Disclosure of Interest: H. Deckx Employee of: Galapagos NV, Belgium, S. Hatch Consultant for: Galapagos NV, Belgium, M. Robberechts Employee of: Galapagos NV, Belgium, S. Dupont Employee of: Galapagos SASU, France, J. Desiret-Youaret Employee of: has been employee of Galapagos SASU, France, H. Coleman Paid instructor for: Covance has been contracted by Galapagos NV to conduct the study, S. Larsson: None declared, A. Struglics: None declared, E. van der Aar Employee of: Galapagos NV, Belgium, A. Fiewe Employee of: Galapagos NV, Belgium


FR01540

IDENTIFICATION OF BIOMARKERS OF OA ASSOCIATED TO DEFECTIVE AUTOPHAGY

I. Lorenzo-Gomez1, N. Oreiro2, J.A. Pinto-Tasende2, F.J. Blanco1,2, B. Carames1.
1Rheumatology Division, Cartilage Biology Group, The Institute of Biomedical Research of A Coruña (INIBIC); 2Clinical Rheumatology Division, Complejo Hospitalario Universitario A Coruña (CHUAC), a coruña, Spain

Background: In osteoarthritis (OA), defects in cellular homeostasis, and in particular in autophagy, are evident and precede joint damage. In this sense, we have shown that there is a defect in autophagy in OA human chondrocytes and cartilage, and pharmacological activation of autophagy protects against joint damage. These data suggest that joint damage could be, at least in part, to a failure of autophagy, by inducing an abnormal accumulation of cellular products related to degradation.

Objectives: These observations represent a unique opportunity to identify and validate potential biomarkers associated with autophagy defects that could facilitate the development of therapeutic strategies to prevent OA progression.

Methods: A comparative analysis of 86 autophagy genes that could facilitate the development of autophagy was performed in blood from non-OA and knee OA patients. Non-OA patients (Age: 61.17±3.370 years; BMI: 25.76±5.897; Sex: Males; n=12) and Knee OA patients (Age: 65.75±1.529 years; BMI: 30.25±0.88; Sex; Males; n=12, OA grade III-IV) were profiled using a human autophagy PCR array (PrimePCR autophagy human panel, BioRad) and analysed using the PrimePCR analysis software, Biorad. In addition, we performed a quantitative proteomic analysis of defective autophagy by genetic deletion of Atg6 in human OA chondrocytes by using iTRAQ (isobaric tags for relative and absolute quantification) labelling coupled with on-line 2D LC/MS/MS. Protein identification and quantification were performed using Protein Pilot Software 4.0. Each MS/MS spectrum was searched in the UniProt/Swissprot database for Homo sapiens.

Results: 16 autophagy-related genes were significantly down-regulated in blood from knee OA patients compared to non-OA patients. No significant up-regulation was observed in blood from Knee OA patients, however a trend toward up-regulation was detected in several genes involved in the mTOR signalling pathway. Importantly, 5 key autophagy-related genes, such as ATG16L2, ATG12, ATG7, ATG4B and MAP1LC3B involved in initiating autophagy, phagophore extension and autophagosome formation were significantly down-regulated in knee OA patients compared to non-OA patients (p<0.05). Interestingly, HSP90A1 and HSP90B1, a chaperone-mediated autophagy genes involved in response stress and protein folding, were significant down-regulated (p<0.001) in blood from knee OA patients. In addition, several regulators of autophagy and apoptosis, such as BNI3, BCL-2 and BCLL1 were significantly down-regulated in OA patients (p<0.01). Total proteome screening in human OA chondrocytes with defective autophagy, showed a significant reduction of Heat shock protein HSP90-alpha (HSP90AA1) (p<0.05), suggesting that reduced autophagy is associated to OA pathology and could be a potential biomarker for OA progression and development.

Conclusions: This approach represents an unique opportunity to identify and validate early-stage biomarkers associated with defective autophagy that could facilitate the development of therapeutic strategies to prevent joint damage.

Disclosure of Interest: None declared


FR01542

POTENTIAL NOCICEPTIVE PAIN RELIEF OF INTRAARTICULAR SALINE CONTROL IN CLINICAL TRIALS OF KNEE OSTEOARTHROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED TRIALS

I. Simsek, T. Phalen, A. Bedenbaugh, J. Tambiah. Samumed, LLC, San Diego, USA

Background: Hyaluronic acid, corticosteroids and platelet-rich plasma (PRP) are widely used intra-articular (IA) therapies for the management of mild to moderate knee osteoarthritis (OA). Many trials evaluating the efficacy of IA-administered therapies commonly use IA saline injections as a placebo comparator arm. A previously published systematic review Altman et al, 2016 showed significant reductions in pain relief with IA saline in both the short (3 months) and long-term (6–12 months).

Objectives: The aim of this updated systematic review and meta-analysis was to assess the clinical benefit and harm associated with use of IA saline in trials of IA therapies for patients with painful knee OA.

Methods: We searched MEDLINE and Embase databases for randomised controlled trials (RCTs) published up to and including October 12th, 2017. Two reviewers independently assessed the eligibility of potential reports and the risk of bias of included trials. We analysed short (≤3 months) and long-term (6–12 months) pain reduction from baseline of the saline arm of included trials using standardised mean differences (SMDs; estimated assuming a null-effect in a comparator group) that were weighted and pooled using a random-effects model. Pain scores were transformed to a 100-point scale when necessary. We summarised and presented treatment-related adverse events (AEs) descriptively.

Results: We included 46 RCTs, of which 44 provided sufficient data to be included in the meta-analysis for benefit. IA saline significantly improved short-term knee pain from baseline vs. a null effect for a comparator group across 36 studies involving 1908 patients (SMD — 0.85, 95% CI — 1.05 to — 0.66, *P* = 0.87). There was also significant reduction in long-term knee pain following IA injection with saline across 25 studies involving 1758 patients (SMD — 0.79, 95% CI — 1.02 to — 0.55) with a substantial degree of heterogeneity (I² = 90%). Thirty-three of the included trials reported on adverse events, none of which found any serious treatment-related AEs following IA injection with saline.

Conclusions: The pain relief observed with IA saline should prompt one to consider the added effectiveness of current IA treatments that use saline comparators in clinical studies, and challenges of classifying IA saline injection a “placebo.”

Disclosure of Interest: None declared


FR01541

INCREASING A PERSON'S OWN PHYSICAL ACTIVITY AND STRENGTH CAN MINIMISE CARTILAGE VOLUME LOSS IN OLDER-ADULTS: A BETWEEN- AND WITHIN-PERSON ANALYSIS ON A POPULATION-BASED PROSPECTIVE COHORT

L.P. Murugappan1, S. Balogun1, K. Willis1, F. Ciocciuti2, G. Jones3, M.L. Callisaya4, D. Alten1.
1Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania; 2Department of Epidemiology and Preventive Medicine, Monash University Medical School, Melbourne, Victoria, Australia

Background: The relationship between physical activity (PA) and osteoarthritis (OA) has been controversial, with some studies showing a detrimental effect and others showing either no effect or a beneficial effect. Traditionally, analysis has focused on examining the effect PA and/or strength have on OA between individuals (between-person comparison). Yet, how the variability in PA and strength over time within the same individual (within-person comparison) is associated with OA is not well recognised. Statistical methods, such as multilevel models that properly capture the within-person processes can be used to tell us whether changes within an individual over time relate to changes in OA outcomes in that same individual.

Objectives: This study aimed to investigate the associations of between-person and within-person variability in PA and leg strength with knee cartilage volume loss over 10.7 years in older adults.

Methods: 479 community-dwelling older-adults (50% female, mean age 61±6 years, range 50–80 years) were studied at baseline, 2.7, 5.1, and 10.7 years. PA (measured objectively as steps/day) and leg strength (measured objectively in kg) were assessed at all four time-points. Knee cartilage volume was measured using MRI at baseline and 10.7 years. Linear mixed-effect regression models were used to estimate the association of between-person and within-person variability in PA and leg strength with cartilage volume loss over 10.7 years. Models were adjusted for age, sex, body mass index and history of knee injury or surgery.

Results: Mean cartilage volume loss over 10.7 years was 465±231 mm³. No between-person associations existed between PA and cartilage volume loss (Beta: 18.8 per 1000 steps/day, 95% CI —6.1, 43.7). However, within-person variability in PA was protectively associated with changes in cartilage volume, such that having higher PA compared to an individual’s average level of PA minimised their cartilage volume loss over time (Beta: 32.8 per 1000 steps/day, 95% CI 20.8, 44.6). Between-person effects showed that participants with greater leg strength lost last cartilage volume over time (Beta: 5.4 per 1 kg, 95% CI 3.1, 7.8). Within-person variability in leg strength was also protectively associated with changes in cartilage volume, such that having higher leg strength compared to an individual’s average strength minimised their cartilage volume loss over time (Beta: 3.3 per 1 kg, 95% CI 2.1, 4.5).

Conclusions: Our unique analysis method adds a new perspective to the PA and OA debate. The implication of these findings demonstrate that individuals can minimise cartilage volume loss by increasing their own PA and strength, which supports the clinical recommendations of promoting PA and strength to prevent and treat OA.

Disclosure of Interest: None declared

Over the 5 years, the average total direct costs were

**Results:**
Of 878 patients with symptomatic knee and/or hip OA, aged between 40 and 75
years, 76.6% women, aged 58.4±9.1 years, duration of the disease 10.5±6.5 years (M±SD).
47 (33.3%) patients had knee and hip OA, 38 (27%) patients had reactive synovitis.
The control group was presented by 36 practically healthy subjects (72.2% female)
aged 57.1±9.95 years (M±SD), 6-sulfatoxyxymelatonin (6-SMT) in urine and
galectin-3 in blood were determined by ELISA. The severity of pain, stiffness,
and physical functioning of the joints were evaluated by the Western Ontario and
McMaster Universities Osteoarthritis Index (WOMAC). Quality of life was eval-
uated by Short Form-36 (SF-36).

**Results:** It was established in patients with OA a decrease in 6-SMT excretion,
(25.3 ± 38.8 ng/ml in control, p<0.001). 6-SMT excretion correlated
with age (r=0.4; p<0.001) and was more significant in patients with knee
and/or hip OA (mean 26.5 vs. 23.0 ng/ml in patients with OA of the knee
only, p<0.001). Lower levels of 6-SMT excretion associated with higher pain and
with lower quality of life. Patients with OA had increased galectin-3 levels in the
blood (mean 16.4 ± 10.1 ng/ml) in the control, p<0.001. In patients with OA of
knee and hip joints were estimated higher levels of galectin-3. Levels of galectin-3
were significantly higher in patients with synovitis (mean 21.5 vs. 13.8 ng/ml with-
out synovitis, p<0.001). The increase of galectin-3 in the blood was associated
with a marked increase of the total WOMAC index and with decrease of life qual-
ity. The level of galectin-3 directly correlated with age, disease duration (r=0.28,
0.23, p<0.01) and inversely correlated with 6-SMT excretion (r=−0.28; p<0.01).

**Conclusions:** Lower levels of melatonin and higher of galectin-3 were associated
with higher WOMAC index and poorer quality of life in patients with OA. This asso-
ciation may reflect possible pathogenic role of melatonin and galectin-3 in OA.

**REFERENCES:**
inflammation and destruction in antigen-induced arthritis. Arthritis Rheum

**Disclosure of Interest:** None declared

---

**DISCUSSION**

**HEALTH RESOURCE USE AND COST-OF-ILLNESS OF SYMPTOMATIC KNEE AND/OR HIP OSTEOARTHRITIS**: DATA FROM KHOALA COHORT

**Methods:**
The KHOALA cohort is a French population-based multicenter cohort
of patients followed for hip and/or knee osteoarthritis from the KHOALA cohort.
**Results:**
Data on the economic impact are scarce.
3

**Conclusions:** These data are important results to describe the cost of care con-
sumption of a sample of patients with symptomatic osteoarthritis of the hip and/or
knee arthritis may reflect possible pathogenic role of melatonin and galectin-3 in OA.

**REFERENCES:**

**Disclosure of Interest:** I. Simsek Shareholder of: Samumed, LLC. Employee of:
Samumed, LLC, T. Phalen Shareholder of: Samumed, LLC. Employee of:
Samumed, LLC, A. Bedenbaugh Shareholder of: Samumed, LLC. Employee of:
Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC. Employee of:
Samumed, LLC