Instrumental assessment of atopic eczema: Validation of transepidermal water loss, stratum corneum hydration, erythema, scaling, and edema

Elisabeth A. Holm, MD,[a] Hans C. Wulf, MD, DMSc, DPharm,[b] Lars Thomassen, MSc,[c] and Gregor B. E. Jemec, MD, DMSc[a]
Copenhagen and Ballerup, Denmark

Background: Quantification of skin diseases can be carried out in many ways. Clinical scores are widely used in atopic eczema (AE), and noninvasive instruments are a relevant supplement.

Objective: Our purpose was to validate 5 noninvasive instruments in quantification of AE severity.

Methods: In all, 101 patients with AE and 30 control subjects were assessed twice in a clinical cross-sectional examination. Assessment of transepidermal water loss, stratum corneum hydration, erythema, scaling, and subepidermal edema was assessed on 3 predetermined skin sites.

Results: The methods discriminated among various severity degrees and correlated significantly with objective assessment of disease severity. High correlations were found among instruments assessing acute symptoms of AE. Threshold values for transepidermal water loss and capacitance were found.

Limitations: No gold standard exists for severity assessment of atopic eczema. Therefore, the methods used cannot be validated in relation to such a standard. Furthermore, atopic eczema is a generalized disease and the methods used assess target lesions. By assessing target lesions, information about the disease is reduced.

Conclusion: Noninvasive instruments are valuable in quantification of disease severity in a mixed group of patients with active AE. Assessment with ultrasound has contributed new information about the pathophysiology in AE. (J Am Acad Dermatol 2006;55:772-80.)

Today, patient history and clinical scoring are the main tools for dermatologists when attempting to assess the morbidity of patients with atopic eczema (AE). These methods, however, frequently show poor interobserver and intraobserver reproducibility, because of the different way doctors assess, for example, erythema or dry skin.[1] In addition, many of the scoring systems include assessment of disease extent, which has been shown to be particularly difficult.[2] New clinical score systems to assess the severity of AE are regularly proposed.[3] To provide objective and reproducible methods, instrumental evaluation of skin morphology and functions have also been proposed. Noninvasive techniques have continuously been developed and improved. Several of these techniques have reached a technologic maturity, which suggests that a more routine use is possible.[4-7]

Abbreviations used:

AE:	atopic eczema
SC:	stratum corneum
SCORAD:	Severity Scoring of Atopic Dermatitis
SLEB:	subepidermal low echogenic band
TEWL:	transepidermal water loss

From the Departments of Dermatology at Roskilde Hospital, Copenhagen University,[a] and Bispebjerg Hospital, Copenhagen Hospital[b]; and Department of Biostatistics, LEO Pharma, Ballerup.[c]

Supported by Eastern Danish Research Forum for Health Sciences (Copenhagen University), The Foundation of Region 3 (east Denmark), Haensch's Foundation, Buchard's Foundation, Bang's Foundation, The Danish Dermatological Society, and an unrestricted educational grant from LEO Pharma. LEO Pharma is a private company and is not tied to any of the 5 noninvasive instruments used.
Conflicts of interest: None identified.
Accepted for publication March 14, 2006.

Reprint requests: Elisabeth A. Holm, MD, Department of Dermatology, Roskilde Hospital, Koegevej 7–13, DK–4000 Roskilde. E-mail: rselho@ra.dk.

Published online June 13, 2006.
0190-9622/$32.00

doi:10.1016/j.jaad.2006.03.036

Particularly the barrier function has been studied and often found to be abnormal in patients with AE. Instruments suitable for studying AE should reflect the different aspects of inflammation and epidermal barrier insufficiency, which play a role in this disease. The increased water evaporation rate and reduced water content of stratum corneum (SC) can be measured as an increased transepidermal water loss (TEWL) and a lower skin capacitance. Measurements of capacitance in SC have been shown to correlate with actual water content.[8,9] Erythema caused by inflammation is present in the acute and chronic phase of eczema. Skin color, including erythema, can be measured by two different principles (ie, reflectance or spectroscopy).[10-12] The associated edema can be studied by high-frequency ultrasound, which identifies the characteristic echo profile of edematous skin.[13,14] Finally, the associated scaling and roughness of the skin can also be measured, although the methods are less standardized. Profilometry is used to describe changes in surface topography and adhesive-coated tape have been used to study scaling.[15]

The data reported in this study were collected as a part of a larger study focusing on the quantification of AE with noninvasive instruments, clinical scores, and quality-of-life methods. Details about clinical scores in relation to noninvasive methods and the results of quality-of-life methods are published.[16,17]

The aim of this study was to obtain objective data on skin functions in AE as a basis for instrument comparisons and disease quantification in predetermined regions. Data from noninvasive instruments assessed on areas with active eczema, uninvolved skin of patients, and normal skin of healthy control subjects were analyzed to determine the range and distribution in a mixed population. The variance of disease severity was assessed both by direct clinical evaluation (involved, uninvolved, and healthy skin) and by an objective measurement of disease severity (objective Severity Scoring of Atopic Dermatitis [SCORAD]) to evaluate the discriminatory validity for the instruments.

METHODS

Participants

In all, 101 patients and 30 healthy control subjects were included. They attended our dermatology division from April 2002 to January 2004. The diagnosis of AE was based on the diagnostic criteria of Hanifin and Rajka.[18] Patients with concomitant ichthyosis vulgaris were excluded. The study population was well defined by patient history and clinically by two separate examinations.

Participants were instructed to refrain from using topical drugs or moisturizers for 1 day before the study. Between the two visits patients continued their routine treatment and no new medical intervention was carried out in the study period. The Declaration of Helsinki protocols were followed and the local ethics committee approved the study. Written informed consent was obtained from all participants.

Instruments and study procedure

Two assessments were carried out at 6-month intervals. On each visit instrumental measurements were performed at 3 different predetermined skin sites: antecubital fossa, back of the forearm, and popliteal fossa. All 3 skin sites were evaluated irrespective of whether active disease was present. For each region the presence of eczema or dry skin was registered. Dry skin was defined as a rough, finely scaling, noninflamed surface that looked and felt dry.[19] Investigations for all patients and control subjects for the two visits were performed in the same room and at the same 3 skin sites. One physician (E. A. H.) carried out all the measurements. Established guidelines and directions for TEWL, skin reflectance, densitometry, and capacitance measurements were followed.[15,19-23] The only deviation was that our room temperature was slightly higher because of our study participants' young age and the requirement that they be at least partially undressed for about 30 minutes. To minimize the seasonal variation, room temperature and relative humidity was continuously measured. If the relative humidity in the examination room was too low an air moistener was activated in the morning, but stopped during measurements. If the humidity was too high examinations were cancelled. Mean room temperature was 24.8°C ± 1.04 (SD). Mean relative humidity was 27.7% ± 8.58 (SD). Skin temperature was assessed with an infrared thermographic scanner (DermaTemp 1001, Exergen Corp, Watertown, Mass). Mean skin temperature for patients was 33.18°C ± 1.03 and for control subjects it was 33.05°C ± 0.91.

Measurements were performed in the following order: TEWL, skin surface hydration (capacitance), skin reflectance spectroscopy of erythema, quantification of scales by densitometry, and finally quantification of structures representing subepidermal edema (subepidermal low echogenic band [SLEB]).

Noninvasive instruments

TEWL was measured (DermaLab, Cortex Technology, Hadsund, Denmark) without an insulating glove or cover grid. Water is lost through the skin as eccrine sweating and transepidermal