

Glucosamine Sulfate Prevents Total Joint Replacement In The Long-Term Follow-Up Of Knee Osteoarthritis Patients

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Purpose: Two recent randomised, placebo-controlled, double-blind, 3-year clinical trials in knee osteoarthritis (OA) indicated that glucosamine sulfate prevents radiographic joint space narrowing (JSN) and relieves symptoms (Reginster et al, *Lancet* 2001;357:251-6; Pavelka et al, *Arch Intern Med* 2002;162:2113-23). The aim of this study was to assess the incidence of joint replacement after a further long-term follow-up.

Methods: Systematic contact was attempted with all knee OA patients from one of the previous studies (Pavelka et al 2002), who had been in the trial for at least 12 months and were then followed by standard care after discontinuation of the study medication. 136 patients (67 formerly on placebo and 69 on glucosamine sulfate), i.e. 78.6% of the original cohort with these characteristics, could be retrieved. They were administered a standardised interview for the occurrence of total knee and/or hip replacement, checked against patient medical records. Incidence of surgery was compared by the chi-square test with calculation of Relative Risk (RR). A subset of 101 patients (47 and 54 in the two former groups, respectively) accepted to perform also a standing antero-posterior knee radiograph according to the same standardised technique used in the trial, for measurement of medial tibiofemoral minimum JSN with a magnifying glass by two readers, randomising the sequence of trial enrolment, trial last and follow-up radiographs; comparisons were performed by ANOVA. All assessments were in double-blind.

Results: Median duration of follow-up after the trial was around further 5 years (64 months, range 40-90 months) without differences in the former two groups, whose pre-trial characteristics were also comparable. A total of 14 patients out of the 136 had undergone knee replacement: 11/67 previously on placebo (16.4%) and 3/69 on glucosamine sulfate (4.3%), with a 73% decrease in risk with the latter (RR=0.27, 95% CI 0.08 to 0.91, p=0.021). When hip replacements were also considered (4 additional patients), RR was still decreased after glucosamine sulfate: 0.37 (0.14 to 0.99), p=0.036.

The subset of glucosamine sulfate patients with x-rays at follow-up had significantly gained joint space during the trial [0.17 mm (0.03 to 0.31) (mean and 95% CI)] vs. a slight loss with placebo [-0.07 (-0.19 to 0.07)] (p=0.017), and still tended to have a lower JSN on the overall 8-year observation period: [-0.47 mm (-0.66 to -0.28) vs. -0.62 mm (-0.82 to -0.41) with placebo (NS: p=0.30)], despite a non-significant trend for a greater loss during the follow-up after drug withdrawal (p=0.53).

Conclusions: Treatment for up to 3 years with glucosamine sulfate in knee OA prevented total joint replacement during a further follow-up of 5 years after drug withdrawal, probably because of the effect on joint structure achieved during treatment.