Skin Barrier Function in Patients with Primary and Secondary Sjögren's Syndrome

Anna Olewicz-Gawlik[1,3], Adriana Polańska[2], Dorota Trzybulska[3], Michalina Nowak-Gabryel[4], Katarzyna Błochowiak[5], Jarosław Kocięcki[4], Jerzy Sokalski[5], Ryszard Żaba[2], Zygmunt Adamski[6], Aleksandra Dańczak-Pazdrowska[6]

[1]Department of Infectious Diseases, Infectious Diseases, Hepatology and Acquired Immune Deficiencies, Poznan University of Medical Sciences, Poznan, Poland; [2]Department of Dermatology and Venereology, Poznan University of Medical Sciences, Poznan, Poland; [3]Department of Rheumatology and Clinical Immunology, Poznan University of Medical Sciences, Poznan, Poland; [4]Department and Clinic of Ophthalmology, Poznan University of Medical Sciences, Poznan, Poland; [5]Department of Oral Surgery, Poznan University of Medical Sciences, Poznan, Poland; [6]Department of Dermatology, Poznan University of Medical Sciences, Poznan, Poland

Corresponding author:
Adriana Polańska, MD
Department of Dermatology and Venereology
Poznań University of Medical Sciences
Poznan
Poland
adriana-polanska@wp.pl

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ABSTRACT Sjögren's syndrome (SS) is a systemic autoimmune disease. A large percentage of patients with SS suffer from dry skin, the cause and pathogenesis of which in this group of patients remains obscure. The aim of the present study was to investigate skin barrier function in patients with SS. Measurements of transepidermal water loss (TEWL) and hydration of stratum corneum (corneometry, CM) were performed in 30 female patients with SS (17 with primary SS and 13 with secondary SS), 20 patients with atopic dermatitis (AD) and 14 healthy controls. There were no statistically significant differences in TEWL values between the three investigated groups, while CM values were significantly decreased in patients with AD when compared with patients with SS and the healthy controls. Based on the obtained results, skin barrier function and hydration in patients with SS showed no functional alterations.

KEY WORDS: xerosis, Sjögren's syndrome, atopic dermatitis

INTRODUCTION

Sjögren's syndrome (SS) is a systemic chronic autoimmune disorder, which can manifest alone as primary (p)SS or in association with other autoimmune rheumatic disease as secondary (s)SS (1). It is characterized by exocrine gland dysfunction and lymphocytic infiltrations. The dominant symptoms, namely xerophthalmia and xerostomia, result from epithelitis which causes glandular destruction. Clinical experience has shown that the majority of patients with SS also suffer from dry skin and xerosis (2). The cause of subjective symptoms, such as dryness sensation or xerosis, clinically manifested as roughness, loss of elasticity, scaling, cracks, and fissures, is unclear. The study by Bernacchi *et al*. showed that cutaneous xerosis in primary patients with (p)SS, unlike xerophthalmia and xerostomia, is not a result of a chronic

lymphocytic infiltrate of the eccrine or sebaceous glands, but is related to peculiar biochemical alterations of the epidermis, similar to those seen in elderly patients (3).

To address the issue of dry skin sensation in patients with SS with differentiation between the primary and secondary variants of the syndrome, we assessed skin functional parameters such as transepidermal water loss (TEWL) and stratum corneum hydration in these groups of patients.

METHODS

We enrolled 30 consecutive female patients with SS to this pilot study (mean age ± Standard Deviation 50.4±13.5, 17 with (p)SS and 13 with secondary (s)SS), all of whom fulfilled the 2002 American-European Consensus Group classification criteria (1). Fourteen age- and sex-matched healthy subjects formed the control group (mean age 50.4±10.1), and 20 patients with atopic dermatitis (AD) formed the disease control (mean age 35±12.3). The protocol of this study was approved by the Institutional Review Board at Poznan University of Medical Sciences (number 211/13) and informed consent was obtained from all investigated subjects before any study procedure was carried out.

The workup comprised the complete medical history and thorough physical examination, which included Schirmer's test and fluorescein tear break-up time (TBUT) test. To assess xerostomia, all patients also completed the visual analogue scale (VAS). Two noninvasive methods were performed to determine the skin barrier functions, namely the measurement of TEWL and hydration of stratum corneum (corneometry, CM). TEWL was determined using Tewameter TM 300 (Courage-Khazaka, Germany) according to the guidelines of the standardization group of the European Society of Contact Dermatitis (at least 20 measurements given as a mean value and expressed in SI units (g/m^2/h) were carried out, normal range: 0-25 g/m^2/h) (4). Corneometry was performed with the use of Corneometer CM 825 (Courage-Khazaka, Germany), the main principle of which is based on the fact that the dielectric constant of water is 81 but is lower for dry skin. A normal value of stratum corneum hydration was accepted as higher than 40 U. Five measurements given as a mean value in arbitrary units (range: 0-130) were determined in accordance with guidelines (5). Both parameters were analyzed within the flexural area of the right extremity – forearm, and in patients with AD the area was without inflammatory lesions. All skin studies were performed by the same trained dermatologist in the same room conditions, after 15-20 minutes of acclimatization. The patients did not use an emollient 24 h before the test. All patients were also asked about the feeling of dry skin in a form of yes/no question. Blood samples from patients were collected at the time of clinical examination on fasting conditions. Routine laboratory tests included measurement of the erythrocyte sedimentation rate (ESR, Westergren method) and detection of antinuclear antibodies (ANA) by indirect immunofluorescence on HEp-20-10 cells (Euroimmun, Germany) and their specification using blot type test (Euroimmun, Germany). All samples were stored at -20 °C before estimations were made.

Table 1. Clinical and laboratory characteristics of patients with Sjögren's syndrome (n=30)

	Primary Sjögren's syndrome patients (n=17)	Secondary Sjögren's syndrome patients (n=13)
Age	48.2±14.9	53.6±10.6
Disease duration (years)	5 (8)	2 (4)
Antinuclear antibodies (%)	15 (88.2)	9 (69.2)
anti-Ro/SSA antibodies (%)	13 (76.5)	5 (38.5)
anti-La/SSB antibodies (%)	8 (61.5)	3 (23.1)
Xerostomia (visual analogue scale, mm)	56 (54.0)	14 (49.5)
Rheumatoid arthritis (%)	0	9 (69.2)
Systemic lupus erythematosus (%)	0	3 (23.1)
Mixed connective tissue disease (%)	0	1 (7.7)
Erythrocyte sedimentation rate (mm/h)	19 (37.0)	20.5 (14.5)
Therapy with low-dose methylprednisolone (%)	3 (17.6)	6 (46.2)
Therapy with chlorochine (%)	0	3 (23.1)
Therapy with methotrexate (%)	0	5 (38.5)
Therapy with azathioprine (%)	1 (5.9)	1 (7.7)
Current smokers (%)	2 (11.8)	1 (7.7)
Data presented as the median (interquartile range), mean ± standard deviation or as n (%).		

Table 2. Skin barrier function parameters in patients with Sjögren's syndrome, atopic dermatitis, and healthy subjects

	primary SS (n=17)	secondary SS (n=13)	Atopic dermatitis (n=20)	Healthy controls (n=14)
Transepidermal water loss (g/m²/h)	9.1 (13.6)	7.2 (9.4)	13.7 (8.2)	9.8 (3.3)
Corneometry (U)	42.3 (24.5)	44.0 (16.8)	30.5 (15.8)	34.6 (11.9)
Data presented as the median (interquartile range); SS: Sjögren's syndrome				

Calculations were carried out with Microsoft Excel 2010 and STATISTICA version 10 software (StatSoft Inc.). Patient demographic data were analyzed using descriptive statistics. Contiguous data were tested for normal distribution using the Kolmogorov–Smirnov test. In case of normally distributed data, results were presented as mean ± Standard Deviation (SD), whereas non-normally distributed data were expressed as median (interquartile range; IQR). Depending on the number of analyzed groups, the differences between them were tested using the Mann-Whitney U test or analysis of variance (ANOVA) by ranks followed by post-hoc multiple comparisons of the mean ranks. Correlations between variables within the group were analyzed using Spearman's rank-order correlation coefficient (r). The differences were considered to be statistically significant at $P<0.05$.

RESULTS

The characteristics of the SS patient group at the time of examination is shown in Table 1.

In the pSS subgroup, 12 (70.6%) patients complained of dry skin, and 10 (76.9%) in the sSS subgroup. Out of 17 patients with pSS, only 3 (17.6%), and in the sSS subgroup only 1 (7.7%), patient had TEWL values above the normal range. The stratum corneum hydration was abnormal in 7 (41.2%) patients with pSS and in 4 (30.8%) with sSS. There were no statistically significant differences in TEWL values between all investigated groups, but CM results were significantly decreased in patients with AD when compared with SS subjects and the healthy controls (Figure 1). The results of TEWL and CM are summarized in Table 2.

In pSS, CM values were significantly associated with xerostomia assessed with VAS ($r=0.51$, $P<0.01$), ESR ($r=0.65$, $p<0.01$) and the titre of ANA ($r=0.5$, $P=0.01$). No other statistically significant correlations were found between skin barrier tests and the rest of studied parameters; in particular the duration of the disease and the presence of ANA, including anti-SSA and anti-SSB antibodies, were not associated with cutaneous dryness measures.

DISCUSSION

The current report focuses on skin barrier function and hydration in patients with pSS and sSS.

Despite a relatively high proportion of patients complaining of dry skin, we did not observe statistically significant differences in TEWL and CM between the SS group and healthy controls. This finding indicates that complaints of dry skin observed in patients with SS are subjective rather than objective and is in agreement with the results of the study of Bernacchi *et al*. (3), who detected no pathological alterations in CM and evaporimetry in patients with pSS and demonstrated that xerosis in pSS is not a feature of chronic autoreactive lymphocytic exocrinopathy. Other pathophysiological hypotheses of skin dryness include neurologic conditions (i.e. neuropathy), frequent in SS (6). However, as no patients underwent electrodiagnostic testing due to lack of clinical indications, the results of the present study could not confirm or exclude neuropathy as a cause of the feeling of dry skin in the investigated subjects.

Moreover, our results point to a distinct pathogenetic mechanism of dry skin in patients with SS and AD. Xerosis is a specific component of AD and, in contrast to subjects with SS, we found reduced stratum corneum water content in the AD group. The observation was in agreement with a previous study, which showed that the skin of patients with AD lacks moisture (7).

CONCLUSION

In conclusion, patients with pSS and sSS present no alterations in skin barrier function and hydration parameters.

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