Medicines Evidence Commentary

commentary on important new evidence from Medicines Awareness Weekly

Osteoarthritis: chondroitin evidence remains of poor quality

A Cochrane Review of 43 randomised controlled trials found that chondroitin (with or without glucosamine) improved pain scores and a composite of pain, function and disability compared with placebo or active control in adults with osteoarthritis. However, for many of the other outcomes assessed there were no statistically significant differences between chondroitin and placebo. The findings of the review were limited by the poor quality of the included studies, and sensitivity analyses that took several limitations into account often did not show statistically significant benefits with chondroitin. This is consistent with the NICE guideline osteoarthritis: care and management in adults that advises healthcare professionals not to offer glucosamine or chondroitin products for the management of osteoarthritis on the basis that the evidence base was poor.

Overview and current advice

The NICE guideline osteoarthritis: care and management in adults recommends the following core treatments for all people with clinical osteoarthritis:

- Access to appropriate information
- Activity and exercise
- Interventions to achieve weight loss if the person is overweight or obese.

In addition, the NICE guideline recommends that the use of local heat or cold and transcutaneous electrical nerve stimulation (TENS) should be considered as adjuncts to core treatments. However, it advises healthcare professionals not to offer glucosamine or chondroitin products for the management of osteoarthritis. This is because the guideline development group concluded that the overall evidence on effectiveness of glucosamine and chondroitin remained very limited and uncertain (see the NICE full guideline on osteoarthritis for details). The guideline also gives recommendations for using oral analgesics, topical treatments and intra-articular injections. It states that paracetamol and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) should be considered ahead of oral NSAIDs, cyclooxygenase 2 (COX-2) inhibitors or opioids. See the NICE guideline for more detail.

There are limitations to the published evidence on treating osteoarthritis. Most studies have focused on knee osteoarthritis, and are often of short duration using single therapies. Although most trials have looked at single joint involvement, in reality many people have pain in more than one joint, which may
alter the effectiveness of interventions. NICE intends to undertake a full review of evidence on the pharmacological management of osteoarthritis in due course (see the Introduction of the NICE guideline for further details).

The NICE Pathway: osteoarthritis brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams. NICE has also produced a Key Therapeutic Topic on NSAIDs.

New evidence
A Cochrane systematic review has considered the benefits and harms of oral chondroitin for treating osteoarthritis. This study included 43 randomised controlled trials (RCTs) in 9110 adults with mostly knee osteoarthritis. The duration of studies ranged from 1 month to 3 years, and in most, chondroitin was taken at a dose of 800 mg/day or higher.

No statistically significant differences between chondroitin and placebo were found for many patient-oriented outcomes assessed, including physical function, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) stiffness, patient global assessment on a visual analogue scale, grip strength, morning stiffness, and disability score. When chondroitin plus glucosamine was compared with placebo, no statistically significant differences were found for most outcomes, including pain.

Compared with placebo, people who took chondroitin had statistically significantly better pain scores in 8 studies (n=1077) that were shorter than 6 months, with a mean difference (a reduction) of 10.14 units (95% confidence interval [CI] 5.71 to 14.58) on a 0 to 100 point pain scale (absolute risk difference [ARD] 10%, 95% CI 6% to 15%; number needed to treat [NNT] 5, 95% CI 3 to 8). The authors considered this to show a clinically meaningful, medium to moderate effect on pain. The reduction in pain with chondroitin compared with placebo in the 6 longer-term studies (n=989) was borderline (mean pain score reduction 9.01, 95% CI 0.34 to 17.68; ARD 9%, 95% CI 0% to 18%). However, the level of evidence was graded as low for these comparisons. The authors commented generally on the poor quality of evidence in this systematic review (see Commentary below for details) and they suggested that more high-quality studies are needed to explore the role of chondroitin in the treatment of osteoarthritis. In 2 studies (n=1253) that provided a high level of evidence, the WOMAC Minimal Clinically Important Improvement (WOMAC MCII Pain Subscale) outcome, a reduction in knee pain by 20%, was achieved in statistically significantly more people taking chondroitin than placebo (53% versus 47%, ARD 6%, 95% CI 1% to 11%, relative risk [RR] 1.12, 95% CI 1.01 to 1.24, NNT 16, 95% CI 9 to 136).

A moderate level of evidence from 7 studies (n=903) shorter than 6 months found that the mean composite measure of pain, function and disability as assessed with Lequesne's Index on a 0 to 24 point scale (lower indicates less pain and disability) was 1.98 points lower with chondroitin than placebo (ARD 8%, 95% CI 5% to 12%, NNT 2, 95% CI 2 to 3). The authors considered this to show a clinically meaningful, but small to medium, effect on Lequesne's Index. In 2 studies (n=922) of at least 6 months that provided a high level of evidence, taking chondroitin was associated with statistically significantly less reduction in minimum joint space width (a disease-oriented outcome) compared with placebo (mean difference 0.18 mm, 95% CI 0.06 mm to 0.30 mm). However, various other comparisons with placebo did not find any statistically significant benefit with chondroitin on radiographic minimum joint space width, mean joint space width or change in mean joint space width.

Moderate evidence from 10 studies (n=2406) found no statistically significant difference between chondroitin and placebo in withdrawals due to adverse events. However, moderate evidence from 6 studies (n=954) found fewer serious adverse events with chondroitin (2.7%) compared with placebo (6.3%).
Commentary

Commentary provided by Medicines and Prescribing Centre

This Cochrane Review of 43 RCTs was an extensive systematic review of the current evidence for chondroitin in osteoarthritis and considered a wide range of outcomes from both short-term and long-term studies¹. In particular it found that chondroitin (with or without glucosamine) improved pain scores and a composite of pain, function and disability assessed with Lequesne’s Index compared with placebo or active control. The authors considered these reported benefits to be clinically meaningful, showing a medium to moderate effect on pain and a small to medium effect on Lequesne’s Index. However, as highlighted by the authors, there are important limitations to the findings. The quality of many of the studies was poor and the results for pain were based only on a low level of evidence and for Lequesne’s index, a moderate level of evidence.

Differences between the studies were found, which makes it difficult to compare between them. Most of the studies were funded by manufacturers of chondroitin and there was evidence of publication bias. In addition, most studies did not report adequate methods of allocation concealment or randomisation and studies were usually small, with only 3 having more than 100 participants. The authors carried out extensive sensitivity analyses to account for these limitations, and studies that had large sample sizes, and those that were of higher quality did not show a statistically significant difference between chondroitin and placebo on pain.

The findings of this Cochrane Review are consistent with the conclusions of the guideline development group for the NICE guideline osteoarthritis: care and management in adults, who concluded that the overall evidence for chondroitin remained very limited and uncertain. The NICE guideline advises healthcare professionals not to offer glucosamine or chondroitin products for the management of osteoarthritis.

Study sponsorship

Most of the studies included in this Cochrane Review were funded by manufacturers of chondroitin.

References


About this Medicines Evidence Commentary

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