Advances in Medical Sciences 63 (2018) 147–151

Contents lists available at ScienceDirect

Advances in Medical Sciences

journal homepage: www.elsevier.com/locate/advms

Original Research Article

PPARγ Pro12Ala and C161T polymorphisms in patients with acne vulgaris: Contribution to lipid and lipoprotein profile

Shohreh Saeidi[a,1], Foroogh Chamaie-Nejad[a,1], Ali Ebrahimi[b,1], Fariba Najafi[b], Ziba Rahimi[a], Asad Vaisi-Raygani[c], Ebrahim Shakiba[c,**], Zohreh Rahimi[a,c,*]

[a] Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran
[b] Department of Dermatology, Kermanshah University of Medical Sciences, Kermanshah, Iran
[c] Department of Clinical Biochemistry, Medical School, Kermanshah University of Medical Sciences, Kermanshah, Iran

ARTICLE INFO

Article history:
Received 29 June 2017
Accepted 26 September 2017
Available online xxx

Keywords:
Acne vulgaris
PPARγ Pro12Ala
PPARγ C161T
Polymorphism
Lipid
Lipoprotein

ABSTRACT

Purpose: The aim of present study was to clarify the role of peroxisome proliferator-activated receptor γ (PPARγ) Pro12Ala and C161T variants in the pathogenesis of acne vulgaris (AV) and their influence on lipid and lipoprotein profile.
Methods: The present case-control study consisted of 393 individuals including 198 patients with AV (mild-, moderate-, and severe-AV) and 195 unrelated age-matched healthy individuals from Western Iran. The PPARγ Pro12Ala and C161T polymorphisms were identified using polymerase chain reaction-restriction length polymorphism method. Also, serum lipid and lipoprotein profile and fasting blood sugar (FBS) were detected in studied individuals.
Results: In women patients with AV significantly higher serum levels of FBS, total cholesterol, low density lipoprotein-cholesterol (LDL-C) and high density lipoprotein-cholesterol compared to healthy women were detected. Neither PPARγ Pro12Ala nor C161T polymorphism was associated with the risk of AV but the Pro allele was a risk factor for AV among all men and women patients ≥20 years. The variant genotype of PPARγ CG (Pro/Ala) was associated with significantly higher levels of total cholesterol and triglycerides compared to CC (Pro/Pro) genotype. We detected a significantly lower level of FBS in the presence of CT + TT genotype of PPARγ C161T compared to CC genotype. Also, carriers of PPARγ TT genotype had significantly lower serum level of total cholesterol and LDL-C compared to CC genotype.
Conclusions: Our results demonstrated the association of PPARγ Pro allele with susceptibility to AV in patients ≥20 years and the influence of PPARγ Pro12Ala and C161T polymorphisms on the lipid and lipoprotein profile.

1. Introduction

Acne vulgaris (AV) is a chronic inflammatory disease of pilosebaceous unit hair follicles in the skin that are associated with an oil gland. The clinical features of AV are seborrhea (excess grease), inflammation, abnormal follicular keratinization and various degrees of scarring [1].

The peroxisome proliferator-activated receptors (PPARs) belong to the family of nuclear hormone receptors that act as transcriptional regulators of a variety of genes including genes involved in lipid metabolism in adipose tissue, liver and skin. The main receptors involved in sebocyte biology are isoforms of PPARα and PPARγ [2]. Activation of PPARγ involves in glucose homeostasis and adipogenesis in subcutaneous fat and also regulation of lipid metabolism in adipocytes [3].

The gene of PPARγ is located at chromosomal region 3p25 [4]. The common single nucleotide polymorphism of cytosine to guanine in exon 2 of PPARγ results in a proline to alanine substitution at codon 12 (Pro12AlaC/G, rs1801282). The polymorphism modulates the transcriptional activity of the gene. The presence of Pro12Ala polymorphism is associated with reduced transcriptional activity of PPARγ [2]. In one available study the Pro12Ala polymorphism had a protective role against AV development [2].

The polymorphism of PPARγ C161T (rs3856806, His447His) at exon 6 results in a silent substitution of histidine residue [5] .There

* Corresponding author at: Department of Clinical Biochemistry, Medical Biology Research Center, Medical School, Daneshgah Avenue, Kermanshah, Iran P.O.Box: 67148-69914, Iran.
** Corresponding author at: Department of Clinical Biochemistry, Medical School, Daneshgah Avenue, Kermanshah, PO Box: 67148 69914, Iran.
E-mail addresses: m.shakiba_d91@yahoo.com (E. Shakiba), rahimizus@yahoo.com, zrahimi@kums.ac.ir (Z. Rahimi).
[1] These authors had equal role in preparing the manuscript.

https://doi.org/10.1016/j.advms.2017.09.003
1896-1126/

is no available study related to the role of this polymorphism in susceptibility to AV.

The aims of present study were to investigate the association of PPARγ Pro12Ala and C161T variants with AV and with lipid and lipoprotein profile in a population from Western Iran with Kurdish ethnic background.

2. Patients and methods

2.1. Sample

We studied 198 patients with AV (13–43 years, mean age 22.1 ± 4.7 years) consisted of 169 females and 29 males and 195 unrelated age-matched healthy individuals including 143 females and 52 males (13–33 years, mean age 22.6 ± 4.2 years, p = 0.33) without systemic and dermatologic disorders. Adult onset acne (onset ≥25 years of age) was detected in 55 patients. Among patients there were 57 patients with the age onset of AV ≤19 years old and 141 individuals with the age onset of AV ≥20 years old. Exclusion criteria for selecting patients were the presence of pregnancy or breast feeding, receiving anti-inflammatory, anti androgens, anabolic androgens, and oral contraceptive pills and the presence of systemic and autoimmune diseases. All subjects were examined by dermatologist. Patients with AV consisted of 89 individuals with mild AV, 53 subjects with moderate AV and 56 persons with severe AV. Mild AV was detected in the presence of comedones without significant inflammation and a few or the absence of papules, moderate AV was determined in the presence of comedones and significant inflammatory papules and pustules and severe AV was detected in the presence of comedones, papules and pustules and inflammatory nodules [6]. Healthy individuals were medical and paramedical students of the Kermanshah University of Medical sciences. All studied patients and healthy individuals were from the Kermanshah province in Western Iran with ethnic background of Kurds.

Written informed consent was obtained from all studied individuals. The study was approved by the Ethics Committee of Kermanshah University of Medical Sciences and was in accordance with the principles of the Declaration of Helsinki II.

2.2. Biochemical analysis

The serum levels of fasting blood sugar (FBS), triglycerides (TG), cholesterol, low density lipoprotein-cholesterol (LDL-C) and high density lipoprotein-cholesterol (HDL-C) were measured using the Bionic Diagnostic Kits (Iran) by the Mindrey BS-480 chemistry analyzer.

2.3. Genotyping

DNA was extracted from venous blood obtained from each individuals using standard procedure of phenol–chloroform [7].

The PPARγ Pro12Ala (C/G) gene variants were detected by polymerase-chain reaction (PCR) – restriction fragment length polymorphism (RFLP) using the forward primer of 5′-GCCAATT-CAAGCCCAGTC-3′ and the reverse primer of 5′-GATATGTTTGCA-GACAGTGTATCAGTGAAGGAATCGCTTTCCG-3′. The 270-bp PCR product was digested with BstU I restriction enzyme. In the presence of C allele (wild type) the 270-bp fragment remains intact while C to G substitution at nucleotide 34 results in creating a BstU I restriction site and the PCR product digests to two fragments of 227-bp and 43-bp [8].

The polymorphism of PPARγ C161T was studied by PCR-RFLP using the forward primer of 5′ −CAA GAC AAC CTG CTA CAA GC −3′ and the reverse primer of 5′ −TCC TTG TAG ATC TCC TGC AG −3′. In carriers of the wild type allele the 200-bp fragment of PCR-product is digested to two fragments of 120-bp and 80-bp by the restriction enzyme of Pml1 but in carriers of mutant allele only one fragment with 200-bp is produced [9].

2.4. Statistical analysis

The allelic frequencies were calculated by the chromosome counting method. The frequency of genotypes and alleles of PPARγ Pro12Ala and PPARγ C161T in patients were compared to controls using chi-square test. Odds ratios (OR) were calculated as estimates of relative risk for disease and 95% confidence intervals (CIs) obtained by SPSS logistic regression. The correlation values of biochemical data with the studied polymorphisms between groups were calculated using independent-sample *t*-test and ANOVA analysis. Statistical significance was assumed at the p value of <0.05. The statistical package for social sciences (SPSS) logistic regression (SPSS, Inc., Chicago, IL) version 16.0 was used for the statistical analysis.

3. Results

Demographic and biochemical characteristics of patients and controls according to the gender have been compared in Tables 1 and 2. As indicated in Tables 1 and 2 both groups were age- and body mass index (BMI)-matched (p > 0.05). A significantly higher concentration of FBS was detected in women patients (80.3 ± 10.3 mg/dl, p = 0.02) compared to women in control group (76.4 ± 17.7 mg/dl). Also, comparing women indicated significantly higher levels of serum cholesterol (134.8 ± 32 mg/dl, p = 0.004), HDL-C (50.3 ± 13.1 mg/dl, p < 0.001) and LDL-C (78.2 ± 26.7 mg/dl, p = 0.004) in patients compared to those in controls (124.3 ± 28.1, 41.8 ± 9.8 and 69.8 ± 21 mg/dl, respectively) (Table 1). However, among men only serum cholesterol concentration was significantly higher in controls (140.2 ± 31.6 mg/dl, p = 0.039) than patients (125.9 ± 24.6 mg/dl) (Table 2).

Distribution of PPARγ Pro12Ala genotypes was in Hardy-Weinberg equilibrium in patients ($\chi^2 = 1.98$, p > 0.1). Also,

Table 1
Characteristics of women in studied groups

Variables	Patients with AV (n = 169)	Controls (n = 143)	P value
Age (years)	22.1 ± 4.7	22.6 ± 4.2	0.33
BMI (Kg/m^2)	23.3 ± 6.7	22.6 ± 4	0.28
Systolic blood pressure (mmHg)	99.5 ± 12.6	99.4 ± 13.3	0.94
Diastolic blood pressure (mmHg)	70.9 ± 9.5	72.8 ± 10.6	0.11
FBS (mg/dl)	80.3 ± 10.3	76.4 ± 17.7	0.02
Cholesterol (mg/dl)	134.8 ± 32	124.3 ± 28.1	0.004
TG (mg/dl)	82.1 ± 50.4	79.6 ± 38.8	0.63
HDL-C (mg/dl)	50.3 ± 13.1	41.8 ± 9.8	<0.001
LDL-C (mg/dl)	78.2 ± 26.7	69.8 ± 21	0.004

AV: acne vulgaris; FBS: fasting blood sugar; TG: triglycerides; HDL-C: high density lipoprotein-cholesterol; LDL-C: low density lipoprotein-cholesterol.

Table 2
Characteristics of men in studied groups.

Variables	Patients with AV (n = 29)	Controls (n = 52)	P value
Age (years)	21.3 ± 4.9	22.3 ± 4.4	0.36
BMI (Kg/m^2)	23 ± 3.3	22.3 ± 3.1	0.34
Systolic blood pressure (mmHg)	109.7 ± 13	108.9 ± 13.1	p = 0.79
Diastolic blood pressure (mmHg)	75.2 ± 12.4	76 ± 16.1	p = 0.82
FBS (mg/dl)	88.3 ± 8.8	85.4 ± 8.5	p = 0.14
Cholesterol (mg/dl)	125.9 ± 24.6	140.2 ± 31.6	p = 0.039
TG (mg/dl)	93.6 ± 56.8	104 ± 44.6	p = 0.36
HDL-C (mg/dl)	44.7 ± 9.2	42 ± 12	p = 0.30
LDL-C (mg/dl)	71.8 ± 22.07	77.9 ± 25.2	p = 0.27

distribution of PPARγ C161T genotypes was in Hardy-Weinberg equilibrium in patients ($\chi^2 = 0.67$, $p > 0.1$).

The frequencies of PPARγ Pro12Ala genotypes and alleles in all patients, patients with mild-, moderate- and severe- AV and controls are demonstrated in Table 3. The genotype of PPARγ GG was not detected among patients and controls. The frequency of CG genotype was 18.2% in all patients compared to 24.6% in controls (p = 0.12). The frequencies of G allele were 9.1% and 12.3% in all patients and controls, respectively (p = 0.14) (Table 3). Considering men and women separately indicated the frequency of CG in 27.6% of patients men and 38.5% of controls men (p = 0.32). In women the frequency of CG genotype was 16.7% in patients compared to 19.6% in controls (p = 0.5). Analysis of all patients with the age of disease onset ≥20 years indicated a higher frequency of CC (Pro/Pro) genotype (83.7%) in patients compared to a frequency of 73.7% in controls that was associated with 1.81-fold risk of AV (p = 0.047) (Table 3). However, considering adult onset AV revealed a nonsignificant increased frequency of CC genotype in patients (78.2%) compared to controls (73.8%, p = 0.57).

The frequency of PPARγ T allele in all patients was 18.4% that was not significantly different compared to controls (19%, p = 0.84) (Table 4). Among men the T allele was found in 22.4% patients and 21.1% controls (p = 0.82). In patients women the frequency of T allele was 17.8% compared to 18.2% in controls women (p = 0.74).

In Table 5 biochemical parameters have been compared between various genotypes of PPARγ in all studied individuals. Significantly higher serum levels of TG and cholesterol were detected in the presence of PPARγ CG genotype (106.1 ± 56.8 mg/dl, and 138.7 ± 32.8 mg/dl, respectively) compared to CC genotype (79.4 ± 42.1 mg/dl, $p < 0.001$ and 129.1 ± 29.5 mg/dl, p = 0.019, respectively)(Table 5). In the presence of CC genotype of PPARγ C161T there were significantly higher levels of FBS (81.3 ± 14.8 mg/dl, p = 0.043) compared to CT + TT genotype (78.5 ± 11 mg/dl). Also, significantly higher serum concentrations of total cholesterol (132.3 ± 30.5 mg/dl, p = 0.015) and LDL-C (76.1 ± 24.2 mg/dl, p = 0.024) in the presence of CC compared to TT genotype (99.9 ± 31.4, and 51.6 ± 21.4 mg/dl, respectively) were detected.

Table 3
Comparison of the frequency of PPARγ Pro12Ala (C/G) genotypes and alleles between patients with AV and controls.

Parameters	All patients n = 198 n (%)	Mild AV n = 89 n (%)	Moderate AV n = 53 n (%)	Severe AV n = 56 n (%)	Controls n = 195 n (%)
Genotypes					
CC	162 (81.8)	75 (84.3)	41 (77.4)	46 (82.1)	147 (75.4)
CG	36 (18.2)	14 (15.7)	12 (22.6)	10 (19.1)	48 (24.6)
	$\chi^2 = 2.42$, p = 0.12	$\chi^2 = 2.82$, p = 0.09	$\chi^2 = 0.089$, p = 0.76	$\chi^2 = 1.1$, p = 0.29	
	All patients ≥ 20 years old (n = 141)	patients ≥ 20 years old, mild AV (n = 62)	patients ≥ 20 years old, moderate AV (n = 44)	patients ≥ 20 years old, severe AV (n = 35)	Controls ≥ 20 years old (n = 148)
CC	118 (83.7)	52 (83.9)	35 (79.5)	29 (82.9)	109 (73.7)
CG	23 (16.3)	10 (16.1)	9 (20.5)	6 (17.1)	39 (26.3)
	$\chi^2 = 3.97$, p = 0.045 OR = 1.81 (95%CI 1–3.3, p = 0.047)	$\chi^2 = 2.94$, p = 0.087	$\chi^2 = 0.86$, p = 0.35	$\chi^2 = 1.75$, p = 0.18	
Alleles					
C	360 (90.9)	164 (92.1)	94 (88.7)	102 (91.1)	342 (87.7)
G	36 (9.1)	14 (7.9)	12 (11.3)	10 (8.9)	48 (12.3)
	$\chi^2 = 2.13$, p = 0.14	$\chi^2 = 2.48$, p = 0.11	$\chi^2 = 0.076$, p = 0.78	$\chi^2 = 0.97$, p = 0.32	

OR: odds ratio; CI: confidence interval

Table 4
Comparison of the frequency of PPARγ C161T genotypes and alleles between patients with AV and controls.

Parameters	All Patients n = 198 n (%)	Mild AV n = 89 n (%)	Moderate AV n = 53 n (%)	Severe AV n = 56 n (%)	Controls n = 195 n (%)
Genotypes					
CC	130 (65.7)	61 (68.5)	34 (64.2)	35 (62.5)	123 (63.1)
CT	63 (31.8)	26 (29.3)	17 (32.1)	20 (35.7)	70 (35.9)
TT	5 (2.5)	2 (2.2)	<2 (3.7)	1 (1.8)	2 (1)
	$\chi^2 = 1.82$, p = 0.40	$\chi^2 = 1.73$, p = 0.42	$\chi^2 = 2.13$, p = 0.34	$\chi^2 = 0.21$, p = 0.89	
Alleles					
C	323 (81.6)	148 (83.1)	85 (80.2)	90 (80.4)	316 (81)
T	73 (18.4)	30 (16.9)	21 (19.8)	22 (19.6)	74 (19)
	$\chi^2 = 0.038$, p = 0.84	$\chi^2 = 0.36$, p = 0.54	$\chi^2 = 0.038$, p = 0.84	$\chi^2 = 0.025$, p = 0.87	

Table 5
Comparison of biochemical parameters according to PPARγ Pro12Ala (C/G) genotypes in all studied individuals and controls, separately.

Variables	All studied individuals (n = 373)		Controls (n = 183)		Patients (n = 190)	
	CC (n = 292)	CG (n = 81)	CC (n = 137)	CG (n = 46)	CC (n = 155)	CG (n = 35)
FBS (mg/dl)	79.9 ± 14.1 p = 0.32	81.4 ± 11.3	78.1 ± 17.7 p = 0.09	81.5 ± 9.7	81.6 ± 9.8 p = 0.9	81.3 ± 13.3
Cholesterol (mg/dl)	129.1 ± 29.5 p = 0.019	138.7 ± 32.8	123.3 ± 27.3 P < 0.001	145.3 ± 31.5	134.2 ± 30.6 p = 0.49	130 ± 32.9
TG (mg/dl)	79.4 ± 42.1 p < 0.001	106.1 ± 56.8	75.3 ± 32 p < 0.001	119.9 ± 49.8	82.9 ± 49.2 p = 0.65	87.9 ± 60.9
HDL-C (mg/dl)	45.9 ± 12.5 p = 0.59	45.1 ± 11.3	41.3 ± 10.2 p = 0.024	43.5 ± 11.05	49.9 ± 12.9 p = 0.23	47.3 ± 11.4
LDL-C (mg/dl)	73.9 ± 23.8 p = 0.23	77.8 ± 26.8	68.8 ± 19.9 p = 0.003	81.9 ± 26.8	78.3 ± 26 p = 0.23	72.4 ± 26.4

4. Discussion

Present study detected alteration in glucose and lipid metabolism among women patients with AV leading to significantly higher serum levels of FBS, total cholesterol, LDL-C and HDL-C in patients compared to healthy individuals.

In our study neither PPARγ Pro12Ala nor PPARγ C161T were associated with the risk of AV in our population. Lower number of men compared to women in our study could be due to higher percent of women with adult acne and higher number of women with AV who refer to dermatologist for beauty treatment of face than men. However, gender-specific differences in the frequencies of both studied polymorphisms were not detected. But the wild genotype of CC (Pro/Pro) was detected to be a risk factor for AV considering patients ≥20 years. Similarly, in one available study among Egyptian patients with AV (15–39 years old) the Ala allele of PPARγ Pro12Ala was reported to be a protective factor against AV development or may attenuate the AV severity [2].

Both PPARγ Pro12Ala and PPARγ C161T polymorphisms are associated with decreased transcriptional activity of the PPARγ gene. The missense PPARγ Pro12Ala polymorphism leads to decreasing transcription of several target genes [9]. The various frequency of the Ala allele has been reported among ethnic populations with a low frequency among Africans and Asians (1–3%) and a high frequency in white populations (20%). Also, homozygosity for the Ala allele is rare among populations [2]. Different frequency of the polymorphism among various populations and life style may affect the association of polymorphism with the risk of AV. PPARγ C161T polymorphism, a synonymous mutation that is an exon splicing enhancer site without amino acid exchange (His/His), was reported to be associated with decreased risk of coronary artery diseases [9].

PPARγ is a critical transcription factor involved in the gene regulation of glucose and lipid metabolism [10]. The natural ligands of PPARs are lipid-derived substrates such as unsaturated fatty acids, eicosanoids, oxidized LDL and VLDL and linoleic acid derivatives. Fibrates and thiazolidinediones are pharmacological agonists of PPARs [11]. In adult patients with diabetes and hyperlipidemia the PPARγ agonists increased sebum production. Since, PPARγ antagonists might decrease sebaceous lipid synthesis they could be useful in the treatment of acne [12].

In the present study PPARγ CG (Pro/Ala) genotype was associated with significantly higher serum levels of total cholesterol and TG compared to CC (Pro/Pro) genotype.

Yang et al. [13] found that the Pro12Ala polymorphism in the PPARγ gene was positively associated with increased fasting TG and waist to hip ratio among Chinese women with polycystic ovary syndrome. It has been reported that the Ala12 allele of PPARγ gene has been positively associated with an enlarged area of small dense low-density lipoprotein particles in a general population [14]. Among Chinese Han population the minor allele of PPARγ Pro12Ala polymorphism was associated with significantly higher LDL-C level [15]. A meta-analysis consisted of 54,953 subjects revealed that in Asian population carriers of Pro/Pro (CC) genotype of Pro12Ala group had significantly lower levels of total cholesterol, LDL-C and higher levels of triglyceride compared to the combined CG + GG genotype group [16]. However, in a Finnish cohort of patients with familial combined hyperlipidaemia the Ala12 allele was associated with a lower body mass index, lower TG and increased HDL-C levels [17].

We found a significantly lower level of FBS in the presence of CT + TT genotype of PPARγ C161T polymorphism compared to CC genotype. Also, carriers of TT genotype had significantly lower total cholesterol and LDL-C compared to CC genotype.

Among Han Chinese population with large-artery atherosclerosis (LAA) ischemic stroke PPARγ CT/TT was associated with lower levels of blood total cholesterol and LDL-C but TG and HDL-C levels were comparable [18]. Also, in Chinese population the T allele of C161T polymorphism through modulating the lipid metabolism and reducing the risk of hyperlipidemia decreased the risk of severe atherogenesis [10]. A meta-analysis by Li et al. in Asian population indicated no statistically significant differences in the levels of TC, TG, high-density lipoprotein cholesterol, LDL-C comparing different genotypes in C161T polymorphism [16]. However, among Chinese Han population the minor allele of C161T polymorphisms was associated with significantly higher LDL-C level [15]. Controversial reports related to the association of PPARγ polymorphisms with lipid and lipoprotein profile could be attributed to differences in the frequency of the polymorphisms among various populations, different lifestyle, effects of environmental factors and also the influence of sample size.

The role of few gene polymorphisms in susceptibility to AV and its severity has been studied [19]. Most of these studies have focused on innate immunity-related genes and genes involved in the steroid hormone metabolism. Some polymorphisms such as minor allele A of the tumor necrosis factor (TNF) −308 G > A was associated with acne and the severity of inflammatory symptoms in women from Central European population. Also, the minor T allele of interleukin (IL)-1α +4845 G > T was associated with the severity of AV symptoms. Among Chinese population the cytochrome P450, family 17 (CYP17) −4T > C was associated with severe AV in male patients [19]. Since, the role of only a handful of genes in the pathogenesis of AV have been studied, it needs to more genetic association studies among various populations to clarify the role of gene variants in the susceptibility and severity of AV symptoms.

Briefly, our study demonstrated significantly higher serum levels of FBS, lipid and lipoproteins in patients with AV compared to healthy individuals. Although, both polymorphisms of PPARγ Pro12Ala and C161T were not associated with susceptibility to acne

vulgaris but the Pro allele was a risk factor for AV among patients ≥ 20 years and the Pro/Ala genotype increased serum cholesterol and TG concentration compared to Pro/Pro genotype. Also, the minor allele of 161T had a benefit effect in lowering FBS, cholesterol and LDL-C.

Conflict of interest disclosures

The authors disclose no conflicts of interest.

Acknowledgments

This work was performed in partial fulfillment of the requirements for MSc degree of Miss Shohreh Saeidi and was financially supported by a grant from Vice Chancellor for Research of Kermanshah University of Medical Sciences, Kermanshah, Iran.

References

[1] Williams HC, Dellavalle RP, Garner S. Acne vulgaris. Lancet 2012;379 (9813):361–72.
[2] Amr K, Abdel-Hameed M, Sayed K, Nour-Edin F, Abdel Hay R. The Pro12Ala polymorphism of the gene for peroxisome proliferator activated receptor-gamma is associated with a lower Global Acne Grading System score in patients with acne vulgaris. Clin Exp Dermatol 2014;39(6):741–5.
[3] Chandra M, Miriyala S, Panchatcharam M. PPARγ and its role in cardiovascular diseases. PPAR Res 20176404638.
[4] Korhonen S, Heinonen S, Hiltunen M, Helisalmi S, Hippeläinen M, Koivunen R, et al. Polymorphism in the peroxisome proliferator-activated receptor-g gene in women with polycystic ovary syndrome. Hum Reprod 2003;18(3): 540–3.
[5] Kuriki K, Hirose K, Matsuo K, Wakai K, Ito H, Kanemitsu Y, et al. Meat, milk, saturated fatty acids, the Pro12Ala and C161T polymorphisms of the PPARgamma gene and colorectal cancer risk in Japanese. Cancer Sci 2006; 97(11):1226–35.
[6] Yang Z, Yu H, Cheng B, Tang W, Dong Y, Xiao C, et al. Relationship between the CAG repeat polymorphism in the androgen receptor gene and acne in the Han ethnic group. Dermatology 2009;218(4):302–6.
[7] Rahimi Z, Merat A, Gerard N, Krishnamoorthy R, Nagel RL. Implications of the genetic epidemiology of globin haplotypes linked to the sickle cell gene in southern Iran. Hum Biol 2006;78(6):719–31.
[8] Hahn S, Fingerhut A, Khomtsiv U, Khomtsiv L, Tan S, Quadbeck B, et al. The peroxisome proliferator activated receptor gamma Pro12Ala polymorphism is associated with a lower hirsutism score and increased insulin sensitivity in women with polycystic ovary syndrome. Clin Endocrinol (Oxf) 2005;62 (5):573–9.
[9] Krasznai M, Szaniszlo K, Kraxner H, Vargha E, Kovacs M, Kaszas E, et al. Association of PPAR polymorphisms with cytokine levels in allergic rhinitis. Eur Arch Otorhinolaryngol 2012;269(2):513–21.
[10] Wan J, Xiong S, Chao S, Xiao J, Ma Y, Wang J, et al. PPAR gamma gene C161T substitution alters lipid profile in Chinese patients with coronary artery disease and type 2 diabetes mellitus. Cardiovasc Diabetol 2010;9:13.
[11] Gupta M, Mahajan VK, Mehta KS, Chauhan PS, Rawat R. Peroxisome proliferator-activated receptors (PPARs) and PPAR agonists: the 'future' in dermatology therapeutics? Arch Dermatol Res 2015;307(9):767–80.
[12] Zouboulis CC, Picardo M, Ju Q, Kurokawa I, Törőcsik D, Bíró T, et al. Beyond acne: Current aspects of sebaceous gland biology and function. Rev Endocr Metab Disord 2016;17(3):319–34.
[13] Yang J, Gong H, Liu W, Tao T. The association of Pro12Ala polymorphism in the peroxisome proliferator-activated receptor-gamma2 gene with the metabolic characteristics in Chinese women with polycystic ovary syndrome. Int J Clin Exp Pathol 2013;6(9):1894–902.
[14] Hamada T, Kotani K, Tsuzaki K, Sano Y, Murata T, Tabata M, et al. Association of Pro12Ala polymorphism in the peroxisome proliferator-activated receptor gamma2 gene with small dense low-density lipoprotein in the general population. Metabolism 2007;56(10):1345–9.
[15] Fan W, Shen C, Wu M, Zhou ZY, Guo ZR. Association and interaction of PPARα, δ, and γ gene polymorphisms with low-density lipoprotein-cholesterol in a Chinese Han population. Genet Test Mol Biomarkers 2015;19(7):379–86.
[16] Li Q, Chen R, Bie L, Zhao D, Huang C, Hong J. Association of the variants in the PPARG gene and serum lipid levels: a meta-analysis of 74 studies. J Cell Mol Med 2015;19(1):198–209.
[17] Pihlajamäki J, Miettinen R, Valve R, Karjalainen L, Mykkänen L, Kuusisto J, et al. The Pro12A1a substitution in the peroxisome proliferator activated receptor gamma 2 is associated with an insulin-sensitive phenotype in families with familial combined hyperlipidemia and in nondiabetic elderly subjects with dyslipidemia. Atherosclerosis 2000;151(2):567–74.
[18] Wei WM, Wu XY, Li ST, Shen Q. PPARG gene C161T CT/TT associated with lower blood lipid levels and ischemic stroke from large-artery atherosclerosis in a Han population in Guangdong. Neurol Res 2016;38(7):620–4.
[19] Szabó K, Kemény L. Studying the genetic predisposing factors in the pathogenesis of acne vulgaris. Hum Immunol 2011;72(9):766–73.