Brief report

Solving the health disparity of eczema assessment: A role for skin tape soluble protein?

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Background: The assessment of erythema in patients with atopic dermatitis (AD) is based on clinical examination. The difficulty of perceiving erythema in Black patients with AD has led to underestimation of AD severity in these patients.
Objective: In this study, we analyzed the concentration of skin tape soluble protein of AD lesions against common AD clinical signs.
Method: A total of 50 children with AD were included. Skin tape total soluble protein was extracted from AD lesions and analyzed against validated AD clinical signs, including erythema, excoriation, edema, oozing, and lichenification.
Results: Concentration of skin tape soluble protein is positively correlated with acute signs of AD, especially erythema.
Conclusion: Determination of concentration of skin tape protein is a potential tool for grading erythema of AD lesions, and it may have an application in improving the health disparity of assessment of eczema severity in Black patients with AD. (J Allergy Clin Immunol Global 2024;3:100180.)

Key words: *Atopic dermatitis, erythema, racial disparity, strip skin tapes, total protein*

Abbreviations used
AD: Atopic dermatitis
SCORAD: SCORing Atopic Dermatitis
TEWL: Transepidermal water loss

INTRODUCTION

It has been shown that the severity of atopic dermatitis (AD) in Black children is underestimated as a result of underperception of erythema.[1] This topic has prompted further clinical studies in an attempt to validate scoring of AD severity in Black patients or patients with skin of color.[2,3] However, a more objective method for grading is needed. Skin tape stripping is a noninvasive technique that has increasingly been used to investigate the stratum corneum of patients with AD.[4] Clausen et al studied skin tape protein and showed that the proportion of skin tape soluble protein was higher in AD lesions than in skin of patients with nonlesional AD and in healthy skin.[5] In a subsequent study, Clausen et al confirmed that the content of skin tape soluble protein in AD lesions was higher than that of nonlesional AD skin and healthy skin.[6] Our goal in this study was to measure the concentration of skin tape soluble protein from AD lesions and analyze it against validated signs, including erythema, excoriation, edema, oozing, and lichenification.

The study was approved by our institutional review board, and consent was obtained from all parents and guardians. A total of 50 pediatric subjects younger than 18 years with AD were recruited. The diagnosis of AD was based on the UK Party diagnostic criteria.[7] Patients were excluded if they had a primary or secondary immunodeficiency, another chronic skin disease such as psoriasis, congenital dermatoses, or an active skin infection. Patients were recruited consecutively as they showed up for their clinical appointment. Severity of AD was based on objective SCORing AD (SCORAD) score,[8] with mild, moderate, and severe AD defined as follows: mild, 0-23; moderate, 24-37, and severe, ≥38.[9] The index lesion, which is the average representative area for the intensity of clinical signs, was used for local SCORAD score calculation based on the 6 objective scoring signs: erythema, excoriation, edema, oozing, lichenification, and dryness.[10] The standard intensity of clinical signs ranges from 0 to 3.[8,11] The score for dryness was determined from a nonlesional area that was at least 4 cm from the lesional area. The total local SCORAD score ranges from 0 to 18. That there had been no washing or application of moisturizers or prescription medications to the index lesion for at least 8 hours before the visit was confirmed with parents or guardians. The index area was prioritized according to the following order: antecubital > forearm > popliteal > thigh > trunk > neck.

Measurement of transepidermal water loss (TEWL) before and after tape stripping was measured by using the Tewameter 300 (Courage+Khazaka Electronic GmbH, Cologne, Germany). Duplicate measurements were taken. All skin tape procedures were performed according to the methods of Clausen et al.[5,12] We limited the number of applications of skin tape on AD lesions in children to a total of 10 to minimize irritation of the lesion. Because the first few tapes may be contaminated with dirt and remnants, we used tapes 6 to 10 (depth 2) for analysis. Briefly, a D-Squame tape (22-mm-diameter; CuDerm, Dallas, Tex) was placed on the index AD lesion using sterile forceps. This was

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TABLE I. Demographics of children with AD in the current study (N = 50)

Characteristic	Value
Age (y), mean ± SD	5.7 ± 4.9 y
Age range (y)	0.5-17
Females/males (%)	42:58
Race/ethnicity, no. (%)	
Hispanic	22 (44)
Black	13 (26)
Asian/Pacific Islander	9 (18)
White	6 (12)
AD severity, no. (%)	
Mild	29 (58)
Moderate	11 (22)
Severe	10 (20)

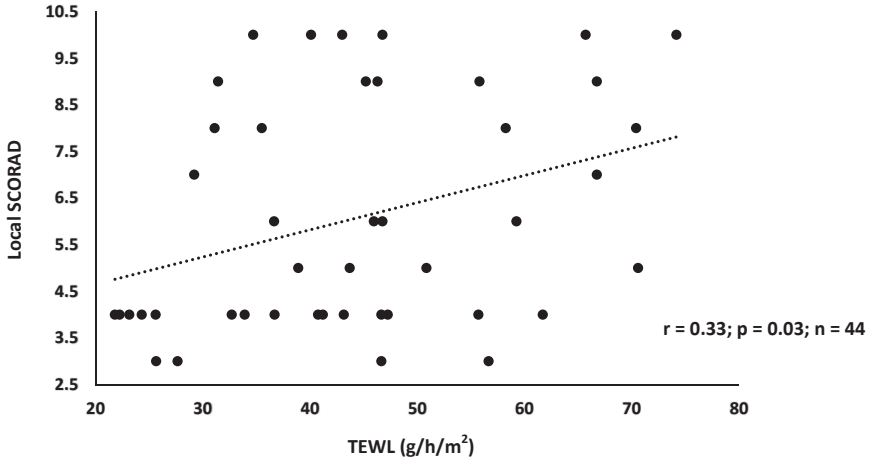

FIG 1. AD index skin lesional severity (local SCORAD score) is positively correlated with TEWL.

followed by pressing on the tape with a standardized pressurizer (D-500-D-Squame, Dallas Tex) for 5 seconds, after which the tape was removed with the forceps. A total of 10 consecutive tapes were placed and removed. Tapes 6 to 10 were pooled into a total of 2 mL of PBS (pH 7.4; 1×) (for details regarding the protein extraction method, please see the Online Repository at www.jaci-global.org). The samples were then stored at –80° C until protein analysis. Bicinchoninic acid protein assay was performed at Alpha Diagnostic, Intl (San Antonio, Tex) and the Aging Biomarkers and Service Core of the University of Southern California (Los Angeles, Calif). Spearman rank was used for correlation testing. One-way ANOVA was used to analyze SCORAD signs versus concentration of soluble protein. An unpaired *t* test was used for the difference between the 2 groups. Significance of the difference between groups was confirmed by the Bonferroni correction test.

RESULTS AND DISCUSSION

A summary of patient demographics and severity is provided in Table I. The distribution of patients with mild, moderate, and severe AD was 58%, 22%, and 20%, respectively.

We verified a significant increase in TEWL on AD lesions after tape stripping. The mean TEWL values before and after tape stripping were 44.3 ± 14.4 g per hour/m^2 (n = 44) and 56.5 ± 19.4 g per hour/m^2 (n = 39), respectively (P = .002). Some children were unable to stay still for the completion of TEWL measurement. TEWL on AD lesions before tape stripping showed a significant positive correlation with local SCORAD score (Fig 1). Fig 2 shows that the concentration of skin tape soluble protein of AD lesions is positively correlated with local SCORAD score. In analyzing each sign of local SCORAD score against concentration of skin tape soluble protein, ANOVA and *t* tests showed significant differences in the mean soluble protein concentrations from grades 1 to 3 erythema (Fig 3). All of the subjects with grade 0 erythema were Black (n = 4). Analysis of the non-Black patients only (n = 37) confirmed that total skin tape protein concentration increases with erythema (see Fig E1 in the Online Repository at www.jaci-global.org), whereas there is no significant difference in the total content of skin tape protein between different grades of erythema in Black patients (n = 13) (see Fig E2 in the Online Repository at www.jaci-global.org). ANOVA analysis was also significant for skin tape soluble protein concentration versus excoriation, but there was no significant difference in the mean soluble protein concentration between grade 2 and 3 excoriation (Fig 4). ANOVA analysis of skin tape soluble protein concentration versus lichenification was not statistically significant (P = .6). There was also no

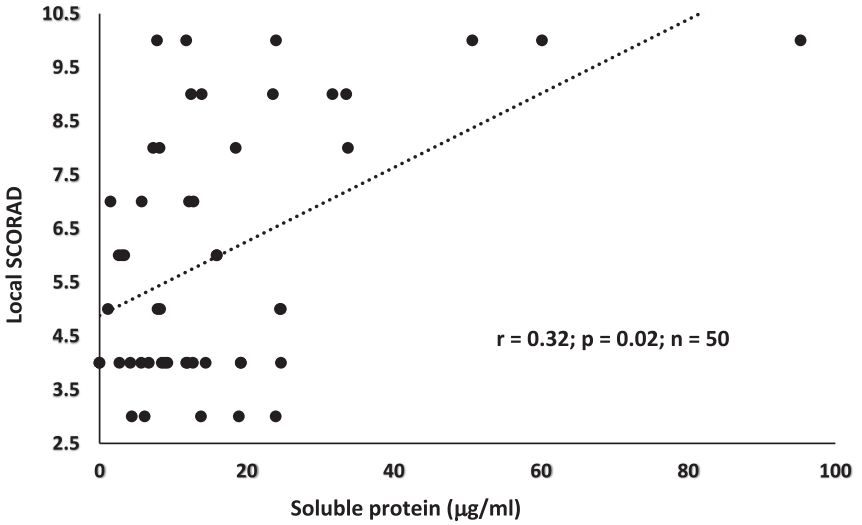

FIG 2. Local SCORAD score is positively correlated with skin tape soluble protein concentration.

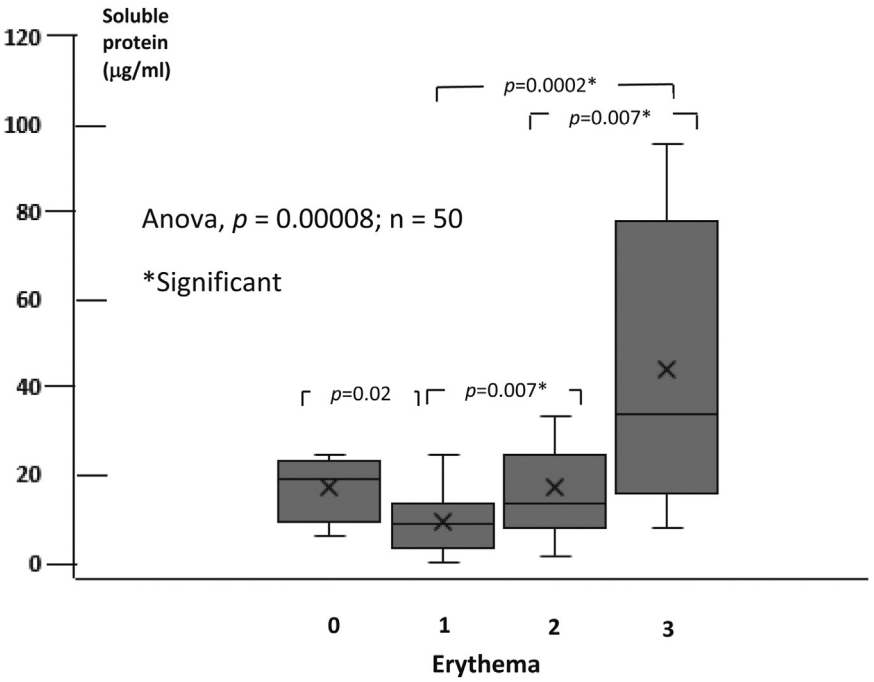

FIG 3. Skin tape soluble protein concentration versus erythema of AD lesions.

statistical difference in skin tape soluble protein concentration between grade 0 to 3 lichenification. The sample size for grade 2 and 3 edema or oozing (n = 0-1) was insufficient for ANOVA analysis. However, the concentration of skin tape soluble protein for grade 1 edema was significantly higher than that for grade 0 edema (19.4 ± 15.7 vs 10.9 ± 7.8 μg/mL [$P = .008$]). The concentration of skin tape soluble protein for grade 1 oozing was also significantly higher than that for grade 0 oozing (51.6 ± 61.9 vs 14.6 ± 12.5 μg/mL [$P = .0008$]).

It has been well documented that erythema in Black patients with AD is underperceived, leading to an underestimation of severity and, therefore, undertreatment or recognition of the morbidity in these patients.[1,13] Clinicians generally perceive erythema in Black patients with AD on the basis of other associated signs such as excoriations or edema.[14] It has also been suggested that clinicians increase the score of erythema by 1 in patients with AD who have a darker skin complexion.[15] Although the assumption of erythema in the presence of other acute AD signs is valid according to our observation and clinical experience in non-Black patients, the grading of erythema in Black patients with AD remains a matter of conjecture. The need for a more objective tool for measuring erythema in Black patients prompted us to

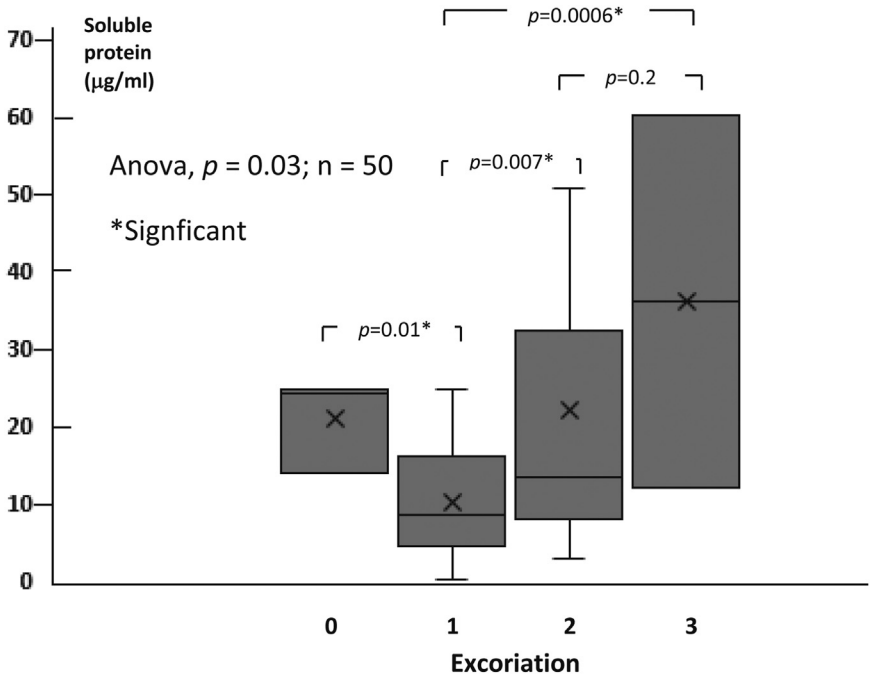

FIG. 4. Skin tape soluble protein concentration versus excoriation of AD lesions.

explore skin tape soluble protein as a potential tool for measurement of AD clinical signs. Our results showed that concentration of skin tape soluble protein from AD lesions is correlated with local severity, especially with the acute signs of AD, which include erythema, excoriation, edema, and oozing.

Skin tape stripping has become a common method in assessing the stratum corneum of patients with AD. Because of its noninvasiveness, skin tape stripping is particularly useful in children. Clausen et al have provided the groundwork for using skin tape for AD by investigating variables including skin depths, tape pressure, and sonication time.[5] Our results are consistent with the observation of Clausen et al that concentration of skin tape soluble protein increases with AD lesional inflammation as a result of an increase in intercellular matrix proteins.[5]

To date, only a few studies have directly studied the clinical signs of AD based on skin tape–specific proteins.[16,17] In our experience, the isolation of specific proteins from skin tapes can be challenging owing to detection limits. Most require the addition of protein extraction reagents such as Tween-20 or Triton X-100, which may interfere with analysis,[5] thus decreasing reproducibility. In contrast, the measurement of total skin tape soluble protein is relatively straightforward, without the need for protein extraction reagents. More importantly, the measurement of total protein concentration will allow for eventual spectroscopic techniques that directly quantify the protein content on the skin tapes (eg, Squame Scan).[5] Our current observation has led us to explore these techniques as a possibility for clinical application.

A limitation of the current study is that our patient population may not represent the general population of children with AD. The majority of our subjects were recruited from a specialty clinic. All but 4 of the Black patients presented with acute symptoms that included erythema. However, the latter observation further highlights the problem that erythema may be underestimated in Black patients with AD. Although the selection and grading of symptomatic AD may be subjective, the strength of our study is completion of clinical assessment before protein measurement, because of which both sets of data were blinded to each other until statistical analyses.

In summary, concentration of skin tape soluble protein increases with acute signs of AD, including erythema, excoriation, edema, and oozing. Our study may provide a basis for further studies in solving the health disparity of assessing severity in Black patients with AD.

DISCLOSURE STATEMENT

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Clinical Implications: Skin tape total protein may help clinicians in a more objective assessment of erythema in Black patients, thus bridging the gap of health disparities in AD care.

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