

## Do glucosamine and chondroitin worsen blood sugar control in diabetes?

### EVIDENCE-BASED ANSWER

Despite theoretical risks based on animal models given high intravenous doses, glucosamine/chondroitin (1500 mg/1200 mg daily) does not adversely affect short-term glycemic control for patients whose diabetes is well-controlled, or for those without diabetes or glucose intolerance (SOR: **A**, consistent, good-quality patient-oriented evidence). Some preliminary evidence suggests that glucosamine may worsen glucose intolerance for patients with untreated

or undiagnosed glucose intolerance or diabetes (SOR: **C**, extrapolation from disease-oriented evidence).

Long-term effects are unknown; however, no compelling theoretical or incidental data suggest that long-term results should be different (SOR: **C**, expert opinion). Further studies are required to clarify the effects of glucosamine on patients with poorly controlled diabetes or glucose intolerance.

### CLINICAL COMMENTARY

#### These products seem to be a safe alternative to NSAIDs

Glucosamine/chondroitin is a popular over-the-counter supplement used by many patients; it appears to be without any serious adverse effects or drug interactions. It does not seem to have much effect on blood sugar for patients with diabetes. It may relieve symptoms for some patients with pain due to osteoarthritis. As such, glucosamine/chondroitin seems to be a safe alternative to nonsteroidal anti-inflammatory drugs (NSAIDs) for patients

with osteoarthritis.

I would monitor blood sugars more frequently for patients with diabetes given the low numbers in the studies cited above. I would avoid glucosamine/chondroitin during pregnancy and lactation for the younger symptomatic female patient. The cost of this product varies widely, and this can be a factor for patients since they are paying out of pocket.

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### Evidence summary

Diabetes mellitus and osteoarthritis commonly overlap in patients, many of whom have looked to the nutritional supplement combination of glucosamine and chondroitin sulfates for pain relief. The effec-

tiveness of these supplements in improving patient-oriented outcomes for osteoarthritis is still being evaluated. However, regardless of their effectiveness they remain popular supplements, representing up to a third of the specialized supplement

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**FAST TRACK****Glucosamine and chondroitin do not have much effect on blood sugar, and may relieve the pain of osteoarthritis for some patients**

market in the US.<sup>1</sup>

The mechanism by which glucosamine is hypothesized to affect blood glucose involves the roles of glucosamine and the hexosamine biosynthesis pathway in the regulation of glucose transport. Overexpression of enzymes involved in this pathway have led to high levels of glucose and insulin resistance in animals given huge doses of intravenous glucosamine (100–200 times higher than oral therapeutic doses in humans).<sup>2</sup> Studies have specifically investigated the effects of intravenous glucosamine infusion in healthy humans, and it did not show any effect on insulin sensitivity or plasma glucose.

A Cochrane systematic review of 20 randomized controlled trials (RCTs) including 2570 patients in order to evaluate the effectiveness and toxicity of glucosamine in osteoarthritis found that glucosamine was as safe as placebo in terms of adverse reactions. However, they did not comment specifically on diabetic patients or hyperglycemia per se.<sup>3</sup>

An RCT published in 2004 tested whether glucose intolerance occurs when healthy adults consume normal, recommended dosages of glucosamine sulfate. Nineteen healthy adults were randomized to receive either 1500 mg of glucosamine sulfate or placebo orally each day for 12 weeks. Three-hour oral glucose tolerance tests were performed using 75 g of dextrose. These occurred before the study, at 6 weeks, and at 12 weeks. There were no significant differences between fasting levels of serum insulin or blood glucose.<sup>4</sup> Glucosamine sulfate supplementation did not alter serum insulin or plasma glucose during the tests. Limitations to the study include the small number of subjects, the short duration period, and the fact that the tests were performed before the patient's daily glucosamine dosing.

A recent study examined insulin and glucose levels with and without the simultaneous ingestion of 1500 mg of glucosamine. Sixteen fasting volunteers with osteoarthritis but without known diabetes or glucose intolerance received 7 g of glu-

cose with or without ingestion of 1500 mg glucosamine sulfate. The authors unexpectedly uncovered undiagnosed diabetes or impaired glucose tolerance in 3 subjects. These 3 subjects showed a statistically significant ( $P=.04$ ) 31% increase in the area under the curve of glucose levels following the test. There was no effect of glucosamine sulfate ingestion on patients with normal baseline glucose testing or on insulin levels. Their results might be important since they are the first to suggest that glucosamine ingestion may affect glucose levels in individuals who have untreated diabetes or glucose intolerance.<sup>5</sup>

One double-blinded RCT evaluated whether oral glucosamine supplementation altered glycosylated hemoglobin (HbA<sub>1c</sub>) concentrations for patients with well-controlled diabetes mellitus. Thirty-eight patients were randomized to receive either treatment with glucosamine/chondroitin at the recommended doses or placebo. After 3 months of treatment HbA<sub>1c</sub> levels did not change and were not significantly different between groups ( $P=.2$ ).<sup>6</sup>

Another study addressed whether glucosamine taken at recommended doses for the treatment of osteoarthritis had any detrimental effect on glucose metabolism. Fourteen patients participated and had a baseline 4-hour meal tolerance test and a frequently sampled intravenous glucose tolerance test, before and after 4 weeks of glucosamine sulfate treatment (500 mg orally 3 times daily). After 4 weeks they found no change in fasting plasma glucose, insulin, glucose tolerance, or difference in insulin sensitivity in the group of subjects.<sup>7</sup> Again, the study was limited by a small subject number and short duration of study.

**Recommendations from others**

The *PDR for Nonprescription Drugs and Dietary Supplements* states that “glucosamine is likely safe for patients with diabetes that is well controlled with diet only or with one or two oral antidiabetic agents (HbA<sub>1c</sub> less than 6.5%). For

patients with higher HbA<sub>1c</sub> concentrations or for those requiring insulin, closely monitor blood glucose concentrations.”<sup>8</sup>

The American Pain Society encourages adults with osteoarthritis to take 1500 mg of glucosamine daily as a dietary supplement but does not specifically recommend it as pharmacologic management for pain.<sup>9</sup> The American College of Rheumatology Subcommittee on Osteoarthritis has no recommendations regarding the use of glucosamine or chondroitin in the treatment of knee osteoarthritis.<sup>10</sup>

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