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SAT0347 DISEASE MODIFYING EFFECT OF ILOPROST IN PATIENTS WITH SYSTEMIC SCLEROSIS AND POSSIBLE ROLE OF CXCL4 CHEMOKINE

K. Stefanantoni[1], I. Sciarra[1], M. Vasile[1], R. Palazzo[2], L. Frasca[2], G. Valesini[1], V. Riccieri[1]. *[1]Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma; [2]National center for research and pre-clinical and clinical evaluation of drugs- Immune-mediated diseases UNIT, Istituto Superiore di Sanità (Nat. Inst. of Health), Rome, Italy*

Background: Iloprost is a synthetic prostaglandine used for vascular manifestation of Systemic Sclerosis (SSc), in particular it is indicated for active digital ulcers (DU) and severe Raynaud Phenomenon (RP) (1). It acts on several receptors such as IP and EP receptors and PPRs. Iloprost is also involved in the regulation of gene expression, fibrosis and inflammation (2,3,4). CXCL4 o Platelet Factor 4, is a 70KDa CXC-chemokine synthesized in megakaryocytes and plasmacytoid dendritic cells, released after platelet activation. In SSc, it seems to be higher in patients with early diffuse SSc and it correlates with mRSS and presence of PAH (5).
Objectives: To evaluate the effect of Iloprost on vascular manifestations, on disease activity and on serum levels of CXCL4 at baseline (T0) and after 1 month (T1), 3 months (T3) and 6 months (T6) of therapy.
Methods: 30 patients (M/F =1/29; mean age =58.2 yrs; mean disease duration =12.8 yrs) with established SSc according to ACR criteria, were enrolled. At T0, T1, T3 and T6 treatment with Iloprost at standard dosage we determined RP VAS, number of DU, European Scleroderma Study Group Activity Index (EScSGAI) and serum levels of CXCL4, measured using commercially available immunoassay kit (Human CXCL4/PF4 R&D SYSTEMS®). All patients underwent to a complete clinical, instrumental and laboratory evaluation.
Results: Regarding RP VAS, we found a statistically significant increase (p=0.04) at T3, corresponding to the colder winter period, while it decreased, although not significantly at T1 and at T6, where this reduction was significant compared to T3 values (p=0.0008). Considering the number of active DU, we have highlighted the same trend of the RP VAS. EScSGAI values showed a statistically significant reduction (p=0.03) comparing T3 to T6. Regarding CXCL4, we found significantly higher levels in SSc patients respect to a group of healthy controls (HC) (p=0.047). No significant difference was found in serum levels of CXCL4 at T0, T1,T3 and T6. Evaluating patients with higher levels of CXCL4 at baseline, respect to the average of HC values (CXCL4>25,000 pg/ml) (11/30 patients), we found that 7 subjects had a significant improvement in disease activity at T6 evaluated by EScSGAI (p=0.015). In these patients we also detected a significant reduction in T3 CXCL4 values (p=0.043) persisting and at T6, although not reaching statistical significance. Moreover higher basal levels of CXCL4 in patients with disease duration less of 60 months (p=0.05) and in patients with pericardial effusion (p=0.037) were detected. Besides we found significantly lower levels of CXCL4 in patients with DU history (p=0.049) and esophageal involvement (p=0.008).
Conclusions: Our study confirms the efficacy of Iloprost on vascular manifestation of SSc and also highlights its effect on the disease activity. Moreover this drug seems to influence, in a subgroup of patients, concentrations of CXCL4, an important chemokine involved in SSc pathogenesis that deserves further investigations.
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SAT0348 ASSOCIATION OF VITAMIN D DEFICIENCY WITH REDUCED IL10-PRODUCING REGULATORY B CELLS IN SYSTEMIC SCLEROSIS

A. Mavropoulos, C. Liaskos, A. Gkoutzourelas, C.G. Katsiari, D.P. Bogdanos, L.I. Sakkas. *Rheumatology and Clinical Immunology, University of Thessaly, School of Health Sciences, LARISSA, Greece*

Background: IL-10-producing regulatory B cells (Bregs), also known as B10 cells, are decreased and functionally impaired in patients with systemic sclerosis (SSc), particularly in those with SSc-associated interstitial lung disease (1). As serum 25-OH-vitamin D (vitD) levels are associated with clinical aspects in patients with SSc (2), we investigated whether there is any link between vitD levels and Breg levels.
Objectives: To assess whether or not vitD deficiency in SSc is associated with the percentages of circulating IL-10-producing Breg cells.
Methods: PBMCs and serum samples were isolated from 55 patients with systemic sclerosis. Serum VitD levels were measured using a commercially available sandwich ELISA kit. Phenotypic analysis of CD19, CD24, CD27, CD38 and intracellular expression of cytoplasmic IL-10 following bacterial CpG (ODN2006) and PMA/ionomycin stimulation was examined by flow cytometry using specific fluorochrome-conjugated monoclonal antibodies (BD Biosciences).
Results: Systemic sclerosis patients were divided into two groups (vitD deficient or not) based on a serum concentration cut off value of 20 ng/ml. The mean vitD levels in the deficient group were 14.11±3.6 ng/ml (n=17) whereas the mean vitD levels in the non-deficient group were 37.5±12.9 ng/ml (n=38). IL-10-producing B cells (B10 cells) were significantly decreased in vitD deficient patients compared to those with medium/high levels (p=0.02). CD19+CD27+ (memory) B cells were also significantly reduced in patients with VitD deficiency (p=0.004). In addition the ratio of naïve/memory B cells was significantly higher in VitD deficient patients (p<0.05). Within the memory B cell fraction, the CD19+CD27+CD24hi cells also known as phenotypic memory Bregs, were mostly decreased (p=0.001). There was no significant association between CD19+CD38hiCD24hi (transitional) Bregs and VitD levels.
Conclusions: Our data suggest that vitamin D deficiency may account for reduced B10 cells in systemic sclerosis
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SAT0349 EVALUATION OF STANDARD SWALLOWING FUNCTION IN ASSESSING ASPIRATION RISK FOR PATIENTS WITH SYSTEMIC SCLEROSIS

L. Yan, P. Yunfeng, Y. Mengru. *Department of Rheumatology, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Swallowing dysfunction is a common symptom of systemic sclerosis, which usually induce aspiration pneumonia to aggravate lung progress. It is necessary to screen swallowing disorders effectively at an early stage.
Objectives: To investigate the value of standard swallowing function assessment (SSA) in aspiration screening for inpatients with Systemic sclerosis.
Methods: SSA and Video fluoroscopic swallowing study (VFSS) were performed in 120 inpatients with Systemic sclerosis from March 2014 to September 2016.The sensitivity, specificity, positive predictive value and negative predictive value of SSA in the diagnosis of aspiration in patients were calculated by taking VFSS examination as the gold standard. The incidence of pneumonia in SSA-positive and SSA-negative patients were compared.
Results: The diagnostic sensitivity of SSA was 81.2%, the specificity was 75%, the positive predictive value was 68.6% and the negative predictive value was 90.3%. The incidence of pneumonia in SSA positive patients was higher than that in SSA negative patients (54.1% vs 28.3%) (P<0.01).
Conclusions: SSA is a valuable screening tool for the evaluation of aspiration risk in patients with Systemic sclerosis.
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SAT0350 DOES A SYSTEMIC SCLEROSIS PATIENT'S CLINICAL PHENOTYPE DEMONSTRATE HIS AUTOANTIBODY STATUS?

M. Boonstra[1], J.A. Bakker[2], M.K. Ninaber[3], N. Ajmone Marsan[4], T.W. Huizinga[1], J.K. de Vries-Bouwstra[1]. *[1]Rheumatology; [2]Clinical Chemistry and Laboratory Medicine; [3]Pulmonology; [4]Cardiology, LUMC, Leiden, Netherlands*

Background: Although antibody status has shown to improve clinical subsetting in Systemic sclerosis (SSc), it is far from perfect. For optimal clinical subsetting as well as for evaluating the possible pathogenic role of SSc specific antibodies, it is relevant to know to what extent clinical SSc phenotypes are determined by presence of these antibodies.
Objectives: To evaluate 1. if clinical relevant subsets of SSc patients are distinguishable using only clinical data, 2. how SSc specific autoantibodies are distributed among these subsets, and 3. whether adding antibody status to cluster analyses improves recognition of SSc subsets.
Methods: Using data from SSc patients of the Combined Care In Systemic Sclerosis (CCIS) cohort, Leiden University Medical Center, hierarchical clustering based on Ward Method was performed on the first obtained factor of principal component analysis of 7 organ systems (skin;lung;heart;kidney;muscle;vascular;gastro-