Short Report: Ibuprofen versus glucosamine sulfate

Treating osteoarthritis pain

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Glucosamine sulfate has been used orally in eight randomized, double-blind trials in humans. Most have shown glucosamine to act as an effective analgesic for osteoarthritis pain, and one found substantial joint space narrowing in the placebo group but not in the glucosamine group.[1]

Despite these trials, use of glucosamine is still controversial; as a meta-analysis of these trials in 2000 concluded, "Trials of glucosamine … demonstrate large to moderate effects, but quality issues and likely publication bias suggest these effects are exaggerated."[2] In 2002, after this meta-analysis was published, a good-quality, 6-month randomized, double-blind trial found glucosamine to be of no benefit.[3] We aimed to help resolve the ongoing controversy by further evaluating the efficacy and side effect profile of glucosamine sulfate in a 12-week double-blind pilot study.

Glucosamine sulfate and ibuprofen were packaged in identical green capsules. The London Health Sciences Centre Pharmacy prepared the capsules and randomly assigned each 12-week supply of capsules a number between 1 and 40. As patients were enrolled in the study, the labeled bottles were given out sequentially. At completion of the trial, the sealed envelopes containing the code were opened.

Patients were eligible for the pilot study if they were 50 years or older; were currently being treated with nonsteroidal anti-inflammatory drugs or acetaminophen for osteoarthritis pain; and previously had been diagnosed with osteoarthritis in any joint (with the exception of osteoarthritis solely in the spine) by their primary care physicians using either x-ray examinations or clinical criteria. Exclusion criteria included previous gastrointestinal bleeding or known gastrointestinal ulcer, any other rheumatic disease, intra-articular injections, known allergy to nonsteroidal anti-inflammatory drugs or glucosamine sulfate; current participation in another study evaluating osteoarthritis treatments; and regularly taking glucosamine sulfate currently or for a period of 6 weeks or longer within the past 3 months. Forty patients were enrolled.

At the initial visit, eligible patients filled out a baseline visual analogue scale of pain and a side effect checklist. Each patient agreed to stop any current analgesic for osteoarthritis. They were randomly assigned in a double-blind fashion to receive either the study drug (glucosamine sulfate, 500 mg three times daily) or the control treatment (ibuprofen, 400 mg three times daily). Bottles of acetaminophen (500 mg) were provided to each participant with instructions to use as necessary as an adjuvant medication for relief of arthritis pain.

Patients were then seen monthly for the next 3 months. In addition to pill counts of study drug and acetaminophen, patients also completed the side effect checklist and a visual analogue scale of arthritis pain intensity and effect. At the beginning and completion of the study, patients' blood was tested for creatinine, serum urea nitrogen, electrolytes, aspartate aminotransferase, γ-glutamyl transpeptidase, and bilirubin levels.

Characteristics of patients who completed the study are shown in **Table 1**. There was no significant difference in characteristics, acetaminophen use, compliance, or side effects between the two groups.

Dr Nowlan *was a resident in family medicine at The University of Western Ontario at the time this study was initiated.* **Dr Wetmore** *is an Associate Professor of Family Medicine at The University of Western Ontario. He currently practises at the Victoria Family Medical Centre in London, Ont.*

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Table 1. Patient groups

PATIENT CHARACTERISTICS	GLUCOSAMINE SULFATE (N = 20)	IBUPROFEN (N = 20)	*P* VALUE
Female: no. (%)	16 (80)	14 (70)	.716
Age: mean (SD)	64.9 (8.01)	65.4 (9.86)	.848
Joints involved			1.0
• Knees: no. (%)	12 (60)	11 (55)	
• Other: no. (%)	8 (40)	9 (45)	
Previously used class of analgesic (alone or in combination)			.245
• Acetaminophen: no. (%)	7 (35)	4 (20)	
• Occasional or weak NSAID: no. (%)	6 (30)	4 (20)	
• Strong NSAID*: no. (%)	6 (30)	7 (35)	
• Codeine + acetaminophen or NSAID: no. (%)	1 (5)	5 (25)	
Baseline pain intensity: VAS score (SD)	5.18 (2.22)	4.97 (2.57)	.804
Baseline pain effect: VAS score (SD)	4.92 (2.50)	5.69 (3.18)	.437

*NSAID—nonsteroidal anti-inflammatory drug, SD—standard deviation, VAS—visual analogue scale (ranging from 1 to 10). *Naproxen (Naprosen) or diclofenac sodium and misoprostol (Arthrotec 50/75).*

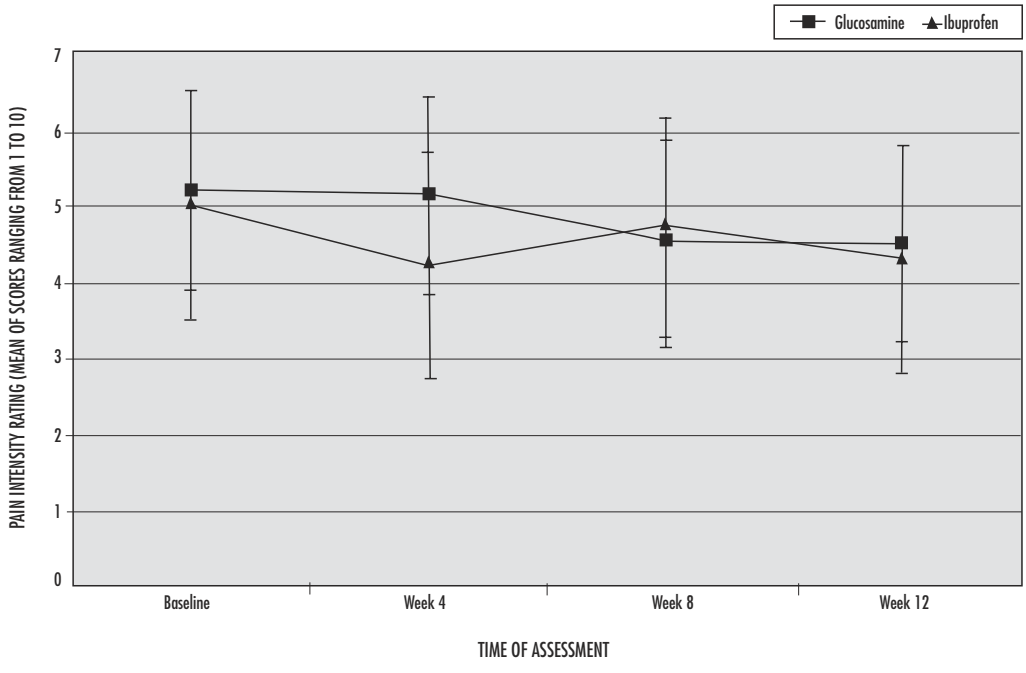
Ten of the 40 patients withdrew before completion. Three patients withdrew from the glucosamine group, stating inadequate pain relief (one patient), dyspepsia (one patient), and palpitations (one patient) as reasons. Seven patients withdrew from the ibuprofen group, stating inadequate pain relief (one patient), on the advice of an internist secondary to rising creatinine levels (one patient), tinnitus (one patient), vertigo (one patient), and dyspepsia (three patients) as reasons.

Five patients developed abnormal laboratory test results during the study. In both the glucosamine and ibuprofen group, mild rises in γ-glutamyl transpeptidase and sodium were not correlated with any clinical event. Both ibuprofen and glucosamine decreased pain compared with baseline, but results did not reach statistical significance (**Figure 1**).

Unfortunately, our pilot study did not achieve enough power to prove that there was no difference between groups (ie, if we had a larger patient population, we might have found a statistically significant difference). Therefore, our pilot study was limited by its small size.

We were unable to reproduce the findings of Vaz, who performed a study similar to ours in 1982 with 40 patients.[4] One noteworthy point is that he did not relate whether his patients had any prior analgesic

Figure 1. Relief of pain with glucosamine and ibuprofen



use, whereas our study was designed to recruit only patients whose pain was such that they were compelled to take regular analgesic medication. If indeed the patient population of Vaz had no prior analgesic use, one might surmise that, as a group, they experienced a milder degree of pain at baseline than our study population. Thus in Vaz's study[4] the relief afforded by the study medication would appear more dramatic and reach statistical significance. The 2002 *Rheumatology* study[3] also hypothesized that "The discrepancy between our results and those of the trial by Reginster *et al.* might suggest that glucosamine has an analgesic effect in mild to moderate [osteoarthritis] but not at the more severe end of the spectrum."

This trial had insufficient power to show glucosamine to be more efficacious for pain relief than ibuprofen. Research to date has found no serious side effects and suggests glucosamine is effective for mild osteoarthritis.

Editor's key point

- This small randomized controlled trial compared ibuprofen with glucosamine for management of osteoarthritis. While both decreased the level of pain, neither was clearly superior.

Point de repère du rédacteur

- Dans ce petit essai randomisé, on a comparé la glucosamine et l'ibuprofène comme traitements, de l'ostéoarthrite. Ces deux substances ont procuré un soulagement, mais aucune ne s'est montrée nettement supérieure.

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Contributors

Dr Nowlan *was responsible for conception, design, funding, and draft versions of the study.* **Dr Wetmore** *supervised designing, funding, and revising the study.*

Competing interests

Physicians' Services Incorporated Foundation provided a $5000 grant; the College of Family Physicians of Canada provided a Janus Research and Education Scholarship worth $1500; Swiss Herbal Remedies supplied the glucosamine sulfate free of charge; McNeil Consumer Products supplied the acetaminophen free of charge; AMCO Pharmaceuticals encapsulated the ibuprofen and glucosamine free of charge.

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