Objectives: We performed a cross-sectional study, enrolling consecutive patients and reporting their clinical and laboratory data. Disease activity was assessed by SLE Disease Activity Index 2000 (SLEDAI-2k). Caffeine intake was evaluated by a 7-day food frequency questionnaire, including all the main sources of caffeine. As previously reported, patients were divided in four groups according to the daily caffeine intake: <29.1 mg/day (group 1), 29.2-153.7 mg/day (group 2), 153.8-376.5 mg/day (group 3) and >376.6 mg/day (group 4). At the end of questionnaire filling, blood samples were collected from each patient to assess cytokines levels. These were assessed by using a panel by Bio-Plex assays to measure the levels of IL-6, IL-10, IL-17, IL-27, IFN-γ, IL-17F and Blys.

Results: We enrolled 89 SLE patients (F/M 87/2, median age 46 years, IQR 144 months, IQR 150). The median intake of caffeine was 195 mg/day (IQR 331). We found that MDCs bone marrow and peripheral blood increased in ESS mice. MSC transplantation ameliorated SS-like syndrome and down-regulated the percentages of MDCs, PMN-MDCs and M-MDCs and promoted their suppressive activity in ESS mice significantly (Figure 1). In vitro, MSCs could down-regulate the differentiation and up-regulate the suppressive ability of MDCs. Mechanistically, MSCs inhibited the differentiation of MDCs and PMN-MDCs via secreting prostaglandin E2, and inhibited the differentiation of M-MDCs by secreting interferon-β (Figure 2).

Conclusion: Our findings suggested that MSCs alleviated SS-like symptoms by suppressing the aberrant accumulation and improving the suppressive function of MDCs in ESS mice via COX2/PGE2 pathway.

References:

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1391

THU0227 CAFFEINE INTAKE MODULATES DISEASE ACTIVITY AND CYTOKINE LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

V. Orfice1, F. Ceccarelli1,2, C. Barbati1, R. Lucchetti1, G. Olivier1, E. Cipriano1, F. Natalucci1, C. Perricone1, F. R. Spinelli1, C. Alessandri1, G. Valesini1, F. Conti1. 1Lupus Clinic, Rheumatology, Sapienza University of Rome, Rome, Italy; 2University of Perugia, Department of Medicine, Rheumatology Unit, Perugia, Italy

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease mainly affecting women of childbearing age. The interplay between genetic and environmental factors may contribute to disease pathogenesis. At today, no robust data are available about the possible contribute of diet on disease outcome.

Methods: We aimed to evaluate the impact of caffeine consumption on SLE-related disease phenotype and activity, in terms of clinimetric assessment and cytokines levels.

Results: We enrolled 89 SLE patients (F/M 87/2, median age 46 years, IQR 144 months, IQR 150). The median intake of caffeine was 195 mg/day (IQR 331). At the time of the enrollment, 8 patients (8.9%) referred a caffeine intake < 29.1 mg/day (group 1), 27 patients (30.3%) between 29.2 and 153.7 mg/day (group 2), 45 patients (51%) between 153.8

Figure 1. MSCs ameliorated SS symptoms and decreased MDCs in NOD mice.
and 376.5 mg/day (group 3) and 9 patients (10.1%) >376.6 mg/day (group 4). A negative correlation between the levels of caffeine and disease activity, evaluated with SLEDAI-2K, was observed (p=0.01, r=-0.26). By comparing the four groups, a significant higher prevalence of lupus nephritis, neuropsychiatric involvement, hematological manifestations, hypocomplementemia and anti-dsDNA positivity was observed in patients with less intake of caffeine (figure 1 A-E). Furthermore, patients with less intake of caffeine showed a significant more frequent use of glucocorticoids (group 4: 22.2%, versus group 1 (50.0%, p=0.0001), group 2 (55.5%, p=0.0001), group 3 (40.0%, p=0.009)). Moving on cytokine analysis, a negative correlation between daily caffeine consumption and serum level of IFNα was found (p=0.03, r=-0.2) (figure 2A); furthermore, patients with more caffeine intake showed significant lower levels of IFNα (p=0.02, figure 2B), IL-17 (p=0.01, figure 2C) and IL-6 (p=0.003, figure 2D).

Conclusion: This is the first report demonstrating the impact of caffeine on SLE disease activity status, as demonstrated by the inverse correlation between its intake and both SLDAI-2K values and cytokines levels. Moreover, in our cohort, patients with less caffeine consumption seems to have a more severe disease phenotype, especially in terms of renal and neuropsychiatric involvement. Our results seem to suggest a possible immunoregulatory dose-dependent effect of caffeine, through the modulation of serum cytokine levels, as already suggested by in vitro analysis.

References:

Figure 1. Prevalence of lupus nephritis (A), neuropsychiatric involvement (B), hematological manifestations (C), hypocomplementemia (D) and anti-dsDNA positivity (E) in the four groups

Figure 2. Correlation between daily caffeine intake and IFNα serum level (A), IFNα (B), IL-17 (C) and IL-6 (D) serum levels in group 1-2 and group 3-4.

Disclosure of Interests: Valeria Orefice: None declared, Fulvia Ceccarelli: None declared, cristiana barbati: None declared, Ramona Lucchetti: None declared, Giulio Olivieri: None declared, enrica ciripino: None declared, Francesco Natafucci: None declared, Carla Perricone: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Consultant of: Novartis, Gilead, Lilly, Sanofi, Celgene, Speakers bureau: Lilly, cristiano alessandri

THU0228 PROTECTIVE EFFECT OF LEFLUNOMIDE ON THE SALIVARY SECRETION OF SUBMANDIBULAR GLAND IN THE NOD MOUSE

C. Yang1, X. Zheng2, L. Wang3, X. Yang2, X. Li1, G. Wang1, X. Li1. 1Anhui Provincial Hospital affiliated to Anhui Medical University, Hefei, China; 2The First Affiliated Hospital of University of Science and Technology of China, Hefei, China

Background: A study of 15 PSS patients showed that leflunomide had no significant effect on the decrease of salivary flow rate and the formation of lymphocytic infiltrates in salivary glands [1]. However, due to the small number of samples included in this study and the small size of human salivary gland biopsies, the therapeutic effect of leflunomide may be underestimated. At present, there is no further study on this issue, the effect of leflunomide on Sjogren’s syndrome is still not clear.

Objectives: To investigate the therapeutic effect of leflunomide on salivary gland secretion dysfunction in the NOD mice with Sjogren’s syndrome.

Methods: The NOD mice were randomly divided into four groups: preventive drug group, preventive control group, therapeutic drug group, and therapeutic control group. Salivary flow rate was measured after pilocarpine stimulation; After hematoxylin and eosin staining, the average number and area of infiltrating lesions were compared; The percentage of CD3+ T, CD4+ T, CD8+ T, CD44+ CD62L+, CD44+ TCD4+ T, CD19+ B, and CD138+ B cells in submandibular gland and spleen were detected by flow cytometry; The levels of serum inflammatory factors TNF-a, IL-17A and IL-6 were detected by CBA method.

Results: The salivary flow rate (t = -5.81, P<0.001; z =-3.61,P<0.05), the number of infiltrating foci(t=3.95,P<0.01; t=4.94,P<0.001) and the average area of infiltrating foci(t=3.18,61,P<0.05; z=2.35,P<0.05) in the treatment groups were significantly ameliorated. CD4+ T cells(t=2.39 P<0.05; t´=3.82 P<0.01) and CD4+ CD62L+CD4+ T cells(t´=3.36,P<0.05; t´=3.67, P<0.001) in the submandibular gland were significantly decreased. CD4+ T cells(t=4.08, P<0.001; t=2.76,P<0.05), CD44+ CD62L+CD44+ T cells(t=3.33, P<0.001; t=3.29, P<0.05), CD19+ B(t=5.88,P<0.001; t=4.23, P<0.01) and CD138+B cells in submandibular gland and spleen were also significantly decreased. In addition, the serum IL-17A of the treatment group reduced to lower level(t=4.1 P<0.01; t=3.61,P<0.05), and the TNF-a level of the preventive drug group decreased(t=4.56; p<0.001).

Figure 1. Leflunomide reduced lymphocyte infiltration and improved salivary gland function in NOD mice. A-D: Histology of the submandibular glands of NOD mice in control and treated groups. E-H: The comparison of the submandibular gland index, salivary flow rate, number of infiltrating foci and average area of the submandibular gland, between the control and treated groups. (means±SD; n=7 per group; * P<0.05, ** P<0.01, *** P<0.001).

Figure 2. Changes of lymphocyte subsets in submandibular gland and spleen A-L: Frequencies of CD3+ T cells, CD4+ T cells, CD8+ T cells, CD44+ CD62L-CD44+T cells, CD19+ + B cells, CD138+ B cells

Disclosure of Interests: Valeria Orefice: None declared, Fulvia Ceccarelli: None declared, cristiana barbati: None declared, Ramona Lucchetti: None declared, Giulio Olivieri: None declared, enrica ciripino: None declared, Francesco Natafucci: None declared, Carla Perricone: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Consultant of: Novartis, Gilead, Lilly, Sanofi, Celgene, Speakers bureau: Lilly, cristiano alessandri

DOI: 10.1136/annrheumdis-2020-eular.21000