Factors Influencing Dry Mouth in Patients with Primary Sjögren Syndrome: Usefulness of the ESSPRI Index

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Abstract

Objective: To evaluate health-related quality of life in a large series of primary SS patients using the recently-proposed ESSPRI questionnaire and to evaluate the relationship between the intensity of oral dryness and other signs and symptoms frequently found in these patients.

Methods: We evaluated 90 primary SS patients seen consecutively; all fulfilled the current classification criteria. All patients completed the ESSPRI questionnaire. We compared the mean values of the ESSPRI-dry mouth item with other ESSPRI items related to sicca features, general symptoms, quality of life, quality of sleep, psychological and psychiatric features, extraglandular involvement, laboratory features and immunological markers and cardiovascular risk factors. Multivariate regression analysis with a backwards stepwise selection method was performed to identify those variables that were independently associated with dry mouth.

Results: Mean intensity of oral dryness measured by the corresponding ESSPRI item was 7.17 ± 0.23. Oral dryness correlated with age both at diagnosis and at study inclusion (p=0.013), but not with gender or with time of disease evolution. No significant correlation was found with the SF-36, HAQ and FIQ questionnaires. We found a significant correlation between the intensity of oral dryness and the quality of sleep (p=0.001), anxiety and depression measured by the GH28 (p=0.004 and 0.024, respectively), and a statistically-significant trend for anxiety and depression measured by the HADS (p=0.08 and 0.07, respectively). No significant correlation was found with the main extraglandular and immunological features; however, a significant correlation between oral dryness and hypertension (p=0.019), type II diabetes mellitus (p=0.005) and hypercholesterolemia (p=0.011) was found. Multivariate regression analysis shows that fatigue measured by ESSPRI (p=0.049), sleep quality (p=0.008) and hypercholesterolemia (p=0.008) were independently associated with dry mouth.

Conclusion: We report on the usefulness of the ESSPRI index in evaluating HRQOL associated with oral dryness in primary SS patients. Oral dryness correlated with age and the other sicca symptoms measured by ESSPRI, but not with the main systemic and immunological SS features. In contrast, oral dryness was strongly correlated with fatigue, pain, psychological distress, poor sleep and vascular risk factors. A multidisciplinary therapeutic approach may be the best way of minimizing oral dryness and its consequences in primary SS patients.

Introduction

Sjögren 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]. Nearly one third of patients may present inflammatory, episodic swelling of the major salivary glands (parotid and submandibular glands) and, less frequently, swelling of the lachrymal glands. The disease overwhelmingly affects middle-aged women, but may also affect children, men and the elderly. The histological hallmark is 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].

Xerostomia (subjective feeling of mouth dryness) is one of the key symptoms in the suspicion of SS, as it occurs in more than 95% of patients; a positive answer to at least one of the three questions about oral symptoms included in the 2002 classification criteria has a positive and negative predictive value of 54-77% and 94-98%, respectively [5]. Reduced salivary volume interferes with speaking or eating and may facilitate local infection and tooth decay, with a lobulated/depapillated red tongue and angular cheilitis being the most frequent oral signs.

Primary SS patients have poor health-related quality of life (HRQOL), which is comparable to that observed in patients with fibromyalgia or chronic pain [6]. Some studies [7] have found that oral disease may have significant social and psychological consequences and contribute to impaired general quality of life in these patients. Patients complain of difficulties in chewing, swallowing food and speaking [8], and consequently may suffer embarrassment or feel self-conscious socially as a result of xerostomia [7]. However, the great majority of studies focused on HRQOL in primary SS have found that a specific cluster of symptoms (fatigue, pain,
sleep disturbances and emotional distress) are the principle reason for poor HRQOL, together with sicca features [9]. It is not clear how the coexistence of these non-specific general features and other SS-related features may influence the intensity of oral dryness.

The aims of this study were to evaluate HRQOL in a large series of primary SS patients using the recently-proposed ESSPRI questionnaire and to evaluate the relationship between the intensity of oral dryness and other signs and symptoms frequently found in these patients (general symptoms, autoimmune features and vascular risk factors).

**Patients and Methods**

Between January and December 2011, we evaluated 90 primary SS patients seen consecutively in the outpatient clinic of the Department of Autoimmune Diseases (Hospital Clinic, Barcelona). All patients were considered to have well-established primary SS after fulfillment of the current classification criteria, either the AECG criteria [5] or the ACR criteria [10], including either positive autoantibodies or salivary biopsy as a mandatory criterion. In all patients, an exhaustive evaluation discarding other causes of sicca syndrome (coexisting systemic autoimmune diseases, chronic viral infections, and pre-existing lymphoma) was made.

Clinical and laboratory data were collected and computerized according to our standard department protocol [4]. The study was approved by the Ethics Committee of the Hospital Clinic (Barcelona, Spain) and all patients gave informed, written consent.

All patients completed the ESSPRI questionnaire (mean score of 0–10 numerical scales for pain, fatigue, and dryness features, including oral, ocular, and global dryness) [11]. The intensity of oral dryness was measured using the corresponding ESSPRI item, which uses a 1 0-cm visual analogue scale (VAS) with the anchor points being ‘No dry mouth’ and ‘Worst possible dry mouth’. We compared the mean values of the ESSPRI-dry mouth item with the following SS features:

- Other ESSPRI items related to sicca features other than dry mouth (VAS for dry eyes, dry nasopharynx, cutaneous and vaginal dryness)
- General symptoms: fatigue and pain using the corresponding ESSPRI items, and the Brief Pain Inventory (BPI) questionnaire
- HRQOL: 0-10 patient global assessment (PGA), SF-36, HAQ and Fibromyalgia Impact Questionnaire (FIQ), VAS for quality of sleep
- Psychological and psychiatric features: Hospital Anxiety and Depression Scale (HADS) and General Health Questionnaire (GH28)
- Extraglandular involvement was evaluated according to the 2010 EULAR SS disease activity index [12].
- Laboratory features and immunological markers (positive ANA, RF, anti-Ro/SS-A and anti-La/SS-B antibodies)
- Cardiovascular risk factors: The following data were retrospectively collected from the medical and analytical records of primary SS patients at the time of the visit: hypertension, current smoking, diabetes mellitus, obesity, hypercholesterolemia and hypertriglyceridemia [13].

**Statistical Analysis**

Descriptive data are presented as the mean and standard deviation (SD) for continuous variables or number and percentage (%) for categorical variables. Spearman correlation coefficients were computed to study the relation between dry mouth and other continuous variables and t-test to evaluate the association of dry mouth with categorical variables. Multivariate linear regression analysis with a backwards stepwise selection method was performed to identify those variables that were independently associated with dry mouth. All significance tests were 2-tailed and p-values<0.05 were considered significant. All analyses were conducted using statistical software package R version 3.0.2 for Windows.

**Results**

**a) Baseline characterization**

The baseline characteristics of the study group are summarized in Table 1. We included 90 patients, 86 (96%) females and 4 (4%) males (female: male ratio, 21:1), with a mean age at diagnosis of 56.32 ± 1.47 years (range, 22-81), a mean age at study inclusion of 63.54 ± 1.48 years (range, 25-84) and a disease evolution ranging from 12 to 252 months (mean, 7.45 years). All patients had xerostomia and xerophthalmia, 81/89 (91%) had altered ocular diagnostic tests (Schirmer’s test and/or rose Bengal/lissamine stainings), 77/79 (97%) altered salivary scintigraphy and 20/31 (65%) a salivary gland biopsy showing lymphocytic infiltrates grade 3 or 4. The main immunologic features were ANA>1/80 in 81 (90%) patients, anti-Ro/SS-A in 40 (44%), RF in 39 (43%), anti-La/SS-B in 32 (36%), low C3 levels in 6/88 (7%), low C4 levels in 2/88 (2%) and cryoglobulinaemia in 9/86 (11%)

**b) Association between oral dryness, non-specific general features and HRQOL**

Mean intensity of oral dryness measured by the corresponding ESSPRI item was 7.17 ± 0.23. Table 2 summarizes the correlation between oral dryness and the intensity of other sicca features measured according to the corresponding ESSPRI items; we found a close correlation between the intensity of oral dryness and the intensity of the other dryness features (p<0.001). With respect to general symptoms, oral dryness correlated with the intensity of fatigue, both mental

**Table 1. Baseline characteristics of a Spanish cohort of 90 patients with primary SS.**

<table>
<thead>
<tr>
<th>Variables at diagnosis</th>
<th>N=90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>56.32 ± 1.47</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>90 (100)</td>
</tr>
<tr>
<td>Dry eyes</td>
<td>90 (100)</td>
</tr>
<tr>
<td>Altered ocular tests</td>
<td>81/89 (91)</td>
</tr>
<tr>
<td>Altered salivary scintigraphy</td>
<td>77/79 (97)</td>
</tr>
<tr>
<td>Positive salivary gland biopsy</td>
<td>20/31 (65)</td>
</tr>
<tr>
<td>Antinuclear antibodies+</td>
<td>81 (90)</td>
</tr>
<tr>
<td>Rheumatoid factor+</td>
<td>39 (43)</td>
</tr>
<tr>
<td>Anti-Ro/SS-A+</td>
<td>40 (44)</td>
</tr>
<tr>
<td>Anti-La/SS-B+</td>
<td>32 (36)</td>
</tr>
<tr>
<td>Cryoglobulina+</td>
<td>9/86 (11)</td>
</tr>
<tr>
<td>Low C3 levels (&lt;0.82 g/L)</td>
<td>6/88 (7)</td>
</tr>
<tr>
<td>Low C4 levels (&lt;0.11 g/L)</td>
<td>2/88 (2)</td>
</tr>
</tbody>
</table>
(p=0.001) and general (p=0.024), and with pain measured by the ESSPRI items (p=0.048), together with a statistically-significant trend for pain measured with the BPI questionnaire (p=0.091).

Table 3 summarizes the correlation between the intensity of oral dryness and HRQOL. No significant correlation was found with SF-36 domains and dimensions except for a statistical trend for physical health (p=0.065). No correlation between the intensity of oral dryness and functional disability measured by the HAQ and FIQ questionnaires was found. However, we found a significant correlation between the intensity of oral dryness and the quality of sleep measured by the Quality of Sleep questionnaire (p=0.001). With respect to psychological and psychiatric features, we found a significant correlation between the intensity of oral dryness and anxiety and depression measured by the GH28 (p=0.004 and 0.024, respectively), and a statistically-significant trend for anxiety and depression measured by the HADS (p=0.08 and 0.07, respectively).

c) Association between oral dryness and SS-related features

Table 4 summarizes the correlation between the intensity of oral dryness and the main epidemiological, clinical and immunological features of primary SS patients. Oral dryness correlated with age both at diagnosis and at study inclusion (p=0.013), but not with gender or with time of disease evolution. No significant correlation was found with the main extraglandular and immunological features.

d) Association between oral dryness and vascular risk factors

Table 5 summarizes the correlation between the intensity of oral dryness and the main vascular risk factors. There was a significant correlation between oral dryness and hypertension (p=0.019), type II diabetes mellitus (p=0.005) and hypercholesterolemia (p=0.011).

Table 2. Correlation between the intensity of oral dryness and the intensity of other sicca features, fatigue and pain measured according to the corresponding ESSPRI items.

<table>
<thead>
<tr>
<th>Other dryness</th>
<th>Correlation Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESSPRI dryness eyes</td>
<td>0.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESSPRI dryness skin</td>
<td>0.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESSPRI dryness nose</td>
<td>0.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESSPRI tracheal dryness</td>
<td>0.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESSPRI vaginal dryness</td>
<td>0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0.24</td>
<td>0.024</td>
</tr>
<tr>
<td>ESSPRII mental fatigue</td>
<td>0.36</td>
<td>0.001</td>
</tr>
<tr>
<td>Pain</td>
<td>0.21</td>
<td>0.048</td>
</tr>
<tr>
<td>BPI total score</td>
<td>0.18</td>
<td>0.091</td>
</tr>
</tbody>
</table>

Table 3. Correlation between oral dryness intensity and HRQOL questionnaires.

<table>
<thead>
<tr>
<th>SF-36 dimensions</th>
<th>Correlation Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF36 health</td>
<td>-0.15</td>
<td>0.172</td>
</tr>
<tr>
<td>SF36 physical function</td>
<td>-0.14</td>
<td>0.208</td>
</tr>
<tr>
<td>SF36 physical role</td>
<td>-0.07</td>
<td>0.523</td>
</tr>
<tr>
<td>SF36 pain</td>
<td>-0.09</td>
<td>0.422</td>
</tr>
<tr>
<td>SF36 emotional role</td>
<td>-0.16</td>
<td>0.140</td>
</tr>
<tr>
<td>SF36 social function</td>
<td>-0.10</td>
<td>0.338</td>
</tr>
<tr>
<td>SF36 vitality</td>
<td>-0.09</td>
<td>0.417</td>
</tr>
<tr>
<td>SF36 mental health</td>
<td>0.07</td>
<td>0.496</td>
</tr>
<tr>
<td>SF36 physical heath sum</td>
<td>-0.20</td>
<td>0.065</td>
</tr>
<tr>
<td>SF36 mental health sum</td>
<td>-0.10</td>
<td>0.377</td>
</tr>
<tr>
<td>PGA score</td>
<td>0.08</td>
<td>0.438</td>
</tr>
<tr>
<td>Quality of sleep</td>
<td>0.33</td>
<td>0.002</td>
</tr>
<tr>
<td>HAQ total score</td>
<td>0.17</td>
<td>0.117</td>
</tr>
<tr>
<td>FIQ total score</td>
<td>0.13</td>
<td>0.269</td>
</tr>
<tr>
<td>HADS anxiety score</td>
<td>0.19</td>
<td>0.080</td>
</tr>
<tr>
<td>HADS depression score</td>
<td>0.19</td>
<td>0.070</td>
</tr>
<tr>
<td>GH28 psychosomatic</td>
<td>0.04</td>
<td>0.705</td>
</tr>
<tr>
<td>GH28 anxiety</td>
<td>0.30</td>
<td>0.004</td>
</tr>
<tr>
<td>GH28 social dysfunction</td>
<td>0.04</td>
<td>0.692</td>
</tr>
<tr>
<td>GH28 depression</td>
<td>0.24</td>
<td>0.024</td>
</tr>
</tbody>
</table>

Table 4. Correlation between the intensity of oral dryness (mean ± SD) and the main epidemiological, clinical and immunological features of primary SS.

<table>
<thead>
<tr>
<th>Age at diagnosis</th>
<th>Correlation Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.26</td>
<td>0.017</td>
</tr>
<tr>
<td>Time of disease evolution</td>
<td>-0.02</td>
<td>0.893</td>
</tr>
<tr>
<td>Antinuclear antibodies+</td>
<td>7.2 ± 2.4</td>
<td>0.931</td>
</tr>
<tr>
<td>Anti-Ro/SS-A+</td>
<td>7.4 ± 2.1</td>
<td>0.310</td>
</tr>
<tr>
<td>Anti-La/SS-B+</td>
<td>7.5 ± 2.2</td>
<td>0.670</td>
</tr>
<tr>
<td>Pulmonary involvement</td>
<td>7.1 ± 2.3</td>
<td>0.525</td>
</tr>
<tr>
<td>Renal involvement</td>
<td>7.2 ± 2.2</td>
<td>0.911</td>
</tr>
<tr>
<td>Peripher neuropathy</td>
<td>7.2 ± 2.1</td>
<td>0.542</td>
</tr>
<tr>
<td>CNS involvement</td>
<td>7.2 ± 2.2</td>
<td>0.828</td>
</tr>
<tr>
<td>Rheumatoid factor+</td>
<td>7.2 ± 2.4</td>
<td>0.955</td>
</tr>
<tr>
<td>Anti-La/SS-B+</td>
<td>7.1 ± 2.5</td>
<td>0.461</td>
</tr>
<tr>
<td>Low C3 levels (&lt;0.82 g/L)</td>
<td>6.2 ± 2.9</td>
<td>0.419</td>
</tr>
<tr>
<td>Cryoglobulins+</td>
<td>7.2 ± 2.2</td>
<td>0.855</td>
</tr>
<tr>
<td>Monoclonal band+</td>
<td>7.2 ± 2.3</td>
<td>0.077</td>
</tr>
</tbody>
</table>

Table 5. Correlation between oral dryness intensity (mean ± SD) and the main vascular risk factors of patients with primary SS.

<table>
<thead>
<tr>
<th>Vascular risk factors</th>
<th>Correlation Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence</td>
<td>6.5 ± 2.7</td>
<td>0.368</td>
</tr>
<tr>
<td>Presence</td>
<td>7.3 ± 2.0</td>
<td>0.332</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6.8 ± 2.3</td>
<td>0.019</td>
</tr>
<tr>
<td>Type II diabetes</td>
<td>6.8 ± 2.3</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>6.6 ± 2.3</td>
<td>0.011</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>7.0 ± 2.2</td>
<td>0.309</td>
</tr>
<tr>
<td>Obesity</td>
<td>7.0 ± 2.4</td>
<td>0.859</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>7.1 ± 2.3</td>
<td>0.207</td>
</tr>
</tbody>
</table>
e) Multivariate model
The multivariate regression model analysed independent variables associated with dry mouth; dryness of other mucosal surfaces was excluded due to the evident correlation. Variables with a p-value < 0.05 in the univariate analysis (fatigue measured by ESSPRI, pain measured by ESSPRI, anxiety and depression measured by GH28, age, quality of sleep, hypertension, diabetes and hypercholesterolemia) were included in the model. Table 6 summarizes the main results: multivariate regression analysis shows that fatigue measured by ESSPRI (p=0.049), sleep quality (p=0.008) and hypercholesterolemia (p=0.008) were independently associated with dry mouth.

Discussion
As in other systemic diseases, measurement of HRQOL in primary SS is an important but complex issue [9]. Several factors may contribute to impaired HRQOL in SS, including dryness, non-specific general symptoms (chronic pain, physical and mental fatigue) and emotional distress [14]. The lack of disease-specific HRQOL questionnaires meant that the first studies carried out in primary SS patients used non-specific disease questionnaires, mainly the SF-36 questionnaire; these studies found that all components of HRQOL were clearly altered in SS in comparison with control groups [15,16]. Disease-specific indexes were developed for specific evaluation of symptoms (subjective features) in SS patients, including the Profile of Fatigue and Discomfort (PROFAD), the Sicca Symptoms Inventory (SSI) [17,18], and the SS Disease Activity Index (SSDAI) for systemic features [19].

Based on the results of these studies, the EULAR has recently promoted an international collaboration between SS experts to develop consensus disease activity indexes. Two indexes have been developed, the EULAR Sjögren’s Syndrome Disease Activity (ESSDAI) for systemic involvement [12], and the EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI), which is based on a patient-administered questionnaire that evaluates subjective symptoms [11]. The ESSPRI index domains were selected according to data from the development of the SSI and PROFAD. The selection of domains and determination of their weighting was determined from the patients’ perspective, using a multiple linear regression model, where patient global assessment was the gold standard. The ESSPRI uses a 0 to 10 numerical scale, with a scale for the assessment of each of the 3 domains: dryness, fatigue and pain (joint and/or muscular) [20]. The ESSPRI index is an independent determinant of HRQOL in primary SS patients in comparison with non-Sjogren’s sicca patients [21].

Our study evaluated how the intensity of oral dryness (using the corresponding ESSPRI item) may be influenced by other features frequently reported by primary SS patients, including not only other sicca features, but also general symptoms, systemic features and vascular risk factors. The intensity of oral dryness correlated closely with the intensity of other forms of dryness, with our results confirming a finding commonly reported by SS patients: the greater the intensity of dry mouth, the greater the intensity of other forms of dryness. The finding of a correlation between the intensity of dry mouth and age might also have been expected. However, we found no correlation with the main systemic features and immunological markers of primary SS, confirming that the association between sicca and systemic symptoms is weak. Studies have shown that ESSDAI (systemic, objective activity) and ESSPRI (subjective symptoms) are not necessarily correlated [20,22], suggesting that patients’ symptoms and systemic complications are two different components of the disease that should be evaluated separately; however, these studies have also showed that ESSPRI is valid to be used as a tool to monitor therapeutic response [23].

With respect to HRQOL, we found a slight correlation between the intensity of oral symptoms and the main non-specific disease questionnaires (SF-36, HAQ, FIQ). Although there was a statistical trend for the majority of items and dimensions, no significant differences were found, suggesting that oral dryness influences general HRQOL, but, in itself, not strongly. Our results differ from those of Enger et al. [24] who found that patients with high levels of oral distress (measured by the Oral Health Impact Profile 14, OHIP-14) scored significantly worse than patients with low levels of oral distress in five of the SF-36 subscales. However, the variable used in this study (oral distress) is different from that used in our study, and therefore the results are not comparable with ours. Other studies have found a poor correlation between the intensity of oral symptoms and HRQOL [25,26].

Most studies have found that non-specific general complaints are the key factors that contribute to worse HRQOL in primary SS patients. Abnormal fatigue is a frequent reason for consultation, with a prevalence in SS of >80% and with a close association with work disability [27,28], together with chronic pain, which is reported by more than 50% of patients. Other non-specific symptoms closely associated with fatigue and pain are sleep disturbances, anxiety, and depression, with prevalence according to recent studies of nearly 15%, 20% and 40%, respectively [28-30]. A recent study by Lendrem et al. [31] found that pain and depression were the two most important predictors of HRQOL (using the EQ-5D questionnaire) using a multiple regression model adjusted for age and gender. Pain and depression accounted for 48% of the HRQOL variability, with anxiety and fatigue being other statistically significant predictors, accounting for <5%. Another recent study found that primary SS patients had higher fatigue levels and also suffered from excessive day time sleepiness. Fatigue, sleepiness, anxiety and depressive

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>t value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>4.56</td>
<td>0.53</td>
<td>8.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESPPRIfatmen</td>
<td>0.15</td>
<td>0.08</td>
<td>2.00</td>
<td>0.049</td>
</tr>
<tr>
<td>ECS</td>
<td>0.21</td>
<td>0.08</td>
<td>2.71</td>
<td>0.008</td>
</tr>
<tr>
<td>HCOL</td>
<td>1.18</td>
<td>0.43</td>
<td>2.73</td>
<td>0.008</td>
</tr>
</tbody>
</table>
symptoms, and sleep onset latency were significantly greater in primary SS patients than in controls [32].

Our results show a close association between the intensity of oral dryness and the main non-specific general complaints, including chronic pain, depression, anxiety and, especially, fatigue. Fatigue is a major predictor of worse HRQOL in primary SS [14,15,33]. In addition, Fox et al. [34] found that oral sicca severity (measured by the PROFAD-SSI questionnaire) was associated with lower energy levels and greater fatigue levels. It is unclear how fatigue could increase the intensity of oral dryness. Fatigue has been linked with poor sleep and discomfort, including joint pain and sicca symptoms [32]; therefore it may be hypothesized that a constellation of different non-specific general symptoms which are closely interrelated (pain, psychological distress, fatigue and poor sleep) might be the key factors involved in the subjective feeling of severe oral dryness in primary SS patients. However, other factors not evaluated in our study (menopause, thyroid disease, drugs with anticholinergic effects) may have also influenced oral dryness intensity.

Interestingly, we found a significant correlation between the intensity of oral dryness and the key vascular risk factors (hypertension, diabetes and hypercholesterolemia); these patients had more severe oral dryness than patients without these risk factors. Improving sicca features by strict control of coexisting metabolic alterations is an attractive possibility and has been suggested in murine models of SS [35]. Some pharmacological agents used in patients with metabolic alterations might have a potential role as future treatments in primary SS, including thiazolidinediones, metformin, antioxidants and statins [36]. Likewise, the hypothesis that the worse the control of vascular risk factors, the worse the intensity of oral dryness, is of interest and opens a pathway to the evaluation of metabolic therapeutic interventions targeted towards improving oral dryness and, globally, improving oral health.

In summary, we report on the usefulness of the ESSPRI index in evaluating HRQOL associated with oral dryness in primary SS patients. Oral dryness correlated with age and the other sicca symptoms measured by ESSPRI, but not with the main systemic and immunological SS features. In contrast, oral dryness was strongly correlated with non-specific general symptoms (fatigue, pain, psychological distress and poor sleep) and vascular risk factors. A multidisciplinary therapeutic approach including specific measures targeting general symptoms, strict control of cardiovascular disease risk factors and specific oral management by the dental team, based on individualized treatment plans that address the severity of salivary dysfunction [7], may, at present, be the best way of minimizing oral dryness and its consequences in primary SS patients.

References


