

Predictors of clinical success in a multidisciplinary model of atopic dermatitis treatment

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ABSTRACT

Atopic dermatitis (AD) is one of the most common pediatric skin disorders. Because treatment involves allergen avoidance, dietary changes, and behavior modification, multidisciplinary treatment models have been used to complement conventional medication therapy. However, predictors of clinical response in these multidisciplinary models have not been studied. This study examined factors associated with a reduction in AD severity in a multidisciplinary outpatient pediatric AD treatment program providing medical, nutritional, and behavioral support. Data were collected from 170 patients between 2001 and 2006. The Eczema Area and Severity Index (EASI) score was determined at the time of each visit. Using a logistic regression model, we investigated the association of baseline demographic and clinical characteristics with clinical outcome. We also analyzed the association between improvement in the EASI score and behavioral changes. One hundred thirty-eight patients had significantly improved EASI scores, and 32 patients were nonresponders. Responders had a median improvement of 79% in their EASI score, whereas nonresponders had a 53% worsening of their EASI score ($p < 0.0001$) and a significantly worse absolute EASI score ($p < 0.001$). Predictors of clinical success included baseline EASI score, baseline age, and improved parental adherence to treatment recommendations. Improvement in the EASI score significantly correlated with quality-of-life measures: decreased itching and scratching, difficulty sleeping, and parental concerns about side effects. A multidisciplinary model of AD treatment has the best clinical outcomes in younger patients with severe AD. Ensuring parental compliance with treatment recommendations is important for clinical response.

(Allergy Asthma Proc 32:377–383, 2011; doi: 10.2500/aap.2011.32.3462)

Atopic dermatitis (AD) is one of the most common pediatric skin disorders. Between 15 and 30% of children are affected by AD and its prevalence has increased two- to threefold in the past 30 years.¹ Acute AD causes erythematous papulosquamous pruritic lesions. Chronic AD results in lichenification and postinflammatory skin changes. The refractory and visible nature of AD impacts the quality of life of patients, with impairments comparable with those reported by parents of children with cystic fibrosis, chronic renal disease, and epilepsy.^{2,3} Parental stress associated with AD stems from sleep deprivation, guilt, financial cost of disease treatment, and worry about the disease and child's self-esteem.^{4–10}

Treatment for pediatric AD includes topical corticosteroids, antibiotics, topical calcineurin inhibitors, and antihistamines.¹¹ Effective treatment also requires lifestyle changes, such as daily baths, frequent moisturization and wraps, behavioral modifications to minimize scratching, dietary restrictions, and environmental

controls.¹¹ Adherence to time-consuming skincare regimens can be challenging and confusing.^{10,12–14}

Given the broad impact of AD on quality of life, multidisciplinary therapies have been used to complement conventional medical therapy. Such programs incorporate specialty medical care, education, and nutritional and psychosocial support. However, these programs are resource and time intensive and are not always efficacious.^{15,16} It is important to understand factors associated with outcome in these multidisciplinary models. No prior studies have investigated whether a multidisciplinary approach is more effective for a specific subgroup of patients with AD.

This study examined factors associated with clinical outcome in a pediatric multidisciplinary outpatient treatment program. We investigated the association of demographic and clinical characteristics with clinical improvement. We hypothesized that parental perception of difficulty following treatment recommendations would be inversely associated with clinical outcome. Furthermore, we proposed that clinical improvement would be associated with change in AD-related behaviors.

METHODS

Program Description

The Atopic Dermatitis Center at Children's Hospital Boston¹⁷ is an outpatient program for children with refractory AD treated by a pediatric allergist, nurse practi-

From the Division of Immunology, Children's Hospital Boston, Boston, Massachusetts
Presented at the meeting of the American Academy of Asthma, Allergy, and Immunology, Philadelphia, Pennsylvania, March 17, 2008

Supported by the Children's Hospital League and the Adams Family Fund for Allergy Research

The authors have no conflicts to declare pertaining to this article

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Table 1 **Multidisciplinary approach to eczema therapy**

Allergist/Allergy nurse practitioner

- Assessment of the patient's AD with the EASI score
- Assessment of food allergies, including skin and specific IgE testing
- Education of parents about food allergies, environmental controls, and AD
- Strategies to increase adherence
 - Eczema action plan detailing where and when to use medications
 - Demonstration of skin care techniques (e.g., application of wraps)
 - Inquiry about barriers to adherence and problem solve to address these with parents
 - Assess understanding of skin care plan and simplify regimen if necessary
 - Assess concerns about medications
 - Assist with a plan for a consistent schedule for skin care and sleep
 - Inquire about barriers to adherence and problem solve if necessary
 - Review importance of follow-up in the AD center

Nutritionist

- Performs calorie count and nutritional assessment
- Provides information about foods containing specific allergens
- Provides information about alternative foods and recipes
- Provides support for food allergy strategies for eating outside the home

Psychologist

- Education about distraction techniques to minimize scratching: activities that keep hands busy (building with Legos, drawing, turning the pages of a book, songs with hand gestures, or crafts) and use of moisturizer or an ice pack to control pruritus
- Coping techniques
 - Fostering "team" approach to eczema so children and parents work together to "beat the itches" and minimize blame
 - Relaxation strategies for older children
- Sleep techniques
 - Children's relaxation CDs to help with sleep onset and refocusing attention away from itchiness
 - Covering up to reduce damage from scratching in their sleep
- Strategies to increase adherence
 - Involve children in treatment and stress the importance of parental monitoring even when children have transitioned to independent skin care
 - Develop skin care schedules
 - Create simple reward plans for children to reinforce cooperation

AD = atopic dermatitis; EASI = Eczema Area and Severity Index.

tioner, nutritionist, and psychologist. Patients are referred by community pediatricians, allergists, and dermatologists. Allergens are diagnosed by skin or specific IgE testing; food challenges are done as needed.¹⁸ Providers offer education, behavior modification, and nutritional guidance, thus combining nonpharmaceutical and medical therapy (Table 1). All patients were treated by the same nurse practitioner and allergist for uniformity of practice style. The providers follow a standard approach based on the Atopic Dermatitis Practice Parameters¹⁹; acute therapy, such as antibiotic use, was individualized for each patient's clinical status. J.S. Chou and J. LeBovide contributed equally to this study.

Study Population and Data Collection

Subjects included 170 patients with AD who attended the center from 2001 to 2006 with at least two

visits. Included patients had persistent eczema despite medical therapy. The AD center does not treat patients without a history of prior eczema treatment or those with skin diseases other than AD. Patient demographics and clinical characteristics were obtained by questionnaire before the first visit and also from a retrospective chart review. At each visit, eczema severity was scored by the pediatric allergist or nurse practitioner and parents rated the frequency of AD-related quality-of-life concerns. This study was approved by the Institutional Review Board at Children's Hospital Boston.

Measures

AD severity was measured using the Eczema Area and Severity Index (EASI), a standardized scoring system ranging from 0 to 72, with 0 indicating no eczema.

The EASI score determines the body surface area affected by erythema, induration/population, excoriation, lichenification, and scaling.²⁰ Because the last visit in the study period may not represent the disease course, we calculated a composite variable reflective of the overall changes in the EASI score. We calculated the percent change in EASI score from the initial score at each follow-up visit; a positive percent change represented worsening eczema, whereas a negative percent change denoted improvement. The percent change in EASI score at each follow-up visit was then averaged over each patient's number of visits to normalize for differences in visit numbers. Patients with a decreased change in the composite EASI score were categorized as "responders," and those with no or increased change were considered "nonresponders."

Parental report of concerns associated with quality of life and treatment adherence was obtained *via* questionnaire each visit. Using a 7-point Likert scale, parents rated the frequency of (a) itching and scratching, (b) difficulty sleeping, (c) child uncooperativeness with treatment, (d) parental difficulty following treatment recommendations, (e) parental stress about managing AD, and (f) concerns about the effects of the prescribed medical treatment. A composite score reflecting change in quality-of-life concerns was calculated in the same way as the composite variable reflecting change in the EASI score.

Statistical Analyses

Normality of the data was assessed using the D'Agostino-Pearson test. The Mann-Whitney *U* test was used to compare differences in composite change scores. The Kruskal-Wallis nonparametric ANOVA was used to compare three groups with nonparametric data.

Univariate logistic regression analysis was performed to examine the relationship between responder status and the following covariates: age at the first visit, gender, age of AD onset, EASI score at the initial visit, number of other atopic diseases, duration of therapy, and number of follow-up visits. Univariate logistic regression analysis was used to analyze the relationship between responder status and change in behavioral factors likely to be associated with adherence: child uncooperativeness with treatment routine and parental difficulty following treatment recommendations. A preliminary binary logistic regression model for identifying predictors of responder/nonresponder status was created using covariates associated with responder status at $p \leq 0.25$ in the univariate analyses. Model fit was examined by individually removing variables with $p > 0.05$ in the bivariate model to create reduced models (described previously).²¹ The likelihood ratio test of these reduced models was compared

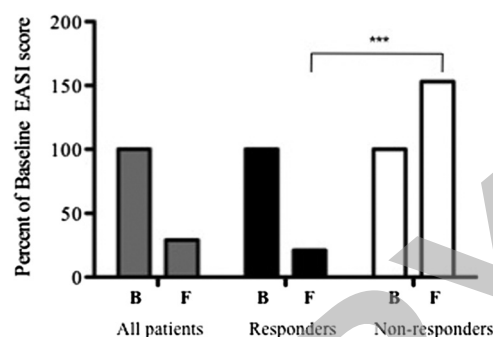


Figure 1. Average percentage change in Eczema Area and Severity Index (EASI) score. Baseline EASI scores (B) are shown at 100%; "F" denotes the composite follow-up score. Scores represent median value. Calculation of the composite follow-up scores are described in the Methods section (** $p < 0.001$, using the Mann-Whitney test).

with the full model. The variable was included in the final model only if the likelihood ratio test of the reduced model had an inferior fit compared with the full model.

Spearman rank correlations were used to examine associations between change in EASI score and change in variables associated with AD-related quality of life, because these data were nonparametric. All analyses were conducted using SPSS (IBM SPSS Statistics, Armonk, NY).

RESULTS

Clinical Outcomes

The median age of the population was 3.1 years (range, 0.3–16.4 years). There were 60 female patients and 110 male patients. Using the composite change in EASI score (see Methods section), the population had a median 71% decrease in the EASI score compared with baseline (Fig. 1). One hundred thirty-eight patients had an improved EASI score (the "responder" group). Responders had an initial median EASI score of 19.9 that decreased by 79% to a median follow-up score of 4.4. "Nonresponders" were patients who had an unchanged or worse EASI score. The median baseline EASI score of the 32 nonresponders was 6.6 and rose by 53% to a median follow-up score of 11.1. The percent change in EASI score from baseline to follow-up differed significantly between responders and nonresponders (79% decrease versus 53% increase; $p < 0.001$), as did the absolute median follow-up scores (4.4 versus 11.1; $p < 0.001$). These two groups are thus distinct, with responders showing less skin involvement at follow-up. The most significant improvement in the responder group occurred after the first visit and was maintained at each follow-up visit (Fig. 2; $p < 0.001$). Additionally, responders had a significantly lower baseline median age of 1.5 years compared with the median age of 2.7 years for nonresponders (Table 2).

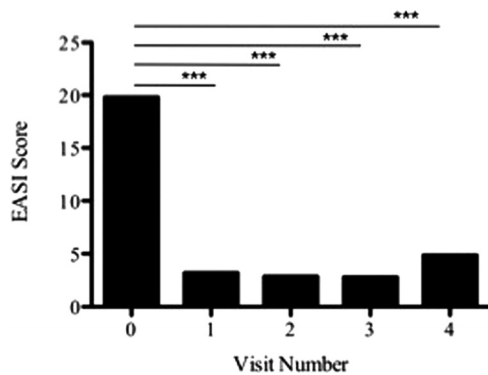


Figure 2. Trend in Eczema Area and Severity Index (EASI) score for responders. Four visits are shown because the 95% confidence interval for visit number ranged from 2 to 4 (** $p < 0.001$, using the Kruskal Wallis nonparametric ANOVA for nonparametric data).

Table 2 Demographic and medical characteristics of study participants

	Responders (95% CI)	Non-Responders (95% CI)
Median baseline age (yr)	1.5 (1.2–2.1)*	2.7 (1.8–4.4)
Gender (%)		
Female	55 (40%)	14 (44%)
Male	83 (60%)	18 (56%)
Ethnicity		
White	71 (51%)	19 (59%)
Black	8 (6%)	1 (3%)
Hispanic	3 (2%)	1 (3%)
Other	37 (27%)	4 (12%)
Not answered	19 (14%)	7 (22%)
Median age of AD onset (mo)	2.0 (2.0–3.0)	3.0 (2.0–6.0)
No. atopic diseases	3 (2–3)	3 (2–3)
Duration of therapy (mo)	18 (12–23)	13.5 (5–33)
No. of visits	3 (2–4)	3 (2–5)

* $p < 0.05$, using the Mann-Whitney test.

AD = atopic dermatitis.

Logistic Regression

Because the study population had two subgroups with distinct outcomes, we used a logistic regression to identify predictors of clinical response. In univariate analyses, a higher baseline EASI score (19.9 for responders versus 6.7 for nonresponders) and reduced parental difficulty in following treatment recommendations were significantly associated with responder status (Table 3). The reduced model for logistic regression included baseline EASI score, baseline age, age of AD onset, and change in parent difficulty following

treatment recommendations. Because eliminating the age of AD onset from the model improved the fit of the final model, the final bivariate logistic regression model included baseline age, baseline EASI score, and change in parent difficulty following treatment recommendations. In this final model, a higher baseline EASI score, a younger baseline age, and reduced parental difficulty in following treatment recommendations were significantly associated with responder status. Importantly, duration of therapy and number of visits did not correlate with response (Tables 2 and 3). All patients had at least two visits to the AD center, but patients with more than two visits did not have greater improvement than those with only two visits (Table 4).

Association between Change in EASI Score and Change in Patients' Behavior

We examined the association between change in EASI scores and quality-of-life measures. As seen in Table 5, an improved EASI score significantly correlated with improvement in itching and scratching, difficulty sleeping, and parental concerns about side effects. Change in parental stress related to AD was not associated with improved EASI scores.

DISCUSSION

Educational and behavioral modification programs are recommended to improve clinical outcome and quality of life for patients with AD.^{22,23} However, a Cochrane analysis concluded that there is limited evidence supporting the effectiveness of multidisciplinary interventions in treating pediatric AD.²⁴ There is no consensus from either single^{16,25,26} or multiple^{14,15,27} intervention studies regarding the best approach or how to maximize efficiency. Differences in intervention type may contribute to differences in outcomes.²⁴ We propose that the multidisciplinary approach is best suited for a specific subpopulation of pediatric eczema patients. This study is the first to investigate predictors of clinical outcome in a multidisciplinary treatment approach to AD. This study is also the first to focus on patients who previously failed conventional medical therapy.

The majority of the study population had clinical improvement with a median decrease of 79% in the EASI score. In our multivariate logistic regression model, predictors of clinical response included a higher baseline EASI score, a younger baseline age, and reduced parental difficulty in following treatment recommendations. Patients with the most severe AD have the most potential for improvement. However, we found that responders had not only a greater change in their EASI scores, but also a lower absolute follow-up score despite having a worse score at the initial visit. Because patients are referred to the AD

Table 3 Logistic regression analysis of potential predictors of responder status

Predictor	Univariate Analysis OR (95% CI)	Multivariate Analysis (reduced model) OR (95% CI)	Multivariate Analysis (final model) OR (95% CI)
Baseline age (yr)	0.93 (0.84–1.03)	0.78 (0.63–0.95)*	0.77 (0.64–0.92)**
Sex	1.17 (0.54–2.55)		
Baseline EASI score	1.11 (1.06–1.17)**	1.15 (1.07–1.24)***	1.15 (1.07–1.24)***
Age of AD onset	0.98 (0.95–1.01)	0.83 (0.96–1.04)	
No. of atopic diseases	0.78 (0.45–1.37)		
Duration of therapy	1.00 (0.98–1.02)		
No. of follow-up visits	1.00 (0.90–1.10)		
Number of atopic diseases	0.78 (0.45–1.36)		
Change in child cooperation with treatment	0.86 (0.55–1.35)		
Change in parental difficulty following treatment recommendations	0.59 (0.35–0.98)*	0.35 (0.16–0.77)**	0.35 (0.16–0.77)**

Results are presented as odds ratios (OR) and confidence intervals (CI).

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

AD = atopic dermatitis; EASI = Eczema Area and Severity Index.

Table 4 Change in Eczema Area and Severity Index (EASI) score of patients with less than two visits compared with those with more than two visits

	No. of patients	Average Percent Change in EASI Score (95% CI)
Patients with less than two visits	36	–52% (–49.6–20.4)
Patients with more than two visits	131	–37% (–40.1–10.9)#

#No significant difference in average percentage change in EASI score between the two groups using the Mann-Whitney test.

center only after failure with conventional therapy, this multidisciplinary approach opens another therapeutic possibility for patients with refractory eczema. A younger baseline age was associated with increased odds of clinical improvement, which may reflect the natural history of the disease. However, introducing behavioral changes and medical interventions earlier addresses the itch–scratch cycle sooner.

The greatest improvement for responders occurred after the first visit. At the first visit, the foundation of the multidisciplinary approach is established with an eczema action plan, a nutritional plan for allergen avoidance, and list of pediatric behavioral techniques (Table 1). A separate study would have to be performed to determine if a single visit at the AD center would result in prolonged improvement. One previous randomized study using a single educational session

Table 5 Correlation between change in Eczema Area and Severity Index score and change in behavioral factors

Average Change in Behavioral Factors	Correlation Coefficient
Itching and scratching	0.19*
Difficulty sleeping	0.28**
Parental stress over managing child's AD	0.14
Parental concern/worries about treatment side effects	0.29**

* $p < 0.05$, using two-tailed Spearman's rank correlation;

** $p < 0.01$, using two-tailed Spearman's rank correlation.

AD = atopic dermatitis.

found that the most significant clinical improvement occurred after 1 month of treatment and was maintained for the 3-month study duration.²⁸ In our study with recurring multidisciplinary meetings, improvement after the first visit was maintained for a longer period; the 95% confidence interval for duration of therapy for responders ranged from 12 to 23 months. The finding that the greatest response occurs after the first visit shows that immediate and significant clinical improvement can occur even after only one educational session. Although providers in the community may not have access to all of the resources of the AD center, they may find it useful to increase the time spent on education for parents with young children affected by refractory eczema.

Positive response was also associated with improvements in parental ability to follow treatment recommendations. Although we did not measure adherence, improved clinical outcome correlated with decreased parental perception of their difficulty in following treatment recommendations. This finding underscores the importance of identifying and addressing aspects of the treatment regimen that parents find difficult. Child cooperation with therapy did not change with clinical improvement, which is not surprising given the young age of our population. Treatments such as applications of creams and wraps can be difficult for toddlers to tolerate. Therefore, parental adherence with treatment regimens is important in this population.

Improvement in disease severity correlated with improvement in quality-of-life measures, including itching and scratching, difficulty sleeping, and concern about treatment side effects. Decreased scratching is necessary for clinical improvement. A reduction in parental concerns about treatment side effects may facilitate increased compliance. There was no association between clinical outcome and parental stress regarding AD. This underscores the difficulty of managing a chronic disease even in a patient who is improving because lifestyle changes must be continued even with quiescent AD.

This study has several limitations. Because this was not a randomized controlled study, we can not quantify the efficacy of a multidisciplinary treatment approach compared with medical therapy alone. However, patients are referred to the AD center only after conventional medical therapy has failed. Furthermore, responders had significantly lower absolute EASI scores at follow-up compared with nonresponders, despite having a higher baseline EASI score. This suggests that multidisciplinary treatment can improve eczema refractory to first-line therapies. Future studies would benefit from a control group receiving conventional medical therapy alone. This study revealed a significant correlation between improvement in the EASI score and quality-of-life measures, such as sleep and scratching. The AD center now collects validated age-specific measures of AD-related quality-of-life concerns.^{20,29}

Despite these limitations, this study is the first to identify factors associated with clinical outcome in a multidisciplinary treatment approach to AD. This study identifies issues relevant to medical practice in the community. Our study revealed that a multidisciplinary treatment approach is helpful when begun early in children with severe disease. Furthermore, the most dramatic improvement occurs after the first visit, suggesting that extra time spent on parental education during one visit can lead to significant clinical improvement even in patients with refractory eczema. With recurrent visits to the AD center, this improve-

ment was maintained for the duration of the study. We have detailed our multidisciplinary approach in this paper for providers to incorporate into their own practice. Given the importance of parental compliance, routinely inquiring about barriers to adherence enables providers to provide additional education or appropriate referrals.

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