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EFFECT OF PATIENT EDUCATION AND SUPERVISED EXERCISE IN PATIENTS WITH HIP OSTEOARTHRITIS. A RANDOMIZED CLINICAL TRIAL

L. Fernandes1, K. Storheim1, L. Nordsletten2, M. Risberg1
1NAR, Orthopaedic Ctr., Oslo Univ. Hosp., Ullevaal, Oslo, Norway; 2Orthopaedic Ctr., Oslo Univ. Hosp., Ullevaal, Oslo, Norway

Purpose: The purpose of the study was to evaluate the effect of a supervised exercise program in addition to patient education for patients with hip osteoarthritis.

Methods: One hundred and nine patients were included and received three sessions of patient education. After completing the patient education the 109 patients were randomized into 1) follow the recommendations of self-management given during the patient education (CG), or 2) follow the recommendations and, in addition, a supervised exercise program (EG). The intervention period lasted for 14 weeks. The patients were followed-up at post-intervention (FU0), six months post-intervention (FU6), and one year post-intervention (FU12). The main outcome was the WOMAC VA3.1, and secondary outcomes were the 36-item Short-Form health related quality of life questionnaire (SF-36v2), the modified Physical Activity Scale for the Elderly (PASE) and the self-efficacy for pain. Linear mixed models analyses were used for between group differences over time, and standardized mean difference for the calculation of effect sizes.

Results: WOMAC physical function showed a significant improved score for the EG compared to the CG (p=0.047, CI 0.6-11.0) over the follow-up period. No significant differences between groups over the follow-up period were seen for WOMAC pain or stiffness subscales. Within-group analysis for the EG showed significantly improved WOMAC pain from baseline to FU0 (p=0.025, CI 0.7-9.7), FU6 (p=0.004, CI 2.5-12.5), and FU12 (p=0.021, CI 0.8-10.1). There were no significant changes over time for the CG. The effect sizes for the EG compared to the CG ranged from 0.26-0.35, 0.16-0.46, and 0.48-0.58 for pain, stiffness and physical function, respectively, over the follow-up period. The secondary outcome, SF-36 bodily pain, showed significantly improved score (p=0.009, CI 2.2-15.5) for the EG over the follow-up period. No significant differences between groups were seen in any of the other SF-36 subscales, in activity level (PASE) or in self-efficacy for pain over the follow-up period.

Conclusions: Physical function (WOMAC) and bodily pain (SF-36) was significantly improved for the EG compared to the CG over the 1 year follow-up period, but there were no significant differences between the two groups for other WOMAC or SF-36 subscales, physical activity level or self-efficacy for pain. There was a small to moderate effect size for pain, stiffness, and physical function for the EG compared to the CG.

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TREATMENT OF CARTILAGE DEFECTS IN THE KNEE USING ALGINATE BEADS CONTAINING HUMAN MATURE ALLOGENIC CHONDROCYTES: A 2-YEAR FOLLOW-UP

A.A. Dholander, K.F. Almqvist, P.C. Verdonk, R. Forsyth, R. Verdonk, G. Verbruggen
Ghent Univ., Ghent, Belgium

Purpose: To determine whether the implantation of alginate beads containing human mature allogenic chondrocytes is feasible and safe for the treatment of symptomatic cartilage defects in the knee.

Methods: A biodegradable, alginate-based biocompatible scaffold containing human mature allogenic chondrocytes was used for the treatment of chondral and osteochondral lesions in the knee. Twenty-one patients were clinically prospectively evaluated with use of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and a Visual Analogue Scale (VAS) for pain preoperatively and at 3, 6, 9, 12, 18 and 24 months of follow-up. Of the 21 patients, 13 had consented to the taking of a biopsy for investigative purposes from the area of implantation at 12 months of follow-up, allowing histological assessment of the repair tissue.

Results: A statistically significant clinical improvement became apparent after 6 months and patients improved during the 24 months of follow-up. Adverse reactions to the alginate/fibrin matrix seeded with the allogenic cartilage cells were not observed. Histological analysis of the biopsy specimens rated the repair tissue as hyaline-like in 15.3 %, as mixed tissue in 46.2 %, as fibrocartilage in 30.8% and as fibrous in 7.7%.

Conclusions: The results of this short term pilot study show that the alginate-based scaffold containing human mature allogenic chondrocytes is feasible and safe for the treatment of symptomatic cartilage defects of the knee. The described technique provides clinical and histological outcomes equal but not superior to those of other cartilage repair techniques.

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THE EFFECTIVENESS OF GLUCOSAMINE SULFATE ON CHRONIC LOW BACK PAIN WITH DEGENERATIVE CHANGES. A RANDOMIZED TRIAL.


Purpose: The aim of this trial is to test whether glucosamine sulfate (GS) can reduce pain and discomfort in patients with chronic low back pain (LBP) and MRI-confirmed degenerative changes. Systematic reviews have reported potential mild effects of glucosamine on knee osteoarthritis (OA), although the scientific quality has been criticized. Though a clear relationship between LBP and lumbar degenerative changes has not been found, GS is increasingly being used in treatment. We have been unable to identify any high quality trials on the effect of GS on chronic LBP. A study of the effect of GS on chronic LBP is therefore needed.

Methods: The study is a randomized, double-blind, placebo-controlled trial. Patients were recruited through primary health personnel and a single newspaper advert. Inclusion criteria: primary LBP and lumbar degenerative changes (LBP and/or psychological) known to influence their LBP. Interventions: Patients were randomized (concealed and computer-generated) to receive 1500mg GS (from Pharma Nord) daily or placebo. Outcome measures were measured 6, 12 and 24 weeks. Primary outcome: A 3 point difference in reduction between glucosamine- and placebo-group measured with the Roland Morris Disability Questionnaire (RMDQ). RMDQ is a self-reported measurement of pain and disability related to LBP. The properties of RMDQ have been studied extensively. Secondary outcomes: Numerical Rating Scale (NRS) for LBP and leg pain when active and inactive; low back stiffness measured by NRS; health related quality of life (EQ-5D); plasma glucose and cholesterol measured pre and post study participation. Statistical analysis: Parametrical or non-parametrical tests (e.g. independent t-tests, ANOVA analysis) will be used in the main analysis depending on the data distribution. SPSS will be used to conduct the analysis and followed the intention to treat principle. The interim analysis reported here utilized repeated
measurements (GLM) to compare the groups. The trial was approved by the regional ethics committee in Norway, Norwegian Medicines Agency and the Norwegian Data Inspectorate. All procedures conformed to the Declaration of Helsinki. The trial was registered at http://www.clinicaltrials.gov under the identifier NCT 0040407. The trial was initiated by Ullevaal University Hospital and financed by the Norwegian LBP organization and not producer financed.

**Results:** This is an interim analysis only. Mean age of the patients (n=250) was 48.5 years. 48.4% were women. Lost to follow up at 6 months was 18 and equal in both groups. GS was not significantly better than placebo in reducing RMDQ score by 3 points. Repeated measurements (GLM) demonstrated no difference between the glucosamine- and the placebo-group. None of the secondary outcomes (NPS, EQ-5D etc) demonstrated any difference between the groups. RMDQ, NPS, LBP duration, race, age, sex, weight, height, BMI, EQ-5D and HSC-L25 were similar in both groups at baseline. No changes in fasting plasma glucose and cholesterol levels were observed post trial participation in either treatment arm. Adverse events were mild, rare and equally distributed among the two groups.

**Conclusions:** Interim results show that daily intake of glucosamine sulfate for 6 months was not effective in reducing low back pain measured with RMDQ.

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**THE EFFECT OF LATERAL-WEDGED INSOLES COMPARED TO VALGUS BRACING IN THE TREATMENT OF MEDIAL COMPARTMENTAL OSTEOARTHRITIS OF THE KNEE: A PROSPECTIVE RANDOMIZED TRIAL**

T.M. van Raaij, M. Reijman, R.W. Brouwer, S.M. Bierva-Zeinstra, J.A. Verhaar

1Erasmus MC, Rotterdam, Netherlands; 2Martini Hosp., Groningen, Netherlands

**Purpose:** The goal was to study the effect of a lateral-wedged insole compared to valgus bracing in patients with symptomatic medial compartmental knee osteoarthritis (OA).

**Methods:** Consecutive patients with symptomatic medial compartmental knee OA who visited the orthopaedic outpatient department of a university medical center were eligible for inclusion. Patients with symptoms not related to medial compartmental OA, younger than 35 years of age, an insufficient command of the Dutch language, or no varus malalignment were excluded. The degree of knee alignment (hip-knee-ankle angle) was assessed on a digitalized whole leg radiograph in standing position. After written informed consent patients were randomly assigned to either an intervention group comprising a shoe inserted leather sole with a lateral-wedged cork elevation of 10 millimeters (6° wedge), or to a control group comprising a commercially available valgus knee brace. The allocation of treatment was concealed until after the participants were included and baseline measurements were executed. One assessor performed all baseline and 6 months follow-up measurements. Primary outcome measure was change in pain severity (VAS). Besides knee function scores (HSS, KSS, WOMAC), percentage responders, varus alignment correction in the frontal plane using the hip-knee-ankle angle, and compliance to the intervention. Responders to the intervention were defined as having an improvement of ≥ 20% compared to the baseline score for pain and function.

**Results:** Between January 2006 and September 2007, 91 consecutive patients were included and randomized (45 insole group; 46 brace group). Pain severity scores improved more in the insole group compared with the bracing group for VAS (-0.9; 95% CI: -1.31; 1.13; effect size 0.04) and WOMAC pain score (-1.43; 95% CI: -1.43; 0.91; effect size 0.004). Knee function was better for the insole group for HSS score (1.69; 95% CI: -3.17; 6.55, effect size 0.16), KSS score (5.47; 95% CI: -12.48; 1.53, effect size 0.34), and WOMAC function score (1.43; 95% CI: -9.39; 6.53, effect size 0.07). There were no significant differences in percentages of responders between the insole and the brace groups (27% vs 25%, respectively). Both intervention had no impact on the varus malalignment. At 6 months 71% of patients in the insole group complied with the intervention, which was significantly (p = 0.015) higher compared to 45% for the brace group.

**Conclusions:** We found no differences in effectiveness of both a 6° lateral-wedged leather shoe inlay and a commercially available valgus brace in the treatment of patients with symptomatic medial OA of the knee joint after 6 months. According to the OMERACT-OARSI set of responder criteria for clinical trials in OA, however, only one fourth of all patients benefited from either the insole or brace intervention.

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**A RANDOMIZED, PARALLEL GROUP, DOUBLE BLIND, PLACEBO AND NAPROXEN CONTROLLED, MULTICENTER PHASE 3 STUDY OF NAPROXINOD IN SUBJECTS WITH OSTEOARTHRITIS OF THE KNEE: EFFICACY RESULTS FOLLOWING 13-WEEK TREATMENT**


**Purpose:** Naproxcinod is a Cyclooxygenase Inhibiting Nitric Oxide Donator (CINOD) under development for the relief of signs and symptoms of OA. Naproxcinod exerts its activity through its two primary metabolites: naproxen and the NO donating moiety. In previous clinical trials, naproxcinod has shown similar anti-inflammatory and analgesic efficacy to conventional NSAIDs, and an improved BP safety and tolerability profile, likely due to its NO donation. The primary objective of the study was to show that naproxcinod 375 mg bid and 750 mg bid were superior to placebo in relieving signs and symptoms in subjects with OA of the knee after 13 weeks of treatment.

**Methods:** In this placebo 13-week and naproxen 26-week controlled study, men and women 40+ years old with a diagnosis of primary OA of the knee meeting ACR criteria and experiencing a flare of pain at baseline after discontinuation of previous anti-inflammatory or acetaminophen treatments were randomized (1:1:1:1) to either naproxcinod 375 mg or 750 mg bid, naproxen 500 mg bid or placebo bid. The three co-primary efficacy variables were the mean change from Baseline at Week 13 in WOMAC™ pain and function subscale scores and subject’s global assessment of disease status. The superiority analysis of naproxcinod over placebo was the primary efficacy analysis. The analysis of each primary efficacy variable was based on an analysis of covariance (ANCOVA) with treatment group as factor, and baseline value as covariate. The primary efficacy analysis was performed using the Intent-to-Treat (ITT) population (all randomized subjects) and was performed on as-randomized basis.

**Results:** A total of 1011 subjects from 129 US centers were included in the ITT population. 71.0% of subjects were female, 78.9% were Caucasian. The mean age was 59.8 years and mean BMI 33.8 kg/m². A total of 766 (75.8%) subjects completed the 13 week study period. Both doses of naproxcinod (375 mg bid and 750 mg bid) demon-