

–319 C > T, R261Q [C > G], and S322N [A > G] and ALOX15 to –272 C > A) or their haplotypes (Ht1: CGCag, Ht2: gGTga, and Ht3: gaCGA). These results suggested that the genetic effects of ALOX12 and ALOX15 for developing AERD may be minimal compared with those of ALOX5.

HYUN-YOUNG LEE, MS
SEUNG-HYUN KIM, PhD
YOUNG MIN YE, MD
GIL SOON CHOI, MD
HAE-SIM PARK, MD, PhD
Department of Allergy and Rheumatology
Ajou University School of Medicine
Ajou University
Suwon, Korea
hspark@ajou.ac.kr

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INTENSE TACROLIMUS OINTMENT THERAPY IN CHILDREN WITH SERIOUS ATOPIC ECZEMA DERMATITIS SYNDROME

Atopic eczema dermatitis syndrome (AEDS)¹ can be considered a 2-faced disease characterized by the presence of early IgE-mediated and delayed T-lymphocyte-mediated allergy. Its pathogenesis is still not completely understood because many patients have an atopic profile with increased secretion of serum IgE and specific IgE sensitizations, but 10% to 30% of all patients have normal serum IgE levels and no specific IgE sensitization.² Topical tacrolimus ointment seems to be safe and effective,³ even in infants, and represents a widespread therapeutic approach for patients with AEDS because of its immunosuppressant action on T lymphocytes.

In this study, we evaluated the effect of intensive topical tacrolimus, 0.03% (Protopic; Astellas Pharma US Inc, Deerfield, Illinois), therapy on peripheral blood T-lymphocyte subsets in children with serious AEDS. All the patients were instructed to apply tacrolimus, 0.03%, ointment over affected skin areas according to the fingertip unit measure,⁴ approximately 12 hours apart, for 12 weeks (the total mean weighed quantity of applied ointment per patient was 193.5 g). Cleared areas were treated for an additional 7 days after clearance. The use of topical corticosteroids, nonsteroidal immunosuppressants, phototherapy, and topical antihistamines was stopped before the first application of tacrolimus and was not permitted in combination with tacrolimus during the study.

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Table 1. Immunologic, Hematologic, and Clinical Findings Across Time in Patients With AEDS

	Value, mean (SD)		P value ^a
	Baseline	End of treatment	
IgE total, U/mL	358 (488)	360 (482)	.98
IgG total, mg/dL	1,092 (168)	1,090 (189)	.97
IgG1, mg/dL	723 (144)	738 (139)	.73
IgG2, mg/dL	265 (143)	278 (165)	.78
IgG3, mg/dL	68 (38)	63 (31)	.64
IgG4, mg/dL	56 (50)	61 (63)	.77
IgM, mg/dL	110 (55)	112 (60)	.91
IgA, mg/dL	98 (45)	95 (43)	.82
RBCs, /mm	4,230,000 (630,000)	4,350,000 (570,000)	.52
Platelets, cell/mm	264,300 (82,440)	263,800 (76,120)	.98
Leukocytes, / μ L	8,760 (1,780)	8,543 (1,103)	.63
Neutrophils, / μ L	2,943 (1,126)	2,928 (1,500)	.97
Lymphocytes, / μ L	3,463 (1,089)	3,462 (1,052)	.99
Eosinophils, / μ L	423 (285)	429 (276)	.94
SCORAD score	37.2 (10.7)	10.3 (12.4)	<.001
SCORAD (atopic) score	36.59 (10.73)	9.5 (13.7)	<.001
SCORAD (nonatopic) score	36.52 (18.95)	10.3 (12.03)	<.006

Abbreviations: AEDS, atopic eczema dermatitis syndrome; RBC, red blood cell; SCORAD, SCORing Atopic Dermatitis.

^a Using the *t* test for paired data.

Data from patients with AEDS before and after 12 weeks of tacrolimus therapy are reported in Table 1. We found a significant improvement in mean (SD) SCORing Atopic Dermatitis scores (37.2 [10.7] vs 10.3 [12.4], $P < .001$), but total peripheral blood lymphocyte counts and serum IgG and serum IgG subclass values remained within the reference range after 12 weeks of therapy. When we compared SCORing Atopic Dermatitis scores between allergic and nonallergic patients, the change from before to after tacrolimus treatment was not statistically significant ($t = 0.136$, $P = .89$). We found no significant change in tested T-lymphocyte subsets in all patients with AEDS after the end of topical therapy (Table 2), and no difference was observed between the 2 subgroups. When we explored the distribution of T-lymphocyte subsets in allergic and nonallergic subgroups of patients with AEDS, we did not find significant modifications. As discussed previously herein for serum IgE levels, peripheral blood T-lymphocyte subsets also seem to have an unclear significance in AEDS. Some authors^{5,6} found an increase in CD4⁺ compared with CD8⁺ T cells, whereas others found a significant decrease in CD3⁺ and CD4⁺ T-lymphocyte levels.

We previously showed⁷ that untreated children with AEDS have decreased levels of CD8⁺ T cells, normal levels of CD3⁺ and CD4⁺ T cells, and a significantly higher CD4:CD8 ratio compared with healthy children in allergic and nonallergic subgroups. Until now, there have been no data on the effect of tacrolimus on peripheral blood T-lymphocyte subsets in children affected by serious AEDS, either allergic or nonallergic.

This study improves the understanding of the course of this disease in childhood, because we did not find any modifications in tested T-lymphocyte markers in patients with AEDS after 12 weeks of therapy. This result suggests that clinical improvement was ap-

Table 2. CD Markers in Patients With AEDS Before and After Topical Tacrolimus Treatment

	Percentage, mean (SD)		P value ^a
	At baseline (n = 21 patients)	12 wk later (n = 21 patients)	
CD3	66.12 (9.73)	63.94 (7.71)	.42
CD4 ⁺	37.87 (9.30)	37.44 (4.41)	.85
CD8 ⁺	24.38 (6.85)	23.62 (4.10)	.68
HLA-DR IN CD3	12.69 (11.79)	10.25 (3.53)	.37
CD57 in CD8	14.75 (10.72)	13.8 (8.70)	.76
CD19	19.68 (8.19)	20.44 (7.29)	.73
CD5 in CD20	51.71 (9.96)	48.87 (10.70)	.36
CD16	10.44 (8.32)	11 (5.83)	.78
CD3-CD56 ⁺	10.50 (7.97)	10.56 (5.85)	.99
CD45Ra in CD4	63.19 (15.51)	65.25 (8.1)	.58
CD25	12.37 (9.32)	10.20 (2.43)	.32
CD4/CD8	1.67 (0.69)	1.56 (0.30)	.80

Abbreviation: AEDS, atopic eczema dermatitis syndrome.

^a Using the *t* test for paired data.

parently not associated with changes in tested T-lymphocyte markers and that the atopic condition did not influence the effect of tacrolimus ointment therapy in children with AEDS.

Furthermore, the lack of changes in T-lymphocyte subsets confirmed that topical tacrolimus therapy did not affect the immune system, in accordance with literature data reporting very low systemic absorption of tacrolimus, 0.03%, ointment, with blood concentrations of the drug ranging from 1 to 2.28 ng/mL.⁸ Finally we suggest that monitoring of peripheral blood T-lymphocyte subsets during topical tacrolimus therapy did not add useful information in the evaluation of therapeutic success in children with AEDS.

SALVATORE LEONARDI, MD
GIOVANNA VITALITI, MD
LUCIA SPICUZZA, MD
MARIO LA ROSA, MD

Pediatric Department
University of Catania
Catania, Italy
leonardi@unict.it

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PROBIOTIC GASTROINTESTINAL ALLERGIC REACTION CAUSED BY *SACCHAROMYCES BOULARDII*

Saccharomyces boulardii medication is a nonpathogenic yeast probiotic that is widely prescribed in a lyophilized form (so-called *S boulardii* lyo) in many countries. Modulation of commensal bacteria of the gut with probiotics has been shown to have an effect on the prevention of food allergy.¹ To our knowledge, there is no contraindication for the patients except for a rare case of fungemia.²

Several fungal species are known to cause cutaneous and respiratory allergic disease.³ The ingestion of yeast can cause clustered sensitivity to allergy, including an anaphylactic reaction.⁴ *Saccharomyces boulardii* is a subtype of *Saccharomyces cerevisiae* known as brewer's or baker's yeast. *Saccharomyces cerevisiae* causes baker's asthma.⁵ However, to our knowledge, allergy caused by the ingestion of *S boulardii* lyo has not been reported. To our knowledge, we report the first case of a gastrointestinal allergic reaction that developed after the administration of *S boulardii* probiotic in a patient with food protein-induced enterocolitis syndrome (FPIES).

A 5-month-old exclusively breastfed boy was admitted to the hospital with vomiting, cyanosis, and lethargy within 4 hours after ingesting approximately 30 mL of soy formula. Two weeks later, an open standard oral food challenge (OFC) with soy formula was performed and soy intolerance was observed. After soy-induced FPIES was diagnosed on the basis of the diagnostic guidelines,^{6,7} iron supplements and breastfeeding exclusively were continued, with no solid intake recommended. However, the mother gave the infant some fruits and vegetables even though we warned of FPIES reactions. Fortunately, no adverse reactions occurred.

At the age of 8 months, presumed bacterial colitis was treated with cefixime (Suprax; Dong-A Pharmaceutical Co, Seoul, Korea); *S boulardii* lyo as Bioflor (Kuhnil Pharmaceutical Co, Seoul, Korea, manufactured under the license of Biocodex, Gentilly, France) was also provided. Two hours later, after taking the medicines, the infant presented to the emergency department with repetitive vomiting and cyanosis and required intravenous fluid resuscitation. Cefixime was excluded as a cause for the infant's symptoms because subsequent exposure to the antibiotic was well tolerated. We presumed that an allergic reaction consistent with FPIES^{6,7} was caused by Bioflor.

One week later, after the infant's bacterial colitis had resolved, an OFC with 1 pack of powdered Bioflor was conducted as described by previous suggestions.^{6,7} After 2 hours, projectile vomiting was detected and soon lethargy with cyanosis followed. The infant's blood pressure was 74/39 mm Hg, and isotonic sodium chloride solution (30 mL/kg) was infused for 1 hour, followed by dextrose saline. After 5 hours of the challenge, the infant's blood pressure normalized to 92/65 mm Hg. No fever developed. In addition, there were no mucocutaneous or respiratory symptoms observed. Eight hours later, stools that were bloody and purulent and had a foul odor

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