Research Abstracts

Glucosamine HCl

Inhibition of articular cartilage degradation by glucosamine-HCl and chondroitin sulphate

Glucosamine and chondroitin sulphate in many animal and human trials has improved joint health. In vitro studies are beginning to clarify their mode of action. The objective of this research was to: 1) determine at what concentrations glucosamine-HCl (GLN) and/or chondroitin sulphate (CS) would inhibit the cytokine-induced catabolic response in equine articular cartilage explants and 2) to determine if a combination of the 2 was more effective at inhibiting the catabolic response than the individual compounds. Articular cartilage was obtained from carpal joints of horses (age 1-4 years). Cartilage discs (3.5 mm) were biopsied and cultured. Explants were incubated with lipopolysaccharide (LPS) in the presence of varying concentrations of GLN, CS, or both. Control treatments included explants with no LPS and LPS without GLN or CS. Media were analysed for nitric oxide (NO), prostaglandin E2 (PGE2) and keratan sulphate. Cartilage was extracted for analysis of metalloproteinases (MMP). Four experiments were conducted. In all experiments, GLN at concentrations as low as 1 mg/ml decreased NO production relative to LPS stimulated cartilage without GLN over the 4 day period. In general, CS at either 0.25 or 0.5 mg/ml did not inhibit NO production. The addition of CS to GLN containing media did not further inhibit NO production. GLN at concentrations as low as 0.5 mg/ml decreased PGE2 production, whereas CS did not effect on PGE2. The combination of GLN/CS decreased MMP-9 gelatinolytic activity but had no effect on MMP-2 activity. The combination in 2 experiments tended to decrease MMP-13 protein concentrations and decreased keratan sulphate levels in media. Overall, the combination of GLN (1 mg/ml) and CS (0.25 mg/ml) inhibited the synthesis of several mediators of cartilage degradation. These results further support the effort to understand the role of GLN and CS in preserving articular cartilage in athletic horses. Orth MW, Peters TL, Hawkins JN. *Equine Vet J Suppl.* 2002 Sep;(34):224-9.

Efficacy of a combination of FCHG49 glucosamine hydrochloride, TRH122 low molecular weight sodium chondroitin sulfate and manganese ascorbate in the management of knee osteoarthritis

OBJECTIVES: The objective of this study was to evaluate the oral combination of glucosamine HCl, sodium chondroitin sulfate and manganese ascorbate for the treatment of osteoarthritis (OA) of the knee. DESIGN: A randomized placebo-controlled study design was implemented. We recruited 93 patients with OA of the knee from a single center. The intervention group received 1000 mg FCHG49 glucosamine HCl, 800 mg TRH122 low molecular weight sodium chondroitin sulfate and 152 mg manganese ascorbate twice daily (Cosamin DS). Patients were evaluated initially and then every 2 months for 6 months. The primary outcome was the Lesquene Index of severity of osteoarthritis of the knee (ISK). RESULTS: Patients with radiographically mild or moderate OA (N=72) in the intervention group showed significant improvement in the ISK at 4 and 6 months (P=0.003 and P=0.04, respectively). The response rate to the medication was 52% vs a 28% response rate to placebo. Patients with radiographically severe osteoarthritis (N=21) did not show significant improvements in the ISK. There was a 17% incidence of adverse events in the intervention group and 19% in the placebo group. CONCLUSIONS: The studied combination of glucosamine HCl, sodium chondroitin sulfate and manganese ascorbate was found to be effective for the treatment of radiographically mild to moderate OA of the knee as measured by the ISK. This is the first U.S. study of these agents. Copyright 2000 OsteoArthritis Research Society International. Das A Jr, Hammad TA. *Osteoarthritis Cartilage*. 2000 Sep;8(5):343-50.

Glucosamine HCl reduces equine articular cartilage degradation in explant culture

Objective To determine whether glucosamine inhibits experimentally induced degradation of equine articular cartilage explants.Methods Articular cartilage was obtained from the antebrachio-carpal and middle joints of horses (2-8 years old) killed for reasons unrelated to lameness. Cartilage discs were harvested from the weight-bearing region of the articular surface and cultured. Media were exchanged daily and the recovered media stored at 4 degrees C. Explants were maintained in basal media 2 days prior to the start of four treatment days. On days 1-4 lipopolysaccharide (LPS, 10 microg/ml) or recombinant human interleukin-1 (rhIL-1, 50 ng/ml) were added to induce cartilage degradation. To test the potential protective effects of glucosamine, the compound was added in three concentrations (0.25, 2.5, or 25 mg/ml) and treatments were performed in triplicate. Controls included wells without LPS, rhIL-1beta, or glucosamine. Nitric oxide, proteoglycan and matrix metalloproteinases (MMP) released into conditioned media and tissue proteoglycan synthesis were measured as indicators of cartilage metabolism.Results Maximal nitric oxide production, proteoglycan release, and MMP activity were detected 1 day after the addition of LPS or rhIL-1beta to the media. The addition of 25 mg/ml of glucosamine prevented the increase in nitric oxide production, proteoglycan release and MMP activity induced by LPS or rhIL-1. Conclusions These data indicate that glucosamine can prevent experimentally induced cartilage degradation in vitro. Fenton JI, Chlebek-Brown KA, Peters TL, Caron JP, Orth MW. *Osteoarthritis Cartilage*. 2000 Jul;8(4):258-65.

Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back: a randomized, double-blind, placebo-controlled pilot study

OBJECTIVE: A 16-week randomized, double-blind, placebo-controlled crossover trial of a combination of glucosamine HCl (1,500 mg/day), chondroitin sulfate (1,200 mg/day), and manganese ascorbate (228 mg/day) in degenerative joint disease (DJD) of the knee or low back was conducted. METHODS: Thirty-four males from the U.S. Navy diving and special warfare community with chronic pain and radiographic DJD of the knee or low back were randomized. A summary disease score incorporated results of pain and functional questionnaires, physical examination scores, and running times. Changes were presented as a percentage of the patient's average score. RESULTS: Knee osteoarthritis symptoms were relieved as demonstrated by the summary disease score (-16.3%; p = 0.05), patient assessment of treatment effect (p = 0.02), visual analog scale for pain recorded at clinic visits (-26.6%; p = 0.05) and in a diary (-28.6%; p = 0.02), and physical examination score (-43.3%; p = 0.01). Running times did not change. The study neither demonstrated, nor excluded, a benefit for spinal DJD. Side effect frequency was similar to that at baseline. There were no hematologic effects. CONCLUSIONS: The combination therapy relieves symptoms of knee osteoarthritis. A larger data set is needed to determine the value of this therapy for spinal DJD. Short-term combination therapy appears safe in this setting. Leffler CT, Philippi AF, Leffler SG, Mosure JC, Kim PD. *Mil Med.* 1999 Feb;164(2):85-91.