

Short reports

Apolipoprotein E alleles in women with severe pre-eclampsia

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Table 1 Frequency of apoE alleles

Allele	Healthy non-pregnant women (n = 101)	Healthy pregnant women (n = 52)	Women with pre-eclampsia (n = 54)
Apo ε2	26 (12.9%)*	11 (10.6%)*	18 (16.6%)*
Apo ε3	159 (78.7%)	80 (76.9%)	82 (75.9%)
Apo ε4	17 (8.4%)	13 (12.5%)	8 (7.4%)

*p < 0.001 McNemar χ^2 test.

Table 2 Frequency of apoE genotypes

Genotype	Healthy non-pregnant women (n = 101)	Healthy pregnant women (n = 52)	Women with pre-eclampsia (n = 54)
ε2/2	4 (4%)	2 (3.8%)	1 (1.9%)
ε2/3	17 (16.8%)	6 (11.5%)*	16 (29.6%)*
ε3/3	63 (62.4%)	31 (59.6%)	29 (53.7%)
ε3/4	16 (15.8%)	12 (23.1%)	8 (14.8%)
ε2/4	1 (1.0%)	1 (1.9%)	0 (0%)
ε4/4	0	0	0

*p < 0.0397 Fisher's test (healthy pregnant v pre-eclampsia).

Abstract

This study investigated the frequency of apolipoprotein E (apoE) alleles among women with severe pre-eclampsia. The presence of the three most common apoE alleles (ε2, ε3, ε4) was determined by polymerase chain reaction-restriction fragment length polymorphism in three groups of white women: non-pregnant healthy (n = 101), pregnant healthy (n = 52), and pregnant with a diagnosis of severe pre-eclampsia (n = 54). The frequency of apo ε2 was highest among women with severe pre-eclampsia (16.6%) followed by non-pregnant women (12.9%), and those experiencing a healthy pregnancy (10.6%). The higher frequency of the apo ε2 allele detected among women with severe pre-eclampsia suggests that apoE may play a role in the development of pre-eclampsia.

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Keywords: apolipoprotein E; pre-eclampsia; gene polymorphism

Apolipoprotein E (apoE) plays an important role in lipid metabolism, and women with pre-eclampsia have raised lipid concentrations. Therefore, we investigated the possible role of apoE in pre-eclampsia by determining the frequency of apoE alleles and genotypes using polymerase chain reaction (PCR) combined

with restriction fragment length polymorphism (RFLP) analysis.

Patients and methods

Participants (207 white women) were drawn from an urban university department and assigned to one of three study groups depending on health status. The three groups included a healthy non-pregnant reference group (n = 101, blood donors) ranging in age from 18 to 62 years (mean, 37); a healthy pregnant 20-41 weeks' gestation (mean, 35.5) control group (n = 52) ranging in age from 17 to 41 years (mean, 26); and a study group of women with severe pre-eclampsia (n = 54) ranging in age from 18 to 45 years (mean, 28.8) who were between 25 and 38 weeks' gestation (mean, 32). The pre-eclampsia group comprised women who were diagnosed with severe pre-eclampsia at our department from 1 October 1996 until 1 September 1997 according to American College of Obstetricians and Gynecologists guidelines.¹ The study protocols were approved in advance by the Semmelweis University Institutional Review Board and informed consent was subsequently obtained from study participants. ApoE genotyping was performed according to accepted protocols.²⁻⁴ Statistical analysis was conducted using McNemar χ^2 test (95% confidence interval (CI)) and Fisher's exact test (95% CI).

Results

Table 1 shows the frequency of apoE alleles. The frequency of the apo ε2 alleles was significantly higher in the pre-eclampsia than the healthy non-pregnant and healthy pregnant control groups by McNemar χ^2 test (p < 0.001; 95% CI).

A significant difference in the frequency of the apo ε2/3 genotype was found between the healthy pregnant group and the pre-eclampsia group by Fisher's exact test (table 2) (p < 0.0397; CI 95%).

Discussion

ApoE is an established genetic marker for dyslipidaemia and atherosclerosis. It may be associated with the hyperlipidaemia observed in patients with severe pre-eclampsia. In this study, we attempted to determine apoE allele frequency in groups of healthy non-pregnant

women (n = 101), healthy pregnant women (n = 52), and women with severe pre-eclampsia (n = 54). The frequency of the $\epsilon 2$ allele appears to be significantly higher among women with pre-eclampsia compared with healthy non-pregnant and healthy pregnant women in this study ($p < 0.001$). We found a higher percentage of women with pre-eclampsia with the apo $\epsilon 2/3$ genotype compared with those experiencing a healthy pregnancy. These results suggest that women with the $\epsilon 2/3$ genotype have a greater than threefold risk of developing pre-eclampsia. However, the sample size is not large enough to draw conclusions regarding other allele combinations.

Although pre-eclampsia is a multifactorial disease, it has a general tendency towards familial clustering, suggesting that genetic factors might play an important role. The work of Husby *et al* has drawn attention to the role of Lp(a) lipoprotein, which is an independent hereditary risk factor for the development of atherosclerosis.⁵ Because the potential roles of lipoproteins and apolipoproteins have not been studied comprehensively in women with pre-eclampsia, this study focused on apoE. This molecule plays an important role in lipid metabolism, especially in the removal of atherogenic remnants of triglyceride rich lipoproteins.⁶ The apoE2 isoform is defective in binding to the low density lipoprotein (LDL) receptor, which is attributable to an altered charge of the molecule, and results in impaired intestinal cholesterol absorption and

clearance of chylomicron remnants. Our findings suggest that the presence of the apo $\epsilon 2$ allele might increase the risk for developing pre-eclampsia. Owing to the relatively small sample size and the sampling approach used in this study, we acknowledge that generalisability is problematical. However, our results support previously published work implicating lipoproteins^{7,8} in the development of pre-eclampsia. ApoE alleles are established genetic markers for dyslipidaemia and coronary heart disease and may also be a risk factor for developing pre-eclampsia.⁸ Our findings provide additional evidence for expanding research in this area.

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