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FRI0231

TREATMENT OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS: PROSPECTIVE COHORT STUDY

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Background: Digital ulcer (DU) is a common clinical manifestation in patients with systemic sclerosis (SSc). About 70% of patients with SSc experience DUs during the first 10 years, which limit daily activities and may result in digital gangrene or amputation. Several vasoactive/vasodilating agents have been suggested for treatment, but few studies have compared the efficacy of those drugs.

Objectives: The objective of our study was to compare the efficacy of medical treatment for SSc related-DUs, focusing on endothelin receptor antagonist (ERA) and phosphodiesterase-5 inhibitors (PDE5inh).

Methods: In this prospective observational cohort study, we recruited patients who had one or more active SSc-related DUs and newly started or changed a medical treatment for SSc-related DUs from 13 medical centers in South Korea. The primary outcome was to compare the time to resolution of cardinal DU (CU) according to the treatments. The secondary outcomes included changes in the size or number of CU and changes in the number of DUs. CU was defined as the most clinically significant DU chosen by the investigators. Patients were followed up at every 4 weeks after enrollment until 12 weeks and finally at 24 weeks.

Results: Seventy-one patients were enrolled. Seven patients were excluded due to follow-up loss or withdrawal of consent. A total of 64 patients were analyzed. Seventy-eight percent (n=50) were female. The mean age at enrollment was 49.6 ± 11.6 year-old, and the mean disease duration was 7.1 ± 5.9 years. Twenty-eight patients (43.8%) were limited SSc. Forty-nine patients (n=76.6%) started ERA treatment (bosentan=49). Eleven patients (17.2%) started PDE5inh treatment (n=9 for sildenafil, n=1 for udenafil, and n=1 for tadalafil). Four patients who started medication other than ERA or PDE5inh classified as other treatment groups. Seventeen patients (26.6%) were on background calcium channel blockers (CCBs). CU healed in 25 patients (39.1%) at 12 weeks and 43 patients (67.2%) at 24 weeks. The mean time to heal CUs were 54.4 ± 22.7 days at 12 weeks and 91.6 ± 49.2 days at 24 weeks. Time to heal CU was comparable among patients on ERA, PDE5inh, and others (p=0.53, figure 1). The CU area was comparable among the three groups at baseline, 12, and 24 weeks. The mean area of CU in patients on ERA at baseline at 12, and 24 weeks was 21.3±19.4 mm², 8.2±14.6 mm², and 4.6±7.7 mm², respectively. The mean area of CU in patients with PDE5inh at baseline at 12, and 24 weeks was 26.2±28.1 mm², 3.5±3.6 mm², and 1.3±4.3 mm². New DUs developed in 4 patients (8.3%) in ERA, whereas 4 patients (40.0%) in PDE5inh at 4 weeks. The use of ERA was significantly associated with less new DUs development than the use of PDE5inh at 4 weeks follow-up (RR for developing new DU patients on ERA, 0.21; 95% CI 0.06-0.70; p=0.02). At 24 weeks follow-up, none of the patients on CCB developed new DUs.

Conclusion: The time to heal CU for ERA and PDE5inh users was comparable in the current study. ERA treatment was associated with reduced new DU occurrence compared with PDE5inh treatment. None of the patients with CCB treatment developed new DU development at 24 weeks.

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Figure 1

FRI0232

ALTERED FIBRIN CLOT PROPERTIES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Vasculopathy in Systemic sclerosis (SSc) is connected with the activation of coagulation. However, the fibrinolytic activity still remains unclear since the most preliminary evidences are discordant (1, 2).

Objectives: To assess the haemostatic function, fibrin clot density and clot lysis time in SSc patients and healthy controls (HC) to determine their relation to disease findings.

Methods: Patients who fulfilled the 2013 ACR/EULAR SSc criteria and have never been treated with endothelin receptor antagonist, phosphodiesterase 5 inhibitors or prostanoids were eligible. Our study included 58 SSc patients [36 limited (lcSSc) and 22 diffuse cutaneous SSc (dcSSc)] and 46 sex/age-matched HC. Clinical evaluation of patients was performed, including high-resolution CT (HRCT), pulmonary function tests and the revised EUSTAR activity index. The interstitial lung disease (ILD) group (n = 15) was defined as moderate or severe changes on HRCT, with a forced vital capacity (FVC) < 85% predicted, without evidence of significant pulmonary arterial hypertension. The serum concentration of ICAM1 and von Willebrand factor antigen (VWF) were measured by ELISA. Haemostatic potential parameters; including overall haemostasis (OHP), overall coagulation (OCP) and overall fibrinolysis (OFF) potential, were assessed and endogenous thrombin potential (ETP) was determined. Maximum absorbance (Cmax), reflects the fibrin clot density and clot lysis time (Lys50t0), reflects fibrinolytic susceptibility, were calculated from OHP and OCP curves (3). Fibrin structure was visualised using scanning electron microscopy (SEM).

Results: The OFF value was significantly decreased, Lys50t0 prolonged (p<0.05), while OHP and ETP were increased (p<0.05) in patients. In dcSSc group ETP, OHP, Cmax and Lys50t0 were higher compared to HC (p<0.05). In SSc group, a positive association was found between coagulation parameters (OCP, OHP, Cmax) and the erythrocyte sedimentation rate (ESR), fibrinogen and ICAM1 (respectively p<0.05). Lys50t0 was positively correlated with ICAM1, ESR and VWF (respectively p<0.001, p<0.05, p<0.05). An inverse correlation was found between Cmax and both the diffusing capacity of the lungs for carbon monoxide (r=-0.408, p<0.01) and FVC (r=-0.318, p<0.01). Increased Cmax was found in ILD respect to HC (p<0.01). Denser plasma clot was associated with active disease (p<0.01). Longer Lys50t0 was observed in pitting scars group (p<0.01). Prolonged Lys50t0 was independently predicted by ICAM1 (OR 1.12, 95% CI 1.03-1.2, p<0.01).

Conclusion: Our results provide evidences of denser plasma fibrin clot among patients with lung involvement and impaired fibrinolysis, selectively presented among SSc patients with pitting scars. Thus, these patients might be at risk for thrombotic complications. Raised ICAM-1 levels could reflect impaired fibrinolysis, giving insight the important role of this molecule in endothelial homeostasis.

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A

B

Figure 1. SEM images of fibrin network in 1 representative sample from a SSc (A) and 1 from HC sample (B).

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FRI0233

IMPACT AND ADHERENCE TO THE MEDITERRANEAN DIET IN SYSTEMIC SCLEROSIS ITALIAN PATIENTS: CORRELATION WITH GASTROINTESTINAL SYMPTOMS, MOOD DISTURBANCES AND QUALITY OF LIFE

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Background: Gastrointestinal involvement (GI) is a common feature of systemic sclerosis (SSc) and can be highly disabling, representing a major cause of morbidity and reduced quality of life (QoL). The impact of dietary habits on GI symptoms, mood and QoL has not been extensively evaluated.

Objectives: To evaluate the adherence to the Mediterranean Diet (MD) in an Italian multicenter cohort of SSc patients, and its impact on GI symptoms and other disease features, depression, anxiety and overall QoL.

Methods: Consecutive SSc (ACR/EULAR2013) patients from 4 Italian cohorts were enrolled. Dietary habits and adherence to the MD were assessed using the 14-item MEDAS and QueMD questionnaires. Presence and severity of depressive/anxious symptoms and QoL were evaluated with the Hospital Anxiety and Depression Scale (HADS) and the SSc-HAQ (S-HAQ). GI symptoms were assessed with the Reflux Disease Questionnaire (RDQ) and the UCLA SCTC GI Tract 2.0 questionnaire (USG). Associations with patients' lifestyle, disease characteristics, and nutritional status were explored.

Results: 265 patients (94.7% females; age 55.8±13.6 years; disease duration 9.1±7.0 years; diffuse SSc 31.8%; Scl70+35.8%; ulcers 23.4%; ILD 29.4%; BMI 23.7±4.4 Kg/m²; obese 11.3%, overweight 23.4%, underweight 4.9%) were enrolled.

Overall MD adherence was moderate (7.5±1.9) according to MEDAS and it correlated with QueMD score (4.53±1.96) (R=-.371, p<0.001). MD adherence was optimal in 39 patients (14.7%), more frequently from Central-Southern Italy (p=0.036); 189 patients (71.3%) had a good and 37 (14.0%) a poor MD adherence.

GI symptoms were moderate/severe according to USG in 37 (14.0%) patients (USG: 0.41±0.40), and heartburn was the most common GI symptom (35.2%). The prevalence of significant anxiety and depression was 24.1% and 17.0%.

An inverse correlation was found between MD adherence and mood disturbances at HADS (MEDAS; R=-0.181, p=0.04), work impairment (QueMD; R=-0.247, p=0.005) and reduced QoL, both for GI (constipation at USG: R=-0.133, p=0.032) and general S-HAQ items (bowel: R=-0.181, p=0.04; severity R=-0.202, p=0.01; Raynaud: R=-0.217, p<0.001; ulcers: R=-0.207, p=0.01). MD adherence directly correlated with lung function (MEDAS; R=0.181, p=0.023 for FVC and R=0.170, p=0.03 for DLCO). Patients with MD optimal adherence had lower HADS depression (p=0.04) and S-HAQ scores (HAQ, p=0.04; Raynaud, p=0.005; ulcers, p=0.02) and lower work impairment and lost work time (p=0.03). No significant correlation emerged between MD adherence and BMI, or specific symptoms. Depression and anxiety directly correlated with the severity of reported upper GI symptoms according to both scales (RDQ-GERD: R=0.261, p=0.001; USG: R=0.263, p<0.001) and general S-HAQ items (HAQ: R=0.136, p=0.032; severity R=0.233, p<0.001; bowel: R=0.135, p=0.04; breath: R=0.133, p=0.03; ulcers: R=0.132, p=0.037). Results were confirmed after exclusion of psychiatric (11.7%) and fibromyalgic (15.5%) patients.

Conclusion: Unsatisfactory MD adherence is associated with a low mood, impaired QoL, work impairment, GI and vascular symptoms in Italian SSc patients. The promotion of a healthy lifestyle could positively impact on QoL and disease status of SSc patients.

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FRI0234

A HIGH NEMO SCORE IN VIDEOCAPILLAROSCOPY IS PREDICTIVE OF FUTURE DEVELOPMENT OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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