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The *CYP17A1* rs743572 Gene Polymorphism and Risk of Development and Clinical Features of Acne Vulgaris in the Uzbek Population

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Abstract

The purpose of this study was to analyze the association between the *CYP17A1* rs743572 SNP and the development and clinical course of acne vulgaris (AV) in the Uzbek population.

The study included 165 AV patients aged from 18 to 30 years (Group AV). All patients were divided into 3 subgroups in accordance with the severity of the disease. SAV1 included 59(35.8%) patients with a mild degree of AV, SAV2 included 64(38.8%) patients with a moderate degree of AV, and SAV3 included 42(25.4%) patients with a severe degree of AV. The control group (CG) consisted of 97 healthy volunteers without a burdened dermatological history. The study revealed a significant association of the *CYP17A1* rs743572 SNP with the risk of AV development in the Uzbek population. The study results showed that the presence of the A2 allele and A2/A2 genotype of the *CYP17A1* rs743572 SNP might be a risk factor for AV in Uzbek ethnicity. It is obvious that the A1/A1 genotype of the *CYP17A1* rs743572 SNP can have a protective effect not only in the formation of AV, but also in the severity of the disease. The functionally unfavorable A1/A2 genotype of the *CYP17A1* rs743572 SNP is more characteristic of patients with a moderate degree of AV, and the homozygote minor allele genotype A2/A2 is more characteristic of patients with a severe degree of AV.(**International Journal of Biomedicine. 2019;9(2):125-127.**)

Key Words: acne vulgaris • single nucleotide polymorphism • *CYP17A1* gene • rs743572

Abbreviations

SNP, single nucleotide polymorphism; **RMI**, recessive model of inheritance; **DMI**, dominant model of inheritance; **GMI**, general model of inheritance

Introduction

Acne vulgaris (AV) is a polymorphic, multifactorial, chronic relapsing inflammatory disease of the sebaceous glands and hair follicles. Epidemiological studies have shown that the prevalence of acne among adolescents and young people reaches of 80%-90%. However, the disease can occur in infants and older adults.[1,2] AV has a multifactorial pathogenesis, of which the key factors are genetic predisposition and hormonal abnormalities (androgens play the key role).[3]

Cytochrome P450 family 17 (CYP17) is one of the key enzymes for the steroidogenic pathway.[4-6] CYP17 is encoded by the *CYP17A1* gene, which is located on the long arm of chromosome 10q24.32.[7] The enzyme mediates steroid 17α-hydrolase and 17, 20-lyase activity in the endoplasmic reticulum.[8] SNP (rs743572) (a common single base pair substitution [−34 T→C]) in the 5'-untranslated region of the *CYP17A1* gene is widely studied, but the functional impact of the T/C change is presently, to our knowledge, not known. The common T allele is referred as A1

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and the variant C allele as A2. The minor allele A2, compared to A1, is postulated to correlate with higher serum levels of various sex steroids in some studies.[9,10]

The purpose of this study was to analyze the association between the *CYP17A1* rs743572 SNP and the development and clinical course of AV in the Uzbek population.

Materials and Methods

The study included 165 AV patients aged from 18 to 30 years (Group AV). All patients were divided into 3 subgroups in accordance with the severity of the disease. SAV1 included 59(35.8%) patients with a mild degree of AV, SAV2 included 64(38.8%) patients with a moderate degree of AV, and SAV3 included 42(25.4%) patients with a severe degree of AV. The control group (CG) consisted of 97 healthy volunteers without a burdened dermatological history. The groups were comparable in sex and age. We used the standard method for analysis of case-control data.

Genomic DNA was isolated from the peripheral blood leukocytes using a modified phenol–chloroform extraction method.[11] PCR was performed in Rotor Gene 6000 (Corbett Research, Australia) using Sintol reagent kits (Russia) according to the manufacturer's instructions (Table 1, Fig. 1).

Table 1.

Polymerase chain reaction amplification conditions

Step	Temperature	Time	Detection	Repeats
Hold	94	3 min	No acquiring	1
Cycling 1	94	20 sec	No acquiring	10
	58	20 sec	No acquiring	
	61	30 sec	No acquiring	
Cycling 2	94	20 sec	No acquiring	30
	58	20 sec	No acquiring	
	61	30 sec	Acquiring on Green, Yellow	

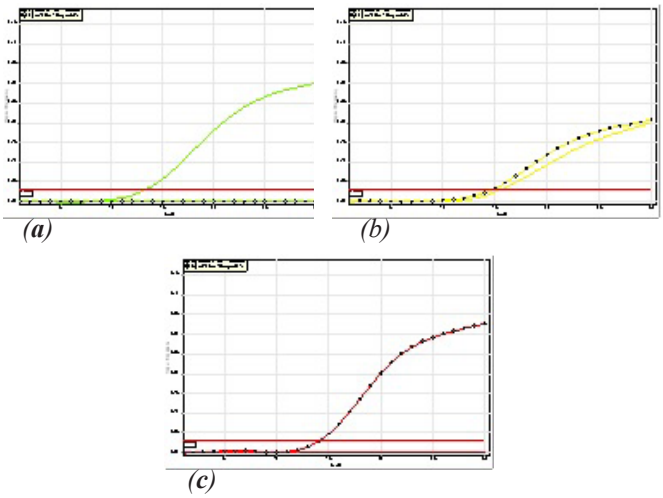

Fig. 1. *The results of real-time PCR for the CYP17A1 rs743572 SNP (a)-homozygous wild-type; (b)-heterozygous mutant; (c)-homozygous mutant.*

Statistical data processing was performed using OpenEpi 2009, Version 2.3. Deviation from Hardy-Weinberg equilibrium and differences in allele distributions between the two groups were assessed by χ2- test with 1 degree of freedom (df). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Chi-square test was used to assess the categorical variables. A probability value of $P<0.05$ was considered statistically significant.

The study was approved by our Institutional Ethics Committee. Written informed consent was obtained from each patient.

Results and Discussion

The frequency of genotypes and alleles of the *CYP17A1* rs743572 SNP in the studied groups is presented in Table 2. The distribution of the genotype frequency was in HWE for both groups ($P>0.05$). In Groups AV and CG, the frequencies of the A1 and A2 alleles were as follows: 56.7% and 43.3% versus 80.4% and 19.6%, respectively. We further used the 3 types of genetic models to test the association between the *CYP17A1* rs743572 SNP and AV. We found a significant prevalence of the carriage of the minor A2 allele in Group AV, compared to CG ($\chi^2=30.5$; $P<0.05$; OR=3.14; 95% CI: 2.07–4.76). The frequency distribution of the A1/A1, A1/A2 and A2/A2 genotypes in Groups AV and CG were as follows: 33.9%, 45.5% and 20.6% versus 67.0%, 26.8% and 6.2%, respectively. We found a significant prevalence of the carriage of the heterozygous genotype A1/A2 and homozygote minor allele genotype A2A2 in Group AV, compared to CG ($\chi^2=26.55$; $P<0.05$; OR=2.28; 95% CI: 1.35–3.92; and OR=3.94; 95% CI: 1.59–9.76). The frequency of the wild A1/A1 genotype in Group AV was significantly lower than in CG, which may indicate a protective effect of this genotype for the development of AV (OR=0.25; 95% CI: 0.15–0.43).

Table 2.

The frequency of genotypes and alleles of the CYP17A1 rs743572 SNP in the studied groups

Group	Allele				Genotype					
	A1		A2		A1/A1		A1/A2		A2/A2	
	n	%	n	%	n	%	n	%	n	%
Group AV	187	56.7	143	43.3	56	33.9	75	45.5	34	20.6
SAV3	18	21.4	66	78.6	2	4.8	14	33.3	26	61.9
SAV2	70	54.7	58	45.3	13	20.3	44	68.7	7	10.9
SAV1	99	83.9	19	16.1	41	69.5	17	28.8	1	1.7
CG	156	80.4	38	19.6	65	67.0	26	26.8	6	6.2

In SAV3, the minor A2 allele was found approximately 5 times more often than in CG ($\chi^2=87.1$; $P<0.05$; OR=15.05; 95% CI: 8.014–28.27). In contrast, the frequency of the A1/A1 genotype was significantly lower than in CG ($\chi^2=45.5$; $P<0.05$; OR=0.02; 95% CI: 0.01–0.11). The carriage of the

A2/A2 genotype was associated with an increased risk of a severe degree of AV in RMI (χ^2=51.3; P<0.05; OR=24.6; 95% CI: 8.76–69.35). The frequency of the heterozygous A1/A2 genotype was not significantly different than in CG.

In SAV2, the minor A2 allele was also significantly more frequent than in CG (χ^2=24.4; P<0.05; OR=3.4; 95% C: I2.07–5.39). The carriage of the A1/A2 genotype was also associated with an increased risk of a moderate degree of AV in GMI (χ^2=34.04; P<0.05; OR=6.01; 95% CI: 3.00–12.02). There were no differences in the frequency distribution of the homozygous A2/A2 genotype between the patient sample and CG, and significant risk was not found in RMI (χ^2=1.17; P=0.28; OR=1.86; 95 % CI: 0.60–5.82).

In SAV1, no significant differences were found in the frequency of the alleles and genotypes of the *CYP17A*1 rs743572 SNP, compared to CG.

The distribution of alleles and genotypes of the *CYP17A1* rs743572 SNP differed significantly depending on the severity of the clinical course of AV. It was found that the minor A2 allele was significantly more frequent in SAV3 than in SAV2 and SAV1 (χ^2=75.721; P=0). It was also noted that the minor A2 allele was significantly more frequent in SAV2 than in SAV1 (45.3% versus 16.1%, respectively; χ^2=24.363; P=0.000). A similar pattern with a more pronounced statistical significance was found in a comparative analysis of the distribution of the homozygous A2/A2 genotype. The A2/A2 genotype was significantly more frequent in SAV3 than in SAV2 and SAV1 (χ^2=60.341, P=0.000). The A2/A2 genotype was also significantly more frequent in SAV2 than in SAV1 (χ^2=4.313; P=0.038). The heterozygous A1/A2 genotype was significantly more frequent in SAV2 than in SAV3 and SAV1 (χ^2=23.087; P=0.0000). Differences in the frequency of the A1/A1 genotype were also significant between SAV1 and SAV2 (χ^2=30.148; P=0.0000), as well as between SAV1 and SAV3 (χ^2=42.047; P=0.0000). It is obvious that the A1/A1 genotype of the *CYP17A1* rs743572 SNP can have a protective effect not only in the formation of AV, but also in the severity of the disease.

Thus, the functionally unfavorable A1/A2 genotype of the *CYP17A1* rs743572 SNP is more characteristic of patients with a moderate degree of AV, and the homozygote minor allele genotype A2/A2 is more characteristic of patients with a severe degree of AV.

The role of the *CYP17A1* rs743572 SNP in the formation and development of acne is not completely clear. Thus, in the Chinese and Iranian populations, there was higher acne risk related to CYP17 (T-34C),[12,13] but in the Polish and Indonesian populations this risk was not found.[14,15] Our study revealed a significant association of the *CYP17A1* rs743572 SNP with the risk of AV development in the Uzbek population. The results of our study showed that the presence of the A2 allele and A2/A2 genotype of the *CYP17A1* rs743572 SNP might be a risk factor for AV in Uzbek ethnicity. Obviously, populations and ethnic groups differ in the frequency of distribution of polymorphic variants of the *CYP17A1* rs743572 SNP and their contribution to the development of various nosologies associated with an imbalance of sex hormones. Further studies need to obtain a more accurate result.

Competing Interests

The authors declare that they have no competing interests.

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