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# Either transepidermal water loss rates or stratum corneum hydration levels can predict quality of life in children with atopic dermatitis

Shan Wang[1] | Chunping Shen[1] | Mutong Zhao[1] | Lei Jiao[1] | Jing Tian[1] | Yang Wang[1] | Lin Ma[1] | Mao-Qiang Man[2]

[1]Department of Dermatology, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China
[2]Dermatology Hospital, Southern Medical University, Guangzhou, China

**Correspondence**
Lin Ma, Department of Dermatology, Beijing Children's Hospital, Beijing 100045, China
Email: bch_maleen@aliyun.com
Mao-Qiang Man, Dermatology Hospital, Southern Medical University, Guangzhou 510091, China
Email: mqman@hotmail.com

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**ABSTRACT**

**Importance:** Patients with atopic dermatitis (AD) display compromised epidermal barrier and suffer from poor quality of life. We hypothesized that quality of life could reflect in the changes in the epidermal barrier function.

**Objective:** To determine whether the epidermal barrier function correlates with the severity of pruritus and/or life quality in children with AD.

**Methods:** A total of 120 children, aged 0–12 years, with moderate AD were enrolled. Children were topically treated with topical corticosteroids (TCS) and an emollient for 2 weeks. The Eczema Area and Severity Index (EASI), visual analogue scale (VAS) for pruritus severity, the Infant's Dermatitis Quality of Life Index (IDQOL) and the Children's Dermatology Life Quality Index (CDLQI) were evaluated. Transepidermal water loss (TEWL) rates, stratum corneum (SC) hydration, and skin surface pH were measured. Correlations of epidermal barrier function with pruritus, life quality, and EASI were determined.

**Results:** Following 2-week treatments, significant improvements were observed in EASI, TEWL, SC hydration, the VAS of pruritus, as well as DQOL ($P < 0.001$ for all). TEWL positively, while SC hydration negatively correlated with VAS pruritus, DQOL, and EASI ($P < 0.001$).

**Interpretation:** Both TEWL and SC hydration levels can serve as indicators of the severity of pruritus and quality of life in children with AD.

**KEYWORDS**
Atopic dermatitis, Transepidermal water loss, Hydration, Quality of life, Pruritus

## INTRODUCTION

Atopic dermatitis (AD) is one of the most common pediatric dermatoses, attributable to multiple genetic causes, compromised epidermal barrier, and immunological dysregulation. Children with AD often have a poor quality of life, mainly due to recurrent intense pruritus, the most vexatious symptom. Because of the links between the severity of pruritus and inflammation, the severity of pruritus is currently assessed by standard clinical scales, such as the Scoring Atopic Dermatitis (SCORAD) index and Eczema Area and Severity Index (EASI).[1,2] However, the association of the severity of pruritus (and resultant sleep disorders) with these related clinical scores is not confirmative.[3] Since dysfunction of the epidermal barrier also plays a pathogenic role in AD,[4]

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we hypothesized that dysfunction of the epidermal barrier could trigger multiple downstream pathways, resulting in pruritus, consequently leading to poor life quality. Therefore, transepidermal water loss rates (TEWL), stratum corneum (SC) hydration, or skin surface pH, which are indicator of epidermal barrier function, could predict the severity of pruritus and quality of life of children with AD.

While the Dermatitis Quality of Life (DQOL) questionnaire is most commonly used approach to assess the quality of life in AD, but it's not convenient, and time-consuming. In contrast, the epidermal barrier function is relatively easy to measure, and has been serving as an objective and reliable indicator for AD status. However, whether TWEL, SC hydration, and/or skin surface pH levels can reflect the severity of pruritus and life quality of AD children has not been demonstrated. In the present study, we determined the correlation of both TEWL and SC hydration levels with the severity of pruritus and life quality in children with AD.

## METHODS

### Ethical approval

This study was approved by the Ethics Committee of Beijing Children's Hospital, Capital Medical University under registration number 2016-135. All procedures were conducted in compliance with the principles of Helsinki Declaration. Written informed consent was obtained from all patient's parents.

### Study design

Children with AD were recruited from the Department of Dermatology, Beijing Children's Hospital of Capital Medical University, from January to December 2018, with the following inclusion criteria for study subjects: (a) between 0 and 12 years old; (b) diagnosed with AD according to UK diagnostic criteria[5] for those below 2 years and Williams criteria[6] for those aged 2–12 years; (c) had an EASI score of 7.1–21.0, indicating moderate disease.[2]

Participants were topically treated with topical corticosteroids (TCS) and an emollient. Children under the age of 2 years (infantile AD) were topically treated with both desonide cream (Huapont Pharm Co., Ltd., Chongqing, China) and emollient (pH 5.8–6.0, Botanee Group Co., Ltd., Kunming, China) twice-daily for two weeks. Children with AD aged 2–12 years were treated topically with mometasone furoate cream (Bayer-China, Shanghai, China) once-daily and emollients twice-daily for 2 weeks. Evaluations of the severity of disease and pruritus for the previous week were carried out according to well-established EASI[2] and visual analogue scale (VAS),[7] respectively, before and after treatments. For those who were unable to evaluate VAS due to age limitations, VAS was evaluated by their parents instead. Life quality in children under the age of 4 year was assessed via Infant's Dermatitis Quality of Life Index (IDQOL),[8] while in children aged 4–12 years was assessed via Children's Dermatology Life Quality Index (CDLQI).[9]

### Measurements of epidermal biophysical properties

Measurements were performed on the lesions of the cheek in children under 2 years old, or the lesions of the cubital fossa in children aged 2–12 years, for consideration of the predilection site in infantile and childhood phase, respectively. The study room was maintained at 20–23°C, 40%–60% humidity. Participants were required to acclimate to the environment for 15 minutes and were not allowed to wash or apply emollients at the lesion for 6 hours before measurements. SC hydration and TEWL were measured with Corneometer CM825 and Tewameter TM300, respectively, connected to an MPA5 system. While skin surface pH was measured with a pH905 pH meter (Courage-Khazaka Electronic GmbH, Köln, Germany) as previously described.[10]

### Statistical analysis

Each measurement was collected three times to allow for calculation of means and analysis of device test-retest reliability. Data are expressed as the mean ± SEM. The Pearson's correlation was used to determine the correlation among epidermal barrier function with pruritus, life quality, and EASI. Paired student's *t*-test was used to compare the parameters before and after treatments. *P* values less than 0.05 were considered to be statistically significant. Stata 14.0 (Stata Statistical Software: College Station, TX: Stata Corp LP) and GraphPad Prism 5 software (San Diego, CA, USA) were used for all statistical analyses.

## RESULTS

### Topical treatments with glucocorticoids and emollient improve both epidermal biophysical properties and DQOL

A total of 120 children with AD, including 70 boys and 50 girls, were enrolled in the study. Patients were aged 3 months to 11.8 years, with an average of 16.0 months (IQR: 6.3–44.8 months). Epidermal biophysical properties, including TEWL and SC hydration, were markedly improved following two-week treatments, while skin surface pH showed no remarkable change (Table 1). Moreover, multiple clinical scores, including EASI, DQOL, and VAS of pruritus, were also significantly improved following 2-week treatments (Table 1). These results demonstrate that this treatment regimen alleviates AD in children.

**TABLE 1** Clinical and barrier characteristics of patients with atopic dermatitis before and after treatment ($n$ = 120)

| Variables | Before treatment | After treatment | Statistics | *P* |
|---|---|---|---|---|
| Epidermal barrier function | | | | |
| TEWL ($g \cdot m^{-2} \cdot h^{-1}$) | 30.36 ± 1.51 | 11.60 ± 0.99 | 11.45† | <0.001 |
| SC hydration (au) | 19.96 ± 1.05 | 34.61 ± 1.10 | −10.92† | <0.001 |
| pH | 6.63 ± 0.07 | 6.77 ± 0.06 | −2.46‡ | 0.140 |
| EASI | 10.50 ± 0.29 | 2.71 ± 0.22 | 25.47† | <0.001 |
| VAS of pruritus | 5.45 ± 0.18 | 1.95 ± 0.16 | 18.84† | <0.001 |
| DQOL | 4.27 ± 0.36 | 1.65 ± 0.13 | 7.05‡ | <0.001 |

Data are shown as mean ± standard error of mean. TEWL, transepidermal water loss; SC, stratum corneum; EASI, Eczema Area and Severity Index; VAS, visual analogue scale; DQOL, Dermatitis Quality of Life. †Paired *t*-test; ‡Wilcoxon signed rank test.

**TABLE 2** Correlation of epidermal barrier function with pruritus and life quality

| Variables | VAS pruritus | | DQOL | | EASI | |
|---|---|---|---|---|---|---|
| | $r^2$ | *P* | $r^2$ | *P* | $r^2$ | *P* |
| TEWL ($g \cdot m^{-2} \cdot h^{-1}$) | 0.244 | < 0.0001 | 0.042 | 0.002 | 0.222 | < 0.0001 |
| SC hydration (au) | 0.174 | < 0.0001 | 0.042 | 0.002 | 0.294 | < 0.0001 |
| pH | 0.003 | 0.3855 | 0 | 0.887 | 0.048 | < 0.0010 |

TEWL, transepidermal water loss; SC, stratum corneum; EASI, Eczema Area and Severity Index; VAS, visual analogue scale; DQOL, Dermatitis Quality of Life.

### Both TEWL and SC hydration correlate with severity of pruritus, DQOL and EASI

We next determined whether epidermal biophysical properties, including TEWL, SC hydration and skin surface pH, correlate with clinical signs and symptoms of AD. Indeed, TEWL positively, while SC hydration negatively correlated with VAS of pruritus, DQOL and EASI. However, skin surface pH only correlated positively with EASI (Table 2). These results suggest that both TEWL and SC hydration could possibly serve as indicators of clinical signs and symptoms of AD in children.

## DISCUSSION

Children with AD experience not only cutaneous discomfort but also poorer quality of life and sleep disturbances,[11] as well as increased behavior problems, such as higher frequency of attention-deficit/hyperactivity disorder (ADHD).[12] The decrease of life quality is mainly due to severe pruritus, which is the most remarkable clinical manifestation of AD. AD also displays prominent abnormalities in epidermal functions, including elevations in TEWL and skin surface pH, and reduced SC hydration,[13] which all can be linked to the development of pruritus because a) both disruption of the TEWL and reduced SC hydration independently increase cytokine release,[14] mast cell density and degranulation,[15] leading to the development of pruritus; and b) either increased TEWL or pH can activate epidermal protease-activated receptor 2 (PAR2), which can directly activating C fibers and further deteriorate epidermal barrier and cutaneous inflammation in AD.[16] Collectively, AD displays cutaneous inflammation and epidermal dysfunction, leading the development of pruritus, and consequently resulting in poor quality of life (Figure 1). Accordingly, improvement in epidermal function can benefit patients with AD.

Previous studies have shown that both TEWL and SC hydration correlate with severity of atopic dermatitis in adults and children,[17,18] while TEWL also correlates positively with pruritus intensity.[19] In agreement with the above findings, we show here that both TEWL and SC hydration correlated with EASI and VAS pruritus in children. In contrast to prior study,[19] we demonstrate here that skin surface pH also correlated positively with EASI. This discrepancy could be due to the differences in body sites of the measurement and subjects' age, which both affect skin surface pH. It is worth noting that although treatment lowered EASI, pH did not change significantly, which is likely due to the adverse effects of glucocorticoids.[20,21] Thus, the change of skin surface pH may not be observed following glucocorticoids treatment. The skin surface pH in these patients was about 6.6, which was unlikely influenced by the pH of emollient (about 5.8–6.0). Be consistent with the previous finding that TEWL correlates with both DQOL and severity of AD,[22] the present study also showed that SC hydration correlated negatively with DQOL, which is no surprise because SC hydration regulates cutaneous inflammation, which, in turn, affect pruritus and DQOL. Nonetheless, the present study results suggest that instead of questionnaire, a time-consuming approach, measurement of either TEWL or SC hydration could be a convenient approach to assess DQOL

and VAS pruritus in children and/or adults with AD.

In some previous concepts, the application of TCS has the potential to enhance the barrier defect. However, in our results, both TEWL and SC hydration improved after TCS treatment. We believe short-term application of TCS could benefit epidermal barrier function in AD due to its anti-inflammatory role, since cutaneous inflammation is one of the most important causes in epidermal function abnormalities of AD.

Limitations of the study include the fact that the methodology of pruritus assessment is not applicable to very young children, which will be instead by parents' evaluation. Additionally, there were slight variations in assessing epidermal biophysical properties in climate and environment variables, although maximal efforts were made to control external variables.

In conclusion, both TEWL and SC hydration correlate with VAS pruritus, DQOL, and EASI. Therefore, either TEWL or SC hydration levels can serve as an indicator of VAS pruritus, DQOL in children with AD.

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## CONFLICT OF INTEREST

None.

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