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Research Article

Relationship Research of PPAR-γ Gene Polymorphisms with Adiponectin and Leptin in Type 2 Diabetes Mellitus

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Abstract: ***Objective:*** To investigate the peroxisome proliferator-activated receptor-γ (peroxisome) in patients with type 2 diabetes mellitus. Proliferators-activated receptors-γ, PPARs-γ (γ) gene polymorphisms about serum lipofuscin and leptin. ***Methods:*** One hundred and twenty patients with type 2 diabetes admitted to our hospital from June 2015 to June 2018 were selected. The patients were divided into an obese group and a non-obese group of 60 patients each according to their waist circumference. A polymerase chain reaction-length polymorphism protocol was implemented in all patients to explore the PPAR-γ gene polymorphism, and blood glucose, lipid, adiponectin and leptin levels were measured in both groups. ***Results:*** PPAR-γ gene polymorphisms in type 2 diabetic patients were dominated by wild-type homozygous; The levels of total cholesterol, triglyceride and LDL cholesterol in the obese group were significantly higher than those in the non-obese group, while the levels of HDL cholesterol were lower than those in the non-obese group. There is significant difference in comparison between groups (P<0.05) Those carrying the A allele had a significant lipid disorder profile and decreased adiponectin levels. ***Conclusions:*** PPAR-γ gene polymorphisms in type 2 diabetes are not significantly associated with adiponectin and leptin, and only in the obese group, the patients with the Allele A showed significant dyslipidemia and a declining trend of adiponectin levels.

Keywords: Type 2 diabetes; Peroxisome proliferator-activated receptor; Gene polymorphism; Adiponectin; Leptin

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Peroxisome proliferators-activated receptors-γ (PPARs-γ) are closely related to adipocyte formation, and regulation of adipocyte gene expression and insulin sensitivity. The human PPAR gene is located on chromosome 3p25, and the 12th coded neutron of exon 2 is most likely to be mutated, allowing proline converted to alanine, which is the Prol2Ala polymorphism. It is located in an insulin-dependent activation region of PPARγ and can alter protein conformation, leading to a decrease in its activity [1, 2]. Some scholars found that the use of lipoplex or leptin alone could only partially improve insulin resistance, and only combination therapy can completely reverse adipose atrophic insulin resistance caused by PPAR-deficiency[3]. To this end, this article discusses the relationship between PPAR-γ gene polymorphisms and lipoplex and leptin in type 2 diabetes mellitus as follows.

1 Information and methodology

1.1 General information

The experimental study was conducted on 120 patients with type 2 diabetes from June 2015 to June 2018, and all the patients were divided into an obese

group and a non-obese group with 60 cases of each group according to their waist circumference (>90 cm for men and >80 cm for women). In the obese group, there were 32 males and 28 females, aged between 48 and 75 years, with a mean value of (61.32±1.54) years old and a disease course of 2-25 years, with a mean value of (12.46 ± 1.58) years; in the observation group, there were 30 cases of each sex, patient age and length of disease are 49-73 years and 1-27 years respectively, with a mean value of (61.45±1.48) years old and (12.56±1.64) years respectively. Inclusion criteria: (1) Patients were diagnosed with type 2 diabetes mellitus by laboratory tests[4]; (2) Patients were at least 40 years old; (3) Patients gave informed consent for this study and actively participated. Exclusion criteria: (1) Patients with substantial organ dysfunction of the heart, brain, liver and kidneys; (2) Patients with concomitant other types of thyroid disease; (3) Patients with type 1 diabetes. There was no difference in baseline data between the groups (P>0.05), and comparisons could be made.

1.2 Methods

2mL of venous blood was drawn from all patients after 2 hours of fasting, and genomic DNA was extracted and stored at -20 ℃. Determination of PPAR-γ Prol2Ala gene using polymerase chain reaction-restriction fragment length polymorphism method Polymorphism. Polymerase chain reaction conditions: initial denaturation at 95 ℃ for 5 minutes, denaturation at 94 ℃ for 35s, anneal to 62 ℃ for 30 seconds, then gradually lower the temperature to 57 °C and raise it to 72 °C for 40s. with a total of 10 cycles; denatured 94 °C for 30s, cooled to 57 °C for 20s, increased to 72 ℃ for 45 seconds, with a total of 22 cycles; the final extension was 72 ℃ for 5 minutes. The above reactions were performed on a thermocycler using 12% non-denaturing polyacrylamide gel electrophoresis to separate the enzymatic products and stained with bromine ingots. The genotypes were observed by placing them under violet light, etc.

1.3 Observational indicators

1.3.1 Comparison of the frequency of PPAR-γ gene Prol2Ala variation between the two groups

A comparison of genotype frequencies between diabetics in the obese and non-obese groups was performed.

1.3.2 Association of Prol-2Ala genotype with blood glucose, lipids and insulin in two groups of patients.

Comparison of different fractions of fasting blood glucose (glucose oxidase method), fasting insulin (radioimmunoassay), total cholesterol (total cholesterol kit), triglycerides (triglyceride assay kit), high-density lipoprotein cholesterol (precipitant precipitation), and low-density lipoprotein cholesterol levels (density gradient ultracentrifugation method) in the two groups.

1.3.3 PPAR-γ gene polymorphism about adiponectin and leptin

PPAR-γ polymorphisms, adiponectin and leptin levels were compared in obese diabetic patients and non-obese diabetic patients.

1.4 Statistical methods

Study data statistically processed by SPSS 22.0 software, the unclassified data (genotype frequencies) was tested by percentage (%). The nominal variable information (blood glucose, lipid, insulin, lipid-linked and leptin levels) were tested by $\bar{x} \pm s$. And P-value less than 0.05 suggests a discrepancy in the data.

2 Results

2.1 Results of comparison of the frequency of Prol-2Ala mutations in the PPAR-γ gene in two groups of diabetic patients

Both the obese and non-obese diabetic groups had wild-type homozygous as the predominant genotype, and the comparison between the two groups was not statistically significant. The differences (P>0.05) are shown in Table 1 below.

Table 1. Comparison of PPAR-γProl-2Ala mutation frequency results between diabetic patients in obese and non-obese groups

Groups	Instances	Genotype Frequency		
		Wild-type homozygous	Hybrid (Zoology)	Mutant Homozygote
Obesity group	60	54(90.00)	5(8.33)	1(1.67)
Non-obesity group	60	52(86.67)	8(13.33)	0(0.00)
χ^2			0.323	
P			0.569	

2.2 Association of Pool-2Ala genotype with blood glucose, lipids and insulin in two groups of patients

Levels of triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol in wild-type homozygous genes in the obese group of diabetic patients lower than patients with non-wild-type homozygous genes, with a statistically significant difference in data comparison (P<0.05), and the levels of triglycerides and LDL cholesterol were higher in the obese group than those in the non-obese group of heterozygous gene patients, and HDL cholesterol levels were lower than those in the non-obese group of heterozygous gene patients, and there was a statistical difference in data comparison (P<0.05). Details of the study are given in Table 2 below.

Table 2. Prol-2Ala genotype association with blood glucose, lipids and insulin in both groups ($\bar{x} \pm s$, mmol/L)

Groups	Typing	Instances	Fasting blood sugar	Fasting insulin	Total cholesterol	Triglyceride	HDL cholesterol	Low-density lipoprotein cholesterol
Obesity group	Wild-type homozygous	54	9.78±0.74	0.90±0.12	5.32±1.21	2.14±0.56	1.21±0.18	2.62±0.45
	Non-wild-type homozygous	6	9.92±0.65	0.92±0.15	5.52±1.07	2.72±0.48	0.92±0.09	3.81±0.72
t_1			0.444	0.378	0.388	2.435	3.871	5.769
P_1			0.329	0.353	0.350	0.009	0.000	0.000
Non-obesity group	Wild-type homozygous	52	9.82±0.45	0.88±0.27	4.81±1.12	1.76±0.24	1.24±0.21	3.36±0.52
	Non-wild-type homozygous	8	10.02±0.26	0.90±0.25	4.32±1.24	1.82±0.35	1.32±0.25	3.21±0.44
t_1			1.220	0.197	0.137	0.618	0.979	0.773
P_1			0.114	0.422	0.130	0.270	0.166	0.221
t_2			0.399	0.173	1.896	4.072	3.711	1.937
P_2			0.348	0.433	0.041	0.001	0.001	0.038

Note: t1 is a comparison between groups, t2 is a comparison between two groups of non-wild-type pure haplotypes

2.3 Relationship of PPAR-γ gene polymorphisms to adiponectin and leptin

There was no statistical difference in the comparison of serum lipoplex and leptin levels between the obese and non-obese groups of diabetic patients with different genotypes (P>0.05), as detailed in Table 3 below.

Table 3. Relationship of PPAR-γ gene polymorphisms to adiponectin and leptin ($\bar{x} \pm s$)

Groups		Instance	Adiponectin(mg/L)	Leptin(μg/L)
Obesity group	Wild type homozygous	54	6.02±1.54	12.01±2.54
	Non-wild type homozygous	6	5.17±1.28	12.27±2.76
	t		1.300	0.236
	P		0.099	0.407
Non-obesity group	Wild type homozygous	52	7.82±1.96	10.82±2.14
	Non-wild type homozygous	8	6.94±1.42	11.26±2.32
	t		1.218	0.536
	P		0.114	0.297

3 Discussions

Type 2 diabetes is the primary type of endocrine system pathology, caused by a combination of genetic and environmental factors, with a significant glycolipid metabolism characteristics of the disorder[5]. The improvement in the standard of living and lifestyle changes have led to a substantial increase in the prevalence of type 2 diabetes, and it is essential to explore the pathogenesis of the disorder

to improve the prognosis of patients with glucose and lipid disorders, clinicians need to focus on the following topics One.

Gene polymorphisms, also known as genetic polymorphisms, refer to the presence of more than one allele at the locus with a frequency greater than 0.01. It uses genetic mutations as the mechanism of formation and is usually evaluated by gene frequency, genotype frequency and phenotype frequency[6]. PPAR is a type of ligand-activated receptor that regulates and controls cellular metabolism, and PPARγ is one of the subtypes of it. It is an essential cellular differentiation transcript factor, expressed to varying degrees in mammalian adipose tissue, vascular smooth muscle tissue, and cardiac muscle tissue[7]. Some scholars thought that elevated levels of free fatty acids can lead to decreased insulin sensitivity and affect the uptake of glucose to muscle, which helps to remove lipids and fatty acids from adipose tissue, reduces the absorption of free fatty acids in muscle tissue, and plays an important role in improving insulin resistance[8]. Adiponectin is an endogenous substance secreted by adipocytes that predicts the progression of type 2 diabetes and coronary artery disease and can resist the development of type 2 diabetes and has the potential to fight diabetes and atherosclerosis[9]. It is the most abundant adipokine in the peripheral blood, with levels of 5-30 μg/mL in healthy individuals, and after binding the receptor, it plays an anti-diabetic role by activating PPAR.

PPAR-γ gene Prol2Ala mutation can lead to decreased free fatty acid uptake in adipocytes and increased liver Very low-density lipoprotein (VLDL) levels. In the case of obese patients, the visceral fat content is higher than in the subcutaneous tissue, the volume count is relatively higher, and the body contains more PPAR- Heterogeneous adipose mass is more abundant and has a distinct Prol2Ala gene. Patients with obese type 2 diabetes carrying the A allele are more likely to have affected lipid levels. Compared with the P allele, the A allele of PPAR-γ and the PPAR reactive element of the controlled gene had lower affinity, affecting protein expression in lipid storage and metabolism. Those carrying the AA genotype have a relative lack of PPAR-γ transcriptional activity, decreased LDL activity, the presence of triglyceride-rich Impaired clearance of lipoproteins increases the degree of disorders of lipid metabolism[10]. Leptin, also secreted by adipose tissue, is a protein hormone that is involved in blood circulation and regulates sugar, fat, and energy metabolism, promoting energy release and having a significant inhibitory effect on adipocyte synthesis, which in turn reduces body weight[11]. An experiment that studied patients with type 2 diabetes[12] showed a positive correlation between serum leptin concentration and fasting insulin levels. Leptin concentrations can be increased by infusion of a moderate amount of insulin because leptin binds to the insulin beta-cell receptor, which affects insulin secretion—stimulating effect. Serum leptin concentrations are lower in insulin-sensitive individuals with the same body mass index than in insulin-resistant individuals, thus indicating that insulin resistance is associated with leptin level effects. The results of the study in the paper show that obese type 2 diabetic patients carrying the A allele have severe lipid disorders and their lipoprotein Levels decreased and leptin levels increased but were not significantly associated with the latter two.

Overall, obesity type 2 diabetes accompanied by the PPAR-γ gene Prol2Ala polymorphism that affects energy metabolism Patients can suffer more significant damage to cardiovascular, hepatic and renal organs on top of increased lipid disorders. Therefore, obese patients with type 2 diabetes should control their weight as early as possible, and timely prevention and intervention from a genetic point of view to improve their quality of life and improved prognosis.

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