Widespread Pain and Sjögren's Syndrome

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ABSTRACT. ***Objective.*** Reports exist of an association between fibromyalgia (FM) and Sjögren's syndrome (SS). Widespread pain is a necessary component of FM. We explored the association of widespread pain and SS.

Methods. Data were abstracted from the records of the most recent 100 patients evaluated in the SS clinic. The subjects included individuals with or without SS who had screened for features of the disorder. Patients with confounding disorders or missing data were excluded. The presence of widespread pain was established by questionnaire in 92 subjects. Widespread pain followed the definition in the 1990 American College of Rheumatology classification criteria for FM. By objective criteria used in the clinic, patients were initially classified into SS (requiring keratoconjunctivitis sicca, positive labial salivary gland biopsy, and serological evidence of autoimmunity), incomplete SS (at least one of the latter objective findings), or non-SS (if all 3 objective findings were negative). For subsequent analyses, the study population was also classified into cases by applying the European criteria for SS, and the subjective or objective components of European criteria. Descriptive statistics and Cochran-Mantel chi-square tests were performed.

Results. Only 2/27 (7%) of those diagnosed with SS reported symptoms of widespread pain. The incomplete SS group consisted of 8/56 (14%), while the non-SS were 1/9 (11%). There was a trend toward greater widespread pain in those 9 of 52 (17%) subjects meeting the European criteria for SS who had widespread pain compared with 2 of 50 (5%) who did not. However, this was not significant ($p = 0.0728$). The greater the subjectivity of the criteria applied to classify cases of SS, the higher was the prevalence of widespread pain. No significant association was found between widespread pain and SS for any of the criteria applied.

Conclusion. No significant association between widespread pain and SS was found in our study population. Further study is indicated to explore a possible lack of association between SS and FM. (J Rheumatol 2001;28:2657–9)

Key Indexing Terms:
WIDESPREAD PAIN SJÖGREN'S SYNDROME FIBROMYALGIA

Pain reported on the right and left side of the body and above and below the waist as well as axially is identified as widespread pain[1]. A common cause of widespread pain observed in patients is due to the fibromyalgia (FM) syndrome[2]. The 1990 American College of Rheumatology (ACR) classification criteria for FM require widespread pain in combination with tenderness at 11 or more of the 18 specific tender point sites[1]. A patient without widespread pain cannot meet ACR criteria for FM. FM is reported to occur in about 2.0% of the general population, with a higher prevalence in women (3.4%) than men (0.5%). However, widespread pain was found to be present in 10.6% of the general population, with rates twice as high in some female age groups[3].

Sjögren's syndrome (SS) is an autoimmune exocrinopathy associated with reduced or absent salivary and lacrimal gland secretion[4]. Estimates of the prevalence of SS in the general population range from 0.05% to 4.8%, with a higher proportion being female[5-9]. It has been reported that a high frequency of patients with SS also have FM[10-14]. We explored the association of widespread pain and SS.

MATERIALS AND METHODS

Records of 100 consecutive subjects evaluated at the NIH Sjögren's Syndrome Clinic were identified in reverse order from most recent. Of these, 96 had all the required information, but 4 were excluded: 2 were primary SS patients who had developed lymphoma, and 2 had secondary SS. For assessment of widespread pain, a questionnaire based on ACR 1990 criteria was completed. The areas of pain included the following: (1) left side of the body, (2) right side of the body, (3) above the waist, (4) below the waist, and (5) axially. A patient had to experience pain in all 5 areas to be diagnosed with widespread pain[1,14]. All subjects had a similar examination.

For diagnosis of SS, our patients initially met 3 specific objective study criteria: a minor salivary gland biopsy with a focus score > 1 (one focus is an aggregation of 50 or more lymphocytes in 4 mm^2 of salivary gland tissue), objective dry eyes by Schirmer's I test with wetting ≤ 5 mm/5 min

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in each eye, and/or Van Bijsterveld score of 4 in each eye using ocular vital dye staining, and any positive serum autoimmune findings, rheumatoid factor ≥ 20 units, anti-SSA, anti-SSB, antinuclear antibodies ≥ 1:40 titer, and elevated immunoglobulins. Since the Sjögren's Syndrome Clinic is located in the dental clinic patients often come to the clinic because of dry mouth symptoms. Patients with SS meeting our objective criteria also had xerostomia. Our criteria were applied to patients visiting the clinics for evaluation or screening of SS or as healthy volunteers. Individuals visited the clinic on the basis of physician referrals, self-referrals, and in response to advertising and the clinic web page on the Internet. The records of these subjects were reviewed and they were classified as SS, incomplete SS, or non-SS controls according to an operational definition. Patients who met some but not all of the criteria for SS were diagnosed with incomplete SS. Non-SS subjects met none of the objective criteria. Necessary data were also collected to determine whether patients met European criteria for SS[15].

Patients with lymphoma, sarcoidosis, hepatitis B or C, human immunodeficiency virus infection, or autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, or scleroderma, as well as those with missing data were excluded. All subjects were seen at the clinic in accord with protocols approved by the Institutional Review Board for screening for SS or for the evaluation of volunteers.

Statistical analysis. Analyses performed using SAS V8.0 included descriptive statistics and Cochran-Mantel-Haenszel chi-squared tests. In addition to the study criteria applied above, we also analyzed the data applying European criteria for SS (ESS), requiring at least 4 of 6 of the following: (1) symptoms of dry eyes; (2) symptoms of dry mouth; (3) objective dry eyes by Schirmer's I test with wetting ≤ 5 mm/5 min in each eye and/or van Bijsterveld score of 4 or more in each eye using ocular vital dye staining; (4) a minor salivary gland biopsy with focus score ≥ 1; (5) salivary gland involvement with ≤ 1.5 ml/15 min of unstimulated whole saliva production; and (6) positive anti-SSA, anti-SSB, or both. In addition, data were analyzed using new International Criteria for SS (ISS), which have the same elements as the ESS. To address concerns that ESS criteria could be met without objective evidence of either exocrine inflammation or autoimmunity, the American European Consensus Group, of which one author (SRP) is a member, has recently revised the ESS criteria and has developed and validated the ISS criteria (Vitali C, unpublished data). The ISS may be fulfilled by meeting 4 of 6 criteria provided that at least the biopsy or autoantibody criterion is met. They may also be fulfilled by meeting 3 of the 4 objective criteria, i.e., criteria 3 through 6 of the ESS. In further separate analyses, the study population was also classified as SS or non-SS on the basis of meeting the subjective dry eye and dry mouth elements of the European criteria and all objective ESS criteria, i.e., elements 3 through 6 of the ESS.

RESULTS

The mean ages (SD) for the 3 groups classified by the initial study criteria were similar (Table 1). The percentage of women differed among the groups. Eleven of 92 (12%) patients reported signs of widespread pain. Only 2/27 (7%) diagnosed with SS reported symptoms of widespread pain. The largest number of patients with widespread pain were from the incomplete SS group, being 8/56 (14%). The non-SS control group had 1/9 (11%) with widespread pain. Table 1 also provides the occurrence of widespread pain by diagnosis according to the study criteria. There was no relationship between widespread pain and SS (p = 0.67). Table 2 shows the results of applying the various criteria to the 92 subjects in the study population. There was a trend toward greater widespread pain in that 9 of 52 (17%) subjects meeting the European criteria for SS had widespread pain, compared with 2 of 50 (5%) who did not. However, this was not significant (p = 0.0728). The number of subjects meeting the various criteria for SS is highest for the subjective criteria, and declines from 61 down to 40 of 92 subjects going down the table. The ages are similar for each classification. The percentage of individuals with widespread pain is lowest for those who meet the objective criteria (OBJ). The odds ratio in each case represents the odds of having widespread pain in those meeting the criterion versus those who do not meet the criterion. Thus, in the table the odds of having widespread pain in those who meet the subjective criteria compared with those who do not meet the subjective criteria is 5.9. The OR decline as the criteria for SS become more objective. However, none of these values were significant.

Table 1.Demographic data and widespread pain by diagnosis.

	Non-Sjögren's Controls	Incomplete Sjögren's	Sjögren's Syndrome
Age (SD), yrs	52 (14.4)	50 (14.3)	52 (15.9)
Female (%)	67	79	93
Widespread pain (%)			
Absent	8 (89)	48 (86)	25 (93)
Present	1 (11)	8 (14)	2 (7)

For widespread pain versus diagnosis: chi-square = 0.82; p = 0.67.

DISCUSSION

Of 92 patients, 27 had SS by our objective study criteria. Only 2 of these 27 (7%) met criteria for widespread pain. This prevalence of widespread pain in SS appears to be lower than in the general population (> 10%). Some rheumatic conditions have been reported to coexist with FM, including studies that found a strong association with SS[10-13,16]. We found no significant association between widespread pain and SS defined by various criteria, which ranged from completely subjective to completely objective.

Widespread pain prevalence by the study criteria for the non-SS control subjects (11%) was similar to that in reports for the general population[3]. The incomplete SS group displayed widespread pain in 8/56 (14%) subjects — less frequently than the subjects who met fully the objective study criteria for SS (7%). Our findings are similar to recent studies[17,18]. Even though there was a preponderance of women in the SS group (Table 1), and widespread pain and FM are more common in women, the SS group reported the lowest frequency of widespread pain. This sex difference further supports a lack of association between widespread pain and SS. However, utilizing the European criteria for SS, which include subjective criteria, we found 17% of the ESS positive patients had widespread pain. These findings suggest that a possible subset of patients who do not meet solely objective criteria for SS may have an increased frequency of widespread pain and possibly FM. This is illustrated in Table 2, where classification of the study popula-

Table 2. Widespread pain in subjects classified by various criteria.

	N	Age, yrs Mean (SD)	Female, %	WP, n (%)	OR (95% CI)	p
SUBJ+	61	50 (13.9)	84	10 (16)	5.9 (0.72, 48.25)	0.0637
SUBJ–	31	52 (16.1)	77	1 (3)		
ESS+	52	51 (14.4)	83	9 (17)	4.0 (0.81, 19.56)	0.0728
ESS–	40	50 (15.2)	80	2 (5)		
ISS+	48	51 (13.9)	83	7 (15)	1.8 (0.46, 6.29)	0.4199
ISS–	44	50 (15.6)	80	4 (9)		
OBJ+	40	52 (14.1)	86	4 (10)	0.7 (0.19, 2.63)	0.6139
OBJ–	52	50 (15.1)	77	7 (14)		

WP: widespread pain; ESS: European SS criteria; ISS: International SS criteria; SUBJ: subjective ESS criteria; OBJ: objective ESS criteria. +: meets criteria; –: does not meet criteria.

tion by various SS criteria showed high odds ratios that declined progressively as the criteria progressed from fully subjective to fully objective. None of the criteria applied revealed statistically significant associations between SS and widespread pain.

Our study has several limitations that must be taken in account in interpreting the data. First, the subjects were evaluated at a referral center, and those who did not have SS may have been biased toward having more features of the disease. This would be expected to decrease differences between those subjects who met criteria for SS versus those who did not. The results do not negate studies indicating that SS is associated with FM, since we only evaluated patients for widespread pain and did not perform tender point examinations. In addition, the sample size may be inadequate to detect a difference in the frequency of widespread pain. Only 2 of 40 patients, who did not meet the European criteria for SS (i.e., ESS negative), as shown in Table 2, had widespread pain, and there was a trend toward greater frequency of widespread pain in ESS positive versus ESS negative subjects ($p = 0.0728$).

Widespread pain and SS were not associated. A possible lack of association between FM and SS merits further study, since widespread pain is a necessary component of FM.

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