Investigation Of Selected Biochemical Markers In Knee Osteoarthritis: The Framingham Osteoarthritis Cohort

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Published in:
Annals of the Rheumatic Diseases

Publication date:
2017

improvements over placebo were seen in 0.03 mg and 0.07 mg treatment arms, achieving statistical significance for PTGA and MDGA. Further studies to identify relevant sub-populations and evaluate the safety and efficacy of SM04690 are ongoing.

SAT0553 | **DETECTION OF SERUM LEVEL CHANGES OF MATRIX METALLOPROTIENASE-13 AND INTER LEUKIN-1 BETA DURING REMISSION AND FLARE-UPS OF PRIMARY OSTEOARTHRITIS OF THE KNEES**

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Background: The diagnosis of osteoarthritis is currently based on radiographic criteria (eg, joint space width) and clinical symptoms (eg, pain and loss of function).

The evaluation of new disease-modifying osteoarthritis drugs (DMOADs) is performed on the same basis, since the regulatory bodies currently require evidence for an impact on radiographic joint space narrowing (JSN) and an impact on symptoms However, the limitations of radiography have led to research into alternative parameters for monitoring osteoarthritis that could serve as biomarkers in drug development.

Objectives: Detection the serum level of MMP-13 and IL-1 β In OA of the knee during remission and exacerbation and if these Biomarkers can be validated as gold biomarkers in assessing OA progression and drug development in OA treatment.

Methods: This study was performed on 60 patients with knee osteoarthritis, 18 males (30%) and 42 females (70%), all diagnosed as osteoarthritis of one or both knees. Their ages ranged from (40 -65) years. The duration of their disease ranged from one to 15years. The control groups were 8 males (32%) and 17 females (68%). their ages ranged from (40–65) years.

- The patients were allowed to continue on the medications that they have pro inflammatory cytokines (IL-1β) and degradative enzymes (MMP-13) are measured.
- Clinical assessing for pain using visual analogue scale (0–10)
- Assessing for pain, stiffness and physical functions by:
  (A) the WOMAC osteoarthritis index
  (B) Lequesne's algo functional index
- Asssesing the flare-ups using Knee Osteoarthritis Flare Ups Score (KOFUS).

Results: Patients who had 3 flare-ups (during one year follow up) showed the statistically significantly highest mean IL-1β & MMP13 level.

There was no statistically significant difference between patients with no flare-up, 1 flare-up and 2 flare-ups; all showed statistically significantly lower mean levels.

There was a statistically significant positive (direct) correlation between IL-1β, disease duration, KL, VAS, stiffness score, pain score, functional score, WOMAC and KOFUS. An increase in all these variables is associated with an increase in IL-1β & MMP13.

Conclusions:

- There is a potential role for IL1 beta and MMP 13 biomarkers in assessing the development in osteoarthritis.
- IL 1 β and MMP 13 were founded to be correlated positively in patients with knee OA this correlation sounded right as the expression of MMP 13 depends on the level of IL1 β.
- Although all medications groups failed to lower the level of IL 1 β and MMP 13,yet there was a numerical difference in favor of Diacerine and NSAID.
- patients on both Diacerine and NSAID had the lowerest rate of flare ups
- It is recommended that the early measurement of biomarkers may detect cases to progress and thus stronger treatment may be given for these groups.

SAT0554 | **INVESTIGATION OF SELECTED BIOCHEMICAL MARKERS IN KNEE OSTEOARTHRITIS: THE FRAMINGHAM OSTEOARTHRITIS COHORT**

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Background: Osteoarthritis (OA) is a major cause of functional impairment and disability among the elderly. There is an unmet need for the development of biomarkers for identifying patients with high risk for OA and for monitoring drug efficacy. Specific and sensitive biochemical markers revealing the turnover of bone, cartilage, and synovial tissue may be useful for investigation and monitoring of OA.

Objectives: To investigate a targeted set of five biochemical markers, which reflect joint tissue turnover, for their ability to evaluate the prevalence of radiographic and symptomatic knee osteoarthritis (OA) in a substudy from the cross-sectional Framingham OA cohort (FOA).

Methods: The subjects from the community-based FOA cohort were divided up based on a terminology proposed by the FNIH-OAI consortium. Two main groups were defined: subjects with radiographic knee OA (RKOA, n=80) and a group with no radiographic OA (NRKOA, n=136). The presence of ROA as any Kellgren-Lawrence (KL) grade =2 or 3. The RKOA group were further divided into two groups; those with persistent symptoms of a joint (RKOA+S, n=30) and those without (RKOA-S, n=50). +S was defined as having pain, aching or stiffness in either knee on most days.

Serum levels of C1M, CRPM and huARGS (matrix metalloproteinases cleaved type I collagen and C-reactive protein neo-epitopes, aggrecanase cleaved ^{374}ARGS neoepitope of aggrecan, Nordic Bioscience) were determined by ELISA. Serum levels of cartilage synthesis and degradation biomarkers, hsPro-C2 and hsAGNx-1 (procollagen type IIB N-terminal propeptide, aggrecanase cleaved TEGE^{373} neoepitope of aggrecan, Nordic Bioscience) were measured by electrochemiluminescence immunoassay (ECLIA). Each measure was fisher transformed in order to be comparable across the biomarkers. The correlation between the biomarkers and covariates was assessed.

The subjects of substudy were segregated into two groups based on the cut-off values of each biomarker. The cut-off values of these markers were set as mean of their reference levels. We used logistic regression to compare these two groups, and to examine the association between each marker and the presence of OA and/or pain. All confounding factors were adjusted.

Results: The two main groups were well-matched by age, sex, and BMI. Two biomarkers correlated negatively with BMI: C1M and CRPM. Aggrecan degradation biomarker, hsAGNx-1 was negatively associated with age while the huARGS was not associated with it (Table 1).

CRPM was associated with a lower risk of RKOA+S. Interestingly, hsPro-C2 was associated with a higher risk of it (Table 2).

Table 1. Subject characteristics of substudy

Covariates	NRKOA (n=136)	RKOA-S (n=50)	RKOA+S (n=30)	Biomarker (Fisher transformed) associations with covariates
BMI, mean kg/m^2 (SD)	31.3 (3.79)	32.3 (6.05)	31.6 (5.12)	C1M, CRPM
WOMAC pain	0.182 (0.657)	0.820 (1.66)	4.83 (3.64)	
Age, mean years (SD)	62.6 (8.18)	63.7 (7.06)	62.4 (7.09)	hsAGNx-1
Sex, n (%) female	82 (60.3%)	33 (66.0%)	18 (60.0%)	C1M

Table 2. Odds ratio of OA in the substudy. Values in bold represent associations of $p \leqslant 0.05$. OR data are for each definition of OA, using logistic regression and adjusted for age, sex, and BMI (Upper: unadjusted, Lower: adjusted). ORs are for comparison with knees with NRKOA subjects.

Biomarker	OR of RKOA-S (95% CI)	OR of RKOA+S (95% CI)
C1M	1.07 (0.54 - 2.10)	0.47 (0.18 - 1.24)
CRPM	0.97 (0.51 - 1.88)	0.41 (0.16 - 1.02)
hsAGNx-1	1.20 (0.61 - 2.38)	0.68 (0.27 - 1.72)
hsPro-C2	1.27 (0.63 - 2.57)	**2.51 (1.10 - 5.73)**
huARGS	1.43 (0.71 - 2.88)	1.19 (0.50 - 2.84)

Biomarker	OR of RKOA-S (95% CI)	OR of RKOA+S (95% CI)
C1M	0.96 (0.47 - 1.95)	0.45 (0.17 - 1.20)
CRPM	0.87 (0.44 - 1.71)	**0.39 (0.16 - 1.00)**
hsAGNx-1	1.11 (0.55 - 2.23)	0.68 (0.27 - 1.72)
hsPro-C2	1.32 (0.64 - 2.72)	**2.55 (1.11 - 5.82)**
huARGS	1.49 (0.73 - 3.03)	1.21 (0.50 - 2.92)

Conclusions: This study provides two major findings: 1) aggrecan degradation is not just aggrecan degradation and different neo-epitopes have distinct clinical relevance; 2) CRPM is a candidate biomarker of disease activity and for patient profiling. These data suggest a reference for interpretation of OA subject biomarker data in future human studies.

SAT0555 | **MRI-DETECTED KNEE OSTEOPHYTE: NATURAL HISTORY AND STRUCTURAL RISK FACTORS AFFECTING CHANGE**

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Background: Although magnetic resonance imaging (MRI) has been proved to be far more sensitive than conventional radiographs to detect OP, the natural history of MRI-detected OP in older adults has not yet been described, and it is unclear whether knee structural abnormalities, including cartilage defects, cartilage volume, bone marrow lesions (BMLs), meniscal extrusion, infrapatellar fat pad (IPFP), and effusion-synovitis, can predict osteophyte change.

Objectives: To describe the natural history of knee MRI-detected OP, and to determine if knee structural risk factors are associated with change of MRI-detected OP in a longitudinal study of older adults.