



Indian J Dermatol. 2019 Mar-Apr; 64(2): 164.

PMCID: PMC6440188

doi: 10.4103/ijid.IJD_58_17: 10.4103/ijid.IJD_58_17

PMID: [30983621](#)

Acetylation Phenotype Variation in Patients with Allergic Contact Dermatitis

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Received 2017 Jan; Accepted 2018 Jul.

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Abstract

Background:

Studies have been done on acetylation phenotype in different diseases but not with allergic contact dermatitis (ACD).

Patients and Methods:

Thirty-five ACD patients and 67 healthy volunteers were enrolled in the study. After an overnight fast, each participant received a single oral dose of 100 mg of dapsone. Three hours later, a blood sample was taken from each participant and plasma was separated to determine dapsone and its metabolite (monoacetyldapsone) using high-performance liquid chromatography.

Results:

Nearly 60% of the patients (21 out of 35 ACD patients) were slow acetylators compared with 72% (48 out of 67 controls), and a statistically significant difference was found. No association between the acetylator status and personal/family history of allergy, patch test positivity, and even the sites of ACD was detected. In the ACD patients with slow acetylators, the lesions of dermatitis presented mainly on the face, neck, and upper limbs, while those with rapid acetylator have predominant lesions in the chest, oral region, and axillae.

Conclusion:

A rapid acetylator status might predispose to ACD without influencing other features of this disease.

KEY WORDS: *Acetylation phenotype, allergens, allergic contact dermatitis, patch test*

Introduction

Contact dermatitis is an inflammatory process of the skin caused mainly by external agents. Its allergic type (allergic contact dermatitis [ACD]) is a cell-mediated hypersensitivity which affects a limited number of people after one or few exposures to an antigenic substance.[1] Acetylation is a major metabolic pathway in the biotransformation of many drugs, which exhibits a genetically controlled bimodal distribution within any given population who are either slow or rapid acetylators.[2] Slow acetylation is inherited in an autosomal recessive fashion which is linked to variations in drug response, adverse reactions, and an increased incidence of certain cancers.[3]

Studies had been done on the relationship between acetylator status and diseases. One revealed a predominance of rapid acetylation in contact dermatitis.[4] This study examined the acetylator phenotype status in Iraqi ACD patients because the Iraqi population, as other middle-Eastern populations, is characterized by a predominance of slow acetylators.[5] Therefore, it is interesting to examine ACD in a predominantly slow acetylator population. In addition, any possible association of the acetylator status on different aspects of ACD was also examined.

Patients and Methods

Thirty-five adult patients of ACD (13 males + 22 females), aged 17–43 years (mean±standard deviation [SD], 27.4±0.9), were recruited from the outpatient clinic of the Department of Dermatology of Al-Kadhimiya Teaching Hospital from May 2015 to October 2016. Clinical diagnosis was made by a dermatologist. A total of 67 healthy adults (40 females + 27 males) participated as a control group in this study. Their ages ranged from 18 to 46 years (mean±SD, 28.3±2.9). Individuals with no history of serious illness and who were normal on physical examination were included in the study. Exclusion criteria were as follows: (a) individuals with glucose-6-phosphate dehydrogenase deficiency, (b) allergy to sulfonamides or dapsone, and (c) individuals on medication within 1 week before the study. Approval to conduct this study was granted by the ethics committee of Al-Nahrain College of Medicine (Reg No. HEC/16/2015/CMANU). The nature of the trial was explained to each participant and consent was obtained. All suspected ACD patients were tested for allergens by patch test using the closed method technique. If the suspected allergen was a cosmetic, medicine, or a fume from liquid, a small amount was poured onto a piece of cotton placed in the bottom of a small glass cup. The cup was then inverted and fastened onto the skin of the upper outer surface of the forearm or the skin of antecubital fossa and covered with an adhesive bandage.[6] If the suspected allergen was a solid such as shoe leather, wood, or rubber, a portion was cleaned and extracted with alcohol 70% over a period of 15 min,[7] and then was applied to the skin in the same manner. The bandage was removed after 48 h to see the reaction. The criteria of the International Contact Dermatitis Research Group were used to categorize the reaction as a doubtful reaction, weak reaction (nonvesicular), strong reaction (edematous or vesicular), extreme reaction (markedly bullous or ulcerative), irritant reaction, and negative reaction.

After an overnight fast, each individual (patients and controls) received a single oral dose of dapsone (AL-NILE Company for Pharmaceutical Industries, Cairo, Egypt) as 1.54 mg/kg body weight.[8] After 3 h from the drug ingestion, 5 ml of the blood sample was taken and put in a heparinized test tube. Within 1 h, plasma was separated and then high-performance liquid chromatography was used to estimate plasma concentrations of dapsone and its metabolite (monoacetyldapsone).[8] Individuals were considered slow acetylators if their acetylation ratio (ratio of monoacetyldapsone to dapsone) was ≤ 0.30 and rapid acetylators if their acetylation ratio was > 0.30 . Statistical analyses were done using SPSS (version 13) (IBM Corp., Armonk, New York., The USA). The results were considered statistically significant if $P < 0.05$. [9]

Results

Nearly 40% of the patients (14 out of 35 ACD patients) were rapid acetylators compared with 28% of controls (19 out of 67 controls), and this was found to be a statistically significant difference [Table 1]. Concerning personal or familial history of allergy, no statistically significant differences were found between slow and rapid acetylators with ACD. Only 26 out of 35 ACD patients returned after 48 h for follow-up of patch test result and no statistically significant differences in patch test results between slow and rapid acetylators were found [Table 2]. The ACD lesions presented mainly in the limbs despite few

occurrences on the mouth and axillae. ACD patients with slow acetylation showed lesions in the upper part of the body (face, neck, and upper limbs) as three times as rapid acetylators, while ACD patients with rapid acetylation showed lesions predominantly in the chest, oral region, and axillae. However, still, the differences were not statistically significant.

Discussion

A predominance of rapid acetylation in ACD was demonstrated in our study as compared with a control group. This result was in agreement with two other studies, which showed a predominance of ACD patients carrying the allele for rapid acetylation.[3,4] Our results showed that rapid acetylation was more common among ACD patients despite the predominance of slow acetylation in the Iraqi population. However, it failed to show an association between acetylator status and different aspects of allergic disease. Besides, no association between acetylator status and positive patch test results was found, although it was reported that variations in N-acetylation in human skin could account for variations in positivity in patch test.[6] Thus, although a rapid acetylator status may predispose to ACD, it does not appear to affect patch test results. In children with atopic dermatitis, an association was found between acetylator status and the severity/the site of the atopic dermatitis lesions.[10,11] Another study showed an association between acetylation status and Behcet's disease, in which the patients had a predominantly slow acetylator phenotype.[5] On the other hand, in other studies, no such association was found between acetylation status and systemic lupus erythematosus.[12]

Conclusion

It appeared that the rapid acetylators could be considered a genetic trait predisposing to ACD. Our study failed to conclude on other aspects of the association which might be due to small number of study subjects.

Financial support and sponsorship Nil.

Conflicts of interest There are no conflicts of interest.

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Figures and Tables

Table 1

Acetylation phenotype in allergic contact dermatitis patients and controls

Demographic characters	Patients (<i>n</i> =35)	Controls (<i>n</i> =67)	<i>P</i>
Slow acetylators			
<i>n</i> (%)	21 (60.0)	48 (72)	0.009
Female/male	13/8	31/17	
Age (mean±SD)	26.8±1.18	28.7±3.9	
Rapid acetylators			
<i>n</i> (%)	14 (40.0)	19 (28)	0.003
Female/male (<i>n</i>)	9/5	9/10	
Age (mean±SD)	28.2±0.61	27.1±2.3	

SD: Standard deviation

Table 2

Acetylation phenotype and patch test in 26 allergic contact dermatitis patients

Patch test	Slow acetylators, <i>n</i> (%)	Rapid acetylators, <i>n</i> (%)	Total patch tests, <i>n</i>
Positive	12 (85.7)	11 (91.7)	23
Negative	2 (14.3)	1 (08.3)	3
Total	14 (100.0)	12 (100.0)	26

P=0.338

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