ESSPRI and other patient-reported indices in patients with primary Sjögren’s syndrome during 100 consecutive outpatient visits at one rheumatological clinic

Marja Pertovaara¹,² and Markku Korpela¹

Abstract

Objective. A European League Against Rheumatism (EULAR) SS disease activity index (ESSDAI) and a patient-reported index (ESSPRI) have recently been developed and validated. In our previous study the ESSDAI correlated significantly with serum β2 microglobulin concentration. We now aim to establish whether the ESSPRI is also associated with serum β2 microglobulin or with other patient-reported indices.

Methods. The data on 100 consecutive visits of patients with primary SS (pSS) were reviewed from the patient charts. Patients who had filled out the ESSPRI questionnaire and fulfilled at least four of the revised American-European consensus group criteria for pSS were included. Data were gathered on the ESSPRI (0–10 cm) and on the patient’s global health assessment [visual analogue scale (VAS) 0–10 cm] (PGH-VAS), pain-VAS (0–10 cm) and HAQ (range 0–3).

Results. The ESSPRI correlated significantly with the PGH-VAS (r = 0.753, P < 0.0001), pain-VAS (r = 0.656, P < 0.0001) and HAQ (r = 0.542, P < 0.0001) (Spearman’s correlation). It also correlated weakly with serum β2 microglobulin (r = 0.214, P = 0.043) and ESR levels (r = 0.235, P = 0.019).

Conclusion. The ESSPRI correlated significantly with other patient-reported indices, serum β2 microglobulin and ESR in patients with pSS. Our results support the view that the ESSPRI is a useful tool in the follow-up of patients with pSS.

Key words: activity index, serum β2 microglobulin, ESSPRI, primary Sjögren’s syndrome.

Introduction

In recent years the use of biologic therapies, in particular those targeting B cells, has been studied in patients with primary SS (pSS) [1–5] and case reports have also recorded promising results with rituximab in severe extra-glandular manifestations of pSS. When new immunomodulating therapies for pSS are investigated or used in clinical practice, it is important to find reliable measures to evaluate the treatment response.

An expert panel of the European League Against Rheumatism (EULAR) has developed indices for the judgement of both the systemic symptoms of pSS [the EULAR SS disease activity index (ESSDAI)] [6] and the patient-reported subjective symptoms [the EULAR SS patient-reported index (ESSPRI)] [7]. The ESSPRI has also recently been validated [8]. In an earlier study we found that the concentration of serum β2 microglobulin, a non-specific marker of immune activation, correlated significantly with the ESSDAI [9]. Serum β2 microglobulin has previously been associated with renal [10, 11] and pulmonary manifestations of pSS [12] and with extra-glandular manifestations of pSS overall [13], and it has also been related to lymphoma development in pSS [10, 14]. In addition, findings in a recent prospective cohort of 395 patients with pSS confirmed that pSS patients with higher serum β2 microglobulin levels had higher ESSDAI indices than others [15]. We now sought...
to establish whether serum β2 microglobulin is also associated with the ESSPRI and, in addition, whether the ESSPRI correlates with other patient-reported indices and biologic parameters such as age, BMI and routine laboratory tests in patients with pSS.

**Subjects and methods**

From the end of the 1990s, all patients attending the rheumatological outpatient clinic of Tampere University Hospital, irrespective of their diagnosis, have been asked to complete questionnaires on such patient-reported indices as the visual analogue scale (VAS) of the patient’s global assessment on disease activity (PGH-VAS) (0–10 cm), pain-VAS (0–10 cm) and HAQ (0–3) before their visit to the attending physician. In addition, from February 2012 onward, patients with pSS were also asked to complete the ESSPRI questionnaire (0–10 cm) [7].

The charts of all patients with pSS who visited the rheumatological outpatient clinic at Tampere University Hospital from February 2012 to May 2013 were reviewed. Data on 100 consecutive visits of patients with pSS who had filled the ESSPRI questionnaire and who fulfilled at least four of the revised American-European consensus group criteria for pSS [16] were included in the study. The mean age of the 100 patients with pSS (93 female, 7 male) was 55 years (s.d. 15, range 22–82) and the mean disease duration was 10 years (s.d. 9, range 0–30).

To evaluate the diagnostic criteria, the following data were gathered from the patient charts: duration of pSS, existence of sicca symptoms in the eyes and mouth, the present status of the mouth, history or presence of recurrent parotid or submandibular gland swellings, Schirmer I test results and ophthalmological examination results, salivary flow rate, results of minor salivary gland histological findings, results of salivary gland US examinations and results of anti-SSA and anti-SSB antibody determinations. In addition, the results of the ESSPRI, PGH-VAS, pain-VAS and HAQ were gathered and data on BMI and routine laboratory tests and immunological findings were recorded.

The standard laboratory tests included whole blood count, ESR and serum CRP. Serum concentrations of IgA, IgG and IgM as well as serum complement (C3 and C4) levels were measured by laser nephelometry (Behring Nephelometric Analyser) and serum β2 microglobulin by electrochemiluminescence. Antibodies to ENAs were measured by enzyme immunoassay.

**Statistical methods**

Correlations were calculated with the Spearman correlation coefficient. Findings were considered statistically significant at $P < 0.05$. Statistical analyses were performed with SPSS Statistics 20 (IBM, Armonk, NY, USA).

**Table 1** Demographic and clinical characteristics of 100 consecutive patients with primary SS visiting one rheumatological outpatient clinic

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (s.d.), years</td>
<td>55 (15)</td>
</tr>
<tr>
<td>Disease duration, mean (s.d.), years</td>
<td>10 (9)</td>
</tr>
<tr>
<td>ESSPRI, median (IQR), cm</td>
<td>3.87 (2.27–5.33)</td>
</tr>
<tr>
<td>PGH-VAS, median (IQR), cm (n = 98)</td>
<td>2.25 (0.65–4.63)</td>
</tr>
<tr>
<td>Pain-VAS, median (IQR), cm (n = 98)</td>
<td>1.60 (0.10–3.80)</td>
</tr>
<tr>
<td>HAQ (range 0–3), mean (s.d.) (n = 98)</td>
<td>0.33 (0.51)</td>
</tr>
<tr>
<td>BMI, mean (s.d.), kg/m² (n = 93)</td>
<td>25.7 (4.93)</td>
</tr>
<tr>
<td>Haemoglobin, mean (s.d.), g/l</td>
<td>132 (9)</td>
</tr>
<tr>
<td>Leucocytes, mean (s.d.), × 10⁹/l</td>
<td>5.6 (2.0)</td>
</tr>
<tr>
<td>Thrombocytes, mean (s.d.), × 10⁹/l</td>
<td>246 (70)</td>
</tr>
<tr>
<td>ESR, mean (s.d.), mm/h</td>
<td>16 (15)</td>
</tr>
<tr>
<td>CRP, mean (s.d.), mg/l</td>
<td>1.71 (2.32)</td>
</tr>
<tr>
<td>Serum IgG, mean (s.d.), g/l (n = 87)</td>
<td>14.5 (5.1)</td>
</tr>
<tr>
<td>Serum IgA, mean (s.d.), g/l (n = 85)</td>
<td>2.4 (1.5)</td>
</tr>
<tr>
<td>Serum IgM, mean (s.d.), g/l (n = 84)</td>
<td>1.27 (0.82)</td>
</tr>
<tr>
<td>Serum β2 microglobulin, mean (s.d.), mg/l (n = 90)</td>
<td>2.38 (0.70)</td>
</tr>
<tr>
<td>Serum C3, mean (s.d.), g/l (n = 78)</td>
<td>1.06 (0.20)</td>
</tr>
<tr>
<td>Serum C4, mean (s.d.), g/l (n = 78)</td>
<td>0.15 (0.06)</td>
</tr>
<tr>
<td>Current or previously</td>
<td></td>
</tr>
<tr>
<td>RF positivity, n (%) (n = 90)</td>
<td>70 (78)</td>
</tr>
<tr>
<td>ANA positivity, n (%)</td>
<td>75 (75)</td>
</tr>
<tr>
<td>Anti-SSA antibody positivity, n (%)</td>
<td>89 (89)</td>
</tr>
<tr>
<td>Anti-SSB antibody positivity, n (%)</td>
<td>38 (38)</td>
</tr>
</tbody>
</table>

ESSPRI: European League Against Rheumatism SS patient-reported index; IQR: interquartile range; PGH: patient’s global health assessment; VAS: visual analogue scale.
Ethical considerations

There is no legal requirement for approval by an ethical committee or informed consent in a study that is based solely on patient charts and does not involve patient contacts. Permission to collect the required data from the patient charts was obtained from the head of the Pirkanmaa Hospital District’s Science Centre, Tampere University Hospital, Tampere, Finland.

**Fig. 1** The correlation of the ESSPRI in 100 visits of patients with pSS with other patient-reported indices.

(a) Patient’s global health assessment visual analogue scale (PGH-VAS); (b) pain-VAS; (c) HAQ; (d) ESR; and (e) serum β2 microglobulin concentration.
Results

The results of the ESSPRI, PGH-VAS, pain-VAS, HAQ and other clinical, immunological and demographic characteristics of the patients are presented in Table 1. The ESSPRI was statistically significantly correlated with disease duration ($r = 0.332, P = 0.001$) and with other patient’s self-reported indices, i.e. with PGH-VAS ($r = 0.753, P < 0.0001$), pain-VAS ($r = 0.656, P < 0.0001$) and HAQ ($r = 0.542, P < 0.0001$) (Fig. 1a–c). There was also a statistically significant positive correlation between the ESSPRI and the BMI of the patients ($r = 0.224, P = 0.031, n = 93$). The ESSPRI correlated weakly but statistically significantly with the levels of blood ESR ($r = 0.235, P = 0.019$) and serum β2 microglobulin ($r = 0.214, P = 0.043$) (Fig. 1d and e). On the other hand, the ESSPRI values did not correlate with those of blood haemoglobin, leucocytes, thrombocytes or serum CRP (data not shown), nor did they correlate with levels of serum IgG, IgM, IgA or with serum complement C3 and C4 levels (data not shown).

Discussion

A significant correlation was found here between the ESSPRI and the PGH-VAS evaluated in 100 consecutive pSS patient visits. Our result is in accord with those in a recent study where 28 patients with pSS were treated with a B cell inhibitor, rituximab, and where the ESSPRI showed a good correlation with patient global health assessment both at baseline and at the follow-up, i.e. after rituximab treatment [17]. Similarly, in a recent large multicentre study validating the EULAR scores for assessment of pSS in evaluations performed at baseline and at 6 months, the ESSPRI was found to correlate significantly with patient global assessment in 395 pSS patients [8].

We also found that the ESSPRI correlated significantly with other patient-reported indices, i.e. with both pain-VAS and HAQ. This is in agreement with a recent study from the UK, where the ESSPRI was found to correlate with functional status and pain in pSS [18]. Altogether, our results support the findings of the EULAR score validation study [8] and the recent rituximab treatment study [17], namely that ESSPRI correlates well with patient-reported indices. However, in our study, the level of the ESSPRI was higher than that of the PGH-VAS or pain-VAS, indicating that it clearly increments the use of other patient-reported indices.

Previously the ESSPRI and the ESSDAI have been suggested to reflect different aspects of disease activity in patients with pSS [8, 19]. Here, however, values of the ESSPRI correlated weakly with both serum β2 microglobulin levels and the ESR. These correlations imply that in addition to the ESSDAI, the ESSPRI at least partly reflects inflammatory disease activity in patients with pSS. The correlation of serum β2 microglobulin with the ESSPRI, which includes sicca symptoms, is in agreement with our previous finding that serum β2 microglobulin is an independent predictor of the development of pSS in subjects with sicca symptoms [20]. However, no correlation was found between the ESSPRI and blood count, serum CRP, serum complement levels or serum immunoglobulin levels. Interestingly, there was also a positive correlation between BMI and the ESSPRI.

Our results from a pSS patient cohort independent of validation studies provide further evidence for the applicability of the ESSPRI in clinical work. In our pSS patient cohort, the ESSPRI correlated significantly with all other patient-reported indices and also with some immunological findings. However, the ESSPRI values calculated with the VAS 0–10 cm scales were higher than with other patient-reported indices, which brings a specifically pSS-related aspect to patient interviews.

Rheumatology key messages

- The European League Against Rheumatism (EULAR) SS patient-reported index (ESSPRI) correlates significantly with patient global health assessment, pain visual analogue scale and HAQ in SS patients.
- The ESSPRI correlated weakly with serum β2 microglobulin and ESR during 100 consecutive outpatient visits.

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Disclosure statement: The authors have declared no conflicts of interest.

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