

Letters

RESEARCH LETTER

Efficacy of Systemic Treatments for Atopic Dermatitis in Racial and Ethnic Minorities in the United States

Most evidence supporting systemic therapy for atopic dermatitis (AD) is derived from randomized clinical trials (RCTs) performed outside the United States, particularly in Europe. However,



Invited Commentary



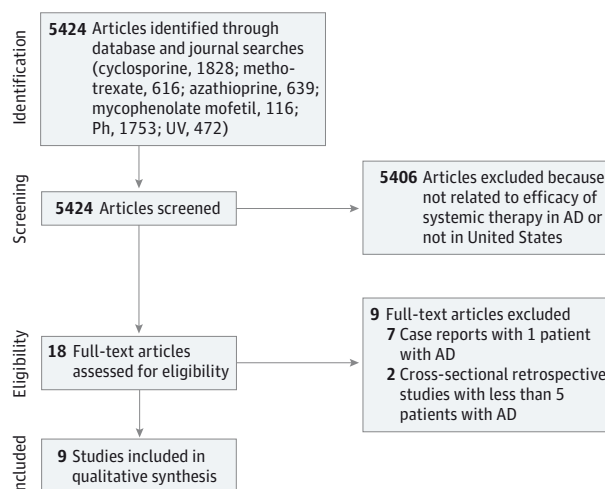
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ever, the US population vastly differs from that of Europe and other regions, with greater racial and ethnic diversity and heterogeneity. This is not a trivial point given recent studies demonstrating greater prevalence¹ and severity of AD and quality-of-life impairment² from AD in blacks. Furthermore, blacks have a distinct clinical presentation with a micropapular, perifollicular erythematous eruption.³ They also seem to have different genetic polymorphisms underlying their disease.^{4,5} Yet, little is known about the efficacy of systemic AD therapy in blacks. It is estimated that blacks will represent 13.4% of the US population in the year 2020.⁶ It is therefore imperative to determine which treatments work best in them and other sociodemographic groups. The aims of this study were to identify US studies involving systemic AD therapy and assess for racial differences in treatment responses.

Methods | We searched PubMed, EMBASE, Cochrane Library, and GREAT databases from 1898 to 2014 for all studies involving “atopic dermatitis,” “atopic eczema,” “phototherapy,” “UV,” “cyclosporine,” “cyclosporin,” “ciclosporin,” “azathioprine,” “methotrexate,” and “mycophenolate.” Only US studies were chosen. We anticipated a small number of studies and therefore decided a priori to include all studies irrespective of study design. Exclusion criteria included studies with fewer than 5 patients with AD and those without efficacy data. The study was approved by the institutional review board at Northwestern University.

Results | A total of 18 studies in the United States concerning systemic AD therapy were identified, of which 9 were excluded (Figure). Of the 9 remaining, 3 were longitudinal prospective studies, and 6 were cross-sectional retrospective studies. The sample size of patients with AD ranged from 5 to 28. Overall, narrowband UV, low-dose UV-A and UV-B, cyclosporine, mycophenolate mofetil, and azathioprine all resulted in good clinical improvement and/or clearance (Table). Surprisingly, only 2 studies reported data on treatment responses in different races or ethnicities (Table). One study of cyclosporine showed that 1 black individual had poorer response than 5 white patients; however, her dose had been reduced owing to the adverse effect of hypertension. A retrospective study of treatment with azathioprine followed by mycophenolate

Figure. PRISMA Diagram of Study Inclusion



AD indicates atopic dermatitis; Ph, phototherapy; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; UV, UV light therapy.

mofetil reports that whites and nonwhites were equally likely to have switched from azathioprine to mycophenolate mofetil.

Discussion | The present study highlights a major deficiency in the reporting of RCT outcomes for AD. There is a dearth of studies demonstrating efficacy of systemic therapy in different racial and ethnic subsets of either children or adults with AD in the United States. Furthermore, the results of our review raise intriguing questions about the generalizability of the results of the extant literature. A fundamental principle of all study designs is to determine whether the study cohort, and by extension the results of the study, is representative of the population. It is difficult to make such conclusions, because most studies did not describe their cohorts in much detail.

Most US studies have been retrospective cross-sectional studies with small sample sizes (the largest had 28 patients), and none were RCTs. These and other weaknesses limit their utility in guiding clinical decision-making for treating recalcitrant AD in racial and ethnic minorities in the United States. In addition, systemic AD treatments have a multitude of potentially serious adverse effects, including increased risk of infection and malignant disease; renal, hepatic, and neurological toxic effects; hypertension; and anemia and other hematologic abnormalities. Currently, we are lacking crucial data to allow for accurately weighing the benefits of treatment against the risks of adverse effects. It is imperative that large-scale RCTs of systemic treatment for AD that include racial and ethnic diversity be conducted in the United States.

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Table. Studies of Systemic Atopic Dermatitis (AD) Therapy in the United States

Source ^a	Treatment	Dose and Frequency	Study Design	Patients With AD, No.	Race, Ethnicity, or Fitzpatrick Skin Type
Tay et al	UV-B	3×/wk	Prospective, longitudinal	5	Type 1, 1; type 3, 3; type 4, 1
Samson Yashar et al	NB-UV-B	NS	Retrospective, cross-sectional	7	NS
Tintle et al	NB-UV-B	3×/wk	Prospective, longitudinal	12	NS
Tuchinda et al	UV-1	Low-dose, 4×/wk	Retrospective, cross-sectional	6	Skin types NS for pts with AD
Frankel et al	Cyclosporine	Initial, 1.0-4.2 mg/kg/d, titrated up as needed	Retrospective, cross-sectional	6	White, 5; black, 1
Heller et al	Mycophenolate mofetil	Initial, 12-40 mg/kg/d, titrated up as needed	Retrospective, cross-sectional	14	NS
Murray et al	Mycophenolate mofetil	Initial, 1 g BID, adjusted according to response	Retrospective, cross-sectional	20	NS
Waxweiler et al	Azathioprine followed by mycophenolate mofetil	Azathioprine, 1 or 3 mg/kg/d; mycophenolate mofetil, 20-40 mg/kg/d	Retrospective, cross-sectional	Azathioprine, 28; mycophenolate mofetil, 12	White, 15; black, 11; Hispanic, 2
Caufield et al	Azathioprine	Initial, 1.0-2.5 mg/kg/d, titrated up as needed	Prospective, longitudinal	12	NS
Source	Duration	Overall Efficacy	Efficacy by Race, Ethnicity, or Skin Type	Adverse Effects	
Tay et al	Mean, 41 tx sessions over 15 wk	Improved, 100% (reduced extent and pruritus); clearance, 0%	NS	Erythema and burning after tx session	
Samson Yashar et al	Mean, 33 tx sessions	Improved, 78%; clearance, NS	NS	AE NS for pts with AD	
Tintle et al	12 wk, or sooner if clearance; mean, 23.5 tx sessions	Improved, 100% (≥50% decrease of SCORAD); clearance, NS	NS	AE NS for pts with AD	
Tuchinda et al	Variable, based on protocols of different medical centers	Improved, >75% (1), 51%-75% (2), 25%-50% (2), <25% (1); clearance, NS	NS	AE NS for pts with AD	
Frankel et al	39-206 wk (mean, 110 wk)	Improved, 100%; clearance, 83%; able to taper, 40%	White, 5 of 5 complete response; black, 1 of 1 partial response (taking a lower cyclosporine dose)	Hypertension, SCC, headache, gastroesophageal reflux, acute viral hepatitis, lymphadenopathy, cellulitis, elevated creatinine level, gastroenteritis, paresthesia, nausea, upper respiratory infection	
Heller et al	8-96 wk	Improved, 93% (>90%, 4; 60%-90%, 5); clearance, 29%	NS	GI tract upset, frequent skin infections (in 2 pts with extensive history of skin infections prior to mycophenolate mofetil)	
Murray et al	5-200 wk	Improved, 90%; clearance, 50%	NS	GI tract complaints, headache, fatigue, skin infections, herpes simplex, herpes zoster	
Waxweiler et al	Azathioprine, mean, 52 wk Mycophenolate mofetil, mean, 30.5 wk	Improved, azathioprine, 82%; mycophenolate mofetil, 67%; clearance, 0%	No difference between whites and nonwhites	Azathioprine: GI tract complaints, elevated liver enzymes, skin infections, low hemoglobin; mycophenolate mofetil: skin infections, low hemoglobin level	
Caufield et al	NS; shortest, 32 wk, tapering begins once stable improvement	Improved, 92%; clearance, 8%	NS	GI tract complaints, elevated liver enzyme level	

Abbreviations: AE, adverse effects; BID, twice daily; GI, gastrointestinal; NB-UV-B, narrowband UV-B; NS, not specified; pt, patient; SCORAD, score for AD; tx, treatment; UV-A1, UV-A; UV-B, UV-B.

^a See the eReferences in the Supplement for complete citations.

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Study concept and design: Both authors.

Acquisition, analysis, or interpretation of data: Both authors.

Drafting of the manuscript: Silverberg.

Critical revision of the manuscript for important intellectual content: Both authors.

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Study supervision: Silverberg.

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6. US Census Bureau. Table 6. Percent of the Projected Population by Race and Hispanic Origin for the United States: 2015 to 2060 (NP2012). 2012 National

Population Projections: Summary Tables. <http://www.census.gov/population/projections/data/national/2012/summarytables.html>. Accessed April 4, 2014.

Supplementary Online Content

Bhattacharya T, Silverberg JI. Efficacy of systemic treatments for atopic dermatitis in racial and ethnic minorities in the United States. *JAMA Dermatol*. Published online September 10, 2014. doi:10.1001/jamadermatol.2014.1674.

eReferences. eReferences for Table

This supplementary material has been provided by the authors to give readers additional information about their work.

eReferences for Table

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