influence on Th17 decreasing and Treg cells increasing in patients with ERA, so we can hypothesise that part of the clinical response is owed to the improvement in T cell balance. Previous data reported that Actinobacteria are strongly correlated with the production of IL-17 and a reduction of Nitrosipea has been associated to increased inflammatory responses and to gut permeability in mice. Lachnospiraceae family play an important role in the maintenance of intestinal homeostasis. The correlation between gut microbiota composition and Th17/Treg axis observed in our patients may suggest the involvement of some bacteria family in Th17/Treg cells balance in the lamina propria of RA patients treated with MTX, even in the early phases of the disease.

REFERENCES:

Disclosure of Interest: None declared

Efficacy of treatment with probiotics in the inflammatory activity of patients with rheumatoid arthritis: Systematic Review of the Literature

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Objectives: To study the effectiveness of the use of probiotics in the control of inflammatory activity of patients with rheumatoid arthritis and analyse its effect on their metabolic profile.

Methods: A bibliographic search was carried out in Medline and Embase. The search strategy included the terms MeSH and the free text of probiotics, bacterium, lactic acid and rheumatoid arthritis. The search was carried out by two authors, which were included according to the type of studies: meta-analysis, systematic reviews and clinical trials, depending on the type of participant: adults with RA who have received probiotics, the main outcome measures: changes in the Disease Activity Score (DAS28), Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI)), as well as each of the parameters that constitute them: C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), visual analogue scale of the doctor and the patient (EVA), number of painful joints (NAP) and inflamed (NAI) and functional status by Health Assessment Questionnaire (HAQ) Secondary variables: number of adverse events and parameters of metabolic activity. The quality of the evidence was analysed following the guidelines of the Scottish Network of Intercollegiate Guidelines (SIGN).

Results: After the selection of 34 articles, 9 articles were finally included. All were randomised, double-blind, placebo-controlled clinical trials (RCTs) with a level of evidence between 1+ and 1++, and a recommendation grade of A and B. Seven CDs showed improvement in arthritis measurements. In Peltonen et al. observed a high rate of improvement in the experimental group than in the control group (3.1 vs 2, p=0.027). Mandel et al. described improvement of the EVA in the experimental group (p=0.046). Zamani et al. described an improvement in DAS28 (−0.3±0.4 versus −0.1±0.4, p=0.01). Vaghef-Mehrabany et al defined this improvement (p=0.01). Pineda et al. showed an improvement in HAQ at 3 months in the experimental group (from 0.97 to 0.80, p=0.02), although not in ACR20 (p=0.33). Allipour et al. found improvements in CRP between the two groups (mean [95% CI]=0.81 [0.54–0.64], p=0.009); NAD: (mean [95% CI]=0.72 [0.25–1.19], p=0.003); NA: (mean [95% CI]=0.35 [0.13, 0.58], p=0.003); EVA: (mean [95% CI]=16.71 [8.91, 24.50] p=0.001); DAS28: (average [CI] 95%)-0.31 [0.61, 0.309]) and in cytokine levels, Hatakka et al observed no significant improvement in the experimental group in HAQ, NAD and NAI, and Nenon et al. Did not observe differences in DAS28. In the last, EC of Vaghef-Mehrabany of 2017 metabolic measures were evaluated without finding significant improvements if an improvement in insulin resistance was observed as measured by the HOMA B index in the study by Zamani et al.

Conclusions: Treatment with probiotics seems to be effective in controlling the inflammatory activity of rheumatoid arthritis.

Disclosure of Interest: None declared

Modulation of endothelial function by proinflammatory cytokines involved in rheumatoid arthritis. Focus on IL-17A, IL-20, IL-23 and IL-9

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Background: Rheumatoid Arthritis (RA) is the most common inflammatory rheumatic disease, characterised by high circulating of pro-inflammatory cytokines. RA is associated with an increased cardiovascular risk secondary to the accelerated atherogenesis which is the consequence of endothelial dysfunction (ED)1. In addition to the well-known cytokines (TNF-α, IL-1β and IL-6), emerging data identified new cytokines such as IL-17A, IL-20, IL-23 and IL-9 as putative key-players of the pathogenesis of RA. To date, whether these cytokines might contribute to RA-associated endothelial dysfunction is not known.

Objectives: This study investigated the effect of IL-17A, IL-20, IL-23 and IL-9 on endothelium-dependent relaxation in response to acetylcholine (Ach) in rat aortic rings.

Methods: Experiments were conducted on thoracic aortic rings from male Lewis rats (11 week old), incubated for 1 hour or 24 hour at 37°C with 2 concentrations of each cytokine (IL-17A: 250 pg/ml and 10 ng/ml; IL-20: 500 pg/ml and 5 ng/ml; IL-23: 80 pg/ml and 10 ng/ml; and IL-9: 300 pg/ml and 10 ng/ml). Incubation with 10 ng/ml TNF-α was used as a positive control and with vehicle as negative control. At the end of the incubation period, endothelial function was studied by assessing concentration-response curves to Ach (10−10−4 mol/L) after phentolamine (10−5–10−4 mol/L) or KCl (30 mmol/L)-induced contractions.

Results: As described in the literature2, a 24-hour but not 1 hour-incubation with TNF-α reduced Ach-induced relaxation. The same result was obtained with IL-17A (10 ng/ml). By contrast, IL-20 did not change Ach-induced relaxation whatever the concentration and the incubation time. Impairment in vascular relaxation was observed after exposure to IL-9 (10 ng/ml), both after 1- and more severely after 24-hour-incubation. As regards IL-23, an effect was observed only after 1 hour incubation and with high concentration.

Conclusions: Our data demonstrated that IL-17A, IL-23 and IL-9 but not IL-20 induced endothelial dysfunction, with different kinetics profiles. Among the cytokines evaluated, IL-9 exhibited the most important effect thus revealing a new putative role of this pleiotropic cytokine in RA-associated cardiovascular risk. Further studies are needed to confirm these data on animal models of diseases.

REFERENCES:

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Prophylactic and therapeutic activity of alkaline phosphatase in arthritic rats: single agent activity and in combination with methotrexate

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Background: Alkaline phosphatase (AP) is a gate-keeper of innate immune system responses by detoxifying (dephosphorylating) inflammation triggering molecules (ITMs) released from endogenous and external sources1 and maintaining physiological barriers.

Objectives: We examined whether AP’s broad mechanism of action may serve as a safe therapeutic, either as single agent or combined with methotrexate (MTX), in rheumatoid arthritis (RA).

Disclosure of Interest: None declared

MODULATION OF ENDOTHELIAL FUNCTION BY PROINFLAMMATORY CYTOKINES INVOLVED IN RHEUMATOID ARTHRITIS. FOCUS ON IL-17A, IL-20, IL-23 AND IL-9

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Scientific Abstracts
1251