Conclusions: A change in the RNA decay rates of COL2A1, DKK1 and ADAMTS5, conferred by the ageing process, may be accountable for the differential gene expression observed for these genes in RNASeq studies of healthy equine articular cartilage. Altered gene expression previously identified following RNASeq studies of the other genes examined here is probably under control of different mechanisms.

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FRAILTY SYNDROME IN THE COMMUNITY DWELLING ELDERLY WITH OSTEOARTHRITIS

R.C. Miguel, R.C. Dias, J.D. Dias, S.L. Silva, T.M. Ribeiro. *UFMG, Belo Horizonte, Brazil*

Purpose: the aim of this study was to characterize and compare community-dwelling elderly people with knee and/or hip osteoarthritis according to the presence of frailty syndrome.

Methods: A cross-sectional study was carried out to evaluate socio-demographic characteristics, comorbidity, depression, anthropomorphic data,subjective evaluations of health, falls, pain,stiffness,physical function and frailty (Fried phenotype)in elderly subjects with osteoarthritis of the knee and hip using a subsample from FIBRA (a study of frailty in Brazilian elderly people).

Results: The final sample consisted of 58 elderly people with an average age of 74 ($\pm$5.5). 17 (29.31%) were classified as non-frail (NF) 28(48.28%) as pre-frail (PF) and 13 (22.41%) as frail(F). F group used more medications (7.00 $\pm$ 2.00) than NF group (4.00 $\pm$ 2.00), ($p = 0.001$). The BMI (Body Mass Index) was lower for the elderly in NF group (average of 27.00 $\pm$4.50 Kg/m2) compared to PF group (average of 30.00 $\pm$ 4.00 Kg/m2) and F group (average of 34.00 $\pm$ 8.00 Kg/m2), ($p = 0.018$). History of depression was more prevalent in frailty group. When comparing the subjects health with the situation one year before, a difference was found between the groups ($p = 0.016$). The majority of the elderly in PF Group (64.3%) believed that their health had deteriorated compared to 46.2% of F Group and in NF group 52.9% believed that their health was unchanged. When present levels of physical activity were compared with those one year before, PF and F Groups considered that the present level was worse ($p = 0.010$). In the case of function, it was found that F Group was worse than the others ($p = 0.023$), and the same was found for fall related self-efficacy ($p = 0.017$).There were no significant differences between the groups for the remainder of the items analyzed.

Conclusions: The elderly with osteoarthritis and frailty use more medications, were more obese, suffered more depression, have less fall related self-efficacy and worse physical function, as well as a poorer perception of their own health and their level of activity in comparison with the previous year. These characteristics may have a negative impact on their quality of life and demand the attention of health professionals.

Biomarkers
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SERUM BIOMARKERS DETECTION CLUSTERS IMPROVE THE DETECTION OF SYMPTOMATIC TREATMENT EFFECT IN KNEE OSTEOARTHITIS PATIENTS: THE RESULTS OF A PHASE IB/IIA STUDY WITH THE B2 RECEPTOR ANTAGONIST FASITIBANT

S. Meini, F. Bellucci, P. Cucchi, C. Catalani, A. Nizzardo, C. Rossi, A. Capriati, C.A. Maggi. *Menarini Ricerche S.p.A., Florence, Italy*

Purpose: The correlation between the clinical outcome and a panel of serum biomarkers indicative of inflammation or cartilage catabolism was investigated in a Phase IB/IIA clinical study, in which the analgesic activity of the bradykinin (BK) B2 receptor antagonist fasitibant was evaluated in knee osteoarthritis (KOA).

Methods: 36 patients with KOA received a single intra-articular placebo or fasitibant dose of 1, 2.5, or 5 mg. Before and 7 $\pm$ 2 days after treatment, patients were asked to assign the WOMAC scores and a blood sample was collected for measuring 22 OA biomarkers in serum (COMP, keratan sulphate, aggrecan, glycosaminoglycans, CTX-II, hyaluronic acid (HA), CRP, MMP-1, MMP-2, MMP-3, MMP-7, MMP-9, TIMP-1, TIMP-2, eotaxin-2, IL-6, IL-15, IL-17, IL-18, VEGF, uric acid) and in the plasma (BK) by using EIA and colorimetric assays. Absolute changes of biomarkers were ANOVA analysed as dependent variable in function of the treatments; in addition, changes (%) of biomarkers were included as covariate in the ANOVA analysis for the evaluation of the WOMAC A-pain, B-stiffness and C functional subscores, and the overall score.

Results: The variance of biomarkers changes , as dependent variable, was significant (P<0.05) for BK, COMP, CRP, HA, MMP-2, MMP-3, MMP-9, TIMP-1, TIMP-2, eotaxin VEGF, and uric acid. On the other hand, basal biomarker concentrations or treatment, as covariates, significantly accounted for the changes of BK, COMP, CRP, eotaxin, HA, MMP-1, MMP-2, MMP-3, MMP-9, TIMP-1, TIMP-2, VEGF and uric acid levels. MMP-2 was statistically significant lower in the OA group treated with 1 mg ($p = 0.0533$) and 2.5 mg ($p = 0.0079$) of fasitibant versus placebo; TIMP-2 approached only the statistical significance due the α level adjustment ($p = 0.0209$ for 1 mg and $p = 0.0651$ for 2.5 mg).

ANOVA models on pain score in function of treatment (with basal pain score, biomarkers change and their interaction with the treatment as covariate) were applied to select those biomarkers which better explain the pain clinical outcome, namely CTX-II ($p = 0.0150$), TIMP-1 ($p = 0.0076$), TIMP-2 ($p = 0.0170$), basal BK ($p = 0.0386$ and $p = 0.0466$), MMP-9, HA, and eotaxin (nearly significant). A factor analysis was then applied to cluster the selected biomarkers, demographics (BMI, age and sex) and OA related variables (onset time, effusion, and knee circumference);then by using a stepwise procedure, WOMAC A, B, and C subscores, and the overall score were analysed in function of the grouped biomarkers (factor 1: CTX-II, HA, TIMP-2, BK; factor 2: MMP-9, eotaxin-2, TIMP-2) and grouped OA and demographic variables, and in function of the relative baseline WOMAC score, the visit and the treatment. None of the covariated factors had a significant influence on the variance of WOMAC A-pain and B-stiffness in the fasitibant versus placebo treated groups, and post hoc test (Student t test) following the ANOVA analysis did not highlight significant differences. Nevertheless the correction by biomarkers factor 1 and OA and demographic factor 1(BMI and knee circumference) contributed to render statistically significant the difference in WOMAC B-stiffness favouring fasitibant 2.5 mg over placebo.

Statistically significant results were also obtained when WOMAC C-function score or overall index were considered as dependent variables. Either demographic, OA characteristics, and differences in changes of MMP-9, eotaxin, and TMP-2 significantly reduced the residual variance of the model. Moreover, higher difference, and consequently higher statistical significance favouring fasitibant 1mg and 2.5 mg over placebo occurred.

Conclusions: The present exploratory investigation suggests the correlation between osteoarthritis biomarkers (reaching statistical significance for MMP-2, TIMP-2) and the symptomatic clinical outcome in patients one week after a pharmacological treatment with fasitibant belonging to the novel class of BK B2 receptor antagonist. Moreover, the study indicates that eotaxin, MMP-9, and TIMP are able to correct and improve the detection of fasitibant clinical benefit over placebo measured by WOMAC score.

	ANOVA	
	Not corrected	**Corrected for biomarkers and OA and demographic variables**
	P	*P*
WO MAC A-pain		
Fasitibant 1 mg versus placebo	0.968	0.8188
Fasitibant 2.5 mg versus placebo	0.238	0.2822
Fasitibant 5 mg versus placebo	0.624	0.0970
WOMAC B-stiffness		
Fasitibant 1 mg versus placebo	0.860	0.0554
Fasitibant 2.5 mg versus placebo	0.210	**0.0233**
Fasitibant 5 mg versus placebo	0.677	0.9220
WOMAC C-function		
Fasitibant 1 mg versus placebo	0.934	**0.0252**
Fasitibant 2.5 mg versus placebo	**0.049**	**0.0015**
Fasitibant 5 mg versus placebo	0.943	0.8225
WOMAC Overall index		
Fasitibant 1 mg versus placebo	0.897	**0.0341**
Fasitibant 2.5 mg versus placebo	**0.049**	**0.0026**
Fasitibant 5 mg versus placebo	0.927	0.7680