Transcultural adaptation of the EULAR activity index for primary Sjögren’s syndrome in Argentine

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Abstract

Objective: To adapt the EULAR Activity Index for primary Sjögren’s syndrome (ESSDAI) to the Argentine population.

Methods: Observational, cross-sectional study that included patients in a period of ten months. Three Argentine rheumatologists adapted and translated to Spanish the original version in English and the final version was translated back into English by a research associate whose mother language was English. In order to estimate the constructive validity of the index, the visual analogous scale (VAS) of disease activity was used by experts. A subgroup of patients attended a second visit in order to evaluate test–retest reliability.

Results: 51 patients were included, 49 (96.1%) were female, the median age was 58 (interquartile range (IQR): 49–69). The median global VAS was 10 (IQR: 4–22.25) and the median total ESSDAI score was 5 (IQR: 3–9). The correlation between the global VAS and the total ESSDAI score was 0.79. The intraclass correlation coefficient was 0.67 (95% CI: 0.32–0.92) for the total score and 0.98 (95% CI: 0.92–0.995) for the global VAS. The results of the correlation coefficient between the VAS and the scale for each domain were: constitutional symptoms: 0.46; lymphadenopathy: 0.76; glandular: 0.78; joint: 0.61; skin: 1; respiratory: 0.83; renal: 1; muscular: (no patient had myositis); peripheral nervous system: 0.72; central nervous system: 0.67; hematological: 0.96; biomarkers: 0.86.

Conclusion: The results of this study showed that the ESSDAI is a reliable and valid index for this pSS argentinian population.

Keywords: Sjögren’s syndrome, systemic disease activity, index, transcultural adaptation, ESSDAI

Introduction

Primary Sjögren’s syndrome (pSS) is a systemic autoimmune disease, characterized by lymphocytic infiltration and progressive destruction of the exocrine glands (1, 2). The systemic involvement may occur either as a form of presentation of the disease or during the disease course (3, 4).

While sicca features cause local complications and affect the quality of life, some systemic manifestations mark the disease prognosis (5, 6).

Internationally validated standardized instruments to evaluate the disease activity are required to define outcomes in clinical trials and to evaluate response to treatments in daily practice (7).

The heterogeneity and clinical variability among patients with pSS have made difficult to develop activity and damage indexes (8, 11).

The EULAR Activity Index for primary Sjögren’s syndrome (ESSDAI) was created by consensus of a large group of international experts. It is the principal tool for assessing systemic activity in pSS and is recommended to be used in trials, observational studies, and daily clinical practice (1, 11-12).

Later, EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI) was developed. ESSPRI is a very simple self-reported index designed to measure the sicca symptoms, fatigue and pain, in pSS (13-15). Both the ESSDAI and ESSPRI were validated in an international cohort that included 395 patients from 15 countries (16). Taking into account the poor correlation observed between both scores, it is suggested to use ESSDAI and ESSPRI as complementary instruments (16).
To validate these tools it is essential to test their properties in several languages and in different populations of patients with pSS (17). Currently, the ESSDAI is available in the English language, and it has been transculturally adapted into Brazilian Portuguese, but it has not been adapted and validated in the Argentine population (17).

The aim of our study was to adapt and validate the ESSDAI in an Argentine population with pSS.

Methods

This is an observational, cross-sectional study, which evaluated the validity at a first cross-sectional point and reliability at a second cross-sectional point. It was conducted at the Bernardino Rivadavia Hospital, in Ciudad Autónoma de Buenos Aires, Argentina. The patients participated during a period of 10 months and attended the first visit to evaluate the instrument validity. A group of patients attended the second visit, 7-21 days from the first visit, to assess reproducibility; in these patients, there were no treatment changes with respect to the previous visit.

Patients

Patients aged >18 years with a diagnosis of pSS according to the American-European Consensus Group (AECG) criteria were included in the study (18). Patients with secondary SS, such as secondary to rheumatoid arthritis, systemic lupus erythematosus, scleroderma, or polymyositis, and patients with uncontrolled fibromyalgia, uncontrolled diabetes, or uncontrolled hypothyroidism, were excluded.

Consecutive SSp patients were recruited from a rheumatology unit at the Bernardino Rivadavia Hospital, Ciudad Autónoma de Buenos Aires, Argentina. All participants were aged >18 years, fulfilled the AECG criteria, and were proficient in the Spanish language. Patients' clinical and sociodemographic data were assessed at baseline. Collected data included age, gender, the AECG criteria, disease duration, and glandular and systemic involvement.

Variables

Instrument

The ESSDAI is a systemic disease activity index, and it includes 12 domains (organ systems). Each domain is divided in 3/4 levels, according to their degree of activity, and scored as 0 (no activity), 1 (low activity), 2 (moderate activity), or 3 (high activity). These scores are then multiplied by an assigned weight factor, ranging from 1 to 6. The index considers disease activity at all current extraglandular manifestation, having excluded those that are secondary to cumulative damage or concomitant pathology. The final score, the sum of all weighted domains scores, ranges between 0 and 123, with 0 indicating no disease activity (1).

Visual analog scales

Taking into account that there is no gold standard to measure disease activity, the visual analog scale (VAS) performed by experts was used for each domain and for the total score to measure the disease activity with a minimum value of 0 (no disease activity) and a maximum value of 100 millimeters (maximum activity). The following active manifestations were evaluated: constitutional, lymphadenopathic, glandular, articular, cutaneous, respiratory, renal, muscular, peripheral nervous system, central nervous system, hematological, and biological markers.

Demographic variables

Gender, age in years, and disease duration in years.

Procedures

Adaptation and validation were carried out according to standard procedures (19).

Translation and back translation

Translation and back translation were carried out according to internationally accepted methodology (20). Three (N.H, L.M, M.L.S) Argentine rheumatologists, whose first language was Spanish, translated at the same time, but independently, the English version of the original scale. Subsequently, a single Spanish version was obtained by consensus. Thereafter, a research associate whose mother tongue was English, performed a retranslation into the original index language for comparison with the original English version.

Finally, 4 rheumatologists (A.S, F.E.R, M.N.M, A.C.C.P) with more than 10 years of experience in pSS management and 4 researchers with similar backgrounds but with <5 years of experience, performed the preliminary assessment of the instrument.

Validation

To assess the construct validity of the index and because, to the best of our knowledge, there is no gold standard to measure the disease activity, the VAS was used in each domain and in the total score to measure disease activity with a minimum value of 0 (no disease activity) and a maximum value of 100 millimeters (maximum activity). The VAS evaluation was conducted by 3 specialists with over 20 years of experience in the management of pSS and two specialists with 5- to 10-year experience. The index was performed by physicians in the final year of specialty training. Both assessments were done independently and blindly.

To evaluate the instrument validity, a complete clinical evaluation, chest radiography, and laboratory tests (blood count, urea, creatinine, electrolytes, bicarbonate, urine, protein dosage, C3, C4, and cryoglobulins) were performed in all patients. In singular cases according to clinical and medical criteria, further tests were performed: anemia characterization, muscle enzyme dosage, immunoglobulin dosage, ammonium overload test (nephrology), parotid ultrasound, thorax high-resolution computed tomography, pulmonary function studies, electromyogram, and neurocognitive tests (neuropsychology).

Reliability

A group of patients attended the 2nd visit, 7-21 days from the first, to assess reproducibility (test–retest reliability). In these patients, no treatment changes with respect to the previous visit were made. Both VAS by an expert and the ESSDAI by physicians in the last year of specialty training was done, again independently and blindly.

Ethical approval

The study was approved by the local Ethics Committee and has been performed in accordance with the ethical standards laid down in the Declaration of Helsinki. All patients gave their informed consent prior to their inclusion in the study.

Main Points

- The development of the ESSDAI has provided a helpful, objective instrument to evaluate systemic involvement in pSS.
- Cross-cultural adaptation aims to produce a comparable instrument applicable to different languages, cultures, and countries.
- The results of this study showed that the ESSDAI is a reliable and valid index for this Argentinian population with pSS.
Discussion

A standardized instrument is a useful tool to measure disease activity and therapeutic responses, both in clinical trials as in daily practice. Cross-cultural adaptation aims to produce a comparable instrument applicable to different languages, cultures, and countries. The measurements performed with this tool also need to be reproducible, among every observer, without changes over time (20, 21).

The development of new biologic agents increases the need of reliable clinimetric tools. These instruments should aim to establish a correct follow-up of disease activity and response to treatments (11).

The development of the ESSDAI has provided a helpful, objective instrument to evaluate systemic involvement in pSS. The ESSDAI has a high content validity and includes the main systemic manifestations seen in the largest series of patients with pSS; its intention is to stratify the items of each domain to treat them, and it has been approved by more than 40 international experts in SS (4).

Also, ESSDAI has been shown to be sensitive to change in studies with different biologic agents, such as rituximab, belimumab, and abatacept (22-25).

An important point when designing a systemic index is to differentiate between the damage and disease activity. The most frequent approach is to contemplate manifestations as active only if they are new or worsening. The problem with these scoring systems, when patients are evaluated at two time points, is that a persistent manifestation will not be rated at the second time point, which may cause an erroneous interpretation of improvement even though the patient’s condition has not changed. To avoid this, all ESSDAI items were defined without reference to a previous assessment, but with an instruction not to score as active, a stable and chronic manifestation related to damage (1, 27).

In our study, the ESSDAI showed to be a valid tool; this was demonstrated by a very good correlation between the total scale score and the global VAS (rho, 0.79). Also, the score for each domain showed a very good-to-excellent range (IQR), according to its distribution. The categorical variables were reported as proportion. The Spearman correlation coefficient was used to quantify the degree of correlation between the VAS and the score for each domain and between the VAS scale and the total score: 0.01-0.20 was considered to indicate a weak correlation, 0.21-0.40 regular, 0.41-0.60 good, 0.61-0.80 very good, and 0.81-0.99 excellent correlation. Intraclass correlation coefficient (ICC) was used to assess reproducibility. A p-value <0.05 after any comparison was considered significant. The Statistical Package for Social Sciences (SPSS) was used.

Results

We included 51 consecutive patients, 49 (96.1%) female, with a median age of 58 (IQR, 49-69) and median time of disease duration of 6 years (IQR, 4-10.8). The median global VAS scale was 10 (IQR, 4-22.3), and the median ESSDAI score was 5 (IQR: 3-9). Their characteristics are reported in Table 1. Systemic involvement measured both by VAS and ESSDAI is presented in Table 2.

The results of the Spearman correlation coefficient between global VAS and ESSDAI, and between VAS and scale for each domain, are presented in Table 3. The correlation between VAS and overall total scale score was 0.79.

In some domains, we found a low percentage of patients with disease activity at the time of evaluation. The cutaneous, renal, and hematological domains showed the higher correlation scores.

Ten patients attended the 2nd visit to assess reproducibility. The ICC was 0.67 (95% confidence interval [CI], 0.32-0.92) for the total score and 0.98 (95% CI, 0.92-0.995) for VAS.

Table 1. Characteristics of 51 patients with primary Sjögren’s syndrome.

| Variables                      | Value (Median, IQR) |
|-------------------------------|---------------------|
| Age m (IQR)                   | 58 (49-69)          |
| Gender (female)               | 49 (96.1%)          |
| Disease duration (years), m (IQR) | 6 (4-10.75)   |
| Ocular symptoms               | 98%                 |
| Oral symptoms                 | 100%                |
| Objective ocular involvement  | 86.27%              |
| Objective oral involvement    | 73.68%              |
| Anti-SSA/Anti-SSB             | 83.67%              |
| Positive salivary gland biopsy| 84.09%              |

Table 2. Number of patients with systemic involvement assessed by VAS and ESSDAI.

| Domains                | VAS | ESSDAI |
|------------------------|-----|--------|
| Constitutional         | 14  | 9      |
| Lymphadenopathy        | 6   | 7      |
| Glandular              | 5   | 5      |
| Articular              | 23  | 21     |
| Cutaneous              | 3   | 3      |
| Pulmonary              | 20  | 17     |
| Renal                  | 4   | 4      |
| Muscular               | 2   | 0      |
| Peripheral nervous     | 4   | 2      |
| Central nervous system | 2   | 1      |
| Hematological          | 14  | 13     |
| Biological             | 32  | 32     |

Table 3. Spearman correlation coefficient between VAS and ESSDAI.

| Domains                                | Spearman correlation (rho) |
|----------------------------------------|-----------------------------|
| Constitutional                         | 0.46                        |
| Lymphadenopathy                        | 0.76                        |
| Glandular                              | 0.78                        |
| Articular                              | 0.61                        |
| Cutaneous                              | 1                           |
| Pulmonary                              | 0.83                        |
| Renal                                  | 1                           |
| Muscular                               | -                           |
| Peripheral nervous system               | 0.72                        |
| Central nervous system                  | 0.67                        |
| Hematological                          | 0.96                        |
| Biological                             | 0.86                        |
| Total score-global VAS                 | 0.79                        |

p <0.05 in all cases.
correlation with the VAS domain, in most cases. We found a very good reproducibility for the ESSDAI and an excellent reproducibility (reliability) for the total VAS.

As a strength of our study, the evaluators were independent and blinded, and their assessment included not only the VAS and total score, but also that of each domain.

The limitation to our study was that the majority of patients included presented a mild to moderate disease activity, in addition to the relative low number of patients. Other limitation of our study is that it was carried out in a single center, and we did not evaluate sensitivity to change.

We found a very good correlation in the total score and in most domains between ESSDAI and VAS. We observed a very good reproducibility of ESSDAI. The results of this study showed that the ESSDAI is a reliable and valid index for this Argentinian population with pSS.

Ethics Committee Approval: Ethics committee approval was received for this study from Ethics Committee of Hospital Bernardino Rivadavia.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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