CHANGES IN FREQUENCIES OF $CD4^+CD25^+FOXP3^+$ REGULATORY CELLS, $CD3^+CD8^+CD28^-$ CELLS AND TH17 SUBSET AND THEIR IMPACT OF THE COURSE OF THE DISEASE IN PATIENTS WITH LUPUS NEPHRITIS.

Marcelina Żabińska, Magdalena Krajewska, Katarzyna Kościelska-Kasprzak, Katarzyna Jakuszko, Marian Klinger

Department and Clinic of Nephrology and Transplantation Medicine, Wroclaw Medical University

Summary

The specific cause of SLE is unknown, although there is a range of immunological abnormalities in SLE, such as disturbances in T-cell homeostasis.

T regulatory cells (Tregs), a subset of $CD4^+$ cells which express the transcription factor FoxP3 are involved in peripheral tolerance maintaining. T helper type 17 (Th17) cells are associated with the pathogenesis of many chronic, inflammatory and autoimmune diseases. These two subtypes of $CD4^+$ T cells play opposite roles in immune tolerance and autoimmune diseases, while they share a common differentiation pathway. The imbalance of Treg/Th17 has been demonstrated in several autoimmune diseases.

Animal models of autoimmunity have also revealed that subpopulation of $CD3^+CD8^+CD28^-$ cells phenotype can act as immunomodulator, and play a role in autoimmune diseases. However the results of studies on the $CD3^+CD8^+CD28^-$ cells are also inconsistent since several studies describe $CD3^+CD8^+CD28^-$ as either immunosuppressive or cytotoxic.

Aims

The aim of the study is to inquire whether the quantitative changes of T cells subpopulations are related to the clinical status of patients with lupus nephritis.

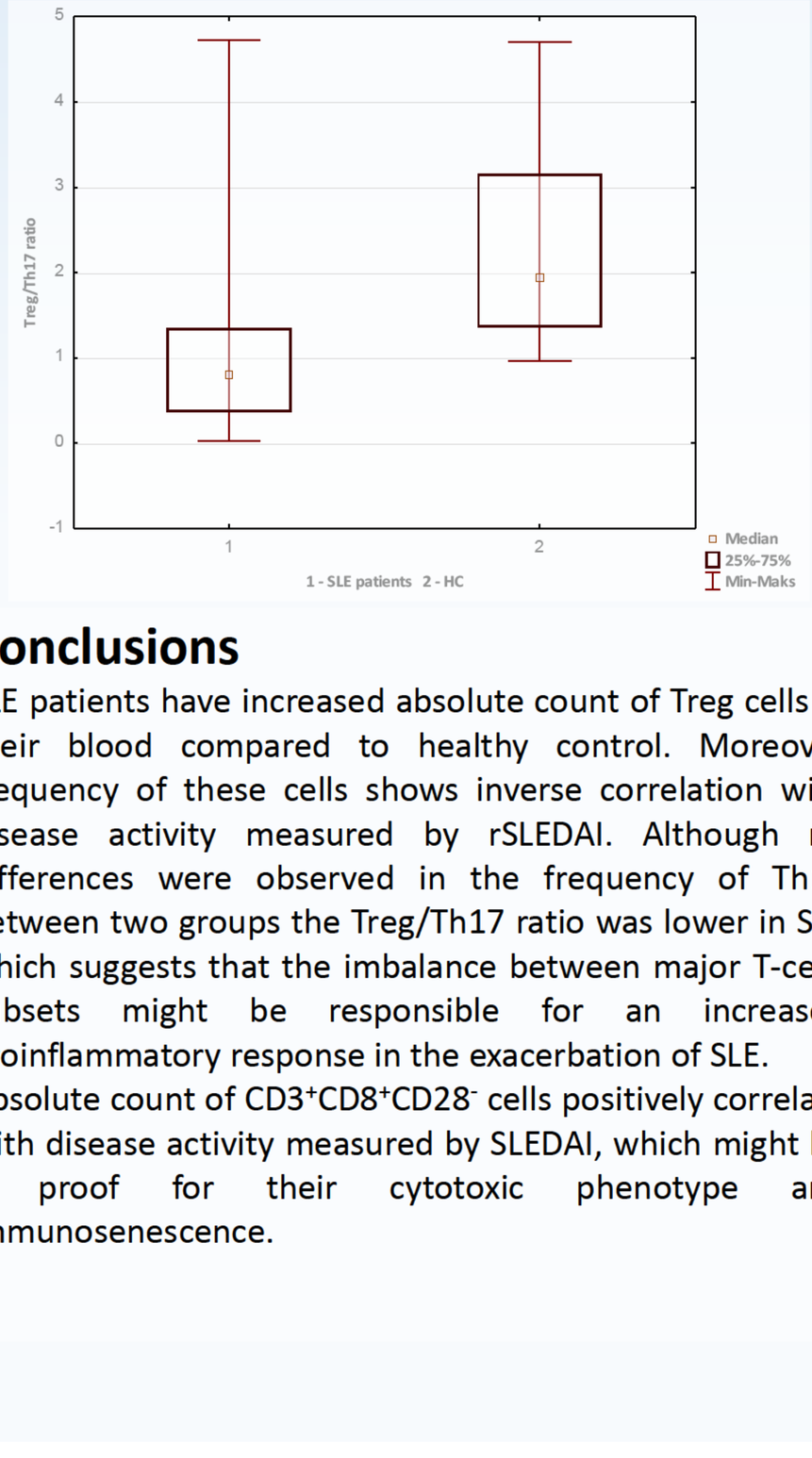
Material and Methods

54 adult SLE pts (96,3% female, mean age 36,5±13,7) were enrolled to the study. Disease activity at the time of evaluation was scored according to the Systemic Lupus Erythematosus Disease Activity Indexes (SLEDAI and rSLEDAI). Patients were divided into two groups according to their SLEDAI score and there were 15 patients in inactive (SLEDAI ≤ 5) and 39 in active (SLEDAI >5) phase of disease. When disease activity was measured by rSLEDAI scale, 14 inactive (rSLEDAI<4) and 40 active (rSLEDAI 4-16) patients were in two groups. Also 19 sex-and-age matched healthy volunteers (89,5% female, mean age 38,3±14,1) were enrolled to the study. We determined absolute count of $CD4^+CD25^+FOXp3^+$, $CD3^+CD8^+CD28^-$ and $CD4^+IL17^+$ subpopulations by flow cytometry. We compared the results with the disease activity measured by the SLEDAI and rSLEDAI scales. The experimental and clinical results were combined and statistically analyzed using STATISTICA 10 software.

Results

The patients with SLE presented significantly lower absolute count of $CD4^+CD25^+FOXp3^+$ cells compare to HC **(p<0,001).** No differences were observed in absolute count of Treg cells between active and inactive SLE patients measured by SLEDAI scale, but there was significant inverse correlation between decreasing absolute number of $CD4^+CD25^+FOXp3^+$ and disease activity measured by rSLEDAI scale **(rs=-0,292, p=0,033)**. No differences were observed in the frequency of Th17 cells between SLE pts and control group, which resulted in decreased Treg/Th17 ratio in SLE pts.

We also observed a statistically significant increase in absolute count of $CD3^+CD8^+CD28^-$ in SLE pts compare to HC **(p<0,001).** Moreover there was weak, but significant positive correlation between increasing absolute count of $CD3^+CD8^+CD28^-$ cells and disease activity measured by SLEDAI **(rs=0,281, p=0,039).**



Conclusions

SLE patients have increased absolute count of Treg cells in their blood compared to healthy control. Moreover frequency of these cells shows inverse correlation with disease activity measured by rSLEDAI. Although no differences were observed in the frequency of Th17 between two groups the Treg/Th17 ratio was lower in SLE which suggests that the imbalance between major T-cells subsets might be responsible for an increased proinflammatory response in the exacerbation of SLE.

Absolute count of $CD3^+CD8^+CD28^-$ cells positively correlate with disease activity measured by SLEDAI, which might be a proof for their cytotoxic phenotype and immunosenescence.

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Katarzyna Jakuszko

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