suppress immune-mediated muscle injury are needed. Glucagon-like peptide-1 (GLP-1) is a peptide hormone with a variety of functions. Although GLP-1 receptor (GLP-1R) agonists have been developed as an anti-diabetic therapy to promote insulin secretion, emerging data suggest that they have pleiotropic actions including anti-inflammatory effects and suppression of muscle wasting². We presumed that GLP-1R agonists have beneficial effect on PM to preserve and recover muscle strength.

Objectives: To examine the effect of a GLP-1R agonist on C protein-induced myositis (CIM), a murine model of polymyositis³, in monotherapy or in combination with prednisolone (PSL).

Methods: Muscle specimens of PM patients and CIM were examined with immunohistological staining for the expression of GLP-1R. The therapeutic effect of PF1801 (ImmunoForge), a GLP-1R agonist (5 mg/kg body weight (BW)/day), in monotherapy or in combination with PSL (20 mg/kg BW/day) on CIM was examined for grip strength, muscle weight and histological muscle inflammation.

Results: GLP-1R was expressed on the plasma membrane of muscle cells of PM patients and CIM. The expression levels were high in the area where inflammatory infiltrates were observed. The treatment of CIM with PF1801 in monotherapy or in combination with PSL suppressed the CIM-induced decrease in grip strength on day 14. The combination therapy with PF1801 and PSL ameliorated the CIM-induced muscle weight loss in quadriceps, while the monotherapy with PF1801 or PSL did not. The histological analysis of muscle specimens on day 14 of CIM revealed that the muscle inflammation was suppressed by the treatments with PF1801, PSL, or the combination of PF1801 and PSL. None of the mice in the combination therapy group developed histologically evident myositis, while the myositis was observed in 90%, 40% and 40 % of the mice in vehicle treated group, PF1801 treated group, and PSL treated group, respectively. The necrotic area of the muscle in CIM was also reduced in the mice treated with PF1801, PSL, or the combination of PSL and PF1801. The CIM-induced increase in spleen weight was suppressed by PF1801, PSL, or the combination of PSL and PF1801. The additive effect of PSL and PF1801 on the suppression of CIM-induced increase in spleen weight was observed.

Conclusion: PF1801 ameliorated CIM-induced muscle weakness and muscle inflammation in CIM. The combination therapy with PF1801 and PSL ameliorated CIM-induced muscle weight loss. PF1801 could be a novel therapy to recover muscle weakness and to suppress muscle inflammation in PM.

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SAT0296

SERUM LEPTIN LEVELS IN SYSTEMIC SCLEROSIS PATIENTS WITH ELECTROCARDIOGRAPHIC ABNORMALITIES

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Background: Electrocardiographic (ECG) abnormalities are described in 25-75% Systemic Sclerosis (SSc) cases and they are associated with other systemic manifestations as well as with a worse prognosis. There is an increasing need for clinical and laboratory biomarkers to ameliorate the diagnostic and therapeutic approaches to patients with ECG abnormalities, due to their actual low sensitivity and specificity. Adipokines are circulating proteins that appear dysregulated in SSc and leptin in particular is synthesized in response to inflammatory conditions and seems to play a proinflammatory and pro-fibrotic action in SSc. Interesting, many studies in the last years have underlined its role in the cardiac remodeling mechanisms and in the development of cardiac fibrosis in other chronic diseases.

Objectives: Aim of our study is to evaluate the role of leptin in the development of cardiac rhythm disorders (CRD) during SSc. Furthermore, by the analysis of the clinical and demographical parameters of our SSc patients, we tried to define other possible features associated with increased serum leptin concentration.

Methods: We included eighty-five SSc patients, fulfilling the 2013 ACR/EULAR classification criteria, attending the Regional Rare Disease Center of Policlinico Umberto I of Rome. Fifty presented significant CRD at non-invasive diagnostic techniques (12 Lead ECG, 24-hour Holter ECG). Demographic, clinical, conventional cardiovascular risk factors were examined; instrumental and laboratory assessments were obtained, together with ECG recordings. Thirty-five SSc patients without pathologic finding at ECG traces, matched for demographic and clinical features, were recruited as the control group. In all cases, after obtaining written informed consent, blood samples were taken to measure serum levels of leptin using an ELISA assay (Life Technologies-Italia).

Results: The fifty SSc patients with CRD (mean age 51±15 years; F:M 41:9) had pulmonary fibrosis (PF) in 32 cases (64%) and a BMI >25Kg/m² in 22 (44%) while in the control group of thirty-five SSc patients (mean age 49±16 years; F:M 33:2) PF was found in 15 (43%) and a BMI >25Kg/m² in 9 (35%); We detected significantly higher median values of serum leptin in SSc patients with CRD compared to the control group (12027 pg/ml IQR 12314 versus 6392 pg/ml IQR 7103; *p* 0,0009). Additionally, SSc patients with a BMI > 25kg/m² (31 cases) as well as those with PF (47 cases) showed a significantly higher median serum leptin levels compared to those with BMI <25kg/m² (13161 pg/ml IQR 13610 versus 8187 pg/ml IQR 8255; *p* 0,0008) and those without PF (11740 pg/ml IQR 11940 versus 7616 pg/ml IQR 7855; *p* 0,0079).

Conclusion: To our knowledge this is the first report on high serum levels of leptin in SSc patients with CRD that also confirms its increase in those cases with a BMI >25kg/m² and with PF, according to scientific literature data. The role of leptin in the pathogenesis of SSc remains unclear although it is already known its involvement in the development of cardiac fibrosis during other chronic diseases. On the basis of these results we speculate on leptin involvement in the pathogenesis of CRD during SSc, although further studies are needed with larger cohort of patients.

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SAT0297

DIFFERENTIAL PHENOTYPES OF DISEASE-SPECIFIC AUTO-REACTIVE B CELL RESPONSES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) carries the highest mortality burden among the rheumatic diseases. >95% of SSc patients harbor autoantibodies. Anti-topoisomerase antibodies (ATA) and anti-centromere antibodies (ACA) are most prevalent, mutually exclusive in individual patients, associate with distinct disease phenotypes and predict disease. Whether and how these auto-reactive B cell responses contribute to disease, however, is currently unclear.

Objectives: To delineate phenotypic and functional characteristics of anti-topoisomerase and anti-centromere specific B cell responses in individual patients with SSc.

Methods: Peripheral blood mononuclear cells (PBMC) obtained from ATA- and ACA-positive SSc patients were cultured without stimulation or in the presence of CD40L-expressing fibroblasts, IL-21 and BAFF. In addition, PBMC were depleted of circulating plasmablasts (CD19+CD20-CD27++) by fluorescence activated cell sorting (FACS), and isolated plasmablasts were cultured separately. ATA- and ACA-IgG and -IgA were measured in culture supernatants by ELISA. B cell