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Pre-hydration is Effective for Rapid Control of Recalcitrant Atopic Dermatitis

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INTRODUCTION

Educating patients and families on proper skin care remains a key component in atopic dermatitis (AD) management. Published treatment guidelines for the management of AD recommend the use of gentle cleansers and the frequent application of emollients.^{1,2} Surprisingly, there are virtually no data available to guide recommendations on optimal bathing practices. Some sources recommend daily bathing for patients with AD, while others, especially in the pediatric realm, have recommend limiting baths to once or twice weekly.³

Bathing practices are likely to significantly influence disease management in AD. On one hand, prolonged or repetitive contact with water can harm the skin barrier, theoretically worsening the disease.^{4,5} Conversely, water contact may be beneficial by hydrating the stratum corneum, allowing for enhanced stratum corneum uptake of topical corticosteroids (TCS).⁶ In our practice, we have long utilized bathing for 15–20 minutes followed by TCS application as a method for inducing clearance of even the most severe disease during the initial patient visits.⁷ Patients are instructed to apply the ointment within three minutes of getting out of the bath tub after a brief “pat dry.” While two studies have shown this “soak and smear” method may have utility in a variety of dermatoses, this technique has not been systematically evaluated in a population of patients with AD.^{7–11} The objective of the current study was to determine the effectiveness of the pre-hydration technique combined with topical steroid therapy in achieving disease control in patients with moderate-to-severe AD.

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METHODS

After receiving Institutional Review Board approval, we performed a retrospective review of the electronic health records of patients attending the outpatient dermatology clinic at Oregon Health & Science University between January 1, 2007, and December 31, 2011. We identified patients using the ICD-9 code of 691.8 (atopic and other eczematous conditions) and applied the following inclusion and exclusion criteria that were determined *a priori*:

Inclusion Criteria

1. The first visit must have been the initial visit to the Department of Dermatology.
2. Disease severity described as moderate or severe in the assessment. Our practitioners routinely include an Investigator Global Assessment (IGA) as part of a patient's initial evaluation, defined as a subjective determination taking into account a patient's severity of the skin disease, extent, and quality-of-life impact.
3. Bathing for 15–20 minutes followed immediately by TCS must have been prescribed at least daily. A detailed representative regimen is shown in Table 1.
4. A follow-up visit must have been scheduled within one to three weeks after the initial appointment.

Exclusion Criteria

1. Investigator Global Assessment (IGA) rated as mild at baseline visit.
2. Patient treated with systemic therapies or phototherapy within two months of their initial visit. This criterion reduced the potential confounding effects of concomitant systemic therapies.
3. Patients in whom the diagnosis of AD was unclear, or did not meet diagnostic criteria for AD.

Outcomes

The primary outcome was the IGA at the first follow-up visit after the initiation of pre-hydration therapy. In cases where the provider did not record the IGA, an IGA was extrapolated using a combination of patient report of disease activity and the physical examination.

Secondary Outcomes

A dynamic scale (Treatment Response Scale) was created to reflect both the patient and provider's assessment of treatment response compared to baseline. Comments regarding treatment response made by the patient or provider were recorded as the following categories: worse, no improvement, moderate improvement, marked improvement, or complete clearing.

Data regarding patient demographics, disease course, and previous treatments were also extracted.

RESULTS

A search for the ICD-9 code 691.8 produced a total of 110 distinct electronic records. Thirty-five patients were excluded for the following reasons: recent systemic therapy (11) or ultraviolet light (4) prescribed by referring physicians, mild disease (6), did not soak in a bath (2), did not satisfy criteria for AD (12), and had no follow-up appointment within the three-week time frame (11). A total of 75 patients were identified as meeting criteria (Table 1). Although 11 patients had only a phone follow-up assessment, these patients were given a Treatment Response Score based on the patient's assessment of treatment response and were not given an IGA score because of the lack of an objective evaluation.

Demographics

Both pediatric and adult patients were represented in our sample (Table 2) and most patients had a history of asthma, food allergies or allergic rhinitis (Table 3). Among the 75 patients, 40 (53%) were female. The number of days between the baseline visit and follow-up visit ranged from two to 21 days, with 36 (48%) patients assessed within one week, 32 (43%) within two weeks and seven (9%) within three weeks after the baseline visit. When evaluating the patients' eczema history, 70 (95%) had onset in childhood, and four (5%) had adult onset (onset was not available in one patient).

Previous Therapy

Most patients reported the use of low-, mid- and high-potency TCS in the past. Patients also reported the use of topical calcineurin inhibitors, systemic corticosteroids, UV therapy, antihistamines and antibiotics, methotrexate, and cyclosporine (Table 4).

Baseline Visit

At the initial visit, 48 (64%) patients had an IGA of severe and 27 (36%) had moderate disease. All subjects were instructed to begin pre-hydration therapy (tub bath for 15–20 minutes) followed by TCS. Mid-potency TCS preparations were prescribed in 49 (65%) of patients (mainly triamcinolone acetonide 0.1% ointment), while 26 (35%) were prescribed high-potency TCS (mainly betamethasone dipropionate 0.05% ointment). Twenty-six (35%) patients also received an oral antibiotic (dicloxacillin or cephalexin) for five days. We had no documented evidence of bleach bath recommendations in the initial visit of any of the patients included in this study. The use of bleach baths is not a component of our routine clearance protocol.

Follow-up Visit

At the follow-up visit, 64 (85%) patients were evaluated with an IGA. The remaining 11 patients were only evaluated with the treatment response scale by phone. No patients persisted with severe disease. Forty-seven (73%) patients were rated as almost clear, and one (2%) was clear (Table 5). Thirteen (20%) patients had mild disease by IGA and three (5%) had moderate disease.

Using the patient's or provider's assessment of treatment response, 59 (79%) had marked improvement and three (4%) patients were clear. Ten patients (13%) noted moderate

improvement, and three (4%) had only slight improvement. No patients had worsened or reported no improvement (Table 6).

We further explored responses of patients who had a history of systemic corticosteroid therapy (oral or intramuscular). Nearly all of these patients (93%) had severe disease when evaluated at the initial visit (IGA). At follow up, 11 patients (73.3%) experienced marked improvement, 2 (13.3%) had moderate improvement and 2 (13.3%) only slight improvement.

Finally, to control for the possible effects that antibiotics may have had on the improvement seen, we stratified our results by those receiving antibiotics versus those who did not and found similar responses in both groups (IGA who were mild, almost clear or clear: 94.7% in the antibiotic group versus 95% in the non-antibiotic group).

DISCUSSION

Our retrospective study found very high response rates to pre-hydration followed by TCS application in both pediatric and adult patients with moderate-to-severe AD. Almost all (95%) achieved an IGA of at least mild after one to two weeks of pre-hydrating baths followed immediately by TCS therapy. These results are striking, especially in light of the fact that many patients had been previously treated with super-potent TCS or systemic therapy. The patients' perceptions of response agreed with the investigator's assessments with 83% of patients noting that they experienced at least marked improvement.

There are several potential reasons why such excellent outcomes were achieved with pre-hydration therapy. The most likely reason is the improved cutaneous uptake of TCS. Water has been considered the most natural and biocompatible penetration enhancer for improving skin permeability.¹² In 1954, Rothman recognized that skin hydration enhanced percutaneous absorption.¹³ In 1963, Cronin and colleagues found that hydration increased the penetration of ethyl nicotinate by six-fold.⁶ Stoughton demonstrated ten-fold greater glucocorticoid permeability when skin was hydrated. Also, pre-soaking with warm water enhanced the reservoir effect five-fold for topical corticosteroids.¹⁴

Other potential explanations for our results include the debriding effects of the bath and improved adherence to the regimen. Bathing may reduce the concentration of bacteria on the skin while removing irritants and allergens. Patient adherence may be improved by treatment success and short follow-up time. Patients frequently diminish adherence after one to two weeks of treatment but studies show that an intensive short course of outpatient treatment promotes good adherence and provides a high level of efficacy in patients with AD.^{15,16} Another study found follow-up visits occurring in one-week improved adherence and treatment outcomes compared to a four-week follow-up visit.^{15,16}

Limitations of this study include its retrospective design and the lack of a validated objective grading scale for determining severity and degree of improvement. The improvement seen in these patients could also represent the natural course of the disease or regression towards the mean, but in our experience patients with moderate-to-severe AD rarely improve in one to two weeks without an intensive intervention. While the study examines a useful technique

for disease clearance, it did not address the optimum regimen for maintenance therapy. The pre-hydration technique is time-consuming and it is not always safe for long-term use. Daily intensive use of TCS can lead to HPA-axis suppression, cutaneous atrophy, striae, rosacea and telangiectasia. Upon follow-up, patients with moderate-severe disease are usually transitioned to steroid-sparing regimens that include emollients, topical calcineurin inhibitors, and maintenance with twice-weekly TCS. Patients whose disease is not stable after the pre-hydration clearance regimen and appropriate maintenance therapy are candidates for phototherapy or use of systemic immunosuppressives.

In conclusion, pre-hydration followed by TCS therapy appears to be a highly effective regimen that achieves rapid control of moderate-severe disease, even in patients who have required systemic therapy. This technique followed by a one- to two-week follow-up visit achieves clearance in the vast majority of patients which then allows for the initiation of steroid-sparing maintenance therapy.

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Table 1**Pre-Hydration Regimen**

1	Patients with severe, recalcitrant AD were given detailed written instructions at the initial visit (24).
2	Baths were used, depending on severity, once or twice daily.
3	Mid-potency corticosteroids (generally triamcinolone acetonide 0.1% ointment) or high-potency corticosteroids (e.g., betamethasone dipropionate 0.05% ointment) were prescribed in ample quantities sufficient to treat until the follow-up visit in one to three weeks.
4	Topical medications were applied as a thin film immediately upon exiting the bath while water remained on the skin — always within three minutes.
5	Face, neck, eyelids and flexures were treated twice daily for three days, then reduced to only one application every three days. Other body areas were treated twice daily the first week, then once daily until the follow-up contact.

Table 2

Age

Age	Patient number (%)
1–5 years old	20 (27%)
6–10 years old	4 (5%)
11–15 years old	8 (11%)
16–20 years old	9 (12%)
21–25 years old	3 (4%)
26–30 years old	7 (9%)
31–35 years old	6 (8%)
Over 35	18 (24%)

Table 3

Atopic history	Number of patients (%)
History of Asthma	27(36%)
Hay fever	27 (36%)
Food Allergies	17 (23%)

Table 4

Previous Therapies

Use of TCS	61 (81%)
Low potency	<u>25 (33%)</u>
Mid potency	<u>27 (36%)</u>
High potency	9 (12%)
Calcineurin inhibitors	<u>15 (20%)</u>
Systemic steroids	<u>15 (20%)</u>
Antihistamines	<u>26 (35%)</u>
Antibiotics	<u>26 (35%)</u>
UV therapy	2 (3%)

Table 5

Investigator Global Assessment

Severity	Initial visit	Follow up Visit
Severe	48 (64%)	0
Moderate	27 (36%)	3 (5%)
Mild	0	13 (20%)
Almost clear	0	47(73%)
Clear	0	1 (2%)

Table 6

Treatment Response Scale

Patient is worse	0
No improvement	0
Slight improvement	3 (4%)
Moderate improvement	10 (13%)
Marked improvement	59 (79%)
Patient is clear	3 (4%)