Research Abstracts

Glucosamine Sulfate

Pharmacokinetics of glucosamine in man

The pharmacokinetics of glucosamine sulfate (CAS 29031-19-4) was investigated in 6 healthy male volunteers (2 per administration route) using 14C uniformly labelled glucosamine sulfate and administering it in single dose by intravenous (i.v.), intramuscular (i.m.) or oral route. The results show that after i.v. administration the radioactivity due to glucosamine appears in plasma and is rapidly eliminated, with an initial t1/2 of 0.28 h. 1-2 h after administration the radioactivity due to glucosamine disappears almost completely and is replaced by a radioactivity originating from plasma proteins, in which glucosamine or its metabolites are incorporated. This radioactivity reaches a peak after 8-10 h and then declines with a t1/2 of 70 h. About 28% of the administered radioactivity is recovered in the urine of the 120 h following the administration and less than 1% is recovered in the feces. After i.m. administration similar pharmacokinetic patterns are observed. After oral administration a proportion close to 90% of glucosamine sulfate is absorbed. Free glucosamine is not detectable in plasma. The radioactivity incorporated in the plasma proteins follows pharmacokinetic patterns which are similar to those after i.v. or i.m. administration, but its concentration in plasma is about 5 times smaller than that after parenteral administration. The AUC after oral administration is 26% of that after i.v., or i.m. administration. The smaller plasma levels of radioactivity after oral administration are probably due to a first pass effect in the liver which metabolizes a notable proportion of glucosamine into smaller molecules and ultimately to CO2, water and urea. Setnikar I, Palumbo R, Canali S, Zanolo G. *Arzneimittelforschung* 1993 Oct;43(10):1109-1113.

Therapeutic activity of oral glucosamine sulfate in osteoarthrosis: a placebo-controlled double-blind investigation

Eighty inpatients with established osteosrthrosis received either 1.5gm of glucosamine sulfate or placebo daily, in three divided daily doses, for 30 days. Articular pain, joint tenderness and swelling, and restriction of active and passive movements were scored at one week intervals, as were possible side reactions. Hematologic analysis, urine analysis, and occult blood in feces were recorded before and after treatment. Samples of articular cartilage from two patients of each group and from one healthy subject were submitted to electron microscopy after the end of treatment. All symptoms decreased in both groups. The patients treated with glucosamine sulfate experienced a reduction in overall symptoms that was almost twice as large (73% vs. 41%) and twice as fast (time to reduce symptoms by 50%: 20 days vs. 36 days) as those who had placebo. The improvement of autonomous mobility was relatively less, compared to improvement in the placebo; with glucosamine sulfate, on the contrary, the improvement was great and as fast as that of the other symptoms. Thus a direct action of glucosamine sulfate on the cartilage is hypothesized. Drovanti A,Bignamini AA, Rovati AL. *Clin Ther* 1980: 3(4):260-72.

Double-blind clinical evaluation of oral glucosamine sulphate in the basic treatment of osteoarthrosis

The efficacy and tolerance of oral glucosamine sulphate were tested against placebo in aprospective double-blind trial in 20 out-patients with established osteoarthrosis. Two capsules of either glucosaminene sulphate (250 mg) or placebo were administered 3-times daily over a period of 6 to 8 weeks. Articular pain, joint tenderness and restricted movement were semi-quantitatively scored 1 to 4 every 3 days, and individually averaged over the treatment period (overall composite score). Possible side-reactions were similarly scored upon positive questioning of the patients. Haematology, erythrocyte sedimentation rate, urine analysis and X-rays were recorded before and after treatment. Significant alleviation of symptoms was associated with the use of the active drug at the prescribed dose. Similarly, patients given glucosamine sulphate experienced earlier alleviation of symptoms compared with those who had placebo. The use of glucosamine sulphate also resulted in a significantly larger proportion of patients who experienced lessening or disappearance of symptoms within the trial period. No adverse reactions were reported by the patients treated with glucosamine, and no variation in laboratory tests was recorded. Pujalte JM, Llavore EP, Ylescupidez FR. *Curr Med Res Opin* 1980;7(2):110-114.

Glucosamine sulphate: a controlled clinical investigation in arthrosis

Efficacy and tolerance of a new preparation of pure glucosamine sulphate, in injectable and oral form, were investigated in 30 patients with osteoarthrosis. Two groups of in-patients with chronic degenerative articular disorders received daily for 7 days either 400 mg glucosamine sulphate or a piperazine/chlorbutanol combination by intravenous or intramuscular injection. During the 2 following weeks, the patients receiving glucosamine had oral glucosamine capsules (6 x 250 mg daily); the other group had placebo. Efficacy was tested by semi-quantitative scoring of pain at rest and during active and passive movements, as well as limitation of articular function, before and after 7 and 21 days of treatment. Patients were positively questioned daily for possible intolerance symptoms. Haematology, circulatory data and urine analysis were tested before and after treatment. During both initial parenteral treatments, each symptom significantly improved, but to a faster and greater extent in the group treated with glucosamine. During the maintenance period, a further improvement was recorded in the patients treated with glucosamine, whereas in those on placebo the symptom scores increased almost to the pre-treatment level. This was considered the major difference between basic therapy, such as with glucosamine, as purely symptomatic treatment. Clinical and biological tolerance were excellent with both treatments, and no definitely drug-related complaints were recorded. It is suggested that parenteral and/or oral treatment with pure glucosamine sulphate should be considered as basic therapy for the management of primary or secondary degenerative osteoarthrosis disorders. D'Ambrosio E, Casa B, Bompani R, Scali G, Scali M. *Pharmatherapeutica* 1981;2(8):504-508.

Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulphate in the management of osteoarthrosis of the knee in out-patients

A double-blind trial was carried out in 40 out-patients with unilateral osteoarthrosis of the knee to compare the efficacy and tolerance of oral treatment with 1.5 g glucosamine sulphate or 1.2 g ibuprofen daily over a period of 8 weeks. Pain scores decreased faster during the first 2 weeks in the ibuprofen than in the glucosamine treatment group. Although the rate of decrease was slower, the reduction in pain scores was continued throughout the trial period in patients an glucosamine and the difference between the two groups turned significantly in favour of glucosamine at Week 8. No significant differences were observed in swelling or any of the other parameters monitored. Tolerance was satisfactory with both treatments, with only minor complaints being reported by 2 patients on glucosamine compared with 5 patients on ibuprofen. Lopes Vaz A. *Curr Med Res Opin* 1982;8(3):145-149.

Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial

BACKGROUND: Treatment of osteoarthritis is usually limited to short-term symptom control. We assessed the effects of the specific drug glucosamine sulphate on the long-term progression of osteoarthritis joint structure changes and symptoms. METHODS: We did a randomised, double-blind placebo controlled trial, in which 212 patients with knee osteoarthritis were randomly assigned 1500 mg sulphate oral glucosamine or placebo once daily for 3 years. Weightbearing, anteroposterior radiographs of each knee in full extension were taken at enrolment and after 1 and 3 years. Mean joint-space width of the medial compartment of the tibiofemoral joint was assessed by digital image analysis, whereas minimum joint-space width--ie, at the narrowest point--was measured by visual inspection with a magnifying lens. Symptoms were scored by the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index. FINDINGS: The 106 patients on placebo had a progressive joint-space narrowing, with a mean joint-space loss after 3 years of -0.31 mm (95% CI -0.48 to -0.13). There was no significant joint-space loss in the 106 patients on glucosamine sulphate: -0.06 mm (-0.22 to 0.09). Similar results were reported with minimum joint-space narrowing. As assessed by WOMAC scores, symptoms worsened slightly in patients on placebo compared with the improvement observed after treatment with glucosamine sulphate. There were no differences in safety or reasons for early withdrawal between the treatment and placebo groups. INTERPRETATION: The long-term combined structure-modifying and symptom-modifying effects of gluosamine sulphate suggest that it could be a disease modifying agent in osteoarthritis. Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, Giacovelli G, Henrotin Y, Dacre JE, Gossett C. *Lancet* 2001 Jan 27;357(9252):251-6.

The preceding abstracts were obtained from the Medline service maintained by the National Institutes of Health.