FRI0234

FACTORS ASSOCIATED WITH THE DEVELOPMENT OF NEOPLASIA IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is characterized by lymphocytic infiltration of the exocrine glands. These patients have a higher risk than the general population of developing non-Hodgkin lymphoma (NHL). This risk also increases with the time of evolution of the disease. pSS is also associated with the development of non-hematological cancer such as thyroid, digestive or gynecological among others.

Objectives: The aim of the study is to explore the association between the development of neoplasia and demographic, clinical or therapeutic factors in pSS.

Methods: The SJOGRENSER registry is a multicenter, cross-sectional study of patients with pSS who meet the American-European consensus criteria of 2002, of 33 Spanish rheumatology units. The demographic, clinical, analytical, therapeutic and neoplastic data were collected through review of the clinical records and interviews with the patients. Previously, all the patients signed informed consent and the approval of the local ethic committees was obtained. Descriptive statistics was used for the analysis of the data. The chi-squared test was used to establish the statistical associations and it was considered a $p < 0.05$ as significant. Bivariate logistic regression models were used to identify the effect of each independent variable on the main variable (neoplasia); the multivariate analysis was used to establish the independent effect of the patient characteristics associated with the dependent variable.

Results: Four hundred and thirty-seven patients were included in SJOGRENSER Registry (female gender 95.19%; median age 58.3 years). We found 30 patients (6.86%) with neoplasia (3 of them with more than one neoplasia): 7 with lymphomas (23.3%) (4 MALT lymphomas, 2 Hodgkin's lymphomas, 1 immunocytoma), 9 with gynecological neoplasia (30%), 2 with digestive malignancies, 2 with hematological, 2 with endocrine, 6 with malignancies in other locations, 3 with multiple myeloma and 2 patients with Waldenstrom macroglobulinemia. The results of the bivariate analysis are shown in the table. The factors significantly associated with the development of neoplasia were older age, glandular inflammatory involvement, lung involvement and use of rituximab. The age at diagnosis of the disease tended to be higher in the group with neoplasia (50.1 ($\pm$ 12.9) vs 54.7 ($\pm$ 11.7), $p = 0.059$). In the multivariate analysis, positive associations were found for the development of neoplasia in older patients (OR 1.045; CI95% 1.010-1.081), patients with glandular inflammation (OR 3.104; CI95% 1.396-6.906), and use of rituximab (OR 3.745; CI95% 1.386-10.118).

Variable	Neoplasia -	Neoplasia +	p
Age (years)	58.3	63.6	0.023
Glandular inflammation (%)	31	53.3	0.012
Lung involvement (%)	8.9	23.3	0.010
Rituximab (%)	6	23.3	<0.001

Conclusion: Thirty (6.86%) patients with pSS from the SJOGRENSER registry developed some neoplasia; the most frequent was gynecological, followed by lymphoproliferative processes. Older age, glandular inflammatory involvement and use of rituximab (presumably indication bias) were associated with the presence of neoplasia.

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FRI0235

DIFFERENCES BETWEEN MALE AND FEMALE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTER EXPERIENCE OVER 20 YEARS OF FOLLOW-UP

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown etiology involving multiple organ systems. It affects predominantly women, and according to different reports only 4–22% of the lupus population is male. Sex differences may influence the clinical and serological expression, therapy and outcome, but the current results varies among different countries and different ethnic groups (1-3). Less is known about the clinical course of male SLE during the follow-up due to the small number of cases collected, but male sex might be a poor factor in SLE prognosis (4-9).

Objectives: The aim of this work was to analyze our male and female SLE patients with an ongoing follow-up.

Methods: Cumulative clinical, serological manifestations, concomitant diseases of patients belonging to the historical SLE cohort with at least one evaluation in the past 15 months were collected from clinical charts. For these patients data regarding the overall and ongoing treatments, damage index (SDI), activity index (SLEDAI-2K) during the last 12 months were collected. For statistical analysis was used Chi-squared test, Fisher exact test, Student T test or Wilcoxon-Mann Whitney when appropriated.

Results: Out of the 550 SLE patients registered until may 2018 we have included for this analysis 345 patients with an active follow-up, 31 males and 314 females, with a male to female ratio of 1:10. A higher number of SLE male had disease onset (13% vs 1.6%) and diagnosis (16% vs 1.6%) after 60 years compared to female ($p=0.001$; OR 9.1; 95%CI 1.92-42.56 and $p<0.0001$; OR11.8; 95% CI 2.73-51.56 respectively). The most relevant differences among male and female patients are reported in the table 1. Males more frequently presented discoid lesions, renal involvement, polyneuropathy and leukopenia compared to female SLE. No difference regarding disease activity during the last 12 months measured by SLEDAI was found. Regarding the damage index, males showed a higher mean SDI and number of patients with a severe damage (SDI>2) compared with women. Analyzing treatment prescribed since the diagnosis of SLE we collected some relevant differences: antimalarials were less prescribed in males than females (87%vs 97%, $p=0.02$; OR 0.19; 95%CI 0.051–0.825), whereas mycophenolate mofetil was more frequently used in males (63%vs36%, $p=0.005$ OR 3.0 95% CI1.3- 6.8). Finally, significant differences regarding the ongoing treatment are reported in table 1: mycophenolate mophetile was more frequently prescribed in males (84,2 vs 25,6) and a highly suggestive trend of significance toward a greater use of steroids in males was also found.

	SLE male N=31 (%)	SLE female N=314 (%)	P value
Clinical and serological manifestation			
Age at the onset (mean $\pm$ SD)	36.2 $\pm$ 15	29 $\pm$ 11.3	<0.001
Age at the diagnosis (mean $\pm$ SD)	39.13 $\pm$ 13.8	30.5 $\pm$ 11.4	<0.001
Discoid lesion	8 (25.8)	36 (11.5)	0.01, OR=3.25, 95%CI 1.236-8.610
Renal involvement	18 (58.1)	116 (36.9)	0.035, OR 2.36, 95%CI 1.055-5.33
Neurological involvement	13 (41.9)	48 (15.3)	0.001, OR 4.8, 95%CI 1.718-13.260
Polyneuropathy	5 (16.1)	7 (4.6)	<0.001, OR 4.43, 95%CI 1.13-32.52
Leukopenia	12 (38.7)	60 (34.5)	0.02, OR 2.67, 95%CI 1.14-6.17
Damage			
SDI (mean $\pm$ SD)	1.94 ($\pm$ 1.83)	1.26 ($\pm$ 1.55)	0.018
Number of patients with SDI=1	24 (77.4)	168 (53.2)	0.01
Number of patients with SDI>2	10 (32.3)	42 (13.3)	0.011, OR 3.08, 95%CI 1.25-7.48
Ongoing treatment			
Steroids	27 (87.1)	238 (75.8)	0.30
Mycophenolate mofetil	16 (51.6)	43 (13.7)	<0.0001, OR 6.72, 95%CI 2.90-15.62

Conclusion: Our study confirmed the presence of differences between male and female SLE patients, both on clinical manifestations and also during the disease course. Our results on currently followed male SLE confirmed that these patients have a more severe disease, in particular with renal or neurological manifestations, that could justify the higher use of mycophenolate mofetil and the higher SDI compared to female SLE.

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FRI0236

MIGHT A 12-WEEK AEROBIC EXERCISE INTERVENTION IMPROVE PATIENT-REPORTED OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

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Background: Despite the relevant advance in treatment options and survival rates in systemic lupus erythematosus (SLE), patient's quality of life (QOL) and other patient-reported outcomes (PROs) do not seem to improve accordingly [1]. PROs provide valuable information about the patient's perceptions across a variety of domains that should be considered in a successful management of this condition [2]. Exercise seems to be a safe way to improve cardiorespiratory fitness [3], and could have also a positive influence on PROs in SLE.

Objectives: To evaluate the effects of 12-week aerobic exercise intervention on PROs (QOL, depression, stress, and fatigue) in women with SLE.

Methods: These are secondary outcomes of a non-randomized clinical trial [NCT03107442]. A total of 58 participants with SLE were assigned to exercise group ($n=26$) or control group ($n=32$). The exercise intervention followed the American College of Sports Medicine guidelines, and consisted of 12-week progressive aerobic exercise on a treadmill (2 sessions/week) between 40%-75% of the individual's heart rate reserve [3]. Attendance of $\geq 75\%$ was set for inclusion in the analyses. The control group received verbal information about a healthy lifestyle. At baseline, and at week 12, PROs were assessed including the physical and mental summary scores of the 36-item Short-Form Health Survey (SF-36), depression (Beck Depression Inventory; BDI-II), perceived stress (visual analogue scale) and fatigue (Multidimensional Fatigue Inventory; MFI-20). A total of 49 women with SLE (age: 44.5 ± 14.2 years) completed all the assessments (exercise=21; control=28) and were included in the per-protocol (primary) analyses. The exercise and control group were comparable in age, disease duration and SLE activity, sociodemographic characteristics, and BMI at baseline, although there were differences in BDI-II scores. Baseline values and BDI-II values were used as covariates in the analyses.

Results: In comparison to the control group, the exercise group showed a significant reduction in general fatigue (mean difference -2.11 units; 95% CI -4.18 to -0.04; $P=0.046$) and physical fatigue (mean difference -3.90 units; 95% CI -6.3 to -1.5; $P=0.002$) following the intervention. There were no between-group differences in the changes from baseline to week 12 either in physical ($P=0.828$) or mental ($P=0.767$) QOL, depression ($P=0.498$), perceived stress ($P=0.247$) or other fatigue dimensions (mental, reduced motivation, reduced activity, all $P>0.05$).

Conclusion: The results of this study suggest that 12 weeks of progressive aerobic exercise might improve relevant dimensions of fatigue in women with SLE, despite absence of effects on QOL, depression or perceived stress.

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FRI0237

OMEGA-3 AND OMEGA-6 FATTY ACIDS IN SJÖGREN'S SYNDROME: CLINICAL IMPLICATIONS AND THEIR ASSOCIATION WITH INFLAMMATION

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Background: Essential ω -3 and ω -6 fatty acids (FA) are natural modulators of inflammation activity; however, their role in primary Sjögren's syndrome (pSS) is unknown.

Objectives: To evaluate the intake and serum levels of ω -3 and ω -6 FA in patients with pSS, and to correlate them with ocular and oral signs and symptoms, disease activity as well as with the presence of a panel of inflammatory chemokines/cytokines in saliva and tears.

Methods: We included 108 patients with pSS according to EULAR/ACG criteria. We excluded patients under ω -3 and ω -6 supplementation. Dietary information was obtained from a semiquantitative food frequency questionnaire of one-day reminder (applied by a trained interviewer), and processed using computerized nutritional analysis software. Fasting blood samples were collected. We measured the serum levels of ω -3 (α -linolenic acid [α -L], eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA]) and ω -6 (linoleic acid [LA], arachidonic acid [AA]) using gas chromatography flame ionization. We assessed the ESSDAI score, ESPPRI, OSDI, tear film break-up time, Schirmer-I test and the SICCA Ocular Staining Score (OSS). In a subgroup of patients, we obtained tears and saliva samples that were frozen at -86°C until assayed. Once defrosted, the levels of CXCL8, CXCL10, CCL2, IL-22 and IL-21 in saliva and CXCL8, CXCL10, CCL2 and CXCL9 in tears were measured by Luminometry.

Results: The median age was 56.12 ± 13.7 years, 94.4% women and median disease duration 10 years. The FA ω -3 and ω -6 intake was 0.43 g/day and 3 g/d, respectively. The levels of α -L were 6.6 $\mu\text{g/mL}$, DHA 26 $\mu\text{g/mL}$, total ω -3 (α -L +DHA) 25.4 $\mu\text{g/mL}$, LA 168.5 $\mu\text{g/mL}$, AA 34 $\mu\text{g/mL}$, and total ω -6 (LA+AA) 205 $\mu\text{g/mL}$. We did not find a correlation among serum levels and food intake. Thus, further analyses were focused on serum results. We found a negative correlation between α -L and the OSDI ($\rho = -0.42$, $p = 0.01$) and ESSDAI ($\rho = -0.26$, $p = 0.03$) as well of DHA and ESSDAI ($\rho = -0.30$, $p = 0.01$). The rest of the variables were not associated. In tears, there was a positive correlation of AA and CXCL9 ($\rho = 0.48$, $p = 0.04$), whereas in saliva, we observed a negative correlation between α -L, DHA and total ω 3 (α -L+DHA) with CCL2. We also observed a negative correlation between total ω 6 (LA+AA) and IL-21, and the ω 6/ ω 3 ratio with IL-22.

Conclusion: Our pSS patients had deficient FA omega intake. We observed lower ocular symptoms, lower ESSDAI scores and salivary levels of CCL2 among patients with higher levels of FA ω -3. Our study suggest that low serum levels of ω -3 might be implicated in the perpetuation of chronic inflammation.

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