LOW AND MODERATE PHYSICAL ACTIVITY REDUCES LOCALISED L-IB IN AN ACUTE MOUSE MODEL OF GOUT BY DOWN-REGULATING TLR2 EXPRESSION ON CIRCULATING NEUTROPHILS

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Background: While physical activity was originally believed to exacerbate inflammation in rheumatic disease, recent studies have shown significant reductions in inflammation with regular exercise. It has been previously shown that down-regulation of toll-like receptor (TLR)2 and TLR4 expression correlates with increased physical activity in humans. Furthermore, bone marrow-derived (BM)-TLR4 knockout mice are resistant to monosodium urate (MSU) crystal-induced gout. Additionally, mesenchymal stem cells (MSCs) can be immunosuppressive by secreting IL-1 receptor antagonist (IL-1RA) and have also been shown to be up-regulated with exercise.

Objectives: The aim of this study was to investigate the mechanism by which exercise suppresses gouty inflammation and to define the potential roles of TLR2, TLR4, and MSCs in the process.

Methods: BM-TLR2 reporter mice (BALC/c-Tg[NFβB-RE-luc]-Xen) were exercised daily by treadmill walking (45 min/day for 2 weeks) at low intensity (35% VO2max; 8 m/min), moderate intensity (55% VO2max; 11 m/min), and high intensity (75% VO2max; 15 m/min). Mice were then injected with MSU crystals (0.5 mg) into the tibio-tarsal joint (ankle). Localised NFκB activity was measured 16 hours later in the injected ankle by bioluminescent imaging. Tissue was collected and processed for immunohistochemical (IHC) analysis and whole blood was collected for both flow cytometry and serum analysis.

Results: Mice in the low/moderate intensity exercise groups had decreased inflammation, F4/80+ macrophages, and MPO+ neutrophils at the site of MSU injection compared to high intensity and non-exercised controls. Similarly, bioluminescent imaging of NFκB activity was significantly reduced locally in both low/moderate intensity groups compared to high-intensity and non-exercised controls. Surface expression of TLR4 on peripheral monocytes or neutrophils showed little difference by flow cytometry, while TLR2 expression on peripheral neutrophils was significantly reduced. In concordance, localised IL-1β expression via IHC was reduced in low/moderate intensity exercise conditions. IL-1RA expression correlated with IL-1β induction locally by IHC and was elevated in serum. Also, bone marrow-derived MSCs were significantly reduced in low/moderate intensity exercise compared to high-intensity or non-exercised controls.

Conclusions: These data show that while low/moderate intensity exercise regimens can reduce the localised MSU crystal-induced inflammation, high intensity training negates this response. Moreover, the exercise-mediated suppression of NFκB activity and IL-1β expression locally can be partially explained by a reduction in peripheral neutrophil recruitment via downregulation of TLR2 expression in the peripheral blood. Although not clearly defined mechanistically in this study, our results also suggest that MSCs may contribute to this immunosuppressive response and are mobilised out of the bone marrow with low/moderate intensity exercise.

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Disclosure of Interest: None declared


FRIDAY, 15 JUNE 2018

Pathophysiology and biomarkers in PsA: what impact?

PRECISION MEDICINE USING DIFFERENT BIOLOGICAL DMARDS BASED ON CHARACTERISTIC PHENOTYPES OF PERIPHERAL T HELPER CELLS IN PSORIATIC ARTHRITIS

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Background: Biological DMARDs targeting TNF-α, IL-17, and IL-12/23 (p40) are available. The high efficacy of these drugs has been proven in numerous clinical trials. However, there are some cases in which a change from one bDMARDs to another one is necessary because of the refractory nature of the disease, and there is no established method to select the optimal bDMARDs according to the individual case, despite the fact that various drugs are available.

Objectives: We sought to identify specific biological DMARDs based on characteristic lymphocyte phenotypes for treating PsA.

Methods: We performed this study to evaluate the efficacy of biologics therapy in 64 patients with PsA after 6 months of therapy, and to compare the results of
peripheral lymphocyte phenotyping using 8-colour flow cytometry, with specific focus on helper T cell subsets, between 26 patients with PsA and healthy donors. In addition, the therapeutic response of 26 patients in whom the optimal bDMARDs was strategically chosen based on the results of peripheral lymphocyte cytometry was evaluated at 6 months of treatment intervention in comparison with 38 patients in whom the standard biological product was used based on the 2011 and 2015 EULAR recommendations. Thus, the possibility of the optimisation of drug selection for bDMARDs therapy based on peripheral blood lymphocyte cytokinetyping was investigated.

Results: The 26 patients with PsA in the strategic treatment group were classified into the following 4 types based on the peripheral blood analysis: a CXCR3+CCR6+CD38+HLA-DR+ activated Th1 cell-predominant type, a CXCR3+CCR6-CD38+HLA-DR+ activated Th17 cell-predominant type, a Th1/Th17-high type, and a Th1/Th17-low type. According, usteukinumab was administered to the activated Th1 cell-predominant patients, secukinumab to the activated Th17 cell-predominant patients, secukinumab or TNF inhibitor to the Th1/Th17-high patients, and TNF inhibitor to the Th1/Th17-low patients. At 6 months of strategic treatment, there was a significant decrease in SDAI (from 28.8 to 25.0), DAS28 (ESR) (from 4.13 to 2.27), and PASI (from 8.0 to 4.20). There were no statistically significant differences in background factors at baseline between these 2 groups. Moreover, the proportion of patients with the combined use of MTX was significantly lower in the strategic bDMARDs treatment group. There were significant decreases in TJC, SJC, PGA, CRP, ESR, DAS28 (ESR), and PASI in both groups at 6 months of therapy. There were no significant differences in the amounts of these decreases between the two groups. However, at 6 months of therapy, the rate of low disease activity achievement according to SDAI, DAS28 (ESR), and ACR20 response rate was significantly higher in the strategic bDMARDs treatment group.

Conclusions: Strategic treatment in which different bDMARDs were selected according to phenotypic differences in helper T cells showed significantly higher efficacy than standard bDMARD therapy. The results of this study provide an important guide to the implementation of more effective therapeutic intervention.

Disclosere of Interest: None declared


FRIDAY, 15 JUNE 2018

The art of diagnosis of axial SpA

OP0322

ARE WE TREATING WITH BIOLOGICAL THERAPIES WOMEN PATIENTS WITH REAL NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS?

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Background: As a result of the development of the ASAS criteria for axial spondyloarthritis (axSpA), a new entity (non-radiographic axSpA - nr-axSpA) was created. In some countries major concerns have been raised with regard to this entity because this could imply administrating TNF inhibitors (TNFi) to non-SpA patients. Especially the possibility of treating women with fibromyalgia has been raised. In some countries major concerns have been raised with regard to this entity because this could imply administrating TNF inhibitors (TNFi) to non-SpA patients. This supports that when treating axSpA women (including nr-axSpA) with BT, we are currently treating axSpA - and not fibromyalgia- patients.

Objectives: To evaluate if the gender distribution and the pattern of patients have changed in clinical practice since TNFi were approved for nr-axSpA.

Methods: Dataset from a prospective cohort including all patients with axSpA treated with biological therapy (BT) since 2000 till August-2017 in a tertiary hospital was analysed. Patients’ and disease’ characteristics and disease activity parameters were collected at baseline. Based on the starting date for the first BT, patients were classified in two groups: i) before 2013 and ii) during or after 2013, according to the approval date for TNFi in the country. In total, 385 axSpA patients initiated BT. Out of these, 266 initiated BT in period i) and 119 in period ii).

Results: Of these 266, 216 initiated BT in period i) and 44 in period ii). The characteristics of patients in both groups are depicted in table 1. Importantly, there were no differences between period i) and ii) in the proportion of men and women, with 38% and 39% of women, respectively. Additionally, during period ii), the percentage of patients with nr-axSpA was similar for both genders and out of all patients with nr-axSpA, the majority (60%) were men. Overall, disease duration was shorter in period ii) for both genders. Women in period ii) had significantly higher ASDAS, BASM1 and CRP than women in period i) and higher ASDAS, BASDAS1 and BASFI than men in period ii).

Conclusions: In the clinical practice, the frequency of women initiating BT have not increased since its approval for nr-axSpA. Additionally, women treated nowadays with BT have more objective parameters of disease activity than they used to do. This supports that when treating axSpA women (including nr-axSpA) with BT, we are currently treating axSpA - and not fibromyalgia- patients.

Disclosere of Interest: None declared


Abstract OP0322 – Table 1 Patients characteristics stratified for starting first TNFi period and gender

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<th>Total</th>
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<tr>
<td>Males</td>
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</tr>
<tr>
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<tr>
<td>44</td>
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<tr>
<td>Female, %</td>
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Abstract OP0323

ARE GENDER-SPECIFIC APPROACHES NEEDED IN DIAGNOSING EARLY AXIAL SPONDYLOARTHRITIS? DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY COHORT

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Background: Although gender differences have been observed in the severity of axial spondyloarthritis (axSpA), gender differences in disease presentation of early axSpA have not been thoroughly investigated.

Objectives: Our aim was to assess if the disease presents differently in males and females, and to evaluate if this has an impact on the diagnostic process.

Methods: Baseline data from the SPondyloArthritis Caught Early cohort, which includes patients with chronic back pain (CBP; ≥3 months; ≥12 years, onset ≤45 years), were analysed. Patients underwent a full diagnostic workup, including MRI and radiography of the sacroiliac joints (MRI-SIJ and X-SIJ), to establish a diagnosis of axSpA. Characteristics of male and female patients with a definite diagnosis of axSpA (based on a level of confidence about the diagnosis ≥7, as expressed by the physician on a 0–10 rating scale) were compared. Regression models were built for i) the whole CBP cohort stratified by gender to study which SpA features were associated most with diagnosis in each gender, and ii) for axSpA patients to test if gender was associated with imaging positivity (MRI-SIJ and/or X-SIJ+).

Results: Of the 719 CBP patients, 275 were male. With 146/275 (53.1%) males and 155/444 (34.9%) females diagnosed as axSpA, males were more likely to be diagnosed with axSpA (OR 2.1, 95% CI: 1.5 to 2.9). Despite similar symptom duration, male axSpA patients were younger at diagnosis (27.4±7.5 vs 29.5±7.8 years; p=0.021). Presence of SpA features was similar in male and female axSpA patients (table 1) except for HLA-B27 and positive imaging features, which were more prevalent in female axSpA patients than in non-axSpA patients, either males (HLA-B27 +23% and imaging 7%) or females (HLA-B27 +34% and positive imaging 11%) (all p<0.001). Nevertheless, both these SpA features were still more prevalent in female axSpA patients than in non-axSpA patients, either males (HLA-B27 +23% and imaging 7%) or females (HLA-B27 +34% and positive imaging 11%) (all p<0.001). Moreover, in multivariable models with diagnosis as