Evaluation of skin barrier function in allergic contact dermatitis and atopic dermatitis using method of the continuous TEWL measurement

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Abstract

Purpose: The aim of study was to determine usefulness of the method of continuous TEWL measurement in the evaluation of skin barrier function in physiological conditions and in allergic contact dermatitis (ACD) and atopic dermatitis (AD).

Material and methods: Study was conducted on a group of 86 persons: 48 patients with allergic contact dermatitis, 18 with atopic dermatitis and 20 healthy individuals. Measurements of transepidermal water loss were made using custom-constructed device for continuous TEWL measurement. In each person the measurements of TEWL were made 4 times: measurement 0 (baseline) – before occlusion with 1% lauryl sulphate for 24 h, measurement 1-15 minutes after SLS patch removal, measurement 2-30 minutes after measurement 1 and measurement 3-30 minutes after measurement 2. Obtained data were statistically analyzed.

Results: TEWL ratio values obtained in measurement 0 were as follows in individual groups of patients: 13.20 ± 8.25 in the AD patients, 10.09 ± 8.29 in ACD patients and 9.02 ± 5.99 in control group. Analogous TEWL values in the subsequent measurements were: in measurement 1 – 16.08 ± 11.17; 11.63 ± 6.43; 17.39 ± 12.41, in measurement 2 – 23.72 ± 14.58; 14.71 ± 6.46; 17,55 ± 8.25, measurement 3 – 24.09 ± 14.93; 16.34 ± 6.32; 18.44 ± 8.26. TEWL ratio values were higher in both groups of patients as compared to control group but not statistically significant (p = 0.1778). After 24 h exposition to SLS, TEWL ratio values increased in all examined groups as compared to baseline (0) measurement. All measurements, except for measurement No 1 in AD group of patients, showed statistically significant differences. The highest increase of TEWL values were observed in group of AD patients.

Conclusions: Delay in skin reaction to SLS in patients with atopic dermatitis provides evidence for different properties of water barrier of the skin in this group as compared to healthy individuals. Increasing tendency in TEWL values 1 hour after SLS removal might reflect persistent damage to water barrier of the skin by detergent. Method of continuous assessment of water barrier of epidermis, through the possibility of multiple measurement by TEWL in examined periods of time, decreased the risk of mistake and increased accuracy of measurement. Measurement of TEWL values allows for assessment of otherwise unnoticed damage to water barrier of the skin.

Key words: skin barrier function, TEWL, continuous measurements, allergic contact dermatitis, atopic dermatitis.

Introduction

The outermost layer of the epidermis, the stratum corneum (SC), plays an essential role in protection the body from water loss. It is commonly known as a skin barrier. It has been shown that correct function of the water barrier depends on many factors, of which the most important are:

1. integrity of the stratum corneum [1,2]
2. proper degree of its hydration [3,4]
3. state of the intercellular lipid matrix [5]
4. size of the corneum cells [6].

A substantial number of non-invasive bioengineering techniques have recently been introduced with the aim to evaluate functional state of the skin barrier [7,8]. Skin surface hydration can be measured by electrical methods such as: measurement of resistance or conductance and capacitance [9-12]. The most direct method, expressing diffusional water loss through the skin, is transepidermal water loss measurement (TEWL). The

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principle of the method is based on measuring water vapour pressure gradient by the use of temperature and humidity sensors at two different levels above the skin surface. TEWL is then calculated and expressed in grams/m^2/h. Transepidermal water loss depends on a number of personal (age, examined region, skin temperature, sweat) and environmental (temperature and humidity, air circulation) factors [13-15]. The impairment of the water barrier and an increase in TEWL is found in pathological conditions with epidermis being damaged and in other diseases with dryness of the skin and matrix lipid disturbance [16-18].

The aim of study was to estimate usefulness of continuous TEWL measurement, using earlier constructed device [19], in evaluation of skin barrier function in physiological conditions, in allergic contact dermatitis (ACD) and atopic dermatitis (AD). We also aimed to determine the influence of SLS on transepidermal water loss in healthy persons and patients with ACD and AD.

Material and methods

Study was conducted on a group of 86 persons divided into 3 subgroups:

I. 48 – 31 female (F) and 17 male (M) – patients, at the age ranging from 17 to 62 (mean 41.5) years with allergic contact dermatitis;

II. 18 (8 F and 10 M) patients, age from 15 to 55 (mean 29.1) years with atopic dermatitis;

III. 20 (18 F and 2 M) healthy volunteers, age from 23 to 50 (mean 29.6) years as a control group.

ACD was confirmed by positive results of patch tests; Hanifin and Rajka criteria were used to recruit patients to AD group. Studies were conducted, after treatment cessation, in the state of remission of the skin lesions. Control group consisted of healthy individuals free of any allergic disease in familial and personal history.

Elicitation of irritant skin reaction by SLS

To determine the influence of SLS on skin barrier function 1% aqueous solution of SLS was used. A cotton patch 1 x 1 cm wet with 0.1 ml 1% SLS was applied for 24 hours on volar surface of forearm in occlusion. After removing the patch with SLS, visual evaluation of the skin was performed in four-step scale considering the presence of dryness, lichenisation and erythema: 0 – absence, 1 – weak, 2 – prominent, 3 – strong.

TEWL measurements

The measurements of transepidermal water loss were made by the use of custom-constructed device and earlier elaborated method was applied for continuous TEWL measurement (*Fig. 1*).

In all persons TEWL was measured 4 times on the volar surface of the forearm:

Measurement 0 – basal TEWL

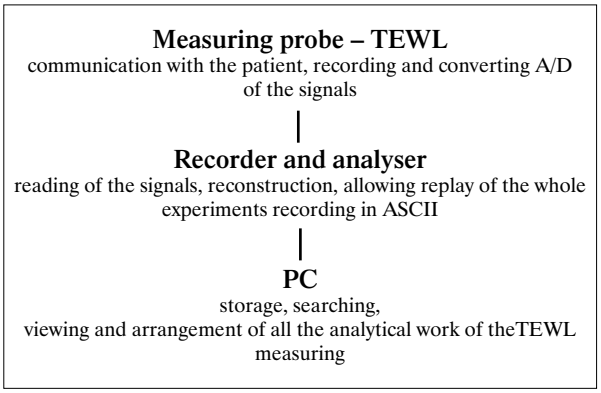
Measurement 1-15 minutes after SLS patch removal

Measurement 2-30 minutes after measurement 1

Measurement 3-30 minutes after measurement 2

The duration of each measurement was 2 minutes (*Fig. 2*).

Figure 1. Method for continuous measurement of TEWL.



In each person median TEWL ratio value and coefficient of variation were calculated for each of 4 measurements.

Statistical analysis

Difference in TEWL values and coefficient of variation between each group of examined persons were estimated using one-factor analysis of variance. Repeated measures analysis of variance was used to evaluate the influence of SLS on TEWL values and coefficient of variation in subsequent measurements. The differences between measurement 0 (baseline) and 1-3 were calculated using t-test for dependent variable.

Results

1. Assessment of the influence of disease and SLS on TEWL ratio values

TEWL ratio values in three examined groups are shown in *Tab. 1*.

Normal distribution of individual measurements has been rejected basing on Shapiro-Wilk test. Logarithmic transformation of data enabled parametric tests to be applied for the analysis [20]. One-factor variance analysis has been used in individual groups of examined persons in order to differentiate TEWL ratio values. Values 0 (baseline measurements) were analyzed for three groups. TEWL ratio values obtained in measurement 0 were higher in both groups of patients with relation to control group but not statistically significant.

Evaluation of the influence of SLS on skin was performed by the use of multidimensional variance analysis with repeated measurements. Increase in TEWL ratio values has been found in all examined groups of patients after 24 hours exposition to SLS as compared to baseline (0) measurement.

Measurements 1-3 have been analyzed in order to determine dynamics of changes in TEWL ratio values after removal of SLS from the surface of the skin. Distribution of mean TEWL ratio values (after logarithmic transformation) is shown in *Fig. 3*.

Student t test, used for dependent variables, was applied to compare analysis of measurement 0 with measurements 1-3 in individual groups (*Tab. 3*). No significant differences ($p=0.123$) were found between measurement 0 and 1 in atopic dermatitis

Figure 2. Continuous recording of TEWL during 2 min test.

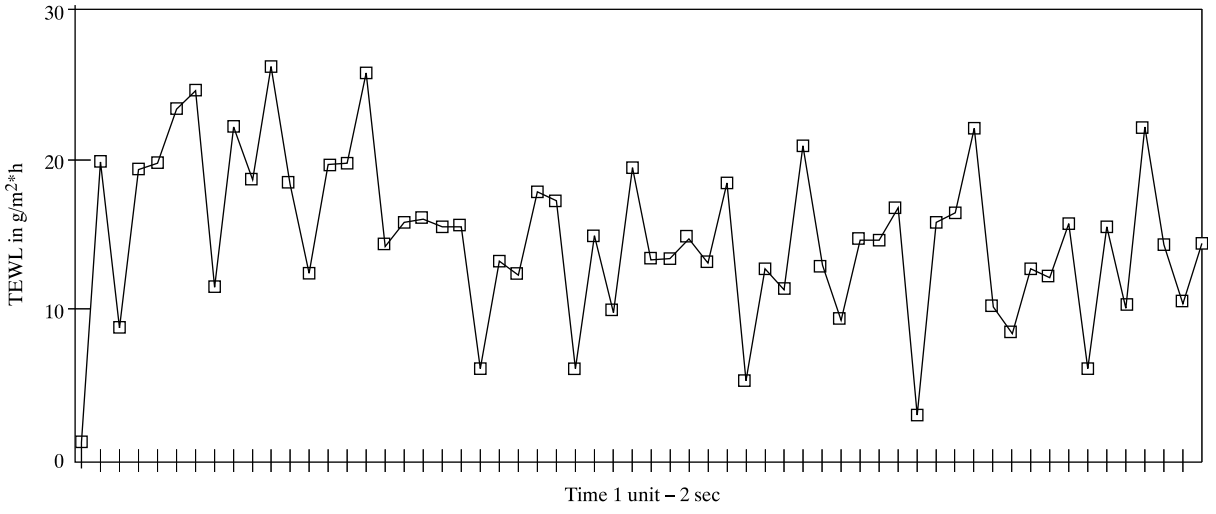


Table 1. Values of transepidermal water loss in patients with allergic contact dermatitis, atopic dermatitis and control group.

	Measurements			
	0 (baseline)	1	2	3
ACD - mean	10.09	11.63	14.71	16.34
Median	7.42	9.86	13.38	15.36
Standard deviation	8.29	6.43	6.46	6.32
AD - mean	13.202	16.08	23.72	24.09
Median	11.67	13.37	21.39	21.15
Standard deviation	8.25	11.17	14.58	14.93
Control group - mean	9.02	17.39	17.55	18.44
Median	7.41	13.54	16.35	16.91
Standard deviation	5.99	12.41	8.25	8.26

Figure 3. Distribution of mean values of logarithms of TEWL coefficients in patients with ACD, AD and control group.

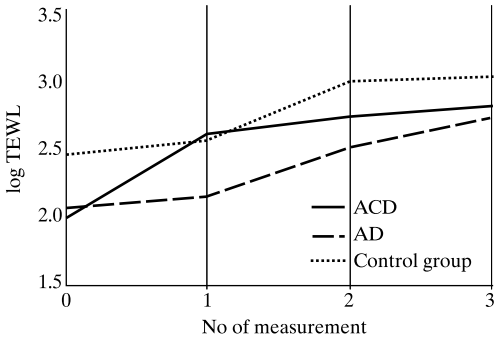
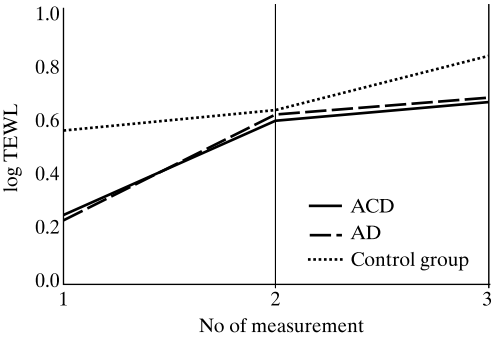


Table 2. Variation of TEWL values coeffictient.

	Measurements			
	0 (baseline)	1	2	3
ACD - mean	69.78	63.08	60.39	53.25
Median	64.24	63.3	61.61	53.48
Standard deviation	30.62	21.66	26.8	15.55
AD - mean	58.37	56.69	41.7	40.59
Median	55.69	54.81	37.09	30.65
Standard deviation	29.52	29.73	18.41	21.06
Control group - mean	67.34	58.8	47.3	44.9
Median	68.54	58.7	46.04	46.34
Standard deviation	16.04	26.19	16.18	16.73

Figure 4. Differences between measurement 0 and measurements 1-3.



group of patients. Remaining measurements showed statistically significant differences. *Fig. 4* shows graph of differences.

2. Evaluation of the influence of disease (ACD and AD) and SLS on variability of TEWL values

Variability of TEWL values is shown in *Tab. 2*.

Coefficient of variation values were analyzed. Basing on Shapiro-Wilk test normal distribution of results of individual measurements in all examined groups was rejected. Logarithmic transformation of data enabled the use of parametric tests for the analysis.

Analysis of TEWL ratio variability has been performed basing on measurement 0 in individual disease (atopic dermatitis vs. contact dermatitis) by the use of one-factor variance analysis. It did not show the influence of the disease on variability of the ratio ($p=0.151$)

Analysis of the influence of the disease and SLS on variability of TEWL ratio, calculated from measurements

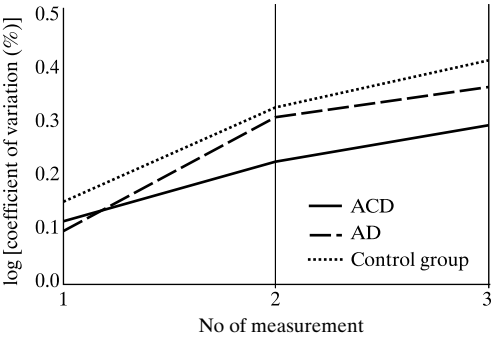
Table 3. Differential analysis of measurement 0 with measurements 1-3 in individual groups.

	P value		
	ACD	AD	Control group
Measurement 1	0.013	0.123#	0.013
Measurement 2	0.0001	0.0001	0.005
Measurement 3	0.0001	0.0001	0.0001

Table 4. Differential analysis of coefficient of variation of measurement 0 with measurements 1-3 in individual groups.

	P value		
	ACD	AD	Control group
Measurement 1	0.176#	0.57#	0.212#
Measurement 2	0.017	0.02	0.02
Measurement 3	0.0033	0.013	0.0053

Figure 5. Mean of values of differences in variation coefficient of baseline measurement and measurements 1-3.



0-3, was done by the use of multidimensional variance analysis with repeated measurements. It showed that variability of TEWL values does not significantly depend on examined group (p=0.108). TEWL ratio values were statistically significant in time-dependent manner (*Tab. 4*, *Fig. 5*).

Discussion

Baseline TEWL values did not differ among the groups of patients involved in the study. 24 hours of skin exposition to SLS caused increase in TEWL values in all examined groups of patients. The character of changes was similar, however, in group of patients with AD shortly after SLS patch removal (measurement 1), no significant changes in TEWL values were observed as compared to measurement 0. This "delay" of skin reaction to SLS in patients with AD, observed in case of coefficient of variation as well, might be reflective of changes in water barrier properties of skin in this group of patients. In case of coefficient of variation of TEWL values it concerned all examined groups of patients after SLS patch removal. It may indicate that skin irritation by SLS could be a second factor influencing TEWL values, independently on disease state.

With regards to basic TEWL values, no significant differences were found between skin of patients with allergic contact dermatitis during remission and healthy individuals, which is consistent with other studies [21,22]. It was shown, however, that skin sensitivity to SLS within unaffected part of the skin in patients with acute stage of contact dermatitis is increased. Agner et al. [23] was able to show significant differences in TEWL values in chronic phase of contact dermatitis which is in opposition to studies performed by Blichman and Serup who noted increase in TEWL values in acute as well as in chronic stage of contact dermatitis [24]. Increased TEWL values observed in examined patients, after skin exposition to SLS, became more explicit in the course of time. It may be indicative of a permanent damage to water barrier of the skin despite removal of the irritant factor. It is worth noting that other authors found higher TEWL values after few hours, or even few weeks, of exposure to 1% SLS. Multiple exposition to detergent caused damage to water barrier of the skin which persisted up to 9 weeks [25].

Despite a relatively high number of publications on different chemical compounds affecting TEWL values, most of them were uncontrolled, performed with temporary recording evaporimeter [26]. Results obtained by this method exhibited substantial inter-study variance. The main limitation of the above studies was, however, possibility of performing only single measurements during the course of clinical test. This could burden the final results with significant mistake.

Modified method, used in our study, decreased the risk of mistake and increased accuracy of measurement through the possibility of taking multiple measurements during 2 minutes of clinical test. We exploited the model used by others [27-29]. It was supplemented with additional triple TEWL measurements taken every 30 minutes which enable dynamic assessment of changes in skin permeability after SLS patch removal. Parallel determination of dispersion of results was additional criterion utilized in this test. Coefficient of variation, reflecting oscillation of measurements around the median value, has been found to be clinically significant.

It seems that coefficient of variation is owing to temporary changes in skin permeability to water, which is to a greater extent dependent on internal conditions than on external ones, such as air motion. In case of both atopic and contact dermatitis, coefficient of variation may reflect temporary changes in skin reactivity to different irritating compounds, such as SLS. To our knowledge there is no information in the literature on potential significance of such dynamic monitoring of water barrier of skin. In our studies we did not find changes in coefficients of variation in all examined groups but we did observe changes in TEWL values. TEWL ratio values were statistically significant in time-dependent manner. It is, however, difficult to judge which method of interpretation is more objective in its ability to assess changes in water barrier of the skin. It seems that evaluation of the status of skin barrier by other biophysical methods, like assessment of its electrical properties, could complement measurements based solely on TEWL method.

In conclusions: 1) delay in skin reaction to SLS in patients with atopic dermatitis provides evidence for different properties of water barrier of the skin in this group of patients as compared to healthy individuals, 2) increasing tendency in TEWL values, one hour after SLS removal, might reflect persistent damage to water barrier of the skin by the detergent, 3) our own method of continuous assessment of water barrier of epidermis, through the possibility of multiple measurement by TEWL in examined periods of time, decreased the risk of mistake and increased accuracy of measurement, 4) measurement of TEWL values allows for assessment of otherwise unnoticed damage to water barrier of the skin.

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