

Correspondence

Use of Glucosamine and Chondroitin Sulfate in the Management of Osteoarthritis

To the Editor: In their article in the March/April 2001 issue, Brief et al¹ provided a concise description of much of the basic and clinical science data regarding the use of glucosamine and chondroitin sulfate in the management of osteoarthritis, and concluded that these supplements should not be used in clinical practice. While we support their conclusion regarding chondroitin sulfate, we believe that currently available data support the use of glucosamine sulfate as part of a comprehensive management program (including components such as exercise, weight loss, analgesics or nonsteroidal anti-inflammatory drugs, and corticosteroid or hyaluronic acid injections) for patients with osteoarthritis of the knee.

Basic science information supporting the clinical use of glucosamine sulfate can be found in articles by Noyszewski et al² and Gouze et al.³ In intact bovine articular cartilage implants, Noyszewski and co-workers demonstrated the uptake and metabolism of glucosamine by explants, as well as its incorporation into cartilage proteoglycan. This observation supports the hypothesis that glucosamine may promote the synthesis of articular cartilage.

In a study involving rat articular cartilage, Gouze et al³ elucidated the ability of glucosamine to inhibit interleukin-1 β (IL-1 β). A cytokine released by synovial cells and macrophages, IL-1 β is responsible for inhibiting biosynthesis of the

main matrix components of cartilage by repressing β -1,3-glucuronosyl-transferase I, an enzyme involved in the priming of glycosaminoglycans. The authors concluded that the ability of glucosamine to inhibit the destructive cascade in articular cartilage initiated by IL-1 β signaling suggests a beneficial effect of glucosamine on the maintenance of articular cartilage in osteoarthritis.

These basic science data take on clinical relevance with the findings from a randomized, double-blind, placebo-controlled trial by Reginster et al.⁴ In that study, 212 patients with mild to moderate osteoarthritis of the knee were randomly assigned to receive either 1,500 mg of oral glucosamine sulfate or placebo once daily for 3 years. At the completion of the study period, the patients who had received glucosamine sulfate were found to have less radiographic evidence of joint-space narrowing and more improvement of symptoms as assessed by WOMAC scores when compared with the patients who received placebo ($P = 0.033$ and $P = 0.016$, respectively). It is notable that similar numbers of patients in the treatment and placebo groups (21 vs 18) withdrew from the study because of adverse effects (e.g., abdominal pain, headache).

In a quality assessment and meta-analysis of studies examining the use of glucosamine and chondroitin for the treatment of osteoarthritis, McAlindon et al⁵ found that although some methodologic problems in selected trials may have led to exaggeration of effect, the evidence of efficacy for glucosamine and chondroitin was clear enough to suggest probable utility in clinical practice.

Where does this leave us as clinicians caring for patients with osteoarthritis of the knee? Although not curative, glucosamine sulfate clearly has the potential to contribute to the relief of pain and the improvement of function with a low likelihood of side effects. Whether or not glucosamine sulfate may also exert a chondroprotective effect is currently incompletely answered. It is to be hoped that this question, as well as the role of chondroitin sulfate, will be clarified by the valuable information expected to be made available at the conclusion of the ongoing National Institutes of Health trials in 2004. In our opinion, the preponderance of scientific and clinical evidence supports the inclusion of glucosamine sulfate, in a dose of 1,500 mg daily, as a component of a comprehensive medical management program for osteoarthritis of the knee, such as that devised by the American College of Rheumatology.⁶

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The Authors Reply: We thank Drs. Arnold and Arnold for their interest in our article. The purpose of

our article was to provide a synopsis of the basic and clinical science data in the literature regarding the use of glucosamine and chondroitin sulfate in the management of osteoarthritis. This endeavor was motivated by reports and accompanying publicity in the popular media pertaining to the use of these drugs as potential chondroprotective agents in repairing articular cartilage and decelerating the degenerative process.

While we agree with Drs. Arnold and Arnold that glucosamine sulfate "has the potential to contribute to the relief of pain and the improvement of function with a low likelihood of side effects," we feel that many unanswered questions remain regarding their long-term effects, the most effective dosage and route of administration, and product purity. At the time of publication, the lack of substantial and conclusive evidence underscored our inability to reach a definitive conclusion regarding their role in

the treatment of arthritis and, we believe, underlies the refusal of the Arthritis Foundation to support their use. As our goal was to summarize the existing documented studies of the use of glucosamine and chondroitin sulfate, we did not venture beyond an objective survey of the data.

Since our publication, further efforts to elucidate the role of glucosamine and chondroitin sulfate have been initiated. We, as well as the rest of the orthopaedic community, eagerly await the results of clinical trials involving large sample sizes and long-term follow-up. In our opinion, the paucity of concrete data at present continues to preclude a ringing endorsement of these agents.

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