

Results of GAIT Study Fail to Demonstrate Clinical Efficacy of Glucosamine or Chondroitin Sulfate in Symptomatic Knee Osteoarthritis

Summarized by Jon Giles, MD

The primary outcome results of the Glucosamine/chondroitin Arthritis Intervention Trial (GAIT) have been published (*N Engl J Med* 2006; 354:795). Prior to its publication, the results of the study were presented at the recent 2005 American College of Rheumatology Annual Scientific Meeting and summarized on this website (Go to <http://www.hopkins-arthritis.org/edu/acr2005/oa-treatments.html#622> for a summary of the results).

In support of and in addition to the previous editorial comments included with the summary, some key points to take away from this study are:

- This was a carefully designed and executed study.
- Only women ≥ 40 years of age with significant knee pain and radiographic evidence of tibiofemoral osteoarthritis were studied.
- The primary outcome, that 24 weeks of treatment with either 1500 mg of daily glucosamine hydrochloride, 1200 mg of daily chondroitin sulfate, or both would be associated with a significantly greater proportion of patients with at least a 20% reduction in knee pain than those treated with placebo, was not achieved.
- The study design included a positive control, 200 mg of daily celecoxib, which was significantly associated with a greater proportion of subjects with a 20% reduction in knee pain than those treated with placebo.
- The response to placebo was extraordinarily high, with 61.7% of subjects who received only placebo reporting a 20% or greater improvement in knee pain and almost 45% of subjects who received only placebo reporting a 50% or greater reduction in knee pain at 24 weeks
- A post-hoc subgroup analysis suggested that the combination of glucosamine hydrochloride and chondroitin sulfate may be more beneficial than placebo in the subset of subjects with a greater severity of reported knee pain. In this subset however, the positive control celecoxib was not effective raising questions as to the validity of the findings
- The study was neither designed nor powered to concentrate on this group, so the finding is not definitive.
- It is possible that these results would not be the same in men or in patients with osteoarthritis at other sites.
- It is possible that these results would not be the same if other formulations of glucosamine (e.g. glucosamine sulfate) were to be used.
- The formulations of glucosamine and chondroitin sulfate used in this study were of pharmaceutical grade and may not be available to consumers.
- No untoward adverse events were reported in this study related to the use of supplements.
- The effect of these supplements on radiographic outcomes in this study have yet to be presented or published.

On balance, even though this study still leaves some issues up in the air, the overall efficacy of either/both of these supplements is underwhelming. Moreover, any improvement achieved in reducing symptoms is very likely to be a placebo effect rather than any physiologic effect of the supplement(s) themselves.