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ACETYLTATION PHENOTYPE VARIATION IN PEDIATRIC PATIENTS WITH ATOPIC DERMATITIS

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Abstract

Background:

Few studies have been done on the relation between acetylator status and allergic diseases.

Aim:

To determine any possible association between acetylating phenotype in pediatric patients with atopic dermatitis (AD) and the disease prognosis.

Patients and Methods:

Thirty-six pediatric patients and forty two healthy children as a control group were participated in the study. All participants received a single oral dose of dapsone of 1.54 mg/kg body weight, after an overnight fast. Using high performance liquid chromatography (HPLC), plasma concentrations of dapsone and its metabolite (monoacetyldapsone) were estimated to phenotype the participants as slow and rapid acetylators according to their acetylation ratio (ratio of monoacetyldapsone to dapsone).

Results:

72.2% of pediatric patients with AD showed slow acetylating status as compared to 69.4% of control individuals. Also, 73% of AD patients with slow acetylating phenotype had familial history of allergy. The severity of AD occurred only in slow acetylator patients. The eczematous lesions in slow acetylators presented mainly in the limbs, while in rapid acetylators, they were found mostly in face and neck.

Conclusion:

This study shows an association between the *N*-acetylation phenotype variation and clinical aspects of AD.

Keywords: *Acetylation phenotype, atopic dermatitis, Hanifin-Rajka scoring system, monoacetyldapsone*

Introduction

Atopic dermatitis (AD) is a common multifactorial disease characterized by an itchy, recurrent, flexural and symmetrical eczematous eruption.[1] Its frequency increases during childhood but it usually resolves by the age of 30 years.[2] Acetylation is a metabolic pathway in a number of drugs[3], which exhibits a genetically controlled bimodal distribution within any given population which is phenotyped as slow or rapid acetylators.[4] Studies had been done to determine acetylation phenotype in Middle East population,[5–8] which showed slow acetylator predominance. Therefore, we examined AD in this population to find any possible association with the disease severity.

Patients and Methods

Thirty-six pediatric patients, 21 males and 15 females, aged from 8 to 11 years (mean 9.66 ± 0.9 SD) besides, 42 healthy children, 27 males and 15 females, aged from 7 to 11 years (mean 8.93 ± 1.1 SD) as a control group, participated in this prospective and open study. Approval to conduct this study, was granted by the appropriate ethical committee in Baghdad College of Medicine. The participants were recruited from the outpatient clinic of Department of Dermatology of Baghdad Teaching Hospital from October 2007 to December 2008. Clinical diagnosis was done. The nature of the trial was explained to the children's parents and their consent was obtained. Then, Hanifin-Rajka scoring system[9] applied to evaluate the disease severity.

After an overnight fast, each individual (patient and control) received a single oral dose of dapsone 1.54 mg/kg body weight.[10] A blood sample (5 ml) was taken in a test tube containing heparin, 3 hours after the drug intake. Plasma was separated within 1 hour of collection and then high performance liquid chromatography (HPLC) was used to estimate plasma concentrations of dapsone and its metabolite (monoacetyldapsone).[10] Individuals were considered slow acetylators if their acetylation ratio (ratio of monoacetyldapsone to dapsone) was less than 0.30 and rapid acetylators if their acetylation ratio was greater than 0.30. Statistical analyses were done using SPSS version. The results were considered statistically significant if the *P* value was <0.05 .

Results

Twenty-six of the 36 AD pediatric patients (72.2%) were slow acetylators compared with 29 of 42 control individuals (69.4%), and this was found to be a statistically non-significant result [Table 1]. In AD patients, a significant relationship appeared between familial history of allergy and slow acetylators who represented 73% (19 out of 26 slow acetylator patients) [Table 2]. Application of Hanifin-Rajka scoring system revealed that 30.5% (11 of 36 AD patients) were severe cases and all were slow acetylators [Table 3]. In the AD patients, eczematous lesions which presented in the limbs (elbows, knees, hands and feet) were found mostly in slow acetylators who represented 84.6% (22 out of 26 eczematous patients), whereas lesions that presented in the face and neck were found mainly in rapid acetylators who represented 60.0% (6 out of 10 rapid phenotypes). This showed a statistically significant difference [Table 4].

Discussion

This study demonstrated that there is a predominance of slow acetylators in AD patients as compared with the control group. The results are in accordance with those of studies that showed a predominance of AD patients carrying the allele for slow acetylation.[5–8]

However, our study succeeded to show a relation between acetylator status and different aspects of the disease course. A significant association was found between the severity of AD and slow acetylator status in which Hanifin-Rajka scoring system determined that a large number of slow acetylator AD patients had scores (≥ 50 points) which means severe cases, while no one is a rapid acetylator. This indicates that *N*-acetylation phenotype variation in human skin could account for variation in the disease severity. This result agreed with that of a study on acetylator phenotype among children with allergic contact dermatitis in which an association was found between the site of allergic lesions and acetylator status.[11]

Conclusion

In a population of slow acetylators, it appears that the slow acetylation phenotype can be considered as a genetic predisposing state for AD and is a clue for severity of the disease.

Footnotes

Source of Support: Nil

Conflict of Interest: Nil.

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Figures and Tables

Table 1

Frequency distribution of acetylation phenotype in AD patients and control

Acetylation phenotype	Patients (<i>n</i> = 36)	Control (<i>n</i> =42)	χ^2	<i>P</i> value
Slow acetylators				
No. (%)	26 (72.2)	29 (69.4)	2.74	0.062
Female/Male (n)	10/ 16	12/ 17		
Age (mean $\pm$ SD)	9.76 $\pm$ 0.81	9.44 $\pm$ 0.79		
Rapid acetylators				
No. (%)	10 (27.8)	13 (30.6)	2.19	0.084
Female/Male (n)	5/ 5	3/ 10		
Age (mean $\pm$ SD)	9.55 $\pm$ 0.98	9.82 $\pm$ 0.77		

Slow acetylators defined as those have acetylation ratio $\leq$ 30;

Rapid acetylators defined as those have acetylation ratio $>$ 30

Table 2

The acetylation phenotype and history of allergy in AD patients

Allergy	Slow acetylators (n = 26)	Rapid acetylators (n = 10)	Total (n = 36)
Personal history	2 (7.7%)	0 (00.0%)	2
Familial history	19 (73.0%)	3 (30.0%)	22
Personal & Familial	1 (3.9%)	3 (30.0%)	4
Non-allergic	4 (15.6%)	4 (40.0%)	8

Data are number and percentage of patients. $\chi^2 = 9.37$ and P value = 0.025

Table 3

The acetylation phenotype and Hanifin-Rajka scoring system in AD patients

Hanifin-Rajka scores	Slow acetylators (n = 26)	Rapid acetylators (n = 10)	Total (n = 36)
>50 points	11 (42.3%)	0 (00.0%)	11
<50 points	15 (57.7%)	10 (100.0%)	25

Data are number and percentage of patients. >50 points = severe cases. $\chi^2 = 9.52$ and P value = 0.016

Table 4

The acetylation phenotype and distribution of eczematous lesions in AD patients

Site of lesions	Slow acetylators (n = 26)	Rapid acetylators (n = 10)	Total (n = 36)
Elbows / Knees	11 (42.3%)	2 (20.0%)	13
Hands / Feet	8 (30.8%)	1 (10.0%)	9
Wrists / Ankles	3 (11.5%)	1 (10.0%)	4
Neck / Face	4 (15.4%)	6 (60.0%)	10

Data are number and percentage of patients. $\chi^2 = 9.28$ and P value = 0.029