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EXPECTATIONS REGARDING KNEE OSTEOARTHRITIS MANAGEMENT: VIEWS FROM PATIENTS AND PRACTITIONERS. A QUALITATIVE INTERVIEW STUDY

S. Alami[1], I. Boutron[2], D. Desjeux[3], M. Hirschhorn[4], G. Meric[5], **S. Poiraudeau**[6]

[1]Interlis, Paris, France; [2]AP-HP, Université Paris 7, Paris, France; [3]Département d'anthropologie, Université Paris 5, Paris, France; [4]Département de sociologie, Université Paris 5, Paris, France; [5]Pfizer, Paris, France; [6]AP-HP, Université Paris 5, INSERM IFR 25, Paris, France

Purpose: Knee Osteoarthritis (OA) is highly prevalent and affects health-related quality of life and healthcare costs. Our objectives were to identify expectations of patients regarding knee OA management, to reveal potential obstacles for improvements of health care strategies, and to explore care providers' perceived difficulties in treating patients with knee OA.
Methods: A qualitative study based on semi structured interviews was performed with a stratified sample of 81 patients (59 women, 21 using alternative medicine) and 29 practitioners (8 women, 11 general practitioners (GPs), 6 rheumatologists, 4 orthopedic surgeons, 8 (4 GPs) delivering alternative medicine).
Results: Patients did not express problems with the way knee OA is diagnosed but GPs sometimes feel uncomfortable with the diagnosis, begin treatment without announcing OA to patients and consider knee x-rays as the gold standard to confirm knee OA. Some practitioners consider knee OA as a common, ineluctable, age-related disease with limited treatment options. This attitude appears to have a negative impact on patient management: it tends to confine treatments to pain medication, and patients feel that their complaints are not taken seriously enough which leads to less compliance to the treatment. Patients also feel that practitioners often act as technicians paying much attention to the knee but less to the individual, and consider that not enough time is spent for information and counseling. This is the reason most often cited for being suspicious of drugs, having the feeling of medical uncertainty toward OA, and switching to alternative medicine. Practitioners, mainly GPs, felt frustrated about the impact of counseling on weight loss but admitted to feel uncomfortable to tackle the subject and sometimes to avoid it. Regarding pharmacological treatments, patients consider that having to take pills at regular interval is a constraint which weakens compliance. They have ambivalent attitude towards NSAIDs, considering that they are effective on pain but with an overall negative opinion due to adverse effects and fears and beliefs about their harmfulness when taken for long time. GPs expect more formation on the disease and more funds for research.
Conclusions: Our results suggest several potential improvements to maximize patients' management: more attention and time should be devoted to patient/practitioner relationship and environmental factors. Patients' profiles should be more precisely defined regarding coping strategies and treatment preferences to propose more adapted and specific options.

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CLINICAL MEASUREMENTS OF GAG SYNTHESIS IN HUMAN ARTICULAR CARTILAGE *IN VIVO*

K.W. Li[1], E.W. Cheng[1], C.R. Allen[2], M.K. Hellerstein[2], S.M. Turner[1]

[1]KineMed, Inc, Emeryville, CA; [2]UCSF, San Francisco, CA

Purpose: Chondroitin sulfate (CS) and hyaluronic acid (HA) are key components of articular cartilage and their regulation may be important in the treatment of OA. An *in vivo* assay has been developed for animal models in which heavy water (^2H_2O) is incorporated into newly-synthesized GAG. The objective of this study was to adapt this assay for use in people to determine the synthesis rates of CS and HA in human articular cartilage after obtaining either cartilage biopsies or synovial fluid (SF) aspirates.
Methods: Patients scheduled for ACL reconstruction surgery were recruited for this IRB-approved study. Five patients were given 2-3 oral doses of ^2H_2O per day for 15-42 days prior to surgery, resulting in ^2H_2O enrichment in body water of 1.5±0.3%. On the day of surgery, small biopsies of articular cartilage (1-2 mg) were harvested during routine notchplasty. A sample of SF also was obtained from all subjects. Body water enrichment was monitored from saliva samples, obtained weekly during the labeling period. Following surgery, HA and CS were isolated from cartilage and SF samples and analyzed by gas chromatography/mass spectrometry. Specifically, fractional synthesis, or the fraction of HA and CS that was newly-synthesized, was determined from the ^2H-enrichment of N-acetyl glucosamine and N-acetyl galactosamine, respectively. Data are mean±SD.
Results: ^2H-enrichments in CS ranged from 0.3-1.3% and increased 0.04% per day ($p<0.01$, $r^2=1$). These ^2H-enrichments were above the sensitivity limit of GC/MS. Expressed as fractional synthesis, the CS in the articular cartilage was synthesized at a rate of 0.8±0.3% per day (Fig. 1; n=5). This represented an interpatient CV of 40%. For patients from which multiple cartilage specimens were obtained, intra-patient variability was higher, with an average CV of 48% (n=4).
Fractional HA synthesis in the cartilage was 0.4±0.2%, 50% lower than the CS turnover rate (p=0.02; n=5). Inter- and intra-patient variability in HA synthesis was 48% (n=5) and 19% (n=3), respectively.

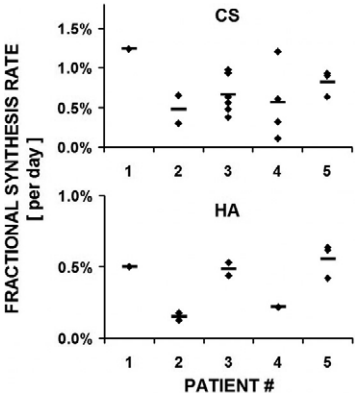

Figure 1. Fractional synthesis rates of CS & HA in individual cartilage biopsies taken from five patients.

The CS from SF had a fractional synthesis rate of 1.9±0.6% (n=5), 2.5X greater than that in the articular cartilage (p=0.03), suggesting that newly-synthesized CS rather than degraded matrix was lost preferentially to the SF. Regression analysis did not indicate a relationship between the CS synthesis measurements in cartilage and SF (n=5, p=0.7, $r^2=0.07$). The HA in SF was nearly completely turned over in this study. Shorter labeling durations would be necessary to measure this parameter. Unlike SF CS, which typically originates from cartilage, the production of SF HA is predominantly mediated by synovium.
Conclusions: We present the first direct *in vivo* measurement of the synthesis rates of CS and HA in "normal" human cartilage, which had half-lives of 92 and 181 days, respectively. These half-lives were much less than those previously shown in *in vitro* systems, which may reflect stimulation from the joint environment induced by traumatic knee injury. This study establishes a physiological baseline for evaluating metabolic alterations that may occur during OA progression and in response to therapeutic intervention.
The majority of CS in SF is bound to aggrecan, indicating that