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Time to stop glucosamine and chondroitin for knee OA?

Prior studies provided conflicting results regarding the efficacy of these medications. This study offers evidence for discontinuing them.

PRACTICE CHANGER

Tell patients with moderately severe osteoarthritis to stop taking their glucosamine and chondroitin as it is less effective than placebo.[1]

STRENGTH OF RECOMMENDATION

B: Based on single, good-quality randomized controlled trial.

Roman-Blas JA, Castañeda S, Sánchez-Pernaute O, et al. Combined treatment with chondroitin sulfate and glucosamine sulfate shows no superiority over placebo for reduction of joint pain and functional impairment in patients with knee osteoarthritis: a six-month multicenter, randomized, double-blind, placebo-controlled clinical trial. *Arthritis Rheumatol.* 2017;69:77-85.

ILLUSTRATIVE CASE

A 65-year-old man with moderately severe osteoarthritis (OA) of the knee presents to your office for his annual exam. During the medication review, the patient mentions he is using glucosamine and chondroitin for his knee pain, which was recommended by a family member.

Should you tell the patient it's okay to continue the medication?

Knee OA in the United States is a common condition and affects an estimated 12% of adults 60 years and older and 16% of adults 70 years and older.[2] The primary goals of OA therapy are to minimize pain and improve function. The American Academy of Orthopedic Surgeons (AAOS) and the American College of Rheumatology (ACR) agree that first-line treatment recommendations include aerobic exercise, resistance training, and weight loss.

Initial pharmacologic therapies include full-strength acetaminophen or oral/topical nonsteroidal anti-inflammatory drugs (either initially or if unresponsive to acetaminophen).[3,4] Alternative medication options for patients with an inadequate response to initial therapy include tramadol, other opioids, duloxetine, or intra-articular injections with corticosteroids or hyaluronate.[3,4] Total knee replacement may be indicated in moderate or severe knee OA with radiographic evidence of OA.[5] Vitamin D, lateral wedge insoles, and antioxidants are not currently recommended.[6]

Prior studies evaluating glucosamine and/or chondroitin have provided conflicting results regarding evidence on pain reduction, function, and quality of life. Therefore, guidelines on OA management do not recommend their use (AAOS, strong; ACR, conditional recommendation).[3,4] However, consumption remains high, with 6.5 million US adults reporting use of glucosamine and/or chondroitin in the prior 30 days.[7]

A 2015 systematic review of 43 randomized trials evaluating oral chondroitin sulfate for OA of varying severity suggested there may be a significant decrease in short-term and long-term pain with doses of ≥800 mg/d compared with placebo (level of evidence, low; risk of bias, high).[8] However, no significant difference was noted in short- or long-term function, and the trials were highly heterogeneous.

Studies included in the 2015 systematic review found that glucosamine *plus* chon-

INSTANT POLL

What percentage of your patients with knee osteoarthritis use/have used glucosamine and chondroitin for their pain?

- ☐ 25%
- ☐ 50%
- ☐ 75%
- ☐ >75%

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droitin did not have a significant effect on short- or long-term pain or physical function compared with placebo. Although glucosamine plus chondroitin led to significantly decreased pain compared with other medication, sensitivity analyses conducted for larger studies (N>200) with adequate methods of blinding and allocation concealment found no difference in pain.[8]

Three studies included in the 2015 systematic review provided data on adverse events when comparing glucosamine plus chondroitin vs placebo, and found no statistically significant difference.[8]

This randomized controlled trial (RCT) from Roman-Blas et al[1] evaluated chondroitin and glucosamine vs placebo in patients with more severe OA. The study was supported by Tedec-Meiji Farma (Madrid, Spain) maker of the combination of chondroitin plus glucosamine used in the study.

STUDY SUMMARY

Chondroitin + glucosamine was not better than placebo for pain

This multicenter, randomized, double-blind, placebo-controlled trial was conducted in 9 rheumatology referral centers and one orthopedic center in Spain. The trial evaluated the efficacy of chondroitin sulfate 1200 mg plus glucosamine sulfate 1500 mg (CS/GS) compared with placebo in 164 patients with Grade 2 or 3 knee OA and moderate to severe knee pain. OA grade was ascertained using the Kellgren-Lawrence scale, corresponding to osteophytes and either possible (Grade 2) or definite (Grade 3) joint space narrowing. Level of knee pain was defined by a self-reported global pain score of 40-80 mm on a 100-mm visual analog scale (VAS).

No significant difference was noted in group characteristics, and the average age in the CS/GS group was 67 years vs 65 years in the placebo group. Exclusion criteria included body mass index of ≥35 kg/m^2, concurrent arthritic conditions, and any coexisting chronic disease that would prevent successful completion of the trial.[1]

The primary end point was mean reduction in global pain score on a 0- to 100-mm VAS at 6 months. Secondary outcomes included mean reduction in total and subscale scores in pain and function on the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index (0–100-mm VAS for each) and the use of rescue medication.

Baseline global pain scores were 62 mm in both groups. Acetaminophen, up to 3 g/d, was the only allowed rescue medication. Clinic visits occurred at 4, 12, and 24 weeks. A statistically significant difference between groups was defined as $P<.03$.[1]

Results. In the intention-to-treat analysis at 6 months, patients in the placebo group had a greater reduction in pain than the CS/GC group (-20 mm vs -12 mm; $P=.029$). No other difference was noted between the placebo and CS/GS groups in the total or subscales of the WOMAC index, and no difference was noted in use of acetaminophen. More patients in the placebo group had at least a 50% improvement in pain or function compared with the CS/GS group (47.4% vs 27.5%; $P=.01$).

In the CS/GS group, 31% did not complete the 6-month treatment period, compared with 18% in the placebo group. More patients dropped out because of adverse effects (diarrhea, upper abdominal pain, and constipation) in the CS/GS group than the placebo group (33 vs 19; $P=.018$).[1]

Placebo was more effective than chondroitin sulfate/glucosamine sulfate in patients with knee OA.

WHAT'S NEW

A pharma-sponsored study finds treatment ineffective

The effectiveness of CS/GS for the treatment of knee OA has been in question for years, but this RCT is the first trial sponsored by a pharmaceutical company to evaluate CS/GS efficacy. This trial found evidence of a lack of efficacy. In patients with more severe OA of the knee, placebo was more effective than CS/GS, and CS/GS had significantly more adverse events. Therefore, it may be time to advise patients to stop taking their CS/GS supplement.

CAVEATS

Cannot generalize findings to CS or GS alone, or different dosages

The study compared only one medication dosing regimen using a combination of CS

and GS. Whether either agent alone or different dosing would lead to the same outcome is unknown.

CHALLENGES TO IMPLEMENTATION

An all-too-common product presents challenges

CS/GC is available over the counter and advertised directly to consumers. With this medication so readily available, identifying patients who are taking the supplement and encouraging discontinuation can be a challenge. JFP

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PRACTICE OPPORTUNITIES