

알도스테론 생성 효소 유전자(CYP11B2) 다형성이 심근 경색증의 발생에 미치는 영향

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The Effects of an Aldosterone Synthase(CYP11B2) Gene Polymorphism on the Risk of Myocardial Infarction

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ABSTRACT

Background and Objectives : Several polymorphisms of the renin-angiotensin-aldosterone system have been found to have pleiotropic effects on cardiovascular diseases. Polymorphism of the aldosterone synthase gene (CYP11B2), which may influence plasma aldosterone levels, has been reported to cause systemic hypertension, influence the left ventricular diameter and mass, and decrease baroreflex sensitivity of the cardiovascular system. Through these mechanisms, it is thought to increase the risk of myocardial infarction (MI). Our study was designed to elucidate whether polymorphism of CYP11B2 increased the risk of MI. **Subjects and Methods :** We analyzed the genotypes of CYP11B2 and the classic risk factors of MI in 188 MI patients and 320 control subjects without history of MI. **Results :** There was no significant difference in the distribution of genotypes between the patient and control groups. Adjusting for the classical risk factors, multiple logistic regression analysis showed no significant effect of CYP11B2 gene polymorphism on the development of MI. However, the presence of the -344C allele is associated with a markedly increased MI risk conferred by classic risk factors including hypertension, smoking, and male sex. In particular, hypertension was not a significant risk factor as compared with non-hypertensive patients in subjects without -344C, but the relative risk was increased to 2.40 (95% CI : 1.05 -5.51, $p < 0.05$) with -344C. The relative risks of smoking and male sex were also increased with the presence of the -344C allele. **Conclusion :** CYP11B2 polymorphism is not an independent risk factor of MI, although hypertension, smoking, and male sex are more potent risk factors for MI in Koreans who possess the -344C allele. (Korean Circulation J 2001;31(12):1261-1266)

KEY WORDS : Cytochrome P-450 CYP11B2 ; Myocardial infarction ; Polymorphism (Genetics).

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가 . , , , , , . CYP11B2

1)

가 , .

2-4)

대상 및 방법

가 대 상

188

100

220

가 , 5)

6)7)

(CYP11B2)

(zona glomerulosa) mitocho -

ndrial P450

. CYP11B2

II

가 5)8)

344C/T

(promoter region) (tr -

anscription factor) SF - 17 thym -

idine(- 344T) cytosine(- 344C)

가 9)

10)11)

(baroreflex)

12) , 11)

13)

CYP11B2 - 344C

유전형 분석

CYP11B2 PCR - RFLP

(restriction fragment length polymorphism)

. Sense antisense primer

5 '- CAG GAG GAG ACC CCA TGA

GAC - 3 ' 5 '- CCT CCA CCC TGT TCA GCC C -

3 ' . 95 10 denaturation 95

1 , 67 1 , 72 2 1 cy -

cle 35 , 72 5

20 µL 5 U HaeIII

37C 2 incubation

2% agarose gel

, ethidium bromide 가

. CYP11B2 - 344T HaeIII 가

273 bp fragment 가 , - 344C

가 202 bp fragmentation

가 (Fig. 1).

통계 분석

Student t - test

CYP11B2



Fig. 1. Genotyping of CYP11B2-344T/C.

Table 1. Characteristics of cases and controls

	MI group (N=188)	Control group (N=320)	p
Age (years)	58.1 ± 11.3	51.8 ± 9.4	<0.001
Sex (Male %)	81.4%	37.2%	<0.001
BMI (kg/m ²)	24.5 ± 3.0	24.0 ± 3.1	0.122
Total cholesterol	193.6 ± 40.9	196.9 ± 38.8	0.380
LDL	122.9 ± 36.2	112.5 ± 32.5	0.001
HDL	41.2 ± 11.0	48.1 ± 13.9	<0.001
DM (%)	28.0	7.6	<0.001
Hypertension (%)	43.0	39.6	0.447
Smoking (%)	76.9	35.4	<0.001

Independent t-test/ ²-test. BMI : body mass index, LDL : low density lipoprotein, HDL : high density lipoprotein, DM : diabetes mellitus

Table 2. Distribution of genotypes between control and MI group

	Control	MI	Control	MI	Control	MI
TT (%)	48.1 (154)	47.9 (90)	48.1 (154)	47.9 (90)	87.2 (279)	90.1 (171)
CT (%)	39.1 (125)	43.1 (81)	51.9 (166)	52.1 (98)		
CC (%)	12.8 (41)	9.0 (17)			12.8 (41)	9.0 (17)
p	0.378		0.956		0.248	

²-test, MI : myocardial infarction

Multiple logistic binary regression analysis

결 과

임상적 특성

58.1 ± 11.3
51.8 ± 9.4 (p<0.001),
LDL, DM, (Table 1).

유전형 분석

CYP11B2 - 344T/C
TT, CT, CC 48.0%(n = 204), 40.6%
(n = 206), 11.4%(n = 58).
Hardy - Weinberg Equation

(Table 2).

LDL

(Table 3).

기존 위험 요인들과의 관련성 분석

CC genotype 가
TT CT CC 가
Wild type TT
가, C
allele 가

(Odd ratio ; 2.40, 95% CI : 1.05 - 5.51).

C allele 가 , Ylitalo ¹³⁾ baro -
(Odd ratio/p : 3.95/0.003 reflex .
6.02/0.001, 2.38/0.087 3.69/0.024).

고 찰

CYP11B2 11B2 - 344C
(filling fraction)
¹²⁾ - 344 C
allele 가 , CC
가 - 344C 가 , Pojoga ¹¹⁾
가 ¹¹⁾ Tamaki ¹⁴⁾ CC CT TT
CYP11B2 - 344 C allele 가 가
- 344C가
¹⁶⁾ ¹⁰⁾가 가
가 CYP11B2 - 344C
가가
CYP11B2
¹⁷⁾¹⁸⁾
¹⁹⁾ CYP11B2가
가
CYP11B2 - 344C
²⁰⁾
²¹⁾가
가 2가 CYP -

Table 3. Relative risks of MI associated with different risk factors with multivariate logistic regression test

	OR	95% CI	p
CYP11B3 - 344TT	1.000		
CYP11B2 - 344CT	1.130	0.454 - 2.814	0.793
CYP11B2 - 344CC	1.234	0.490 - 3.111	0.656
Obesity (BMI >27 kg/m ²)	1.965	0.981 - 3.935	0.057
Sex (Male)	3.237	1.559 - 6.724	0.002
Age (years)	1.083	1.051 - 1.115	<0.001
DM	4.621	2.344 - 9.108	<0.001
Smoking	3.571	1.829 - 6.973	<0.001
Hypertension	0.727	0.418 - 1.265	0.260
LDL	1.011	1.003 - 1.018	0.007

Multiple binary logistic analysis. CI : confidence interval, OR : odds ratio, DM : diabetes mellitus, LDL : low density lipoprotein, BMI : body mass index

Table 4. Comparison of potency of classic risk factors between with and without 344C allele

	CYP11B2-344T/T			CYP11B2-344C/T or C/C		
	OR	95% CI	p	OR	95% CI	p
Age (years)	1.07	1.03 - 1.12	0.001	1.10	1.05 - 1.15	<0.001
Male	2.38	0.88 - 6.43	0.087	3.69	1.19 - 11.5	0.024
Smoking	3.95	1.59 - 9.85	0.003	6.02	2.06 - 17.5	0.001
DM	3.72	1.58 - 8.75	0.003	3.28	1.08 - 9.94	0.035
Hypertension	0.79	0.37 - 1.70	0.546	2.40	1.05 - 5.51	0.038
Obesity	2.38	0.92 - 6.16	0.074	1.73	0.60 - 4.97	0.309
LDL	1.01	1.00 - 1.02	0.046	1.01	1.00 - 1.02	0.122

Multiple binary logistic analysis. CI : confidence interval, OR : odds ratio, DM : diabetes mellitus, LDL : low density lipoprotein

11B2 - 344C 가 .

- 344C/T C allele Dominant ef -

- 344C 가 , T allele Co - dominant effect

가 가 CC CT

- 344CC

- 344C가 2 가

- 344C

CYP11B2 - 344C 가

가 .

- 344C

TT, CT, CC ,

26.5%, 50.1%, 23.4% ,

TT CT Data ,

(homozygous mutant) 가

CC 11.4% 가

(CC : 9.28%).¹⁴⁾ - 344C

요 약

가

가 배경 및 목적 :

가

가

가 (CYP11B2)

가

가

가 , - 344C가

가 , - 344C

가 2.4 가 CYP11B2

(95%CI 10.5 5.51, p=0.038)

가 3.95 6.02 2. 방 법 :

38 3.69 가 188

- 344C 가 , 100

가 220

- 344C ,¹⁸⁾ , PCR - RFLP CYP -

가 ,¹³⁾ 11B2 - 344T/C

결 과 :

가 가 (: CC 12.8%,

CT 39.8%, TT 48.1%, : CC 9.0%, CT 43.1%,
TT 47.9%),
가

CYP11B2 - 344C
가 가
- 344C
가 ,
Odd Ratio ; 2.40(95% CI : 1.05 5.51 p<0.05)

결 론 :

, CYP11B2
,
가 , ,
가 .

중심 단어 : ; ; .

(HMP - 00 - GN - 01 - 0001).

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