

# American Family Physician

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### FPIN's Clinical Inquiries

#### Glucosamine and Chondroitin for Osteoarthritis

##### Clinical Question

Does glucosamine or chondroitin reduce pain, improve functional status, or improve prognosis in patients with osteoarthritis?

##### Evidence-Based Answer

Glucosamine reduces pain and improves function in patients with knee or hip osteoarthritis. (Strength of recommendation: B, based on systematic reviews and a meta-analysis)

Glucosamine may be beneficial in other forms of osteoarthritis as well. (Strength of recommendation: B, based on a randomized controlled trial [RCT])

Chondroitin has not consistently been found to improve pain or functional status. (Strength of recommendation: B, based on a systematic review and a meta-analysis)

Combination glucosamine and chondroitin therapy with camphor improved pain when applied topically. Combination therapy with methylsulfonylmethane given orally results in improved pain relief, function, and swelling. (Strength of recommendation: B, based on RCTs)

Glucosamine may slow the progression of joint space narrowing, but there is no evidence that directly relates it to symptoms or prognosis of knee osteoarthritis. (Strength of recommendation: B, based on a meta-analysis and an RCT)

##### Evidence Summary

Reports from European trials suggest that glucosamine relieves the pain of osteoarthritis, although some of the earlier RCTs were of marginal quality and potentially biased because of manufacturer sponsorship.<sup>1</sup> Chondroitin has been investigated less often and in a greater variety of dosages. One systematic review<sup>1</sup> suggested that glucosamine and chondroitin improved pain relief and function; however, poor-quality trials and publication bias made the data difficult to interpret. Another systematic review<sup>2</sup> found that glucosamine significantly reduced pain compared with placebo and nonsteroidal anti-inflammatory drugs (NSAIDs). A subsequent meta-analysis<sup>3</sup> compared either glucosamine or chondroitin with placebo in persons with hip and

knee osteoarthritis and found that five persons with osteoarthritis had to be treated with glucosamine or chondroitin for one to benefit.

Three small RCTs found no improvement in pain relief or function with glucosamine treatment of knee osteoarthritis for less than six months; however, another study found improvement in functional pain of temporomandibular joint osteoarthritis treated for this same period.<sup>4</sup> Two trials compared glucosamine with placebo over three years and demonstrated improvement in pain and function.<sup>4</sup>

One recent RCT<sup>5</sup> evaluated glucosamine given for 12 weeks to persons with knee osteoarthritis. Two different glucosamine preparations were utilized during the trial because the manufacturer withdrew the original supply. There was no significant difference between the glucosamine and placebo groups regarding the mean changes in pain, stiffness, or function. There was a decrease in pain scores seen during the RCT, but it was not statistically significant. A larger mean change in pain scores was seen in those receiving glucosamine hydrochloride than in those receiving glucosamine sulfate; however, this was not statistically significant. Another RCT<sup>6</sup> evaluated flares of osteoarthritis and pain, stiffness, and function in patients receiving glucosamine compared with those receiving placebo over a six-month period. There was similar disease flare in patients receiving glucosamine and placebo, and no differences in pain and function.

No RCTs evaluated glucosamine in combination with chondroitin; however, two RCTs compared glucosamine, chondroitin, and manganese with placebo with conflicting results.<sup>4</sup> Persons with knee osteoarthritis showed a greater reduction in pain at eight weeks using a topical preparation of glucosamine, chondroitin, and camphor compared with placebo but with no statistically significant change in function or stiffness.<sup>7</sup>

Another study<sup>8</sup> evaluated glucosamine, methylsulfonylmethane (a form of dimethyl sulfoxide), a combination of the two, and placebo in patients with mild to moderate osteoarthritis. The glucosamine, methylsulfonylmethane, and combination groups experienced a reduction in pain and swelling, with combination therapy resulting in a more rapid and significant improvement in symptoms than either compound alone.<sup>8</sup>

Three RCTs used joint space narrowing to measure disease progression of knee osteoarthritis.<sup>4</sup> Methodologic difficulties in standardization of joint space width measurements and knee radiographs limited definite conclusions on the effectiveness of glucosamine as a disease-modifying agent; however, in two RCTs,<sup>3</sup> patients receiving glucosamine in a dosage of 1,500 mg per day for three years demonstrated 0.27 mm less joint space narrowing than those taking placebo (95% confidence interval, 0.13 to 0.41 mm). Another study<sup>9</sup> demonstrated that in mild and severe knee osteoarthritis, approximately five patients needed to be treated with glucosamine to prevent one patient from experiencing joint space narrowing of at least 0.5 mm over three years.

Recommendations from Others

The American Pain Society recommends that adults with osteoarthritis be encouraged to take 1,500 mg of glucosamine daily as a dietary supplement but does not specifically recommend it as pharmacologic management for pain.<sup>10</sup>

The American College of Rheumatology Subcommittee on Osteoarthritis currently has no recommendations regarding the use of glucosamine or chondroitin in the treatment of knee osteoarthritis<sup>11</sup>; however, during their 2005 annual meeting, preliminary results from the Glucosamine/chondroitin Arthritis Intervention Trial (GAIT) were revealed. It was indicated in the presentation that glucosamine and chondroitin in combination may be effective in treating knee osteoarthritis, but final recommendations await the publication of results.<sup>12</sup>

### Clinical Commentary

Sufficient evidence exists from studies of persons with hip or knee osteoarthritis to support the use of glucosamine as a safe and effective alternative treatment. With the potential harmful effects of chronic NSAID and acetaminophen use and a reluctance to begin chronic narcotic therapy for mild osteoarthritis, glucosamine and possibly chondroitin offer viable, low-cost treatment options or adjuvant medications. Patients should be advised to take 1,500 mg of glucosamine daily, either once daily or in divided doses three times daily, and to continue therapy for at least four to eight weeks to allow for onset of benefit. It remains to be seen whether one preparation of glucosamine is more effective than another and whether dosing should be in a single daily dose or divided.

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