Conclusion: The DIAPS might be a valid score system for the assessment of APS-related damage and QoL.

REFERENCES:

- [1] Miyakis S, Lockshin MD, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006;4:295–306.
- [2] Grika EP, Ziakos PD, et al. Morbidity, mortality, and organ damage in patients with antiphospholipid syndrome. *J Rheumatol* 2012;39:516–523.
- [3] Amigo MC, Goycochea-Robles M V, et al. Development and initial validation of a damage index (DIAPS) in patients with thrombotic antiphospholipid syndrome (APS). *Lupus* 2015;24:927–934.

Figure 1. Relative involvement of the organ domains included in the DIAPS according to diagnosis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4295

Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models

AB0089

SILDENAFIL COUNTERACTS THE ACTIVATION OF CXCR3/CXCL10, -11 AXIS IN SCLERODERMA FIBROBLASTS EXPOSED TO REACTIVE OXYGEN SPECIES

C. Antinozzi¹, I. Dimauro¹, P. Sgrò¹, D. Caporossi¹, F. Del Galdo^{2,3}, L. Di Luigi¹.
¹University of Rome Foro Italico, Movement, Human and Health Sciences, Rome, Italy; ²University of Leeds, Institute of Rheumatic and Musculoskeletal Diseases, Leeds, United Kingdom; ³NIHR Biomedical Research Centre, University of Leeds, Leeds, United Kingdom

Background: Oxidative stress associated with vascular damage represents one the major contributor in the pathogenesis of systemic sclerosis (SSc) [1]. Indeed, different studies demonstrated that excessive free radicals production can contribute to the activation of fibrotic process in the skin and visceral organs [1]. CXCL10 and CXCL11, together with their receptor CXCR3, are involved in vascular damage and in fibrosis [2]. Furthermore, these chemokines have been proposed as biomarkers of vascular damage progression and severe SSc prognosis [3]. Emerging evidences highlight the beneficial effects of the phosphodiesterase type 5 (PDE5) inhibitor, sildenafil, to protect different cell types from reactive oxygen species (ROS)-induced DNA damage, *in vitro* [3]. This effect has been linked to modulation of CXCL10 concentration in different pathological conditions [4,5].

Objectives: Here we set out to investigate the effects of sildenafil, in modulating the CXCR3/CXCL10, -11 inflammatory axis in dermal fibroblasts exposed to oxidative stress, *in vitro*.

Methods: Human dermal fibroblasts isolated by SSc skin biopsies were treated for 24h with 100μM of hydrogen peroxide (H₂O₂), in the presence or not of sildenafil (1μM). Dermal fibroblasts from healthy skin were used as controls. CXCL10 and CXCL11 were evaluated in cell medium by luminex technology assay; expression of chemokine receptor (CXCR)3 and peroxisome proliferator-activated receptor (PPARγ) (a regulator of CXCL10,-11 mRNA) was evaluated by western blot assay.

Results: As showed in figure 1, SSc fibroblasts (grey bar) showed similar basal levels of CXCL10 (A) and CXCL11 (B) to healthy controls (black bar). H₂O₂ induced a significant increase of both chemokines only in SSc fibroblasts (by 4.6 fold for CXCL10 and by 4.2 fold for CXCL11) (*P<0.05 and **P<0.01 vs. c; #P<0.05 vs. healthy controls). Sildenafil pre-incubation reduced by approximately 50% the effects of H₂O₂ on chemokines release (Figure 1A and B) (§P<0.05 vs. H₂O₂), and reduced the expression of CXCR3 and PPARγ induced by hydrogen peroxide exposure (data not shown).

Conclusion: *In vitro* study on dermal fibroblasts support clinical studies to determine the efficacy of sildenafil in the preventing tissue damage and fibrosis in SSc, by reducing the pro-inflammatory activation induced by oxidative stress.

REFERENCES:

- [1] Di Luigi L, Sgrò P, Duranti G, Sabatini S, Caporossi D, Del Galdo F, Dimauro I, Antinozzi C. Sildenafil Reduces Expression and Release of IL-6 and IL-8 Induced by Reactive Oxygen Species in Systemic Sclerosis Fibroblasts. *Int J Mol Sci.* 2020 Apr 30;21(9):3161. doi: 10.3390/ijms21093161. PMID: 32365773; PMCID: PMC7246497.
- [2] Koper OM, Kamińska J, Sawicki K, Kemona H. CXCL9, CXCL10, CXCL11, and their receptor (CXCR3) in neuroinflammation and neurodegeneration. *Adv Clin Exp Med.* 2018 Jun;27(6):849-856. doi: 10.17219/acem/68846. PMID: 29893515.
- [3] Crescioli C, Corinaldesi C, Ricciari V, Raparelli V, Vasile M, Del Galdo F, Valesini G, Lenzi A, Basili S, Antinozzi C. Association of circulating CXCL10 and CXCL11 with systemic sclerosis. *Ann Rheum Dis.* 2018 Dec;77(12):1845-1846. doi: 10.1136/annrheumdis-2018-213257. Epub 2018 May 14. PMID: 29760155; PMCID: PMC6241615.
- [4] Giannattasio S, Corinaldesi C, Colletti M, Di Luigi L, Antinozzi C, Filardi T, Scolletta S, Basili S, Lenzi A, Morano S, Crescioli C. The phosphodiesterase 5 inhibitor sildenafil decreases the proinflammatory chemokine IL-8 in diabetic cardiomyopathy: in vivo and in vitro evidence. *J Endocrinol Invest.* 2019 Jun;42(6):715-725. doi: 10.1007/s40618-018-0977-y. Epub 2018 Nov 10. PMID: 30415310; PMCID: PMC6531405.
- [5] You N, Li J, Huang X, Wu K, Tang Y, Wang L, Li H, Mi N, Zheng L. COMMD7 activates CXCL10 production by regulating NF-κB and the production of reactive oxygen species. *Mol Med Rep.* 2018 May;17(5):6784-6788. doi: 10.3892/mmr.2018.8706. Epub 2018 Mar 8. PMID: 29532873.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.459

AB0090

THE BIOCHEMICAL BASIS OF ANIMAL MODEL OF SYSTEMIC SCLEROSIS

B. Doskaliuk¹, L. Zaiats¹, R. Yatsyshyn². ¹Ivano-Frankivsk National Medical University, Pathophysiology, Ivano-Frankivsk, Ukraine; ²Ivano-Frankivsk National Medical University, Internal Medicine #1 Clinical Immunology and Allergology, Ivano-Frankivsk, Ukraine

Background: Systemic sclerosis (SSc) is a heterogeneous autoimmune pathology, which detailed pathogenetic mechanisms of initiation and progression still require further investigations. It could be achieved with implementation of reliable experimental modeling techniques.

Objectives: This study was aimed to determine the state of oxidant/antioxidant system, dysregulation of collagen synthesis in laboratory animals and evaluate effectiveness of the considered model of SSc induction.

Methods: Thirty adult Wistar rats (220-240 g) were included in the study. The experimental group consisted of 20 animals, which received 3 subcutaneous injections of 0.5 ml of 5% sodium hypochlorite solution (NaClO) with an active chlorine concentration of 190 g / dm³ for 6 consecutive weeks. The control group consisted of 10 rats injected with isotonic solution according to the previously described scheme.

Results: The level of catalase in the experimental group was lower than in the control 9.69 ± 0.67 g / l and 11.1 ± 0.87 g / l respectively (p = 0.002). Protein oxidative modification (POM) products were higher in the experimental group (0.0722 ± 0.023 vs 0.0527 ± 0.023, p = 0.014). Malondialdehyde (MDA) was also higher in the experimental group compared to the control (4.30 ± 0.26 and 3.85 ± 0.23, respectively, p = 0.010). The concentration of oxyproline in the serum of laboratory animals subjected to repeated administration of NaClO was significantly higher compared to the control group (34.03 ± 5.01 and 33.23 ± 2.40, p = 0.020).

Conclusion: As a result of the use of NaClO for the reproduction of SSc in laboratory animals, there is a violation of oxidative-antioxidant homeostasis and increased fibrotic processes. These changes are comparable with those in SSc patients, which makes this modeling technique a promising tool for a detailed investigation of SSc pathogenesis.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.732