Original Article

Wet Wrap Therapy in Children with Moderate to Severe Atopic Dermatitis in a Multidisciplinary Treatment Program

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What is already known about this topic? Atopic dermatitis (AD) remains a complex, common, chronic, and relapsing skin disorder. National and international AD guidelines discuss treatment of AD based on severity of AD and include wet wrap therapy (WWT).

What does this article add to our knowledge? Although WWT was first described in the AD treatment literature in 1987, only 15 studies of WWT have been published. This study is the largest to date of patients treated with WWT by using a validated outcomes tool and the only one in which WWT was administered under direct nursing supervision.

How does this study impact current management guidelines? WWT plays an important role as an acute therapeutic intervention for management of moderate-to-severe AD. WWT should be considered as a treatment option ahead of the systemic therapies for patients for whom topical therapy failed.

BACKGROUND: Atopic dermatitis (AD) is the most common chronic, relapsing inflammatory skin disease of children and is a global public health problem. National and international AD guidelines address AD care in a stepwise fashion. Wet wrap therapy (WWT) is a therapeutic intervention for moderate-to-severe AD.
OBJECTIVE: This cohort study evaluated the effectiveness of WWT as part of a multidisciplinary AD treatment program to improve disease severity. Patients treated in this unique outpatient program had moderate-to-severe AD and had multiple therapies that failed.
METHODS: An observational cohort study was completed. The primary outcome was improvement in AD severity as measured by SCORAD (Scoring Atopic Dermatitis). Demographics; clinical management of AD, including use of antibiotics and systemic treatments; and WWT methodology were comprehensively described.
RESULTS: Seventy-two children with a mean ± SD age of 4.6 ± 3.12 years were included. By using a paired *t* test, the SCORAD at admission and at discharge showed significant differences in mean ± SD values, of 49.68 ± 17.72 versus 14.83 ± 7.45, respectively (t, 18.93; *df,* 71; *P* < .001). None of these patients required systemic immunosuppressive therapy during the treatment program. By using a previously published parent-administered outcomes tool, patients were shown to maintain clinical improvement of their AD 1 month after discharge.
CONCLUSION: To our knowledge, this study is the largest to date of WWT for pediatric patients with moderate-to-severe AD by using a validated outcomes tool. None of the patients required systemic immunosuppressive therapy, and only 31% were treated with an oral antibiotic. This study demonstrated the benefit of incorporating WWT as an acute intervention in a supervised multidisciplinary AD treatment program with lasting benefit 1 month after discontinuing this intervention. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;2:400-6)

Key words: *Wet wrap therapy; Atopic dermatitis; Management; Outcomes*

Atopic dermatitis (AD) remains a complex, common, chronic, and relapsing skin disorder of infants and children but can affect patients of any age. The prevalence has increased to 20% in children and approximately 3% of adults in the United States and other industrialized countries.[1] More than half of these patients develop asthma and allergies.[2] AD occurs in genetically predisposed individuals with a defective skin barrier and abnormal immune responses to irritants, allergens, and microbial organisms.[3] AD is characterized by abnormal skin barrier function associated with abnormalities in cornified envelope genes, reduced ceramide levels, increased levels of endogenous proteolytic enzymes, and enhanced transepidermal water loss.[4] The skin barrier also may be damaged by exposure to exogenous proteases

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Abbreviations used
AD- Atopic dermatitis
ADP- Atopic Dermatitis Program
ADQ- Atopic Dermatitis Quickscore
MRSA- Methicillin-resistant Staphylococcus aureus
SCORAD- Scoring Atopic Dermatitis
WWT- Wet wrap therapy

from *Staphylococcus aureus.* Skin barrier abnormalities contribute to increased allergen absorption and microbial colonization. Patients with AD have severe pruritus, and their disease disrupts sleep and negatively impacts the quality of life of patients and families.[5] When AD remains in poor control, patients and caregivers experience multiple medical and psychosocial problems. This illness places a significant economic burden on the patient, family, and society.

National and international guidelines emphasize basic treatment of AD at every level of severity to establish the foundation of AD management by addressing the skin barrier defect with regular use of moisturizers and skin hydration, along with the identification and avoidance of specific and nonspecific trigger factors. Further treatment based on the severity of AD can be done in the stepwise manner described in the PRACTALL Consensus[6] or the more recent update of the Practice Parameter treatment algorithm (Figure 1).[7]

In severe cases that cannot be controlled with topical treatment, the guidelines indicate systemic treatment options, including systemic corticosteroids, cyclosporine A, and UV light.[7] All of these therapies have potential risks and are not approved for use in children. Wet wrap therapy (WWT) for AD in children was first described in the AD literature in 1987.[8] Limited objective evaluation of WWT is available, especially when supervised by registered nurses. To our knowledge, no studies have evaluated long-term benefit after discontinuation of WWT. The primary objective of this study was to evaluate the effectiveness of WWT in a multidisciplinary treatment program in pediatric patients with moderate-to-severe AD for whom outpatient therapy failed. Demographics; clinical AD management, including use of oral antibiotics; and WWT methodology also were comprehensively described in this study.

METHODS

Patients

This was a cohort of pediatric patients admitted to the AD Program (ADP) in the pediatric care unit at National Jewish Health in Denver, Colorado, with a primary or secondary diagnosis of moderate-to-severe AD who had failed previous outpatient therapy. This cohort was a subset of a larger study designed to investigate the relationship between disease severities and associated psychosocial problems among pediatric patients with AD compared with patients with asthma. This study protocol was approved by the institutional review board at National Jewish Health.

AD management

Treatment in our ADP was previously described in detail. [9-11] This program allows for comprehensive evaluation, treatment, and education of patients in an outpatient setting, typically over the course of 5 to 10 days. Patients and caregivers interact with members of the multidisciplinary team primarily from 8 AM to 5 PM but can be observed overnight and even admitted as inpatients if necessary. Most patients and families spend the night in a nearby hotel. Standard of care treatment for this cohort included a 10- to 15-minute bath in warm water, immediately followed by application of a topical medication to eczematous lesions and moisturizers to the clear areas. No additives to the bath water were used. A gentle cleansing bar or wash, formulated for sensitive skin, was used as needed. Based on clinical severity, the patients were prescribed 2 to 3 supervised baths per day, with each bath followed by topical medications or moisturizer applications, and WWT. Topical medications usually were ointments and were not diluted or compounded. The most commonly used topical corticosteroid for moderate-to-severe AD to the body and extremities was triamcinolone acetonide 0.1%, and the most commonly used topical corticosteroid used for moderate-to-severe AD on the face was desonide ointment 0.05%.

A step-by-step detailed description of how the ADP implements WWT is outlined in Table I. WWT was done by using children's normal cotton-blend clothing. The patients were assisted by the registered nursing staff. The only area treated with gauze or dressings was the face. The face was wrapped only when there was severe facial involvement. Wet wraps were left in place a minimum of 2 hours. In general, wet wraps were removed after 4 to 6 hours, although they could be left on overnight if the patient fell asleep with wet wraps in place. Direct demonstration of proper skin care during treatment in the ADP included topical application of agents and techniques such as WWT and supervision of bathing by a registered nurse.

Measures of AD severity and statistical analysis

This study determined the magnitude of improvement in the severity of the AD by using 2 published instruments: Scoring Atopic Dermatitis (SCORAD) and AD Quickscore (ADQ). The SCORAD index was the primary measure used to assess improvement in the severity of AD. The SCORAD index is the most extensively used AD severity index nationally and internationally. Validity, reliability, and sensitivity have been demonstrated in multiple AD clinical trials.[12-15] The SCORAD index combines evaluation of the percentage body surface area involved, intensity of skin lesions, and subjective symptoms (daytime pruritus, sleep loss).[14] The SCORAD index produces a continuous score that indicates disease severity. In addition, severity classifications are determined from SCORAD index scores: mild (<25), moderate (25-49), and severe (>50).

Each subject had a detailed skin assessment on admission and at discharge completed by using SCORAD by 1 of 2 physician assistants who participated in the parent study. These staff members have well-documented competencies in completing this tool, and a duplicate assessment also was done to ensure interrater reliability. Neither of these physician assistants was involved in the preparation or review of this study or article. The ADQ is a parent-administered AD scoring tool and has been validated against the SCORAD index with Pearson correlations of the 2 scales.[16] ADQ assesses skin involvement and pruritus of 7 body parts. ADQ was scored at admission, discharge, and 1 month after discharge from the ADP.

Data were recorded and entered into the JMP software solution (SAS Institute Inc, Cary, NC) by clinical research coordinators with extensive check-and-balance processes to ensure accuracy of the data. The SCORAD index and ADQ scores produce continuous variables that can be used with parametric statistics. The length of time between admission and

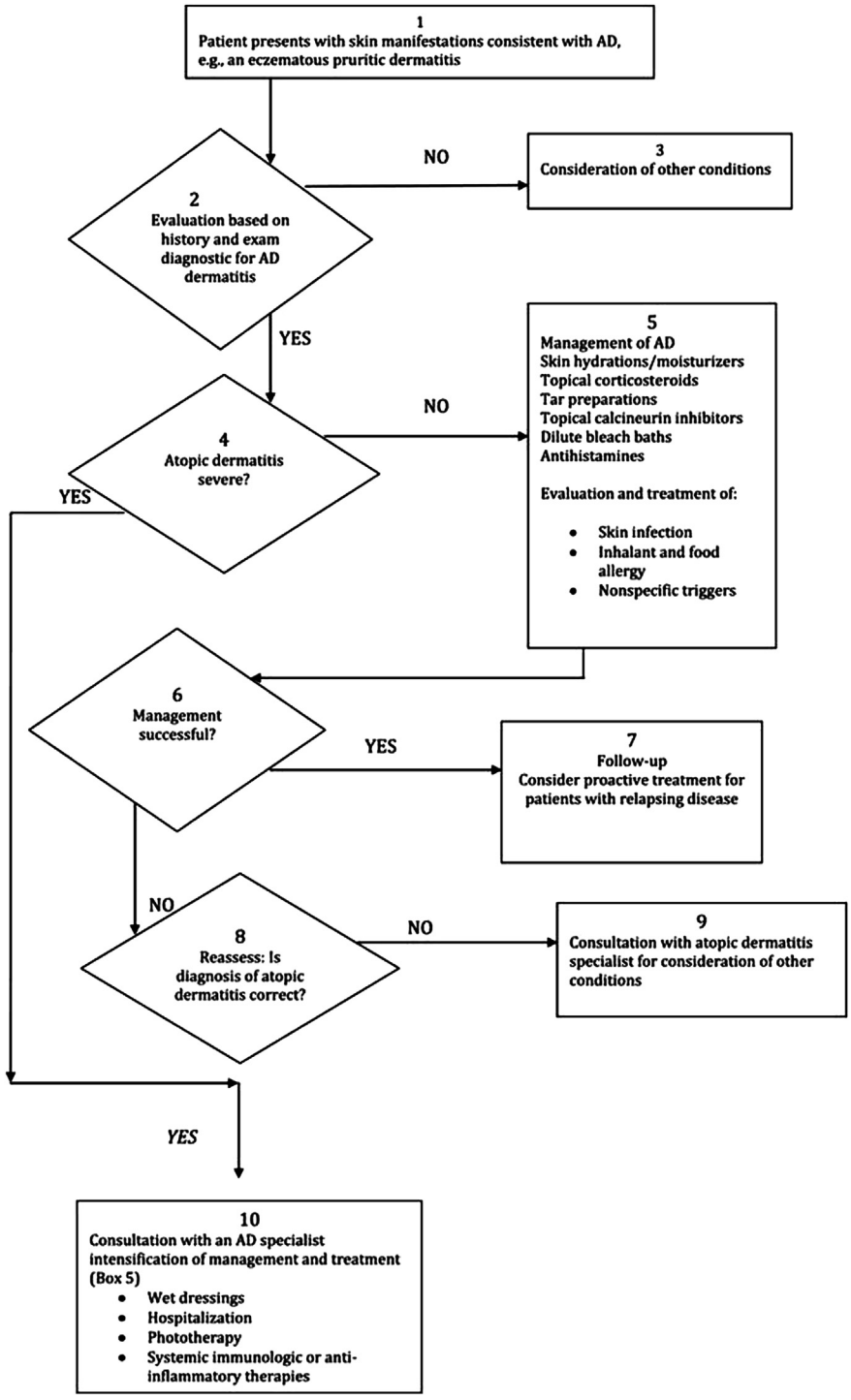

FIGURE 1. Treatment algorithm from the update to the AD Practice Parameter. Reproduced with permission from Schneider et al.[7]

discharge SCORAD varied among patients because the length of stay in the ADP depended on multiple factors. Factors included evaluation of comorbid conditions, the need of the family for discharge based on family issues, in addition to clinical improvement of AD. For statistical analysis of SCORAD and ADQ data, paired *t* tests were used to compare means of variables at 2 time points that were paired within subjects, for example, baseline and discharge SCORAD values. Two-sample *t* tests were used to compare mean values among different groups of subjects.

RESULTS

Patients

Patient demographics, clinical characteristics, and treatment are listed in Table II. The mean ± SD age at admission was

TABLE I. ADP WWT protocol: WWT will be used to relieve inflammation, itching, and burning of AD. Wet wraps facilitate the removal of scale and increase penetration of topical medications in the stratum corneum. Skin protection provided by the wraps allows healing to take place. WWT should only be used under the supervision of a health care provider during flares of AD. They should not be used as routine maintenance therapy

Supplies
1. Topical medications and moisturizers.
2. Tap water at a comfortably warm temperature.
3. A basin for dampening of dressings.
4. Clean dressings of approximate size to cover involved area.
a. Face: 2-3 layers of wet clinging gauze bandages held in place with expandable orthopedic or surgical net covering.
b. Arms, legs, hands, and feet: 2-3 layers of wet clinging gauze bandages gauze held in place with elastic bandages or tube socks, or cotton gloves, or wet tube socks, followed by dry tube socks; tube socks may be used for wraps for hands and feet, and larger ones work as leg and/or arm covers.
c. Total body: combination of above or wet pajamas or long underwear and turtleneck shirts covered by dry pajamas or sweatsuit. Pajamas with feet work well for the outer layer.
5. Blankets to prevent chilling.
6. Nonsterile gloves if desired.
Procedure
1. Be certain that the patient's room is warm and ensure privacy. Gather supplies appropriate to the individual.
2. If wraps are to be applied to a large portion of the body, work with 2 people if possible. It is necessary to work rapidly to prevent chilling.
3. Explain the procedure to the patient and parent.
4. Fill the basin with warm tap water.
5. The patient will have had a 15-20−min soaking bath in warm water without additional additives before this procedure. Pat skin dry with a towel.
6. Apply the appropriate topical medications to affected areas and moisturizer to nonaffected areas immediately after pat drying the skin. Use clean plastic spoons or tongue depressor to avoid contamination of products in jars. This allows large areas to be covered quickly and prevent caregivers from unnecessary exposure to topical medications.
7. Soak the dressings in very warm water because they cool quickly in this process. Squeeze out excess water. Dressings should be wet, not dripping.
8. Cover an area with wet dressing chosen for the area and the patient. Immediately after wrapping, cover with appropriate dry material, such as an elastic bandage, socks, or pajamas. Start at the feet and move upward. Use wet, long underwear or wet pajamas covered by dry pajamas or a sweatsuit with total body involvement in place of wet gauze.
9. Take steps to avoid chilling. A blanket can be put in a dryer to warm it, and cover the patient, but do not overheat the patient. Wraps can be removed after 2-4 hours or can be re-wet. A warm blanket and snuggling help pass the time.
10. If the patient is known or suspected to have an infection of the involved areas, place dressings in the appropriate bag and dispose according to infection control procedure.
11. After all dressings are removed, moisturizers may be applied to the entire body.

4.6 ± 3.12 years, with 62.5% being boys. All 72 pediatric patients were treated with WWT during their ADP stay. The frequency of WWT was decreased as AD severity improved. No patients were discharged if they were still being treated with WWT. Based on the length of stay in this program, the patients in this cohort were treated with WWT for a minimum of 2 days and for a maximum of 16 days, with the mean ± SD ADP stay being 7.5 ± 2.6 days. None of the 72 patients received oral glucocorticoids, cyclosporine A, mycophenolate, methotrexate, intravenous immunoglobulin, or UV light therapy during this AD treatment program. Oral antibiotics were the only systemic therapy used in this cohort, although a positive skin culture was not the only indication for treatment with oral antibiotics. Of 72 patients, only 5 (6.9%) had culture-proven methicillin-resistant *S aureus* as documented in the patient's medical record.

Oral antibiotics were not used in 50 patients (69.4%). For the remaining 22 patients (30.6%), amoxicillin-clavulanic acid combination was used with 2 patients (2.8%) with comorbid diagnosis of sinusitis, 18 patients (25.0%) were prescribed cephalexin for clinically secondarily infected AD, 1 patient (1.4%) was prescribed clindamycin for clinically secondarily infected AD, and 1 patient (1.4%) was prescribed erythromycin for clinically secondarily infected AD. It should be noted that 2 of the patients with documented methicillin-resistant *S aureus* did not receive oral antibiotics and had AD improvement by SCORAD. Of 72 patients, 4 patients (5.6%) developed folliculitis while on WWT. Only 1 of these 4 patients received oral antibiotics. All the patients diagnosed with folliculitis in this cohort had improved AD severity as measured by SCORAD and had sustained improvement as measured by ADQ, irrespective of whether folliculitis was treated or not treated with oral antibiotics.

On admission, individuals with bacterial infections who received oral antibiotics had significantly higher baseline SCORAD index scores (mean ± SD, 62.96 ± 16.47 [n = 22]) compared with those who did not receive antibiotics (mean ± SD, 44.22 ± 15.27 [n = 50]) ($P < .001$). A change in SCORAD between admission and discharge also was significantly greater ($P < .001$) in those individuals who received oral antibiotics (mean ± SD, 46.10 ±16.37 [n = 22]) compared with those who did not receive antibiotics (mean ± SD, 30.22 ± 12.81 [n = 50]).

AD severity improvement during the program

This study enrolled 72 patients who met the inclusion criteria and who had a pre- and post-SCORAD. The mean ± SD SCORAD index on admission was 49.68 ± 17.7 and the mean ± SD SCORAD index on discharge was 14.83 ± 7.4. When using a paired *t* test, the differences between SCORAD index means at admission and discharge were significant (*t*, 18.93; *df*, 71; $P < .001$). This finding of improved disease severity in this patient population, as measured by SCORAD index change, demonstrates a significant clinical improvement as a result of being treated with WWT in the ADP. Twenty-five of the 33 patients with severe conditions improved to mild and 8 of the 33 patients with severe condition improved to moderate with every patient with a severe condition that showed improvement based on AD severity classification. The admission SCORAD index (blue bar) and the discharge SCORAD index (red bar) for each of the 72 patients are compared in Figure 2. Of note, the

TABLE II. Demographics of patients with AD, clinical characteristics, and treatment

Pediatric patients with AD (N = 72)	
Age at admission (y), mean ± SD (range)	4.6 ± 3.12 (0.5-12.8)
Days in the unit (included week-end) (mean ± SD) (minimum, maximum)	7.5 ± 2.6 (2, 16)
Sex, no. (%)	
Girls	27 (37.5)
Boys	45 (62.5)
Race or ethnicity, no. (%)	
Asian	5 (7)
Black	5 (7)
Hispanic	9 (12)
White	51 (71)
Other	2 (3)
Child lives in Colorado, no. (%)	
Yes	25 (34.7)
No	47 (65.3)
Child lives with, no. (%)	
Both parents	66 (92)
Mother only	2 (3)
Other	4 (5)
Caregiver's work status, no. (%)	
Full-time homemaker	18 (25)
Working full or part time outside home	38 (53)
Looking for work outside home	1 (1)
Not working due to other reasons	5 (7)
Not working due to child's health	10 (14)
Use of oral antibiotics before admission	
Yes	51 (70.8)
No	15 (20.8)
Unknown	6 (8.4)
Number of confirmed food allergies, no. (%)	
0	16 (22.2)
1	7 (9.7)
2	47 (65.3)
3 or more	2 (2.8)
AD admission severity (SCORAD index), no. (%) (range)	
Severe (>50)	33 (45.8) (52-86)
Moderate (25-50)	34 (47.2) (25-47)
Mild (<25)	5 (7.0) (20-24)
SCORAD index change, mean ± SD*	
Admission	49.68 ± 17.7
Discharge	14.83 ± 7.4
WWT used, no. (%)	
Yes	72 (100)
No	0 (0)
Bacterial infection-culture positive staph-MRSA, no. (%)	
Yes	5 (6.9)
No	67 (93.1)
Oral antibiotics given, no. (%)	
Yes	22 (30.6)
No	50 (69.4)
Oral antibiotic prescribed, no. (%)	
None	50 (69.4)
Amoxicillin/clavulanate (sinusitis)	2 (2.8)
Cephalexin	18 (25.0)
Clindamycin	1 (1.4)
Erythromycin	1 (1.4)
Folliculitis documented during stay, no. (%)	
Yes	4 (5.6)
No	68 (94.4)
Topical prescription antibiotic used, mupirocin, no. (%)	
Yes	10 (13.9)
No	62 (86.1)
Topical calcineurin inhibitor used, no. (%)	
Yes	50 (69.4)
No	22 (30.6)
Herpes infections present, no. (%)	
Yes	1 (1.4)
No	71 (98.6)
Oral immunosuppressive given, no. (%)	
Yes	0 (0)
No	72 (100)

MRSA, Methicillin-resistant *Staphylococcus aureus.*
*Paired *t* (*t,* 18.93; *df,* 71; $P \leq .0001$).

gap between blue and red bars gets smaller from left to right, which demonstrates that the greater the severity of AD at admission, the greater the improvement.

AD severity improvement 1 month after discharge from ADP

The study determined if the achieved improvement at discharge from the ADP was sustained at 1 month as measured by the ADQ. In this cohort, ADQ scores and the SCORAD index were well correlated. The mean ± SD ADQ scores were 43.28 ± 12.03 at admission, 12.33 ± 8.42 at discharge, and 15.59 ± 12.53 1 month after discharge (Figure 3). Although the discharge and the 1-month means both differed significantly from the admission mean ($P < .001$), the discharge and 1-month means did not ($P = .36$). Analysis of these results indicates that patients had significant improvement from admission to discharge, which was consistent with SCORAD. In addition, analysis of these results also indicates that patients were able to maintain the improvement of AD that was achieved by discharge.

DISCUSSION

This study assessed a therapeutic intervention in a unique treatment program for children with moderate-to-severe AD who had multiple outpatient therapies that failed. Although WWT was first described by one of us (N.H.N.) in 1987,[8] limited evaluation by using validated AD scoring tools has occurred and rarely in an environment where WWT is supervised by registered nurses. In addition, no study has previously evaluated sustained benefit after discontinuing WWT when using a published AD scoring tool.[16] It is important to recognize that WWT

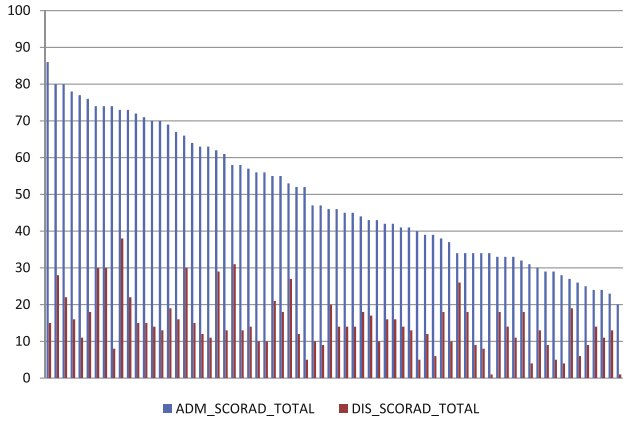

FIGURE 2. SCORAD on admission (blue bars) and at discharge (red bars) paired for 72 patients, sorted by SCORAD at admission (high to low). By using a paired *t* test, differences between SCORAD index means at admission and discharge were significant (t, 18.93; *df*, 71; $P < .001$). Of note, the gap between the blue and red bars gets smaller from left to right, which demonstrates that the greater the severity of AD at admission, the greater the improvement.

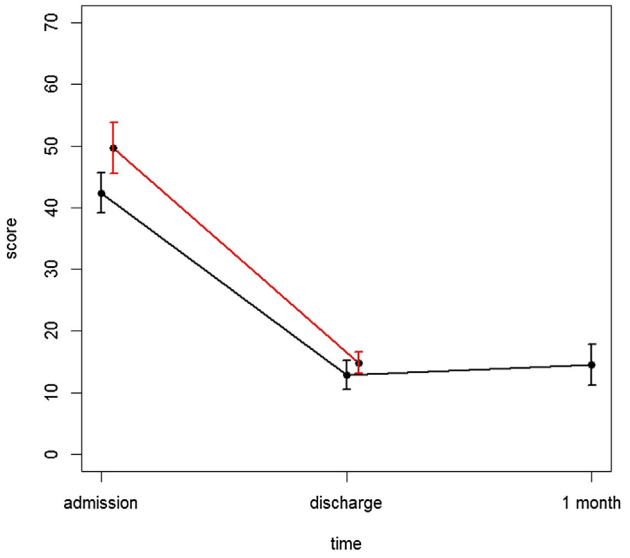

FIGURE 3. Mean ADQ (black) vs SCORAD (red), with 95% confidence limits. The mean ± SD ADQ scores were 43.28 ± 12.03 at admission, 12.33 ± 8.42 at discharge, and 15.59 ± 12.53 1 month after discharge. The mean ± SD SCORAD index on admission was 49.68 ± 17.7, and the mean ± SD SCORAD index on discharge was 14.83 ± 7.4.

methodology has not been standardized and that wide variation in WWT methods have limited proper interpretation and comparison of results. A recent retrospective 30-year review of a WWT study at a single institution found it to be highly efficacious; however, there was no standardized or objective formal scoring of AD or evaluation of patients after discontinuing WWT.[17] Only 15 WWT studies have been published, and only 8 incorporated a validated AD severity outcomes tool, with the largest patient sample being 45 children.[18-25] None of these studies were completed in a supervised environment, and the WWT techniques varied considerably. Importantly, none of the 15 WWT studies had a follow-up assessment as part of the study. The extended benefit seen after discontinuing WWT in our study is supported by studies that demonstrated that skin barrier function was improved 1 week after WWT was discontinued.[26]

Efficacy and safety of wet-wrap dressings as interventions for children with severe and/or refractory AD was previously assessed in a review of the literature.[27] The use of wet-wrap dressings with diluted topical corticosteroids for up to 14 days has been shown to be a safe intervention treatment in children with severe and/or refractory AD, with temporary systemic bioactivity of the corticosteroids as the only reported serious adverse effect.[27] In contrast to other studies in which WWT was used over an extended period,[25] our study emphasized that WWT should be considered an acute treatment intervention. This approach is less likely to be complicated by secondary infections or other adverse effects reported in some studies[25] because only 4 of our 72 study patients developed folliculitis. Of practical importance, the WWT methodology used in our study was much simpler and less expensive for families to incorporate into a treatment regimen than many of the published methods. Education of patients and caregivers is critical to the success of WWT.[9-11] This crucial education is increasingly difficult to accomplish in a typical outpatient clinic visit but can be coordinated with dedicated nurse educators or other allied health professionals working with the physician and the attending health care team. An important educational strategy is direct demonstration of proper skin care, which includes topical application techniques and WWT. If patients are allowed to continue WWT at home, then frequent follow-up visits should be scheduled.

There were limitations with this observational study. It was not possible to include a control group not treated with WWT for comparison because the patients were sent to the ADP for treatment that included WWT. These limitations are offset by the fact that this was a real-world study of pediatric patients with moderate-to-severe AD referred to the ADP after multiple outpatient treatments failed. This study is not generalizable to the adult population due to the study design. However, anecdotally, we have successfully treated adult patients in our ADP with WWT by using the same methodology and procedures.

Future WWT studies need to carefully describe all components of WWT procedures. Incorporation of the SCORAD index or other validated outcomes tools would help with interpretation of future studies when using WWT.[28] Studies need to address differences in methodology of the WWT, including topical preparations and the appropriate application technique of that preparation; type of wrap, bandages, and/or dressing; application frequency; wetting or rewetting of the first layer of wraps; wraps left in situ; area treated; duration of treatment; and location of treatment.[29] Two additional practical points need to be considered: first, the specifics of skin care immediately before WWT, and, second, skin care, if any, immediately after WWT needs to be described.

Because WWT appears to play an important role in the improvement of acute moderate-to-severe AD, this therapy should be considered as a treatment option ahead of the systemic therapies such as those listed in national[7] and international guidelines.[6] Our study of WWT in a cohort of children with moderate-to-severe AD after multiple outpatient therapies failed, including oral corticosteroids, demonstrated that extended

improvement can be achieved while avoiding the need for systemic immunosuppressive therapy.

CONCLUSION

To our knowledge, this study is the largest to date of patients with moderate-to-severe AD who received WWT by using a validated outcomes tool. The study population consisted of 72 children ages 6 months to 12.8 years. This study demonstrates the benefit of supervised WWT as an acute intervention in improving AD severity. Patients treated in this unique outpatient ADP had acute moderate-to-severe AD and multiple therapeutic interventions that failed. This study showed that these patients could be managed without systemic immunosuppressive therapy and were able to transition off of WWT before discharge from the program. The patients also were able to maintain improvement of their AD 1 month after discharge.

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