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# Assessing the effects of topical cannabidiol in patients with atopic dermatitis

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To the Editor:

Atopic dermatitis (AD), a chronic relapsing inflammatory disorder characterized by pruritus, erythema, and dry skin, is estimated to affect up to 20% of children and 3% of adults [1]. Pruritus is one of the most distressing symptoms for patients with AD and when severe, can negatively impact patients' quality of life [2]. Current treatments for AD, including topical corticosteroids, are effective yet limited by unfavorable side effects [4,5]. Complex neuro-cutaneous signaling in pruritus has proven to be a significant therapeutic challenge for physicians and patients. However, recent studies elucidating this mechanism has provided opportunity to explore neuromodulators, such as topical naltrexone, capsaicin, and cannabidiol (CBD), as off-labeled therapies for inflammatory skin disease [3,5,6]. Cannabinoids have demonstrated anti-inflammatory and anti-pruritic properties in both in vitro and in vivo studies and thus may be of clinical utility in the treatment of AD [2]. To our knowledge there have been no clinical studies assessing the effects of cannabidiol (CBD) on AD patients. Herein, we present a pre-post observational study, which aims to appraise the effects of topical CBD as a therapeutic option for AD.

This pre-post observational study was approved by an independent IRB and performed between January 2019-August 2019 in the United States. Participants

met with board-certified dermatologists for eligibility assessment and voluntarily agreed to participate. The inclusion criteria consisted of the following: 1) being 18 years of age or older, 2) a diagnosis of AD/eczema confirmed by a board-certified dermatologist prior to study enrollment, 3) consideration previously of the use of topical CBD, and 4) currently not pregnant or breastfeeding.

Patients were provided with means to obtain a 1% CBD-infused gel containing a vehicle of dimethicone and polysilicone-11 as well as hemp oil (1% cannabidiol and 0% THC), as verified by third party test results from a CBD testing laboratory. Application frequency was tracked using the eczema care log. Patients were instructed to immediately discontinue CBD application and call the investigator if any discomfort or side effects occurred.

## Survey measures

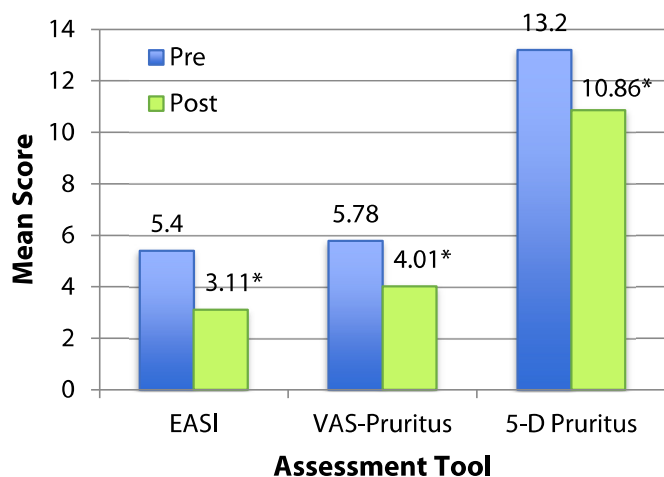
Subjects were provided with a seven-item questionnaire assessing age, gender, disease duration, recent medication use, and satisfaction with their current eczema medication. Disease severity and pruritus were assessed using the Eczema Area and Severity Index (EASI), Visual Analogue Scale-Pruritus (VAS), and 5-D Pruritus Scales, respectively. These assessment tools were repeated following the 14-day application. An additional six questions were administered at the end of the study to determine frequency of application, difficulty in topical use, degree of side effects if any, and overall participant satisfaction.

**Table 1.** Demographic patterns of participants.

Characteristics of Participants	
Age, in years	
Mean (SD)	51.36(16)
Median (Range)	57.5 (25-73)
Gender, N(%)	
Male	11(78.6%)
Ethnicity/Race, N(%)	
Caucasian	7(50%)
African American	4(%)
Asian	2(%)
Onset of disease, in years	10.28

### Eczema Area and Severity Index

Eczema Area and Severity Index is a validated physician-assessment tool that measures the extent and severity of atopic eczema [7]. It assesses four main body parts: the head and neck (H), upper extremities (UE), trunk (T), and lower extremities (LE). There are two components of EASI, the *area* and *severity* scores. The area score assesses the extent of disease involvement in each of the four body regions from a scale of 0, reflecting no eruption, to 6, which reflects 90-100% of surface area involvement. Additionally, the severity score measures disease severity by assessing four symptoms (erythema, induration/papulation/edema, excoriations, and



**Figure 1.** Mean scores in assessment tools pre- and post-use of topical cannabidiol.

\*Overall change in mean score of Eczema Area and Severity Index (EASI), Visual Analogue Scale (VAS)-pruritus, and 5-D Pruritus Scale following a 2-week use of topical 1% CBD gel in AD patients was significant ( $P < 0.05$ ).

lichenification) in each of the four body areas. Each symptom is graded from a scale of 0 (none) to 3 (severe). The overall score is the sum of each individual average symptom score.

### Visual Analogue Scale (VAS)-Pruritus

Visual Analogue Scale-Pruritus was used to assess patient perspective and consisted of a single question assessing the intensity of pruritus from 0 to 10 with the latter being the worst itch of their life [8].

### 5-D Pruritus Scale

5-D Pruritus Scale has been recognized as a valid and sensitive tool used to quantify the impact of pruritus on patients' quality of life over time. It consists of four major elements that include degree, duration, disability, and distribution of itch within the past two weeks [9].

### Statistical analysis

A paired t-test was performed to compare the mean score from baseline to the end of two weeks use of the CBD-infused gel. Statistical measurements were performed on EASI, VAS-pruritus, and 5-D itch scale scores. A P value  $< 0.05$  was the threshold for significance. SPSS 20.0 version was used for analysis.

Fourteen subjects participated in this study (mean [SD] age, 51.36 [16]; 11 M (78.6%); 53.84% white). The average disease onset was 11 years (**Table 1**). Ten subjects (71.4%) perceived their eczema to be poorly to moderately controlled (1-5); four (28.57%) believed that their eczema was well controlled (6-9).

### Eczema Area and Severity Index

A significant reduction in the overall mean EASI score was noted at the follow-up visit (5.4 at baseline and 3.10 at two weeks post-use,  $P < 0.005$ ), (**Figure 1**).

### Visual Analogue Scale-Pruritus

Following two weeks of CBD application, all subjects experienced a 29% average decrease in intensity of pruritus (mean score: 5.78 versus 4.01,  $P < 0.05$ ), (**Figure 1**).

### 5-D Pruritus Scale

Using 5-D pruritus, an average of 14% reduction in impact of pruritus on quality of life was also noted following two weeks course (mean score: 13.21 versus 10.85,  $P < 0.05$ ), (**Figure 1**).

### Side effects

Of the 14 participants, eight (80%) did not encounter any reaction to the CBD topical. Five subjects noted some discomfort and stinging upon application (35%) but four of the five opted to continue with application of the topical and saw a 34.5% reduction in EASI scores. One subject experienced transient erythema when first applied, but overall erythema for the subject decreased by 27% over the course of two weeks.

There were significant differences in baseline excoriation scores between the groups that experienced stinging and those that did not (3 versus 0.78,  $P < 0.01$ ), which may indicate that stinging is likely to occur in subjects with broken skin from scratching; thus topical CBD would be contraindicated for individuals with broken skin. Two subjects reported worsening of their eczema and discontinued application.

In this observational study, we determined that a topical gel containing 1% CBD could be a reasonable option among AD patients as assessed by a significant reduction in EASI score ( $P < 0.05$ ), VAS-Pruritus ( $P < 0.05$ ) and 5-D Pruritus Scales ( $P < 0.05$ ). Despite our small sample size, these findings are meaningful, as traditional therapeutic routes (e.g. topical corticosteroids) have unfavorable long-term effects on skin and alternative options are needed. The physiologic effects of CBD, including anti-inflammatory and anti-pruritic properties, along with epidermal barrier restoration have been elucidated in previous studies [10-13]. As illustrated by this study, topical CBD resulted in a significant improvement in itch, as measured by both VAS-pruritus and 5-D scale.

Previous studies highlighted the safety and tolerability of oral CBD but the safety profile of the topical formulation is still under-investigation [13]. A few subjects in this study experienced stinging, transient erythema, or discomfort. None of the

subjects required systemic and/or topical treatment. The reporting of stinging was inconsistent with a previous study using the same topical. However, the population for the previous study were individuals with self-reported eczema. We believe this may be related to the relative severity in AD between subjects seeking treatment from a dermatologist in this study versus those that have not yet engaged with a dermatologist because their AD is still tolerable.

### Limitations

Clinicians were not blinded during the study period; external validity is an issue inherent to single-center studies. Additionally, short-term follow-up makes it difficult to assess the long-term effects of topical CBD. The observational design and lack of control group makes efficacy hard to fully judge.

To conclude, AD is a chronic, relapsing inflammatory disorder with a multifactorial etiology. Given the implications of neuro-skin physiology pathways in AD pathogenesis, cannabinoids may be a promising therapeutic alternative. To the best of our knowledge, this is the first pre-post study that demonstrates statistically significant clinical improvement in the use of topical CBD and its effects on pruritus, excoriation, erythema, lichenification, and edema. Despite our findings, large-scale human studies are necessary to further support the role of CBD in AD as a treatment. Until then, dermatologists should consider screening patients for the use of CBD products and counsel patients on the current evidence on efficacy and safety of its use for dermatologic conditions such as AD.

### Potential conflicts of interest

Drs. Yardley, Lio, and Dellavalle are shareholders in CQ Science. Dr. Yardley is employed by CQ Science. Drs. Dellavalle and Lio are medical consultants to CQ Science.

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