Glucosamine, Chondroitin Didn't Ease Joint Pain

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FROM THE BRITISH MEDICAL JOURNAL

Neither glucosamine nor chondroitin, alone or combined, reduced joint pain or preserved joint space, according to Swiss researchers, who conclude that these supplements should not be prescribed, and if they are, health insurance should not cover them.

Meanwhile, despite a growing body of recent evidence showing the popular supplements to be ineffective, global sales of glucosamine and chondroitin have more than doubled since 2003. As of 2008, the sales of these supplements approached $2 billion and are projected to reach $2.3 billion in 2013, according to the same research team, which published its findings from a meta-analysis of data from 10 randomized, controlled trials.

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The paradox of a market for a medication growing as its evidence base shrinks is probably merely the result of a predictable delay between evidence and adoption, said Dr. Peter Jüni, an epidemiologist at the University of Bern (Switzerland), lead author of the study.

High-quality evidence from large randomized controlled trials is relatively recent in the field of osteoarthritis, Dr. Jüni said in an interview, Sept. 17. "Only in the last 5-10 years has it become established in this field to do large-scale clinical trials," he said. Of the 10 published randomized placebo-controlled trials Dr. Jüni and colleagues identified for their analysis, one was published in 1994 and the rest in the past decade, with the most recent in 2008.

"At the end of the 1990s and beginning of the 2000s, there were moderately small studies that actually made it into meta-analysis and into treatment guidelines" showing favorable results from glucosamine and chondroitin," Dr. Jüni said. "Physicians were very reluctant to accept these then." Eventually, of course, they did, and now "it will take time for the bad news to sink in, just as it took time for the good news in the 1990s." Currently, Dr. Jüni noted, two more large nonindustry trials of glucosamine and chondroitin are underway. These "could put the nail in the coffin – or, you never know, could reopen the book."

For their research, Dr. Jüni and colleagues analyzed results from randomized, placebo-controlled trials – seven of them industry-sponsored – enrolling 200 or more patients with knee or hip osteoarthritis (3,803 patients total). Using complex statistical modeling that allowed for comparisons at varied time points, the team assessed changes in levels of perceived pain after patients took glucosamine, chondroitin, or placebo daily for between 1 and 36 months. Six of the trials also measured joint narrowing (BMJ 2010;341:c4675[doi:10.1136/bmj.c4675]).

The 10 trials differed significantly in design. The majority enrolled patients with osteoarthritis of the knee only, though one enrolled patients with osteoarthritis of the hip or knee, and another included just patients with osteoarthritis of the hip. Supplements used included glucosamine sulfate, glucosamine hydrochloride, chondroitin sulfate, and combinations of these. All the

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glucosamine supplements were tested at 1,500 mg daily, while the chondroitin supplements varied between 800 and 1,200 mg daily.

Some of the trials took place in the United States, where supplements are not standardized for quality, and some in Europe, where they are. In eight, the supplements were evaluated to ensure correct concentrations of glucosamine or chondroitin, and in two the quality of the supplements was unclear. Patients ranged in age from 58 to 66 years, and the median percentage of women participants was 68%.

On a 10-cm visual analogue scale, Dr. Jüni and colleagues found, the overall difference in pain intensity compared with placebo was –0.4 cm (95% confidence interval, –0.7 to –0.1 cm) for glucosamine, –0.3 cm (–0.7 to 0.0 cm) for chondroitin, and –0.5 cm (–0.9 to 0.0 cm) for the combination. "For none of the estimates did the 95% credible intervals cross the boundary of the minimal clinically important difference," the investigators wrote. "The differences in changes in minimal width of joint space were all minute, with 95% credible intervals overlapping zero."

The seven industry-sponsored trials were more likely to detect an effect, however limited, than the non-industry trials ($P = .02$ for interaction). In industry independent trials, estimated treatment effects "were minute to zero and by no means clinically relevant," Dr. Jüni and colleagues wrote in their analysis.

A possible reason that glucosamine and chondroitin are perceived widely as effective, Dr. Jüni said, is because osteoarthritic pain tends to fluctuate naturally. If people take a supplement when their symptoms are worse, "it leads you to perceive that it works perfectly" as they gradually subside, and the theoretical mechanism of the supplement is biologically plausible. In the end, he said, it may come down to need – as much as 30% of the adult population suffers joint pain, he said. Glucosamine and chondroitin are demonstrably safe, and there are few truly safe long-term treatments for joint pain.

The study was funded by grants from the Swiss National Science Foundation's National Research Program. Neither Dr. Jüni nor any of his colleagues declared conflicts of interest. ■