AB0535

EFFECT OF METFORMIN ON THE ABSOLUTE NUMBER OF CD4+ T CELL SUBSETS IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

X. Sun¹, H. Yao¹, J. He¹, G. Chai¹, L. Wei¹, J. Xie¹, C. Gao², X. Li¹, J. Li¹.
¹Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China; ²Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, USA

Background: Primary Sjogren's syndrome is a chronic inflammatory autoimmune disease characterised by the infiltration of lymphocytes into exocrine glands such as the salivary gland and lacrimal gland. Although its etiology and pathogenesis is unclear at present, we consider immune dysfunction plays a significant role in the process. A lot of studies have confirmed that the formation of Treg and Th17 cells interact between each other, and their balance can affect the immune response results, notably reflected in various autoimmune and inflammatory diseases, including primary Sjogren's syndrome. However, there are few studies on the absolute number of CD4+T cells in peripheral blood of patients with primary Sjogren's syndrome. In addition, metformin can affect the balance of Th17/Treg cells through the AMPK-mTOR pathway.

Objectives: To explore whether metformin can affect the balance of Th17/Treg cells in peripheral blood of patients with primary Sjogren's syndrome, and then be applied in the treatment of pSS patients.

Methods: The number of Treg cells(28.74 (21.22,38.68) vs 34.05 (30.14,42.31), $P=0.023$)significantly increased after the treatment. At the same time, there was a significantly decrease in the ratio of h17/Treg cells(0.25 (0.08,0.44) vs 0.18 (0.04,0.32), $P=0.014$). Besides, after the treatment the absolute number of Th17 cells were increased, but it was not statistically significant(4.5 (3.64,14.23) vs 7.87 (2.37,19.89), $P=0.835$). In addition, the clinical symptoms of the metformin group were obviously improved, while the dosage of prednisone, leflunomide or hydroxychloroquine reduced significantly.

Results: The number of Treg cells(28.74 (21.22,38.68) vs 34.05 (30.14,42.31), $P=0.023$)significantly increased after the treatment. At the same time, there was a significantly decrease in the ratio of h17/Treg cells(0.25 (0.08,0.44) vs 0.18 (0.04,0.32), $P=0.014$). Besides, after the treatment the absolute number of Th17 cells were increased, but it was not statistically significant(4.5 (3.64,14.23) vs 7.87 (2.37,19.89), $P=0.835$). In addition, the clinical symptoms of the metformin group were obviously improved, while the dosage of prednisone, leflunomide or hydroxychloroquine reduced significantly.

Abstract AB0535 – Figure 1

Conclusions: Metformin can increase the absolute number of Treg cells and decrease the ratio of Th17/Treg cells in the peripheral blood of patients with pSS, while reducing the use of hormones and DMARDs drugs. And it may be one of the mechanisms adopted in the treatment for pSS.

REFERENCES:

- [1] Matsui K, Sano H. T Helper 17 Cells in Primary Sjogren's syndrome [J]. Journal of Clinical Medicine 2017;6(7):65.
- [2] Saito M, Otsuka K, Ushio A, et al. Unique Phenotypes and Functions of Follicular Helper T Cell and Regulatory T Cell in Sjogren's Syndrome. [J] Curr Rheumatol Rev 2017;13(999).
- [3] Lee SY, Moon SJ, Kim EK, et al. Metformin Suppresses Systemic Autoimmunity in Roquin (sar/san) Mice through Inhibiting B Cell Differentiation into Plasma Cells via Regulation of AMPK/mTOR/STAT3[J]. Journal of Immunology 2017;198(7):2661.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2255

AB0536

RAPAMYCIN ATTENUATES SYMPTOM AND RESTORES THE BALANCE OF TH17/TREG IN REFRACTORY PRIMARY SJOGREN'S SYNDROME

Z. Hao¹, M. Miao¹, Y. Guo¹, X. Zhang¹, X. Li¹, C. Gao², X. Wang¹. ¹The Second Hospital of Shanxi Medical University, TaiYuan, China; ²Harvard Medical School, Boston, USA

Background: Primary Sjögren's syndrome (pSS) is one of the more common rheumatological diseases. Despite continued advances, the use of conventional drugs or biologic agents in patients with pSS did not provide expected efficacy and a targeted treatment of pSS is not available at present. We have shown that absolute number of peripheral CD4⁺CD25⁺FOP3⁺regulatory T cells (Tregs) decreased in pSS patients. And rapamycin is an inhibitor of mTOR that can decrease Th17 cells but increase regulatory T cells (Treg cells).

Objectives: To observe the effect of rapamycin on Th17/Treg cell balance in patients with refractory pSS.

Methods: Twenty-eight refractory SS patients (26 women and 2 men) and 93 health controls were enrolled, with a mean duration of 76.64±49.66 months and mean age of 52.39±10.62 years. They fulfilled the 2002 PSS international classification criteria and were treated with glucocorticoid and immunosuppressant for more than one year, but had not yet reached the disease relief. After the eligible patients are given rapamycin in combination with conventional therapy at 0, 12, 24 weeks, we respectively collect the clinical symptoms, blood routine, urine routine, ESR, the absolute number of Th17 and Treg cells, the ratio of Th17/Treg, and the dosage of corticosteroids and immunosuppressant. Alleviation criteria: no clinical symptoms, inflammation normal range, no organ damage.

Results: The absolute number of Treg cells decreased significantly in peripheral blood of pSS patients compared with that of healthy controls. By rapamycin combined with conventional therapy, flow cytometry showed the absolute number of Treg cells in refractory SS patients was increased from 25.51 cells/μl (at week 0) to 27.88 cells/μl (at 12 weeks) and 29.6 cells/μl (at 24 weeks) ($P>0.05$) respectively. The ratio of Th17/Treg decreased from 0.38 (at week 0) to 0.21 (at 12 weeks) and 0.22 (at 24 weeks) ($P>0.05$). There was no significant difference in the usage of prednisone, whereas 5 patients gradually stopped using CTX at 24 weeks. Also, the dose of hydroxychloroquine and leflunomide were markedly diminished.

Conclusions: Our results suggest that rapamycin combined with the conventional treatment greatly alleviated symptoms of patients with pSS, and gradually reduced the use of DMARDs. The absolute number of peripheral Tregs decreased in pSS patients and restored by this combined therapy. It still needs to be further confirmed by large sample studies.

REFERENCES:

- [1] Ferro F, Marcucci E, Orlandi M, Baldini C, Bartoloni-Bocci E. One year in review 2017: primary Sjögren's syndrome. Clin Exp Rheumatol 2017 Mar-Apr;35(2):179–191. Epub 2017 Mar 15. Review.PMID: 28337967.
- [2] Zheng Y. The mTOR kinase differentially regulates effector and regulatory T cell lineage commitment. [J].Immunity 2009;30(6):832–844.

Acknowledgements: Wurujie contributed collection of information of outpatients. Wuqi contributed contacted and bought reagents.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4373

SLE, Sjögren's and APS – clinical aspects (other than treatment)

AB0538

INCREASED BODY MASS INDEX MAY NOT BE A RISK FACTOR FOR THE DEVELOPMENT OF LUPUS NEPHRITIS

Y.P. Chock¹, A. Danve¹, on behalf of Yale University School of Medicine, M. Petri², W. Fu². ¹Yale University School of Medicine, Connecticut; ²Johns Hopkins University, Baltimore, USA

Background: Studies have indicated that elevated body mass index (BMI) increases risk of Chronic Kidney Disease (CKD). Obesity is a low grade inflammatory state which leads to CKD by glomerulosclerosis. Systemic Lupus Erythematosus (SLE) is associated with high leptin levels and dyslipidemia. We hypothesised that obese SLE patients may be at increased risk of nephritis.

Objectives: We studied BMI as possible predictor for development of lupus nephritis (LN) in SLE.

Methods: We performed a retrospective cross sectional study on a longitudinal lupus cohort. Patients were enrolled from year 1987 to 2015. We compared demographics, clinical information, labs between patients with and without LN (table 1) and between patients with SLE with and without obesity. Mean and standard