Influence of clinical and immunological parameters on the health-related quality of life of patients with primary Sjögren's syndrome

R. Belenguer[1], M. Ramos-Casals[1], P. Brito-Zerón[1], J. del Pino[3], J. Sentís[2], S. Aguiló[1], J. Font[1]

[1]Department of Autoimmune Diseases and [2]Statistics Unit Department of Public Health, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clínic, Facultad de Medicina, Universitat de Barcelona, Barcelona, and [3]Department of Rheumatology, Hospital Universitario de Salamanca, Universidad de Salamanca, Salamanca, Spain.

Abstract

Objective

To evaluate health-related quality of life (HR-QoL) in patients with primary SS patients using the SF-36 questionnaire and to analyse the association between the main clinical features and the SF-36 scales.

Methods

We studied 110 patients (105 women and 5 men, mean age of 56 years) with primary SS seen consecutively in the outpatient clinic of our Department. We used the population-based reference values for the Spanish version of the SF-36 health survey as control values for a healthy population.

Results

Comparison between patients with primary SS and the control population showed lower scores in all SF-36 scales ($p < 0.001$). Analysis of the SF-36 scales by gender showed a significant correlation between age and the values for physical functioning ($p = 0.013$) and bodily pain ($p = 0.016$) scores. No significant differences in SF-36 scores were found when comparing patients according to the presence or absence of sicca features. Women with vaginal dryness had lower scores for social functioning (61.9 vs. 74.4) and general health (37.2 vs. 44.7) than those without, although the differences were not statistically significant ($p > 0.05$). Patients with extraglandular involvement had lower scores for the vitality scale (40.8 vs. 54.5 $p = 0.007$), social functioning (67.0 vs. 79.8, $p = 0.010$), bodily pain (49.5 vs. 62.5, $p = 0.018$) and general health (38.6 vs. 49.4 $p = 0.001$) than those without.

Conclusion

Patients with primary SS had clearly lower HR-QoL scores than the healthy population; with significantly lower scores in all SF-36 scales and in both summary measures. We identified several epidemiological and clinical SS features related to these lower SF-36 scores. Age at protocol correlated with physical functioning and bodily pain. Vaginal dryness was the sicca feature that most affected the HR-QoL of female SS patients, and a poor HR-QoL was also observed in those patients with a systemic expression of the disease, with pulmonary involvement being the extraglandular manifestation that most contributed to a poor HR-QoL. Our results highlight the importance of earlier diagnostic and therapeutic management of patients with primary SS, which, together with a close follow-up, may contribute to a significant improvement in their HR-QoL.

Key words

Primary Sjögren's syndrome, health-related quality of life, SF-36 questionnaire, extraglandular manifestations.

Please address correspondence to:
Dr. Manuel Ramos-Casals, Department of Autoimmune Diseases, Hospital Clínic, C/Villarroel no. 170, 08036 Barcelona, Spain. E-mail: mramos@clinic.ub.es

Received on October 18, 2004; accepted in revised form on January 21, 2005.

© *Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2005.*

Introduction

Sjögren's syndrome (SS) is a systemic autoimmune disease that mainly affects the exocrine glands and usually presents as persistent dryness of the mouth and eyes due to functional impairment of the salivary and lachrymal glands (1). In the absence of an associated systemic autoimmune disease, patients with this condition are classified as having primary SS. The histological hallmark is a focal lymphocytic infiltration of the exocrine glands, and the spectrum of the disease extends from an organ-specific autoimmune disease (autoimmune exocrinopathy) (2) to a systemic process with diverse extraglandular manifestations (3, 4).

The measurement of health-related quality of life (HR-QoL) is a useful parameter when evaluating the benefits of health care interventions and the impact of social influence on rheumatic diseases. Quality of life encompasses a broad spectrum of domains including health status, economic resources, work status, leisure activities, environment and relationships (5). There are several questionnaires for evaluating the quality of life in patients with systemic and rheumatic autoimmune diseases. The most common is the Medical Outcomes Study 36-Item Short-Form Healthy Survey (SF-36), a generic instrument that has been validated and used in patients with rheumatoid arthritis, fibromyalgia and systemic lupus erythematosus (6-8). The HR-Qol of patients with primary SS has been usually studied in small series of patients (9-12), focusing on the comparison with other rheumatic diseases (9, 11-13), and the study of functional disability (11), psycological well-being (12) and fatigue (13).

The aims of this study were to evaluate health-related quality of life in a large series of primary SS patients using the SF-36 questionnaire and to analyse the association between the main epidemiological, clinical and immunologic characteristics of patients and the SF-36 scales.

Patients and methods

Between January 2002 and December 2003, we studied 110 patients with primary SS seen consecutively in the outpatient clinic of our Department. All patients fulfilled 4 or more of the 1993 European Classification Criteria for SS (including as mandatory criterium, either positive immunological markers or salivary lip biopsy) (14). Seventy eight percent of patients also fulfilled the recent 2002 classification criteria for primary SS (15). We used the population-based reference values for the Spanish version of the SF-36 health survey (16), which included 9,151 non-institutionalized subjects as control values for a healthy population.

Written consent was obtained from all patients who completed the SF-36 questionnaire. The questionnaire was administered by a trained interviewer (MR-C, PB-Z, RB), who spent between 30 to 45 minutes for each patient. The taxonomy of the SF-36 measurement model has 3 levels: (1) items, composed of 36 questions; (2) eight scales [physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE) and mental health (MH)] that aggregate 2-10 items each; and (3) two summary measures that aggregate scales (physical and mental health). Each item is used in scoring only one scale. All items are scored on a scale from 0 to 100, with 100 representing the highest level of functioning possible. The scores are then averaged for a final score within each of the 8 dimensions measured. Summary measures are scored in the same way.

We compared the mean values of the SF-36 scales with the following SS features:

- Sicca features (xerostomia, xerophthalmia, nasopharynx, cutaneous and vaginal dryness)
- Extraglandular involvement (articular, cutaneous, muscular, pulmonary, neurological, renal, Raynaud's phenomenon), defined according to previous studies (3, 4)
- Cytopenia (anemia, leukopenia and thrombocytopenia), defined according to previous studies (4)
- Analytical features (hypergammglobulinemia and high ESR), defined according to previous studies (4)

- Immunological findings (positive ANA, RF, anti-Ro/SS-A and anti-La/SS-B antibodies) defined according to previous studies (3, 4)

Statistical analysis

For comparison between quantitative and qualitative parameters, the Student t-test was used in large samples of similar variance, and the nonparametric Mann-Whitney U test for small samples. For comparison of quantitative variables, the Pearson's coefficient correlation was used in large samples of similar variance and the nonparametric Rho Spearman for small samples. Statistical significance was established at $p < 0.05$. Statistical analysis was performed using the SPSS program (SPSS, Chicago, IL).

Results

Of the 110 patients, 105 (96%) were female and 5 (5%) male, with a mean age at the time of study of 56.06 years (range 23-80). All were Caucasians. The marital status was: married 72 (65%), single 13 (12%), widowed 13 (12%) and divorced 12 (11%). Current occupational status was: house work in 39 (35%), disabled or unemployed in 34 (31%), retired in 29 (26%) and currently employed in 8 (7%). Twenty (18%) patients had a history of hospitalization due to SS and 44 (40%) reported having a painful or emotional episode that might have influenced the onset of the disease. The main clinical and immunological features are summarized in Table I.

At protocol, therapy included artificial tears in 102 (93%) (70 requiring more than 3 application per day), nonsteroidal anti-inflammatory drugs in 55 (50%), antidepressants in 40 (36%), eye ointment in 26 (24%), N-acetylcisteine in 22 (20%), oral corticosteroids in 21 (19%), antimalarial drugs in 17 (16%), artificial saliva in 11 (10%), oral pilocarpine in 9 (8%) and anetholtrithione in 3 (3%). Due to severe cutaneous and nasal dryness, 89 (81%) of patients used hydrative lotions and 25 (23%) humidifiers.

When asked about sources of SS information, 108 (98%) said they received full information from their specialist while 24 (22%) received the information from their primary health-care center. Additional sources of information included books and magazines in 7 (6%), internet in 7 (6%), family and friends in 5 (5%) and the SS patients associations in 4 (4%) patients. With respect to family or social support, 105 (96%) patients said they had received support from their physician, 78/90 (87%) from their spouse, 41/104 (39%) from their sons/daughters, 16/93 (17%) from their co-workers and 26 (24%) from the health system.

Table I. Main clinical and immunological features in 110 patients with primary SS.

	Number of patients (%)
Clinical features	
Xerophthalmia	109 (99%)
Xerostomia	108 (98%)
Articular involvement	43 (39%)
Xerosis	37 (34%)
Vaginal dryness	20/105 (19%)
Raynaud's phenomenon	17 (16%)
Parotidomegaly	16 (15%)
Pulmonary involvement	5 (5%)
Cutaneous vasculitis	5 (5%)
Renal involvement	1 (1%)
Analytical features	
Leukopenia	32 (29%)
ESR > 50 mm/hr	30 (27%)
Anemia	27 (25%)
Hypergammaglobulinemia	19/94 (20%)
Thrombocytopenia	14 (13%)
Immunological features	
ANA	98 (89%)
RF	49 (45%)
Anti-Ro/SS-A	40 (36%)
Anti-La/SS-B	30 (27%)
Cryoglobulins	5/88 (6%)

SF-36 measurements in primary SS and control group

Distribution of the SF-36 questionnaire score is summarized in Table II. With a maximum value of 100, the following

Table II. Distribution of scores of the SF-36 quality of life scales and summary measures in 110 patients with primary SS.

	Mean (SD*)	Highest possible score[1] n (%)	Lowest possible score[2] n (%)
Scales			
Physical functioning (PF)	65.2 (27.6)	8 (7.3)	3 (2.7)
Role-physical (RP)	50.0 (45.7)	45 (40.9)	43 (39.1)
Role-emotional (RE)	73.6 (42.6)	78 (70.9)	25 (22.7)
Vitality (VT)	46.9 (26.5)	2 (1.8)	2 (1.8)
Mental health (MH)	53.8 (23.7)	3 (2.7)	0 (0)
Social functioning (SF)	72.7 (26.1)	32 (29.1)	1 (.9)
Bodily pain (BP)	55.3 (29.0)	15 (13.6)	3 (2.7)
General health (GH)	43.4 (16.7)	0 (0)	0 (0)
Summary measures			
Physical health	53.5 (25.0)	0 (0)	0 (0)
Mental health	61.8 (25.3)	1 (0.9)	0 (0)

*Standard deviation. [1]Number of patients who had the highest score for each scale; [2]number of patients who had the lowest score for each scale.

mean values for the different SF-36 subscales in primary SS patients were found (in decreasing order): 73.6 ± 42.6 for the role emotional scale, 72.7 ± 26.1 for the social functioning scale, 65.2 ± 27.6 for the physical functioning scale, 55.3 ± 29.0 for the bodily pain scale, 53.8 ± 23.7 for the mental health scale, 50.0 ± 45.7 for the role-physical scale, 46.9 ± 26.5 for the vitality scale and 43.4 ± 16.7 for the general health scale. Scores for the summary measures were 61.8 ± 25.3 for mental health and 53.5± 25 for physical health. Comparison between patients with primary SS and the control population showed lower scores in all the SF-36 scales (Table III): Role-physical (50.0 vs. 83.2, $p < 0.001$), role-emotional (73.6 vs. 88.6, $p < 0.001$), vitality (46.9 vs. 66.9, $p < 0.001$), mental health (53.8 vs. 73.3, $p < 0.001$), social functioning (72.7 vs 90.1, $p < 0.001$), bodily pain (55.3 vs. 71.0, $p<0.001$), physical functioning (65.2 vs. 84.7, $p < 0.001$) and general health (43.4 vs 68.3, $p< 0.001$).

Table III. Comparison between the Spanish healthy population (ref. 14) and 110 patients with primary SS.

Scales	Primary SS n = 110 Mean (SD*)	Healthy population n = 9151 Mean (SD*)	p value
Physical functioning (PF)	65.2 (27.6)	84.7 (24.0)	< 0.001
Role-physical (RP)	50.0 (45.7)	83.2 (35.2)	< 0.001
Role-emotional (RE)	73.6 (42.6)	88.6 (30.1)	< 0.001
Vitality (VT)	46.9 (26.5)	66.9 (22.1)	< 0.001
Mental health (MH)	53.8 (23.7)	73.3 (20.1)	< 0.001
Social functioning (SF)	72.7 (26.1)	90.1 (20.0)	< 0.001
Bodily pain (BP)	55.3 (29.0)	79.0 (27.9)	< 0.001
General health (GH)	43.4 (16.7)	68.3 (22.3)	< 0.001

*Standard deviation.

Table IV. SF-36 scale scores for primary SS patients according to extraglandular manifestations.

Scales	Primary SS patients without extraglandular manifestations n = 49 Mean (SD)*	Primary SS patients with extraglandular manifestations n = 61 Mean (SD)*	p value
Physical functioning	68.8 (28.8)	62.4 (26.5)	0.229
Role-physical	58.7 (46.1)	43.0 (44.5)	0.074
Role-emotional	78.2 (40.0)	69.9 (44.6)	0.313
Vitality	54.5 (26.4)	40.8 (25.2)	0.007
Mental health	58.2 (23.3)	50.4 (23.5)	0.084
Social functioning	79.8 (24.4)	67.0 (26.1)	0.010
Bodily pain	62.5 (28.0)	49.5 (28.6)	0.018
General health	49.4 (17.6)	38.6 (14.3)	0.001
Summary measures			
Physical health	59.8 (25.1)	48.4 (23.8)	0.016
Mental health	67.7 (25.0)	57.0 (24.8)	0.028

*Standard deviation.

Association between SF-36 measurements and SS features

We found a significant correlation between age and the values for physical functioning ($p = 0.013$) and bodily pain ($p = 0.016$) scores. No significant differences in SF-36 scores were found when comparing patients according to the presence or absence of sicca features, except for vaginal dryness. Thus, women with vaginal dryness had lower scores for social functioning (61.9 vs. 74.4, $p=0.053$) and general health (37.2 vs. 44.7, $p = 0.072$) than those without, although the differences were not statistically significant. Patients with extraglandular involvement (defined as the presence of articular, muscle, lung or kidney involvement, polyneuropathy and/or serositis) had lower scores for the vitality scale (40.8 vs. 54.5 $p = 0.007$), social functioning (67.0 vs. 79.8, $p = 0.010$), bodily pain (49.5 vs. 62.5, $p = 0.018$) and general health (38.6 vs. 49.4 $p=0.001$) than those without.

With respect to the summary measures, patients with extraglandular features had lower scores in physical (23.8 vs. 59.8, $p = 0.016$) and mental health (57.0 vs. 67.7 $p = 0.028$) compared with those without, (Table IV). No significant differences were found between patients with or without articular involvement, neuropathy, Raynaud's phenomenon and cutaneous vasculitis. However, patients with lung involvement had significantly lower scores for role physical (10.0 vs. 51.9, $p = 0.045$), role-emotional (33.3 vs. 75.5, $p = 0.030$) and body pain (30.0 vs. 56.5, $p = 0.045$) and the physical health summary score (29.2 vs. 54.6, $p = 0.026$) than those without. Finally, no significant differences were found between patients with or without cytopenia, high ESR (> 50 mm/hr), hypergammaglobulinemia, antinuclear antibodies, anti-Ro/La or rheumatoid factor on any of the SF-36 scales.

Discussion

Health-related quality of life (HR-QoL) is a concept that refers to the individual's perception of their mental and physical status over time. It has been used to measure the effects of chronic illnesses in diverse groups of patients in order to better understand how illnesses interfere with the patients' day-to-day life and to identify those patients with poor physical or mental health requiring specific strategies. Some studies have analysed HR-QoL studies in patients with primary SS, usually analyzing less than 50 patients (9-12). In spite of the apparently low grade disability that sicca features may originate, their impact on HR-QoL of primary SS is significant,

as demonstrated by the lower scores detected in all SF-36 scales in comparison with the values observed in a healthy Spanish population. It should be noted, however, that this control population was not matched for age, sex and social parameters with our SS population.

The greatest differences were observed in physical scales (physical role and physical functioning), vitality and general health, while the smallest differences were found in the social and mental scales (Fig. 1). This poorer HR-QoL in primary SS patients was also described by Strombeck *et al*. (9), Tensing *et al*. (13) and Strombeck *et al*. (17), underlining the impact of the disease on the physical, psychological and social well-being of the patient. A recent study by Bowman *et al*. (18) has used a new questionnaire to measure fatigue and discomfort in patients with primary SS. In addition, the existence of coexisting processes such as fibromyalgia in SS patients might have an important role in the lower HR-QoL found in these patients in comparison with the healthy population (19). The frequent delay in diagnosis and lack of social support may also be contributing factors to the reduced HRQoL seen in primary SS patients, in contrast with other rheumatic/autoimmune diseases that count on more social and medical support (9).

Based on the understanding that primary SS is a systemic disease, which in itself can affect the HR-QoL, we specifically analyzed the correlation between the main epidemiological, clinical and immunological SS features and the scores of the eight SF-36 scales. Only 2 SF-36 scale scores (physical functioning and bodily pain) correlated with age of the patient. The poor perception that these women had of their health may be partly explained by symptoms of depression, probably related to the chronic nature of the disease and the worsening of pain with age, although depression may also contribute to the patterns of disease expression in these patients. In fact, almost 40% of women in our study were receiving antidepressant treatment. It has been hypothesized that if pain were

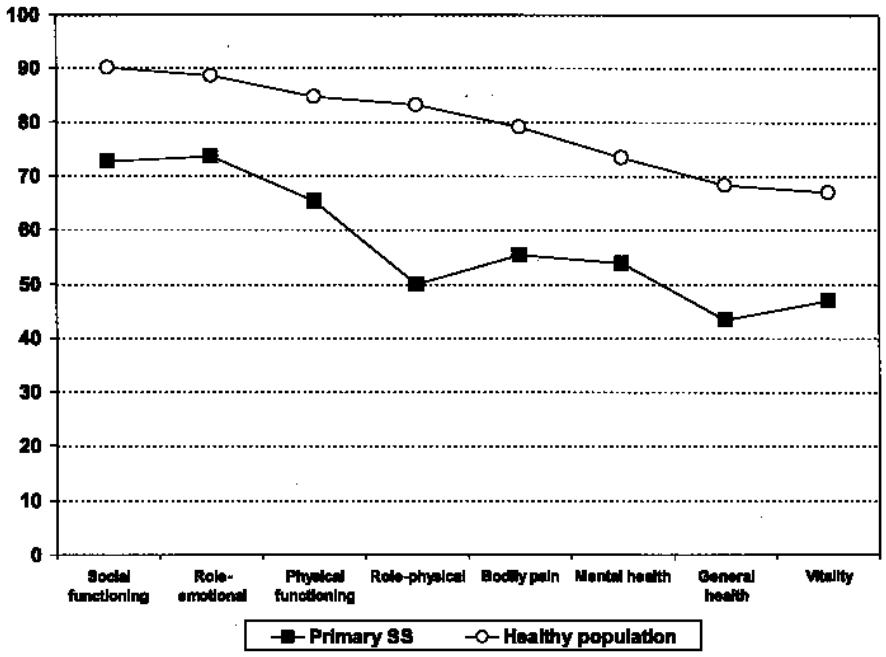

Fig. 1. Mean values of the SF-36 scales in patients with primary SS compared with the healthy Spanish population (ref. 14).

reduced, there would be a substantial improvement in the HR-QoL of these patients (9).

Although chronic dryness constitutes *per se* the most disabling feature of primary SS, only vaginal dryness seems to contribute significantly to the poorer well being of women with primary SS in our study (although the differences were not statistically significant). Vaginal dryness and dyspareunia are important causes of pain in women with primary SS, affecting both social activities and health perceptions. A recent study (20) showed that women with different vulvovaginal disorders (including dyspareunia) experienced more depression than those without. In contrast, the systemic manifestations of primary SS had a very substantial influence on all aspects of HR-QoL in primary SS. Patients with extraglandular involvement had lower scores for the vitality, social functioning, bodily pain and general health scales than patients with a sicca-limited disease, with the differences being significant for both summary measures. These results highlight the role of SS-related systemic features in reducing the HR-QoL of patients with primary SS. However, individual analysis of extraglandular features showed no statistical differences for the main SS manifestations, including articular, cutaneous and vascular involvement. The extraglandular manifestation that had the greatest impact on the HR-QoL of our patients was pulmonary involvement, predominantly in the physical scales. While articular involvement, purpura or Raynaud's phenomenon are clinically mild in patients with primary SS, pulmonary involvement (including either interstitial or obstructive lung disease) may significantly affect the physical activities of patients, limiting their daily activities and work, resulting in poor physical health. Sutcliffe *et al*. (11) analysed functional disability and end organ damage in patients with primary SS compared with SLE and SS associated with SLE, and found that although end organ damage was uncommon in primary SS, the degree of functional disability is as great as in patients with SLE. Due to the influence of extraglandular features on the HR-QoLof patients with primary SS, physicians should be more aware of the importance of early diagnostic and therapeutic management in these patients including a more extensive assessment of the clinical evaluation and a closer follow-up.

In conclusion, patients with primary SS

had clearly lower HR-QoL scores than the healthy population; with significantly lower scores in all SF-36 scales and in both summary measures. We identified several epidemiological and clinical SS features related to these lower SF-36 scores. Age at protocol correlated with physical functioning and bodily pain, and vaginal dryness was the sicca feature that most affected the HR-QoL of female SS patients. A poor HR-QoL was also observed in those patients with a systemic expression of the disease, with pulmonary involvement being the extraglandular manifestation that most contributed to a poor HR-QoL. In contrast, hematological, analytical and immunological markers were not correlated to the SF-36 scales. Our results highlight the importance of earlier diagnostic and therapeutic management of patients with primary SS, which, together with a close follow-up, may contribute to a significant improvement in their HR-QoL.

References

1. DANIELS TE, FOX PC: Salivary and oral components of Sjögren's syndrome. *Rheum Dis Clin North Am* 1992; 18: 571-89.
2. MOUTSOPOULOS HM: Sjögren's syndrome: autoimmune epithelitis. *Clin Immunol Immunopathol* 1994; 72: 162-5.
3. GARCIA-CARRASCO M, RAMOS-CASALS M, ROSAS J *et al*.: Primary Sjögren's syndrome: clinical and immunologic disease patterns in a cohort of 400 patients. *Medicine* (Baltimore) 2002; 81: 270-80.
4. RAMOS-CASALS M, FONT J, GARCIA-CARRASCO M *et al*.: Primary Sjögren's syndrome: hematologic patterns of disease expression. *Medicine* (Baltimore). 2002; 81: 281-92.
5. BURCKHARDT CS, ARCHENHOLTZ B, MANNERKORPI K, BJELLE A: Quality of life of Swedish women with fibromyalgia syndrome, rheumatoid arthritis and systemic lupus erythematosus. *J Musculoskel Pain* 1993; 1: 199-207.
6. BARTLETT SJ, PIEDMONT R, BILDERBACK A, MATSUMOTO AK, BATHON JM: Spirituality, well-being, and quality of life in people with rheumatoid arthritis. *Arthritis Rheum* 2003; 49: 778-83.
7. DA COSTA D, DOBKIN PL, FITZCHARLES MA *et al*.: Determinants of health status in fibromyalgia: a comparative study with systemic lupus erythematosus. *J Rheumatol* 2000; 27: 365-72.
8. GRECO CM, RUDY TE, MANZI S: Effects of disease activity, pain, and distress on activity limitations in patients with systemic lupus erythematosus. *J Rheumatol* 2004; 31: 260-7.
9. STROMBECK B, EKDAHLC, MANTHORPE R, WIKSTROM I, JACOBSSON L: Health-related quality of life in primary Sjögren's syndrome, rheumatoid arthritis and fibromyalgia compared to normal population data using SF-36. *Scand J Rheumatol* 2000; 29: 20-8.
10. THOMAS E, HAY EM, HAJEER A, SILMAN AJ: Sjögren's syndrome: a community-based study of prevalence and impact. *Br J Rheumatol* 1998; 37: 1069-76.
11. SUTCLIFFE N, STOLL T, PYKE S, ISENBERG DA: Functional disability and end organ damage in patients with systemic lupus erythematosus (SLE), SLE and Sjögren's syndrome (SS), and primary SS. *J Rheumatol* 1998; 25: 63-8.
12. VALTYSDOTTIR ST, GUDBJORNSSON B, HALLGREN R, HETTA J: Psychological well-being in patients with primary Sjögren's syndrome. *Clin Exp Rheumatol* 2000; 18: 597-600.
13. TENSING EK, SOLOVIEVA SA, TERVAHARTIALA T *et al.*: Fatigue and health profile in sicca syndrome of Sjögren's and non-Sjögren's syndrome origin. *Clin Exp Rheumatol* 2001; 19: 313-6.
14. VITALI C, BOMBARDIERI S, MOUTSOPOULOS HM *et al.*: Preliminary criteria for the classification of Sjögren's syndrome. Results of a prospective concerted action supported by the European Community. *Arthritis Rheum* 1993; 36: 340-7.
15. VITALI C, BOMBARDIERI S, JONSSON R *et al.*; European Study Group on Classification Criteria for Sjögren's Syndrome. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 2002; 61: 554-8.
16. ALONSO J, REGIDOR E, BARRIO G, PRIETO L, RODRIGUEZ C, DELA FUENTE L: [Population reference values of the Spanish version of the Health Questionnaire SF-36]. *Med Clin* (Barc) 1998; 111: 410-6.
17. STROMBECK B, EKDAHL C, MANTHORPE R, JACOBSSON LT: Physical capacity in women with primary Sjögren's syndrome: a controlled study. *Arthritis Rheum* 2003; 49: 681-8.
18. BOWMAN SJ, BOOTH DA, PLATTS RG: UK Sjögren's Interest Group: Measurement of fatigue and discomfort in primary Sjögren's syndrome using a new questionnaire tool. *Rheumatology* (Oxford) 2004; 43: 758-64.
19. RIVERA J, GONZALEZ T: The Fibromyalgia Impact Questionnaire: a validated Spanish version to assess the health status in women with fibromyalgia. *Clin Exp Rheumatol* 2004; 22: 554-60.
20. JENSEN JT, WILDER K, CARR K, ROMM J, HANSEN A: Quality of life and sexual function after evaluation and treatment at a referral center for vulvovaginal disorders. *Am J Obstet Gynecol* 2003; 188: 1629-37.