Research Article

The Correlation Between ApoE Genetic Polymorphism and Serum Lipid Levels

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Abstract

Objective: To explore the correlation between apolipoprotein E genetic polymorphism and serum lipid levels.

Methods: The genechips method was adopted to detect the ApoE genotype in people undergoing physical examination.The serum lipid levels were compared among the populations with different ApoE genotypes.

Results: The ApoE gene showed the polymorphic distribution in populations,in which the distribution frequency of E3 allele was highest,the population containing E2 allele had higher triglyceride level in serum, the population containing E4 allele had higher total cholesterol level in serum.

Conclusion: The ApoE gene presents the polymorphic distribution in populations. The E2 allele is correlated with serum high triglyceride level. The E4 allele correlated with serum high total cholesterol level.

1. Introduction

Apolipoprotein E (ApoE) was the major apolipoprotein in the serum.ApoE played the crucial role in the lipid metabolism,which was the key part of very low-density lipoprotein (VLDL), high-density lipoprotein(HDL) and chylomicrons [1-3]. The recent study showed that triacylglycerol (TAG) hydrolysis mediated by lipoprotein lipase in VLDL. The surface material containing phospholipids, free cholesterol and ApoE and ApoCs (CII and CIII) were also evolved in the process [2]. The released components were received by HDL, so the new HDL-sized ApoE-

containing molecule are also induced. Decreased HDL particles or abnormalities in their structure is correlated to unfavorable changes in the features of VLDL remnants [3].

ApoE encoding gene was located in the 19th chromosome, including 4 exons and 3 introns. The exon includes 3 alleles, named E2, E3 and E4, which generated 6 phenotype (E2/E2, E3/E3, E4/E4, E2/E3, E2/E4, E3/E4). Its genetic polymorphism is an important genetic factor affecting lipid metabolism. The studies showed approximately 14-17% variation of plasma cholesterol concentration can be associated with genetic polymorphism [4-7]. Echeverria et al reported the impact of 13 polymorphisms of nine genes affecting lipid metabolism [8].

At present, more and more studies on the relationship between ApoE gene polymorphism and lipid metabolism were reported. The purpose of the research was to provide valuable data about diagnosis and treatment of abnormal lipid metabolism and disease in Chongqing.

2. Methods

2.1 Research population

A total of 327 people (172 male and 155 female) was recruited from January to September of 2017 in The First Affiliated Hospital of Chongqing Medical University. All the patients were negative for hypertension, the disease from liver, kidney and internal secretion. This study was approved by the Institutional Review Board (IRB) committee of The First Affiliated Hospital of Chongqing Medical University. Written consent given by the patients was waived by the approving IRB. Anticoagulation with EDTA was applied in vitro to detect ApoE gene polymorphism .The serum was applied to detect serum lipid.

2.2 Blood lipid detection methods

Total cholesterol (TC) and triglyceride (TG) were measured with enzymatic assay (Roche Company). High-density lipoprotein cholesterol (HDLC) and low-density lipoprotein cholesterol (LDLC) were using direct method (Roche Company). ApoA1, ApoB, ApoE, and Lp(a) were tested using immunoturbidimetry (provided by WAKO Co., Ltd, Japan).

2.3 ApoE gene polymorphism analysis

The nucleic acid was extracted from anticoagulation blood and PCR amplification. Once combined with a hybridization buffer (Sinochips Corporation), the products were placed in a BioMixer chip hybridization instrument (Sinochips Corporation) for hybridization. Then products were put in a slidewasher 8 chip dry cleaning instrument (Sinochips) for washing and drying. Finally, the chip was placed in chip identification system for scanning and interpretation (Sinochips Corporation).

2.4 Statistical analysis

The number of groups between the use of t-test or analysis of variance, composition than with the Chi-square test, correlation analysis using Spearman rank correlation analysis.

3. Results

3.1 ApoE genotype and allele distribution rate

In the recruited people, the E3 allele of ApoE gene has the highest distribution rate, so the rate of E3/E3 genotype was the highest (Table 1). Compared to the male, the distribution rate of ApoE allele and genotype of female was no statistically different (P>0.05).

Sex	**n**	**ApoE genotype**						**ApoE allele**		
		E2/E2	E3/E3	E4/E4	E2/E3	E2/E4	E3/E4	E2	E3	E4
Male	172	3(1.7)	119(69.2)	2(1.2)	23(13.4)	6(3.5)	19(11.0)	32(14.5)	161(73.2)	27(12.3)
Female	155	3(1.9)	102(65.8)	3(1.9)	30(19.4)	5(3.2)	12(7.7)	38(18.8)	144(71.3)	20(9.9)

Table 1: ApoE genotype and the allele distribution rate

3.2 ApoE gene polymorphism and serum lipid levels

In order to study the pure effects of alleles E2 and E4 on blood lipids, E2/E4 type was removed and divided into three groups according to different genotypes: E2/E2+E2/E3, E3/E3, and E3/E4+E4/E4. The Table 2 showed that the levels of TC, TG and LDLC in ApoE genotype E3/E4 + E4/E4 were significantly higher in hemodialysis group (P<0.05).

Gene type	n	TC (mM)	TG (mM)	HDL-C (mM)	LDL-C (mM)	ApoA1 (g/L)	ApoB (g/L)	ApoE (mg/L)	Lp(a) (mg/L)
E2/E3+E2/E2	59	3.41±0.57	1.31±0.59	1.09±0.11	1.87±0.65	1.12±0.14	0.85±0.31	35±11	335±159
E3/E3	221	3.87±0.52	1.59±0.49	1.01±0.17	2.08±0.65	1.08±0.21	0.95±0.21	37±10	205±143
E4/E4+E3/E4	36	4.21±0.61	2.01±0.74	1.25±0.63	2.31±0.71	1.37±0.29	0.91±0.22	45±6	266±4
P		0.046*	0.008*	0.052	0.024*	0.095	0.647	0.017*	0.086

*P<0.05

Table 2: The blood fat level in the people with different ApoE genotype (X±S)

4. Discussion

Lipoid and neutral fat were included in blood fat. The most ingredient of blood fat was TG and cholesterol. Abnormal blood lipid refers to the abnormal serum lipid metabolism, included the increased TC, TG, LDL-C and HDL-C.

The ApoE gene contained 3 major alleles, which consisted of 6 genotypes.The previous study reported that the frequency of E3 alleles was the highest. E3/E3 genotype was the most common type in the population. There were significant regional and racial differences in gene polymorphism.The frequency of E3 alleles was 80% in Chinese population, which was similar to the Japanese, but the frequency of European was less than 80% [9]. The frequency of genotypes was depended on the racial and regional differences[10]. ApoE has played an important role in the

transport, storage, utilization and excretion of lipids. The affinity between the ApoE2 and LDL receptor was low, so the VLDL residue in ApoE2 was eliminated slowly. Then the LDL receptor was up-regulation, which induced the LDL-C level decreased and hypocholesterolemia. Otherwise, the VLDL residue in ApoE4 was eliminated quickly to decrease LDL receptor, which induced LDL-C increased and hypercholesterolemia [11]. Therefore, most studies demonstrated E2 allele was beneficial mutations and E4 allele was adverse mutation. The mutations of the ApoE allele was induced by the adjustment of the diet [12]. The study demonstrated that E2 could decrease the TC level,but E4 was correlated to higher TC level to induce hyperlipidemia [13].

In conclusion, our study demonstrated ApoE gene polymorphism was related to the level of serum lipid level. The genotype induced the abnormal index of serum lipid level. ApoE gene polymorphism was also related to the diseases like coronary heart disease, hyperlipidemia, cerebral infarction. We should reinforce early detection, rapid diagnosis, and standardize therapy, in order to reduce the risk of the diseases related to abnormal lipid metabolism.

5. Acknowledgements

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6. Conflict of interest

The authors declare no conflicts of interest.

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