AB0574

BENEFITS OF ILOPROST IN LONG – TERM STABILIZATION OR IMPROVEMENT IN NEOANGIOGENESIS IN SYSTEMIC SCLEROSIS: A 15 YEARS OBSERVATION COHORT

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Background: In Systemic Sclerosis (SSc) fibrosis is due to microcirculation damage with capillary necrosis, arteriolar intimal proliferation and local ischemia. Iloprost (ILO) is used IV for the treatment of severe Raynaud phenomenon (RP) and digital ulcers (DU) in (SSc). We have already described (1) an improvement of peripheral vascularization with ILO, observed after 3 years treatment by capillaroscopy with an increase in the capillary number and mild regression of avascular areas and pericapillary oedema

Objectives: Our aim was to observe capillaroscopic changes in a cohort of 26 patients treated with ILO, once a month (25 – 50 ng each infusion) for an average time of 15 years

Methods: We evaluated the initial and 2019 capillaroscopic picture of 26 SSc patients (24W,2M; median age 63.8Y) in continuous treatment with monthly infusion of ILO from 2004 to today. 6/26 were SCL70 positive; the remainder was positive for anticentromere Ab

Results: We documented stability of capillaroscopic picture in 62% of patients, an improvement in 19% and a worsening (mainly from early to active pattern) in 19%. Low adherence to therapy was observed among the worsened patients. Out of 8 patients with onset ulcers, only 3 patients still have skin ulcers, all with late stable capillaroscopic picture from onset. We have not documented serious adverse events

Conclusion: Our observations confirm the efficacy and safety of ILO in the treatment of SSc even after many years of treatment, resulting in a stabilization of microvascular damage, independent of disease severity.

References:

- [1] Possible role of iloprost (stable analog of PG12) in promoting neoangiogenesis in systemic sclerosis. Faggioli P, Giani L, Mazzone A. Clin Exp Rheumatol. 2006 Mar-Apr;24(2):220-1. No abstract available

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AB0575

THE ROLE OF LONG-TERM AND INTENSIVE IV ILOPROST TREATMENT IN REDUCTION OF PULMONARY ARTERY PRESSURE AND PRO-BRAIN NATRIURETIC PEPTIDE (PBNP) IN SCLERODERMA PATIENTS

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Background: Systemic sclerosis (SSc) is a chronic immune-mediated connective tissue disease with heterogeneous organ involvement that reduces the life expectancy of these patients. In particular cardiopulmonary manifestations, such as pulmonary arterial hypertension (PAH), are currently the primary cause of death and stabilizing this condition may represent an important therapeutic goal (1,2). An increased NT-proBNP is predictors of PAH in SSc and use of these markers should result in improved PAH risk stratification (3). Some studies have suggested the role of intravenous iloprost in preventing the incidence of most severe vascular complications in long term treated patients (4).

Objectives: The aim of our study is to evaluate the evolution of the disease, with particular focus on cardiopulmonary function, in a group of consecutive patients chronically treated with iloprost at the Rheumatology Unit of Catania Hospital, Italy, from 2006 to 2019.

Methods: 68 SSc patients (58F, 52.88 ± 12.6 years). At baseline, 67.6%, 25% and 5.9% had a limited, diffuse and early scleroderma type respectively and 20.6% had interstitial lung disease. The follow-up period of the study was of 9.9 ± 2.9 years. Iloprost was administered with a regimen of 6 infusions per month (6 hours/day, 0.5-2.0 ng/kg/min) to treat secondary Raynaud's phenomenon (RP), diagnosed at an average age of 46.6 ± 13.7 years. We evaluated: skin score (SS), systolic pulmonary arterial pressure (PAPs), plane tricuspid annular systolic excursion (TAPSE), lung diffusing capacity of carbon monoxide (DLCO), forced vital capacity (FVC), alveolar volume (VA), DLCO/VA, pro-brain natriuretic peptide (pBNP), and NYHA class. We analyzed the patients as a whole group (68 subjects), as a group who continued the treatment (57 subjects) and as a group who stopped the treatment during the follow-up (11 patients).

Results: After the long follow up period in the study (almost 10 years) in the whole group of patients, PAPs and pBNP showed statistically significant improvement from baseline (30.91 ± 6.4 vs 27.36 ± 7.1 and 97.20 ± 69.3 vs 66.65 ± 44.3 respectively, p < 0.0001 for both) while the other parameters showed no significant changes: SS (4.70 ± 5.3 vs 3.86 ± 4.2 mm), TAPSE (22.07 ± 2.4 vs 22.06 ± 3.8 mm), DLCO (83.68 ± 13.5 vs 77.70 ± 14.6 mmol/kPa.min), FVC (107.09 ± 14.5 vs 107.72 ± 18.7 liters), VA (91.12 ± 13 vs 90.30 ± 14.4 liters), DLCO/VA (88.48 ± 13.5 vs 89.5 ± 16.3) and NYHA class (1.0 ± 0.0 vs 1.0 ± 0.0). A subgroup analysis indicated a significant improvement in addition to PAPs and pBNP also for skin score for 57 patients who continued the treatment (5.09 ± 5.7 vs 3.30 ± 4.2, p < 0.0001) and a significant worsening of this parameter as early as the first year of suspension (p < 0.05 year 1, p < 0.01 year 2 and 3) in 11 patients who stopped the treatment.

Conclusion: Cardiac involvement is recognised as a poor prognostic factor among systemic sclerosis (SSc) patients, significantly to mortality and N-Troponin B peptide may represent a surrogate marker for cardiac involvement in SSc, selectively identifying patients with severe impairment of cardiac function. Our intensive (6 infusions/month) and chronic regimen of iv iloprost administration seems improve the long-term evolution of disease in SSc patients, as suggested by the improvement of cardiopulmonary parameters and the significant improvement of SS.

References:

- [1] Rheumatology 51, 1027-36 2) Best Pract Res Clin Rheumatol.32, 223-240 3) Arthritis Rheum. 2008 58, 284-9 4) Rheumatol Int 2012;32:1933-8.

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AB0576

INCIDENCE AND CLINICAL MANIFESTATIONS OF RAYNAUD'S PHENOMENON IN RHEUMATIC DISEASES

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Background: Systemic sclerosis (SSc) is a connective tissue disease (CTD) most frequently associated with Raynaud's phenomenon – RP (96%), followed by mixed CTD (MCTD) (86%), systemic lupus erythematosus – SLE (31%), undifferentiated CTD (30%), rheumatoid arthritis – RA (22%) and Sjogren's disease – SD (13%)¹. RP can manifest as a classical triple-colour change with pallor (ischaemic phase) followed by cyanosis (deoxygenation) and erythema (reperfusion)^{2,1}. However, this triple-colour change only occurs in 19% of cases^{2,3}. Majority of patients report an episodic double-colour change, consisting of pallor and cyanosis, pallor and erythema or cyanosis and erythema². In a 4.8-year follow-up, 37.2% of RP patients developed rheumatic diseases (RD), 8.1% had other causes, in 54.7% RP remained primary⁴.

Objectives: To study the incidence and manifestations of secondary RP in RD.

Methods: A questionnaire survey conducted in 230 patients with RD.

Results: RP was detected in 45.6% of RD patients (n=105), 54.4% of patients with RD had no RP (n=125). RP was 4 times more frequent in females than in males (F:M 4:1). In RP group, 87 patients (82%) had autoimmune RD: SSc (55.2%), SLE (17.1%), RA (6%), dermatomyositis (3.8%), cross syndrome (3.8%), MCTD (1.9%), SD (0.9%).

Only 84% of RP patients had positive answers to all three questions that characterize RP (1. Is there an unusual sensitivity of fingers to cold? 2. Do fingers change color when exposed to cold? 3. Do they turn white and/or bluish?). Biphasic color changes (whitening-blueness; whitening-redness; blue-redness) were observed in 33 (31.4%) patients with RP, three-phase changes – in 32 patients (30.5%). Blueness of fingers to cold was more frequent in SLE than in SSc (p=0.027). Redness of fingers to cold occurred more often in cross syndrome, MCTD, SD, RA, vasculitis than in SSc (p<0.001) and in vasculitis than in SLE (p=0.035). In SSc patients, whitening of fingers to cold was more common than redness (p=0.037) and two-/three-phase changes of fingers color in the cold were more frequent than single-phase changes (p<0.001).

The frequency of RP attacks was detected more than once a day in 44 (42%) patients. In 73% of cases, RP did not show signs of deep digital ischemia. Digital ulcers (active) were observed in 13 (12.3%) patients, fractures in a finger area – 23 (21.9%), digital scars – 15 (14.2%), phalange amputations – 7 (6.6%).

Conclusion: Patients with RD and secondary RP most often have SSC (55%), less often – SLE (17%), RA (6%), DM (3%). In SSC and SLE patients, Raynaud's reddening of fingers to cold is less common than in other RD. In SSC, two-/three-phase changes of fingers color in the cold are more frequent than single-phase changes. In SLE, fingers turn blue in the cold more often than in SSC.

References:

- [1] Prete M, Fatone MC, Favoino E, Perosa F. Raynaud's phenomenon: from molecular pathogenesis to therapy. *Autoimmun Rev* 2014;13:655–67.
- [2] Linnemann B, Erbe M. Raynaud's phenomenon – assessment and differential diagnoses. *Vasa* 2015;44:166–77.
- [3] Heidrich H, Helms J, Fahrigr C, Hovelmann R, Martini N. Clinical characteristics of primary, secondary and suspected secondary Raynaud's syndrome and diagnostic transition in the long-term follow-up. A retrospective study in 900 patients. *Vasa* 2008;37 (Suppl. 73):3–25.
- [4] Pavlov-Dolijanovic S, Damjanovic NS, Vujasinovic Stupar NZ, Radunovic GL, Stojanovic RM, Babic D. Late appearance and exacerbation of primary Raynaud's phenomenon attacks can predict future development of connective tissue disease: a retrospective chart review of 3035 patients. *Rheumatol Int* 2013;33:921–6.

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AB0577

ENDOTHELIAL DYSFUNCTION AND ATHEROSCLEROSIS IN SYSTEMIC SCLEROSIS: A MULTIPARAMETRIC ANALYSIS USING IMAGING TECHNIQUE AND LABORATORY MARKERS OF INFLAMMATION AND VASCULAR FUNCTION: SCLERODERMA CV RISK STUDY

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Background: Systemic sclerosis (SSc) patients have an increased risk for atherosclerotic cardiovascular disease (CVD), possibly mediated by inflammatory and fibrotic mechanisms¹. However, pathogenesis of accelerated atherosclerosis in SSc remains to be elucidated. Endothelial dysfunction is the key initial event in atherosclerosis. Predictors for rapid evolution of cardiovascular complications would be highly desirable for CV risk stratification. This study aims to assess endothelial function and atherosclerosis in SSc, in context of markers of inflammation and vascular function in SSc patients.

Objectives: To assess endothelial function and atherosclerosis in SSc in context of markers of inflammation and vascular function in SSc patients.

Methods: A cross-sectional study was performed in 20 SSc patients meeting the 2013 European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) classification criteria and 18 healthy controls matched for age and sex. Flow-mediated dilatation (FMD) assessed by AngioDefender and CIMT measured ultrasonographically. Disease-specific measures included: Disease duration, Modified Rodnan Skin Score (mRSS), EUSTAR activity score in SSc. We also assayed markers of inflammation, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), proinflammatory cytokines (interleukin IL-1, IL-6, and IL-17), and endothelial dysfunction including lipids, serum nitrite and TBARS (marker of oxidative stress). Quality of life measured by Scleroderma Health Assessment Questionnaire (SHAQ).

Results: FMD is significantly lower in SSc patients compared with controls (6.13±0.35% vs. 9.12±0.25%, p<0.05). CIMT is significantly higher in SSc patients compared with controls (0.071±0.04cm vs. 0.035±0.02cm p<0.05). Compared with controls, SSc patients had significantly (p<0.05) elevated mRSS, EUSTAR score, ESR, CRP, IL-1, IL-6, IL-17, nitrite, TBARS and SHAQ whereas HDL levels are significantly reduced in SSc compared with controls (p<0.05). In SSc, FMD inversely correlated with EUSTAR score, mRSS, IL-6 (Fig. 1A), serum

nitrite (Fig. 1B), TBARS (Fig. 1C) and CIMT (Fig. 1D). CIMT positively correlated with age (Fig. 2A), disease duration, CRP (Fig. 2B) and IL-17 (Fig. 2C) and inversely correlated with HDL (Fig. 2D) (p<0.05).

Conclusion: In the present study, FMD and CIMT are impaired in SSc, indicating endothelial dysfunction and accelerated atherosclerosis, respectively. EUSTAR score, mRSS, IL-6, serum nitrite, CIMT and TBARS predicted endothelial dysfunction. Age, disease duration, CRP, IL-17, HDL and impaired FMD predicted accelerated atherosclerosis. SSc-related inflammatory mechanisms (IL-6, IL-17) and markers of vascular function (CRP, serum nitrite and TBARS) may all be involved in the development of vascular disease in SSc. Cytokine-triggered inflammation mediated by nitrite and TBARS is associated with endothelial dysfunction and accelerated atherosclerosis in SSc. These markers would possibly serve as predictors of endothelial dysfunction and atherosclerosis and more importantly therapeutic targets to prevent premature atherosclerosis and cardiovascular disease in SSc.

References:

- [1] Pagkopoulou E, Poutakidou M, Garyfallos A, Kitas G, Dimitroulas T. Cardiovascular risk in systemic sclerosis: Micro- and Macro-vascular involvement. *Indian Journal of Rheumatology* 2017;12:S211-7.

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AB0578

LONG-TERM TOLERABILITY OF AMINAPHTONE IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS IN CONCOMITANT STANDARD THERAPY

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