SAT0360 BACTERIAL TRANSLOCATION IN THE ADJUVANT INDUCED ARTHRITIS MODEL: PRELIMINARY STUDY AND IMPACT OF NSAIDS

S. Hecquet1, R. Bordy2, C. Prati1, D. Wendling1, C. Demougeot2, F. Verhoeven1, C. Prati1, D. Wendling1, C. Demougeot2, F. Verhoeven1, C. Prati1, D. Wendling1, C. Demougeot2, F. Verhoeven1.
1CHRU Jean Minjoz, Rheumatology, Besançon, France
2UMRS 1319, UVSQ, CNRS, Bio-Medical Sciences, Villejuif, France

Background: In patients with spondyloarthritis, the presence of intestinal inflammation and an increase in digestive permeability responsible for bacterial translocation has been described. No data are available on the effect of non-steroidal anti-inflammatory drugs (NSAIDs) on this bacterial translocation in patients with spondyloarthritis. Zonulin and lipopolysaccharide (LPS) have been described as good biomarkers of intestinal permeability and bacterial translocation, respectively. Adjuvant-induced arthritis (AIA) is a model of recent arthritis characterized by ossification and ankylosis in the post arthritis period. This model can be considered as a model of reactive arthritis in which our previous work has reported a clear efficacy of NSAIDs with differences between molecules at the structural and vascular levels.

Objectives: To test the hypothesis that there is an increase in digestive permeability and bacterial translocation in the AIA model and to show the influence of different NSAIDs on these two parameters.

Methods: Adjuvant-induced arthritis (AIA) was induced in 6-week-old male Lewis rats by an injection at the base of the tail of Mycobacterium butyricum. A group of non-AIA (control) rats received saline. At the first signs of arthritis, the AIA-rats were evaluated (arthrosis score 0-6) and treated daily intraperitoneally with naproxen (10 mg/kg/day), diclofenac (5mg/kg twice daily), celecoxib (3 mg/kg/day) or saline solution (AIA-vehicle group). After 21 days of treatment, the rats were sacrificed and serum levels of zonulin and LPS were measured.

Results: Compared to the control group, there was a significant increase in zonulin concentration (p < 0.001) in the AIA group. There was no significant difference in the concentration of LPS between the two groups. The levels of zonulin were correlated with the TNF-α levels (R= -0.42; p=0.032) and the arthritis score (R=0.45; p=0.013) but not with the level of IL1-β (R= -p 0.018; p=0.39). Treatment with NSAIDs significantly and equivalently decreased the arthritis score in each group. Compared to the vehicle group, treatment with naproxen significantly decreased the radiographic score (p<0.001), TNF-α, IL1-β (p < 0.01), zonulin (p<0.001) and LPS (p < 0.03). Celecoxib decreased radiographic score (p < 0.001), IL1-β (p < 0.01) but increased zonulin levels (p < 0.05) without effect on LPS. Diclofenac also decreased radiographic score (p < 0.001), TNF-α (p < 0.01), and IL1-β (p < 0.01) but increased both zonulin (p < 0.01) and LPS (p < 0.001).

Conclusion: We have demonstrated an increase in serum zonulin levels in the AIA model and a beneficial effect of naproxen on intestinal permeability and bacterial translocation in contrast to celecoxib and diclofenac. Moreover, the plasmatic zonulin levels were correlated with TNF-α supporting a pivotal role of TNF-α on the tight junctions in this model.

Disclosure of Interests: Sophie Hecquet: None declared. Romain Bordy: None declared. Clément Prati: None declared. Daniel Wendling: None declared. Céline Demougeot Grant/research support from: From an institutional support from Pfizer., Frank Verhoeven: None declared

DOI: 10.1136/annrheumdis-2020-eular.3508
ASSOCIATION OF GUT DYSBIOSIS WITH STRUCTURAL DAMAGE AND ACTIVITY IN AXIAL SPONDYLOARTHRITIS PATIENTS. DATA FROM THE COSPAR REGISTRY.

G. G. Ignacio1,2,3, I. Moreno-Indias4,5, M. D. C. Castro Villegas1,2,3, M. D. C. Abalos-Aguilera1,2,3, M. Ladehesa Pineda1,2,3, I. C. Aranda-Valera1,2,3,

Background: The etiopathogenesis of axial spondyloarthritis (AxSpA) is multifactorial. The possible role of alteration in gut microbiome (dysbiosis) has been recently suggested. However, the association of dysbiosis with structural damage is still unknown and further studies are needed to assess its association with disease activity.

Objectives: To determine the alterations in the gut microbiota in AxSpA patients. To evaluate whether changes in the gut microbiota in AxSpA patients are associated with structural damage.

Methods: Fifteen AxSpA patients and 15 healthy donors (HDs) were included in a cross-sectional study. Disease activity variables such as C-reactive protein and ESR were measured. Structural damage was determined by lateral X-rays of the cervical and lumbar spine to establish the mSASSS index. Axial mobility was evaluated using the BASMI index and the enthesal alteration was evaluated using ultrasonography. The gut microbiome was measured using the Ion Torrent SS platform and sequences were processed using the QIIME2. Chi-square and Mann-Whitney U were used, and correlations were determined using the Spearman Rho test. Significant differences were considered p < 0.05.

Results: Alpha diversity indexes, such as the number of observed OTUs group and the phylogenetic index, showed a greater richness in AxSpA compared to HDs (p=0.03 and p=0.01). A significant decrease in families Bacteroidaceae and Bifidobacteriaceae were found in the microbiota of AxSpA (p=0.036, p=0.049). According to genera, Bacteroides decreased in AxSpA (p=0.006), while Dialister and Bidibacterium increased (p=0.010 and p=0.046). Positive correlation among lumbar mSASSS (r=0.508, p=0.019) and Synergistaceae was found. This family was also increased along with the increase in enthesal damage (mASEI index (r=0.656, p=0.028)) and axial mobility by the BASMI index (r=0.529, p=0.011). Correlation studies between the decrease in Bacteroidaceae and Bifidobacteriaceae with disease activity measured by ASDAS (r=-0.697, p=0.025; r=-0.770, p=0.009) was also significant. Positive correlation was observed between Dialister with mSASSS (r=0.549, p=0.010) and BASMI (r=0.512, p=0.015).

Conclusion: 1) AxSpA patients had a significant alteration of the gut microbiota. 2) These alterations are associated with radiographic damage, disease activity, affection of enthesis and axial mobility.