra-articular corticosteroids were associated with joint space narrowing.[1]

Evidence Profile

No. of studies: 27

No. of randomized clinical trials: 27

Study years: Conducted, 1954-2014; published, 1958-2015

No. of participants: 1767

Male: 39% **Female:** 61%

Race/ethnicity: Not reported

Age, mean (range): 63 years (42-71 years)

Settings: Outpatient clinics in rheumatology, surgery, physical medicine and rehabilitation, anesthesia and pain management, and general practice

Countries: Australia, Belgium, Brazil, Canada, Curaçao, Denmark, France, Italy, the Netherlands, Russia, Scotland, Spain, Sweden, Turkey, United Kingdom, United States

Comparison: Intra-articular corticosteroids compared with sham injection or no intervention in patients with knee osteoarthritis

Primary outcomes: Change in pain and physical function

Secondary outcomes: Quality of life, any adverse events, withdrawal due to adverse events, serious adverse events, joint space narrowing

Discussion

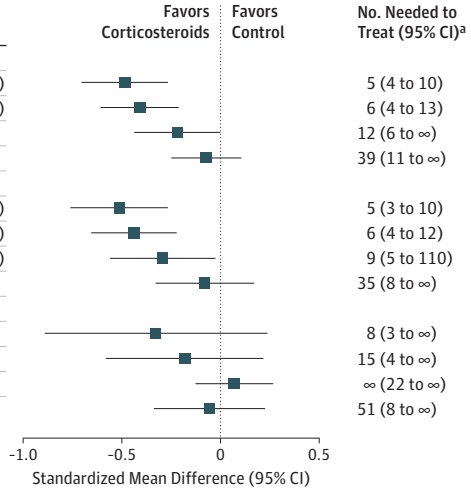
Intra-articular corticosteroids may be associated with moderate improvement in pain and a small improvement in physical function. However, the quality of evidence is low. Associations of intra-articular steroids with benefit decreased over time. There was no association of intra-articular steroids with benefit at 6-month follow-up.

Limitations

First, the quality of the evidence was generally low, there was considerable heterogeneity among trials, and there was evidence of small study effects. Heterogeneity estimates and associations with benefit decreased when analyses were restricted to trials with appropriate concealment of allocation, nonindustry funding, moderate to large sample

Figure. Associations of Intra-articular Corticosteroids With Knee Pain in Randomized Clinical Trials of Knee Osteoarthritis

Length of Follow-up	No. of Trials	No. of Patients	Standardized Mean Difference (95% CI) in Severity of Knee Pain	No. Needed to Treat (95% CI)[a]
All trials[b]				
1-2 wk	16	1042	-0.48 (-0.70 to -0.27)	5 (4 to 10)
4-6 wk	22	1529	-0.41 (-0.61 to -0.21)	6 (4 to 13)
3 mo	18	1233	-0.22 (-0.44 to 0)	12 (6 to ∞)
6 mo	7	526	-0.07 (-0.25 to 0.11)	39 (11 to ∞)
Small trials				
1-2 wk	14	838	-0.51 (-0.76 to -0.27)	5 (3 to 10)
4-6 wk	20	1221	-0.44 (-0.66 to -0.22)	6 (4 to 12)
3 mo	15	835	-0.29 (-0.56 to -0.03)	9 (5 to 110)
6 mo	5	333	-0.08 (-0.33 to 0.17)	35 (8 to ∞)
Moderate to large trials[c]				
1-2 wk	2	204	-0.33 (-0.89 to 0.24)	8 (3 to ∞)
4-6 wk	2	308	-0.18 (-0.58 to 0.22)	15 (4 to ∞)
3 mo	3	398	0.07 (-0.13 to 0.27)	∞ (22 to ∞)
6 mo	2	193	-0.06 (-0.34 to 0.23)	51 (8 to ∞)



[a] To derive from standardized mean differences, a probability of treatment response in the control group of 31% was assumed, with response defined as 50% or greater decrease in pain from baseline.[1] The ∞ symbol reported for the point estimate or 95% CI of the number needed to treat (NNT) indicates that the corresponding estimate was in favor of control (ie, the risk difference used to generate the NNT, which is the inverse of the risk difference, was negative, indicating that patients in the control group were more likely to respond to treatment than those receiving corticosteroids).

[b] Trials assessed pain using self-reported instruments such as a 10-cm visual analog scale.

[c] Included 50 or more patients per trial group.

sizes, or use of viscosupplementation or joint lavage as cointerventions in both groups.[1] Findings were similar for physical function. Second, point estimates were imprecise and we cannot exclude an association between corticosteroids and clinically relevant benefits or harm.

Third, none of the included trials focused on patients with intermittent osteoarthritic flares, and only 2 trials had eligibility criteria compatible with the predominant inclusion of patients with acute or subacute exacerbations of symptoms.[2,3] Therefore, it is not possible to draw conclusions about the association of corticosteroids with benefit in patients with acute or subacute worsening of symptoms after minor trauma or physical activity with signs of local inflammation, effusion, or both.

Comparison of Findings With Current Guidelines

The findings are consistent with the 2013 guidelines of the American Academy of Orthopaedic Surgeons, which did not provide any recommendations for or against the use of intra-articular corticosteroids because the evidence was inconclusive.[4] The 2012 guidelines of the American College of Rheumatology conditionally recommend intra-articular steroids for knee osteoarthritis.[5] The 2014 National Institute for Health and Care Excellence guidelines recommend that clinicians consider the use of corticosteroids as an adjunct to core treatments. Our findings are formally consistent with these recommendations.[5,6] The 2014 Osteoarthritis Research Society International guidelines[7] state that intra-articular corticosteroids are appropriate for knee osteoarthritis, which somewhat differs from our conclusion.

Areas in Need of Future Study

Adequately powered trials are needed to confirm or refute clinically relevant short- to midterm benefits of intra-articular corticosteroids in patients with stable disease, and in patients with intermittent exacerbations of their osteoarthritis symptoms. The trials should have a sham injection control group, and use ultrasound guidance to ensure accurate intra-articular needle placement.[2]

ARTICLE INFORMATION

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