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The association of fibromyalgia and systemic lupus erythematosus change the presentation and severity of both diseases?

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ABSTRACT

Introduction: The association of fibromyalgia (FM) and systemic lupus erythematosus (SLE) has been investigated, with conflicting results regarding the impact of a condition on the other.

Objectives: To determine the frequency of FM in a sample of patients with SLE treated at the Hospital Complex of Sorocaba (CHS) and the impact of FM in SLE activity and quality of life, as well as of SLE in FM.

Materials and Methods: Descriptive and correlational study. Patients who met the American College of Rheumatology (ACR) criteria for SLE and/or FM were included. The total sample was divided into three groups: FM/SLE (patients with association of SLE and FM), SLE (SLE patients only) and FM (FM patients only). The following variables were used: Fibromyalgia Impact Questionnaire (FIQ), activity index of SLE (SLEDAI), Indices of Diagnostic Criteria for Fibromyalgia 2010 (SSI end GPI) and SF-36.

Results: The prevalence of patients with FM among SLE patients was 12%. FIQ showed no difference between groups, indicating that SLE did not affect the impact caused by FM alone. The presence of FM in SLE patients did not influence the clinical activity of this disease. A strong impact of FM on the quality of life in patients with SLE was observed; the opposite was not observed.

Conclusions: The prevalence of FM observed in SLE patients is 12%. The presence of FM adversely affects the quality of life of patients with SLE.

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A associação fibromialgia e lúpus eritematoso sistêmico altera a apresentação e a gravidade de ambas as doenças?

Palavras-chave:
Fibromialgia
Lúpus eritematoso sistêmico
Atividade clínica
Qualidade de vida
Associação

RESUMO

Introdução: A associação da fibromialgia (FM) e de lúpus eritematoso sistêmico (LES) tem sido investigada com resultados conflitantes em relação ao impacto de uma condição na outra.
Objetivos: Determinar a frequência de FM em uma amostra de pacientes com LES atendidos no Conjunto Hospitalar de Sorocaba (CHS) e o impacto da FM na atividade do LES e na qualidade de vida, bem como do LES na FM.
Material e métodos: Estudo descritivo e transversal. Incluíram-se pacientes que preenchem os critérios de classificação para LES e/ou de FM do Colégio Americano de Reumatologia (ACR). A amostra total foi dividida em três grupos: FM/LES (pacientes com associação LES e FM), LES (somente pacientes com LES) e FM (somente pacientes com FM). As seguintes variáveis foram Questionário de Impacto da Fibromialgia (FIQ), Índice de Atividade do Lúpus Eritematoso Sistêmico (Sledai), Índices dos Critérios Diagnósticos de Fibromialgia de 2010 (IGS E IDG) e o SF-36.
Resultados: A prevalência de pacientes com FM entre os pacientes com LES foi de 12%. O FIQ não apontou diferença entre os grupos e indicou que o LES não interferiu no impacto causado pela FM isoladamente. A presença da FM em pacientes com LES não influenciou a atividade clínica dessa doença. Observou-se um forte impacto da FM na qualidade de vida nos pacientes com LES e não foi observado o contrário.
Conclusões: A prevalência de FM observada nos pacientes com LES é de 12%. A presença de FM afeta adversamente a qualidade de vida dos pacientes com LES.

Introduction

Fibromyalgia (FM) is a rheumatic condition that has as main features a diffuse chronic pain, hyperalgesia and allodynia. Fatigue, sleep disturbances, morning stiffness, headache and paresthesia are symptoms often present.[1] Comorbidities like depression, anxiety, irritable bowel syndrome, myofascial pain syndrome and nonspecific urethral syndrome are also associated.[2]

This syndrome, whose etiology and pathogenesis have not been fully elucidated yet, has as its most important mechanism the amplification of the transmission of painful stimuli, with changes in the perception of pain.[1] An imbalance in neurotransmitters involved in the physiology of pain was also observed. Among other abnormalities, na increase of substance P and nerve growth factor in the cerebrospinal fluid (CSF) of individuals with fibromyalgia was found.[3]

Although few Brazilian epidemiological data have been published, some studies show a prevalence of about 2.5% in the general population; mostly they are women aged 35–44 years old.[4] The mean age of patients is around 29.8 years old. A relationship with low family income was also noted.[5]

The clinical assessment can be done through scales of intensity of symptoms, by specific instruments to assess the disease like the Fibromyalgia Impact Questionnaire (FIQ),[6] and by generic questionnaires on quality of life.[7]

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease involving multiple organs, especially the skin, joints, kidneys, blood vessels, heart and lungs. It is a rare disease, with more frequent incidence in young women, i.e., in the reproductive phase, in a ratio of nine to ten women to one man, and with its prevalence ranging from 14 to 50/100,000 inhabitants.[8–12]

SLE causes significant morbidity and mortality due to inflammatory disease activity, infectious processes secondary to the disease-induced immunosuppression and its treatment, and to cardiovascular complications.[13]

The disease assessment can be made by clinical observation, laboratory tests and imaging studies of the organs involved, evidence of inflammatory activity, evidence relating to autoimmunity, specific questionnaires for the assessment of disease activity such as the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)[14] and generic questionnaires to assess quality of life.[15]

The association of FM and SLE has been investigated by several authors, with conflicting results regarding the impact of a condition on the other.[16–22] The prevalence of a concomitant association between the two diseases is around 20%.[16] Thus, the presence of FM in SLE patients is much greater than in the general population. No study of this association was held in the Brazilian population; and taking into account the personal and cultural nature of the impact of chronic diseases on the quality of life, we believe that knowing the nature of this association in a Brazilian sample can contribute to this discussion. The objectives of this study are to determine the presence of FM in a sample of patients with SLE treated at the Hospital Complex of Sorocaba (CHS) and the impact of FM on SLE clinical activity and on the quality of life of these patients, as well as of SLE in FM.

Materials and methods

This is a descriptive cross-sectional study involving patients from the Rheumatology outpatient clinic, Sorocaba Hospital Complex (CHS). Female patients who met the American College of Rheumatology (ACR) criteria for SLE and/or FM were included.[23,24]

The patients were assessed by a rheumatologist who checked the fulfillment of ACR criteria. The total sample was divided into three groups: FM/SLE (patients with an association of SLE and FM), SLE (SLE patients only) and FM (FM patients only).

Data were obtained from medical records and through interviews conducted for the questionnaires' administration, since the medical records of patients with SLE did not present specific tools for FM; and the medical records of patients with FM had no specific tools for LES. Besides these, the following data were obtained through questionnaires: disease duration, clinical activity and severity of the disease, and the impact on the patients' quality of life. The instruments used in this assessment are described below.

The number of patients in each group was determined by the number of patients with the association of SLE and FM in the outpatient clinic of CHS. Twenty patients were selected for each group. During the study, patients who were lost to follow-up with the rheumatologist for unknown reasons were excluded, as well as patients whose data on their medical records were incomplete and patients whose questionnaires were not fully answered. There was no refusal by any patient to answer the questionnaires. Although the number of subjects in this research can be considered small, the study design aimed to show the reality of a particular service and, therefore, a number compatible with the size of the outpatient clinic where the study was conducted was used. Despite the exclusions, a number of 20 for each group was reached.

The impact of SLE on FM was evaluated using FIQ,[25] which proved to be a valid and reliable instrument to measure functional capacity and health status of these patients. FIQ consists of questions that evaluate the difficulty that FM imposes on day-to-day activities, the occupational impact and the intensity of the main features of the syndrome. The FIQ total score ranges from 0 to 100, 0 being the milder impact and 100 being the worst impact. This is a specific instrument; therefore, it should only be used in groups with patients who meet the classification criteria for FM and not in the SLE-only group.

SLEDAI[16] was used to evaluate the activity index of SLE and the impact that FM may have on this condition, using clinical parameters present in SLE. SLEDAI is a scale that assesses 24 variables associated with SLE activity and grouped into nine systems, wherein the presence of each commitment receives different weights; thus, weight 8 to lesions of the central nervous system and vascular injuries; weight 4 for renal, musculoskeletal and osteoarticular disorders; weight 2 for skin, serous and immunological changes; and weight 1 for constitutional and hematological symptoms. The scores were obtained from the medical records on the day the questionnaire was administered. SLEDAI is a specific instrument; thus, it should only be used in groups with patients who meet the classification criteria for SLE and not in the FM-only group.

Through the Symptom Severity Index (SSI),[26] the severity of the main symptoms in patients with FM, except for the pain, was verified. This questionnaire has a range from 0 to 12, 0 being the lowest and 12 the highest intensity of symptoms.

Generalized Pain Index (GPI)[26] was used to evaluate the extent of pain. GPI shows the number of areas of the body having pain. This index varies between 0 and 19.

Both GPI and SSI are indexes that comprise the Preliminary Diagnostic Criteria for Fibromyalgia, 2010.[26] By being specific, GPI and SSI are instruments that should only be used in groups of patients who fulfill the criteria of classification for FM and not in SLE-only groups.

SF-36[27] is a generic questionnaire for assessing the quality of life, consisting of eight domains: functioning capacity, physical limitations, general health, vitality, mental health, and social and emotional aspects. Each scale has a score ranging from 0 to 100, where zero is the worst possible quality of life and 100 the best QoL scenario.

For the analysis of the results, the following tests were used: Mann–Whitney test with the aim of comparing the FM and FM/SLE groups in relation to the FIQ and SSI values; analysis of variance of Kruskal–Wallis for the purpose of comparing SLE, FM and FM/SLE groups with respect to the values of VAS, GPI and the eight domains of SF-36; and the chi-squared test with the aim of comparing SLE, FM and FM/SLE groups with respect to percentages of presence of hypertension, diabetes mellitus and osteoarticular diseases.

Results

Sixty patients with FM, SLE and FM associated with SLE were studied from September 2011 until August 2012, being distributed equally into three groups, namely, FM, LES and FM/LES. The prevalence of patients with FM among patients with SLE followed at CHS was 12%. The average age of the interviewed patients was 44 years for FM group, 40 for SLE group and 43.5 for FM/LES group.

Similarly, the presence of co-morbidities – diabetes mellitus (DM) and systemic arterial hypertension (SAH) – showed no significant difference. The variables "diagnosis of depression prior to the study" and "other osteoarticular diseases (OAD)" were more present in FM-presenting groups (Table 1). Regarding OAD, patients with FM referred myofascial pain (5 patients), low back pain (4 patients) and tendinopathy (6 patients). Patients with SLE reported tendinopathy (7 patients) and low back pain (4 patients). On the other hand, patients of FM/SLE group mentioned arthritis (1 patient), tendinopathy (7 patients) and low back pain (10 patients).

Table 2 shows the clinical characteristics and impact on quality of life. The comparison of the impact of fibromyalgia by FIQ showed no statistically significant difference between FM and FM/SLE groups, indicating that LES did not affect the impact of FM alone. Although no level of significance ($p = 0.0881$) was observed, there is a tendency that, in this sample, patients with FM in association with SLE present a minor impact on quality of life than those only with FM.

Table 1 – Clinical data of patients evaluated.

Variables/groups	FM	SLE	SLE/FM	P
Age of disease onset (median)	36	28	31.5/35.5	0.0638
Presence of DM (*n*, %)	2 (10%)	0	1 (5%)	0.3499
SAH (*n*, %)	6 (30%)	12 (60%)	8 (40%)	0.1496
Presence of OAD (*n*, %)	15 (75%)	11 (55%)	18 (90%)	0.0426[a]
Presence of previous depression (*n*, %)	16 (80%)	3 (15%)	12 (60%)	0.0001[a]

n, number; DM, diabetes mellitus; SAH, systemic arterial hypertension; OAD, osteoarticular diseases; $p < \text{or} > 0.05$.

[a] FM and SLE/FM > SLE.

Considering that the patients were studied in the tertiary sector of health care, in the case of patients with fibromyalgia we expect an important participation of emotional issues such as depression. In the present study it was not possible to conclude what is the influence of depression on the quality of life of the two groups, since this variable has not been studied with specific instruments.

Through GPI and SSI, we observed a greater intensity of symptoms of fibromyalgia in patients who only had this syndrome, in comparison with those FM patients with an association with SLE. This finding may explain the tendency for a lower impact, cited above, observed with the use of FIQ. The presence of FM in SLE patients did not influence the clinical activity of this disease, when assessed by SLEDAI.

Regarding the quality of life measured by SF-36, it can be seen that the groups with FM had a more negative physical, social, emotional and mental impact, when compared to the SLE-only group in all its scales. The domains most affected by fibromyalgia were physical aspects, pain and emotional aspects. In SLE patients, this analysis did not detect differences between domains. On the other hand, in the group FM/LES the most altered scales were also physical and emotional aspects – thus, a finding similar to the FM group, again suggesting a strong influence of FM in SLE, and not otherwise.

Discussion

SLE is an autoimmune disease that can affect various organs, especially the skin, musculoskeletal system and kidney, among others.[10] The literature has pointed to a higher prevalence of FM in patients with SLE, than in the general population. The prevalence identified of FM in SLE patients in this study was 12%, slightly lower than that found in the literature,[16–22] ranging from 17 to 22%.

In the evaluation of the characteristics of pain and symptom intensity through VAS, GPI and SSI questionnaires, the worst performances occurred in the groups presenting FM alone or in association with SLE. Thus, the presence of FM has a significant negative impact on the quality of life of patients with SLE. It should be emphasized, however, that most of the patients pertaining to the group of SLE in this study presented no disease activity (SLEDAI = zero).

These findings are in agreement with the literature, since studies have shown that FM, besides being common in SLE patients, is the primary determinant of the frequency and severity of symptoms. In addition, FM causes incapacity for daily activities.[17] Therefore, it is likely that a better control of FM would result in improvement in the quality of life of patients with SLE.

In most SF-36 domains, we observed a worse outcome in the FM-only group. The FM/SLE group showed intermediate values, which may indicate that FM contributes to the worsening of health status. These patients are more symptomatic and dysfunctional than patients exclusively with LES. Fibromyalgia causes a significant negative impact on the quality of life of patients, showing a strong correlation with intensity of pain, fatigue and decreased functional capacity.[18,28,29]

According to a Canadian study, the presence of FM in SLE patients was not related to an increase of the parameters that

Table 2 – Data from clinical activity and impact on quality of life.

Variables/groups	FM	SLE	SLE/FM	P
FIQ	71.3	–	59.89	0.0881
SLEDAI	–	0.1	0.3	0.9892
GPI	15.05	–	11.75	0.0001
SSI	10.4	–	8.2	0.0152
SF-36 functional capacity limitations due to physical aspects	30.75	70.25	48.25	0.0008
Pain	87.5	35	71.25	0.0004
General health	17.9	73.68	37.6	<0.0001
Vitality	45.5	63.25	37.85	0.0067
Social aspects	21.25	59.75	33	0.0009
Limitation due to emotional aspects	44.43	76.25	55.63	0.0023
Mental health	88.23	33.3	73.3	0.0014
Variables/groups	33.15	70.8	38	0.0003

make up SLEDAI; however, the presence of FM has a strong correlation with the eight domains of SF-36.[29] Thus, FM is not related to disease activity in SLE, but can generate a misinterpretation of its activity, due to the clinical features of FM, besides contributing to worsening the quality of life in patients with SLE.[29]

Despite the contribution of FM to the worsening of the health status of patients with SLE, it has been shown in the literature that FM causes little or no impact on the activity of SLE,[19,29] which corroborates the findings of our study, where no change in SLEDAI of respective groups (SLE, FM and SLE/FM) was noted.

In our study, patients with SLE presented with a stable clinical picture; thus, our results may not reflect the reality in the acute phases of SLE.

The sample of patients with both FM and SLE differs in relation to what is observed in the community. Patients with FM are those individuals refractory to a standard treatment, since they are seen at a tertiary level center, while SLE patients are generally treated at tertiary centers. Therefore, our sample may not reflect the general population of patients with fibromyalgia. A complement to this study intends to propose the assessment of patients seen at primary and secondary sectors.

Conclusion

The frequency of FM observed in patients with SLE treated at CHS is 12%. The patients had a mean age of 40–44 years in the three groups. The presence of SLE has not determined a greater impact on quality of life of patients with SLE/FM, when assessed by FIQ. FM, in turn, also did not result in higher levels of LSE activity measured by SLEDAI. A higher intensity of symptoms in the FM-only group, in relation to the association SLE/FM, was noted. The presence of FM adversely affects the quality of life of patients with SLE.

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Conflicts of interest

The authors declare no conflicts of interest.

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