AN ORAL PREPARATION CONTAINING HYLAURONIC ACID (ORALVISC®) CAN NORMALIZE THE TURNOVER OF HYALURONIC ACID IN SYNOVIAL FLUID OF OSTEOARTHRITIC KNEE PATIENTS


Purpose: Osteoarthritis (OA) is a degenerative joint disease in which articular cartilage matrix is no longer in homeostatic balance, resulting in a net loss of chondroitin sulfate (CS)-rich glycosaminoglycans (GAGs). The pro-inflammatory environment of synovial fluid has been shown to result in an increase in hyaluronic acid (HA) turnover. Consequently the turnover of CS and HA are considered key parameters to evaluate the degree and evolution of OA. We conducted a double blind randomized clinical trial to determine if there would be changes in turnover of CS and HA in the synovial fluid (SF) of knee OA patients treated with a patented hyaluronic acid formulation for oral use (Oralvisc®) as compared to placebo.

Methods: 51 symptomatic knee OA patients were recruited sequentially at the time of an outpatient visit for OA. Subjects were between the ages of 50-75 years, had knee effusion, and a pain visual analog score (VAS) >50mm. 40 patients completed the study. 21 had been randomly selected to receive 80 mg daily of Oralvisc® and 19 had received placebo. Each month they were evaluated for VAS and WOMAC pain and joint function. A subset of 10 subjects per treatment group began a 2-day long oral administration of heavy water (35 mL 2H2O TID for 2 days) at the conclusion of the treatment phase (Week 12), followed by a synovial fluid aspiration in the affected knee. Synovial fluid lavage samples were analyzed for 2H-labeling of component GAGs by gas chromatography/mass spectrometry (GC/MS) to obtain fractional synthesis rates of HA and CS in SF.

Results: The age, sex, race, BMI, KL scores, as well as VAS pain and WOMAC function were balanced between groups at the beginning of the trial. Treatment with oral HA during 3 months resulted in a significant improvement in VAS pain (p=0.0035), WOMAC pain (p=0.0259) and WOMAC function (p=0.0132) compared to placebo. The stable-isotope mass spectrometry method was successfully implemented for the clinical study of SF GAG kinetics. The rate of HA turnover was 0.78±0.42 /day (i.e., 78% per day) in placebo-treated OA patients (n=10; Fig. 1). With 12 weeks of oral HA treatment, the mean rate of HA turnover declined by 45% to 0.42±0.24 /day (p=0.046). While we have not directly compared the rate of HA turnover in normal vs. osteoarthritic knees, comparison of the current results with data from a previous study in ACL patients suggests that these osteoarthritis patients (0.78 /d) have elevated HA turnover relative to “normal” subjects (0.25 /d), and that oral HA partially normalized the HA turnover rate. CS molecules in the SF were also highly enriched, with the majority of the patients recording the maximum measurable turnover rate for this assay (>1400 /d). Thus, virtually all of the SF-derived CS was recently synthesized, suggesting a defect in the retention of potential repair molecules in osteoarticular cartilage.

Conclusions: This is the first study of its kind to show that the use of an oral HA (Oralvisc®) agent in knee OA patients can lead to a significant impact on HA turnover in synovial fluid. The normalization in HA turnover was paralleled by an overall decrease in pain scores and improvement in joint function. Further studies are needed to investigate its mechanism but this novel form of oral HA may provide a safe alternative treatment to correct the homeostatic imbalances in the progression of OA.