

## 한국인 남자에게서 식이와 Apolipoprotein E 유전자 다형성이 혈청 지질의 변동에 미치는 영향

박정식<sup>1</sup> · 오성주<sup>1</sup> · 김광석<sup>1</sup> · 안승혜<sup>2</sup> · 김영기<sup>3</sup>

### Effect of Diet and Apolipoprotein E (Apo E) Polymorphism on the Variation of Serum Lipid Profile in Korean Males

Jeong Sik Park, MD<sup>1</sup>, Seung Joo Oh, MD<sup>1</sup>, Kwang Seok Kim, MD<sup>1</sup>,  
Seung Hye Ahn<sup>2</sup> and Young Kee Kim, MD, PhD<sup>3</sup>

<sup>1</sup>Department of Internal Medicine, <sup>2</sup>Clinical Pathology, Seoul Adventist Hospital, Seoul,

<sup>3</sup>Department of Clinical Pathology, College of Medicine, Korea University, Seoul, Korea

#### ABSTRACT

**Background and Objectives** : Diet is the basic and principal therapeutic modality for hyperlipidemia. However, diet therapy alone showed variable responses in lowering lipid levels in different studies. This research is to prove the effect of diet and Apo E polymorphism on the variation of serum lipid profile in Korean males.

**Materials and Methods** : To evaluate the gene-diet interaction, serum total cholesterol (Chol), triglycerides (TG), HDL-cholesterol and LDL-cholesterol (HDLc, LDLc), lipoprotein (a) (Lp (a)), and fasting blood glucose (FBS) were measured with Apo E genotyping in vegetarians (group A, n = 154) and in healthy Korean male adults (group B, n = 150) of similar mean age (50.1 vs. 49.3). **Results** : Lipid profiles showed significantly lower levels in group A compared to group B (Chol 168.3 ± 30.5 mg/dL vs. 181.3 ± 33.4 mg/dL, p < 0.001 ; TG 131.0 ± 62.9 mg/dL vs. 149.4 ± 76.7 mg/dL, p = 0.023 ; HDLc 56.0 ± 11.0 mg/dL vs. 56.9 ± 11.5 mg/dL, p = 0.509 ; LDLc 92.5 ± 28.1 mg/dL vs. 100.6 ± 29.9 mg/dL, p = 0.016 ; Lp (a) 22.1 ± 14.6 mg/dL vs. 26.9 ± 13.8 mg/dL, p = 0.004 ; FBS 85.1 ± 14.1 mg/dL vs. 102.7 ± 16.6 mg/dL, p < 0.001). The Apo E genotyping showed 3/3, 64.1% ; 3/4, 20.7% ; 2/3, 11.8% ; 2/2, 1.3% ; 4/4, 0.6% in the combined groups. The distribution was similar in both groups. Chol and LDLc were significantly (p < 0.05) higher in 3/4 allele group compared to other allele groups among non-vegetarians. On the other hand, Chol and LDLc were significantly (p < 0.01) lower in vegetarians compared to non-vegetarians only in 3/4 allele group.

**Conclusion** : Vegetarian diet significantly lowered Chol, TG, LDLc, Lp (a) and FBS levels. Significant lipid lowering effect of vegetarian diet was noted in Apo E allele 3/4 group which had significantly higher Chol and LDLc levels without diet intervention. These data suggest that the influence of diet on serum lipid profiles differ according to apo E genotypes. (**Korean Circulation J 1999;29(3):266-275**)

**KEY WORDS** : Apolipoprotein E · Genotype · Vegetarian diet · Serum lipids.

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: (02) 210-3501 · : (02) 249-0403

E-mail : sjpark@www.amc.seoul.kr

## 서 론

, Lp(a)

가

(National Cholesterol Education Program)

## 대상 및 방법

<sup>1)2)</sup>

대 상

1997 5 1998 1  
35  
154 (A )  
150 (B )  
A

가

<sup>1-4)</sup>

lacto - ovo - vegetarian

가

. B

A

50.1 , B 49.3

apolipoprotein apolipoprotein( apo) (body mass index, BMI)  
A - , apoA - , apoB, apoC - , apo E lipoprotein (Table 1).  
lipase

<sup>3-7)</sup>

apo E

48%가

, 44%가

, lipoprotein(a)( Lp(a)), apo E

## 방 법

Apo E

12

1

**Table 1.** Comparison between vegetarian and non-vegetarian groups

Age	35 - 40	41 - 50	51 - 60	≥ 61	Total	Mean age	BMI* (kg/m <sup>2</sup> )	Mean BP <sup>†</sup> (mmHg)
Vegetarian	19	62	60	13	154	50.1 ± 7.9	22.8 ± 2.7	98.5 ± 15.6
Non-vegetarian	30	63	39	18	150	49.3 ± 9.6	24.3 ± 2.6	94.4 ± 15.3

\* ; body mass index, <sup>†</sup> ; blood pressure

24 . Apo E  
 EDTA -40  
 DNA . DNA XTRAX  
 TM DNA extraction kit(Gull Laboratories, USA)  
 cholesterol(HS) reagent(E - CHEM, Santafe  
 Springs, USA) triglyceride  
 reagent(E - CHEM, Santafe Springs, USA)  
 (Abbott EPX, USA)  
 . HDL EZ HDL TM cholesterol kit  
 (Sigma Diagnostics, St. Louis, USA) , LDL  
 LDL - cholesterol kit(Sigma Diagnostics, St.  
 Louis, USA) Embiel Auto Glu  
 Test(Embiel, , )  
 (Abbott, USA) . Lp(a) Lp(a)  
 Auto " DAIICHI " (Daiichi pure chemicals Co.,  
 Ltd., Tokyo, Japan) (Cobas  
 Mira, Switzerland)

#### Apo E genotype 검사법

Apo E Kontula <sup>8)</sup>  
 Bowden <sup>9)</sup>  
 . Oligonucleotide primer  
 ( , )

P1 = 5' - AAGGAGTTGAAGGCCTACAAAT - 3'  
 (nucleotides 3537 - 3616)  
 P2 = 5' - TCGCGGGCCCCGGCCTGGTACA - 3'  
 (nucleotides 3914 - 3893)  
 P3 = 5' - GAACAACCTGAGCCCGGTGGCGG - 3'  
 (nucleotides 3649 - 3670)  
 P4 = 5' - GGATGGCGCTGAGCCGCGCTC - 3'  
 (nucleotides 3943 - 3922)

1 DNA

. 50  $\mu$ L

. Oligonucleotide primer P1

P4 1.0  $\mu$ M, dNTP 0.2 mM, Tris -  
 HCl(pH 8.3), 10 mM ; MgCl<sub>2</sub>, 1.5 mM ; dithio -  
 threitol, 1 mM ; bovine serum albumin, 500 mg/L

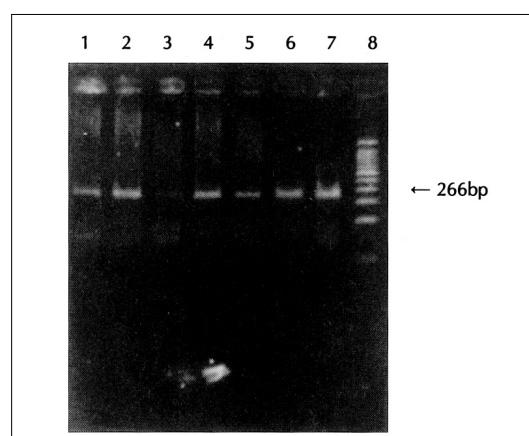
DNA 2  $\mu$ L(50-200 ng/ $\mu$ L ; 100 ng/ $\mu$ L)

thermal reactor(Perkin Elmer  
 9600, USA) 95 5 72  
 Taq polymerase(Takara, Japan) 1.5 U  
 . 96 60 , 55 60  
 , 72 60 30  
 . DNA 1  $\mu$ L  
 oligonucleotide P2 P3  
 .  
 DNA Hha I(Takara, Japan) 0.5 U/ $\mu$ L  
 37 18  
 MetaPhor agarose(FMC BioProducts, ME,  
 USA)  
 4% . 0.5X Tris - borate  
 . Hha I 6 cm  
 minigel 50 V 80  
 UV transilluminator

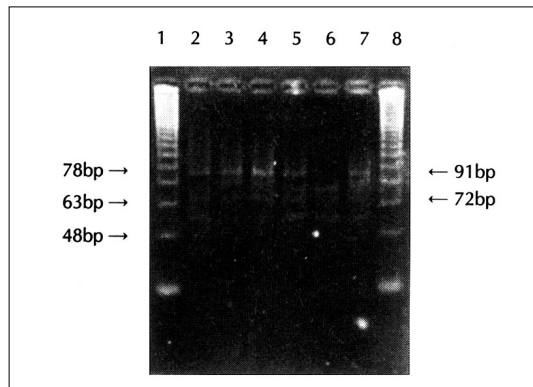
DNA .  
 266 bp size 2 (Fig. 1)  
 가 apo E (Fig.  
 2) . apo E  
 fragment size 2 91, 78, 63 bp  
 , 3 91, 63, 48 bp ,  
 4 72, 63, 48 bp .

#### 자료 및 통계처리

± ,



**Fig. 1.** The second amplification products of 266 bp size are seen in all lanes with primer 2 and primer 3. The 8th lane is 100 bp DNA ladder size marker.



**Fig. 2.** Apo E gene restriction fragment length polymorphism by Hha I. Lane 1 and 8, 20 bp DNA ladder size marker. Lane 2, 3/3, Lane 3, 2/2, Lane 4 2/3, Lane 5, 3/4, Lane 6, 4/4, Lane 7, 2/4.

Apo E

SAS

t

## 결 과

채식자군과 비채식자군의 혈청지질 및 지단백 농도 (Table 2)

, LDL Lp(a) 가  
85.1 ± 14.1 mg/dL  
102.7 ± 16.6 mg/dL  
HDL  
56.0 ± 10.9 mg/dL  
56.9 ± 11.5 mg/dL 가

Apo E 유전자형 분포 (Table 3)

apo E  
2/2, 2/4, 4/4 0.6 1.3%  
3/3 64.1% 가  
3/4 20.7% , 2/3 11.8%  
가  
2 0.067, 3 0.80, 4 0.133  
2 0.078, 3 0.796, 4 0.126

**Table 2.** Lipid profiles and fasting blood glucose level in vegetarians and non-vegetarians (mg/dL)

	Vegetarian (n = 154)	Non-vegetarian (n = 150)	p
Cholesterol	168.3 ± 30.5	181.3 ± 33.4	<0.001
Triglyceride	131.0 ± 6.9	149.4 ± 76.7	0.023
HDL-C	56.0 ± 11.0	56.9 ± 11.5	0.509
LDL-C	92.5 ± 28.1	100.6 ± 29.9	0.016
Lp (a)	22.1 ± 14.6	26.9 ± 13.8	0.004
Glucose	85.1 ± 14.1	102.7 ± 16.6	<0.001

**Table 3.** Comparison of apo E genotypes and gene frequencies between vegetarians and non-vegetarians  
No. observed (%)

	Vegetarians	non-vegetarians	Total
2/2	3 ( 1.9)	1 ( 0.7)	4 ( 0.13)
2/3	15 ( 9.8)	21 ( 14.0)	36 (11.8 )
2/4	1 ( 0.7)	1 ( 0.7)	2 ( 0.66)
3/3	100 ( 64.9)	95 ( 63.3)	195 (64.1 )
3/4	33 ( 21.4)	30 ( 20.0)	63 (20.7 )
4/4	2 ( 1.3)	2 ( 1.3)	4 ( 0.13)
Total	154 (100.0)	150 (100.0)	304
Gene frequencies			
2	0.067	0.078	0.072
3	0.800	0.796	0.798
4	0.133	0.126	0.130

각 Apo E 유전자군내에서의 채식자군과 비채식자군간의 각종 혈청 지질과 지단백 및 공복혈당 농도의 변화 (Table 4)

LDL 가 3/4  
(p<0.01).  
3/4  
(p<0.05).

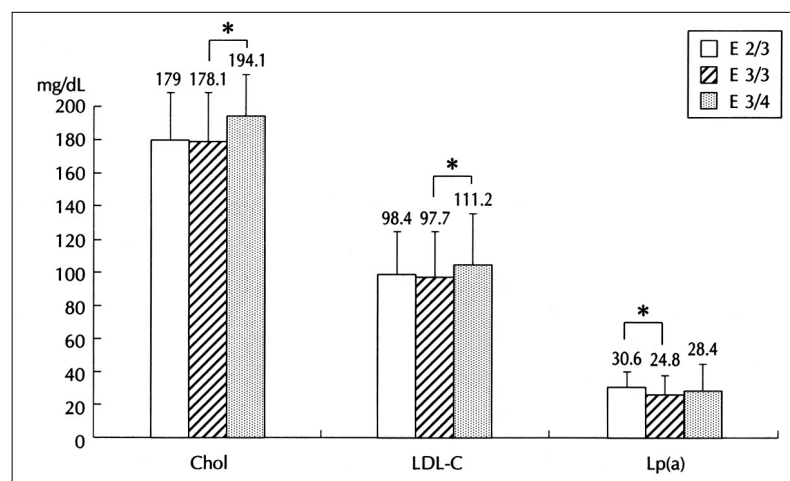
채식군,비채식군 및 전체군내에서 Apo E 각 유전자형 군간의 혈청지질과 지단백 및 공복혈당 농도의 변화 (Fig. 3)

apo  
E  
LDL

**Table 4.** Lipid profiles in various Apo E allele groups

	Group	Chol	TG	HDL-C	LDL-C	Lp (a)
2/2	A <sup>†</sup> (n=3)	184.0 ± 46.6	185.0 ± 89.3	70.7 ± 20.6	83.0 ± 86.7	13.2 ± 6.3
(n=4)	B <sup>‡</sup> (n=1)	186.0	147.0	61.6	111.0	32.6
2/3	A <sup>†</sup> (n=15)	180.5 ± 46.4	128.1 ± 60.7	57.5 ± 13.8	105.0 ± 45.3	24.7 ± 16.2
(n=36)	B <sup>‡</sup> (n=21)	179.0 ± 27.6	151.4 ± 86.2	59.6 ± 12.0	98.4 ± 30.1	30.6 ± 8.4
2/4	A <sup>†</sup> (n=1)	132.0	94.0	41.6	74.0	19.7
(n=2)	B <sup>‡</sup> (n=1)	171.0	69.0	56.7	104.0	20.3
3/3	A <sup>†</sup> (n=100)	179.1 ± 103.4	131.0 ± 63.9	55.9 ± 9.9	94.7 ± 28.4	22.1 ± 13.9
(n=195)	B <sup>‡</sup> (n=95)	178.1 ± 32.9	150.5 ± 78.7	55.5 ± 12.4	97.7 ± 30.9	24.8 ± 12.8
3/4	A <sup>†</sup> (n=33)	166.3 <sup>§</sup> ± 29.1	118.4* ± 52.8	57.7 ± 13.1	88.6* ± 22.1	23.8 ± 16.1
(n=63)	B <sup>‡</sup> (n=30)	194.1 ± 38.3	151.8 ± 69.8	58.9 ± 9.2	111.2 ± 29.7	28.4 ± 12.9
4/4	A <sup>†</sup> (n=2)	156.5 <sup>§</sup> ± 10.6	155.5 ± 47.4	51.6 ± 4.7	85.0 ± 5.7	24.8 ± 0.9
(n=4)	B <sup>‡</sup> (n=2)	163.5 ± 14.9	102.5 ± 36.1	59.0 ± 1.5	87.8 ± 3.9	23.4 ± 17.0

<sup>†</sup> ; vegetarian, <sup>‡</sup> ; non-vegetarian, \*p<0.05, <sup>§</sup>p<0.01



**Fig. 3.** Lipid profiles in various Apo E alleles among Apo E alleles among non-vegetarians. \*p<0.05

가 3/4 (p<0.01). , 가 LDL 가 4S (Scadinavian Simvastatin Survival Study)<sup>10)</sup>

가 3/4 LDL (national cholesterol education program)<sup>11)</sup> 2

가

고 안

가

Ornish<sup>12)</sup> Life Style Heart Trial 11% very low fat diet

가 가 가 가

<sup>13)</sup> 가  
<sup>14)</sup> Los Angeles VA data base Framingham study cononary risk analysis  
가 9%  
<sup>15)</sup> Finland  
가 <sup>16)</sup> Lyon  
Heart Study 가 apo  
E 가  
<sup>3-7)</sup> Apo E chylomicron, VLDL,  
가 <sup>17)</sup> HDL  
ligand . Apo E 2,  
<sup>12)18)19)</sup> , 3, 4 가  
2/2, 3/3, 4/4 homozygous 2/3,  
2/4, 3/4 heterozygous  
19 3597  
<sup>4)</sup> medium chain  
, , (C<sub>12</sub>), (C<sub>14</sub>), (C<sub>16</sub>) apo E 112 158  
, arginine cysteine  
(C<sub>18</sub>) ancestral form 4 112 arginine, 158 arginine  
<sup>20)</sup> Medium chain , 3 112 cysteine, 158 arginine  
<sup>21)</sup> 2 112 cysteine, 158 cysteine  
, whole grain <sup>29)30)</sup> 4, 3 LDL  
, LDL, VLDL 2 100 VLDL - apo  
<sup>22)</sup> seven country study E4 LDL  
가 <sup>23)</sup> 가  
LDL, <sup>29)</sup>  
VLDL 가 HDL  
<sup>24)25)</sup> Lp(a) , LDL 가 가  
, , 가 , 2 가 가 가  
Lp(a) <sup>31)</sup> apo E  
<sup>26)27)</sup> Lp(a) 가 22± 14 17% <sup>29)</sup> ,  
14.6 mg/dL, 27 ± 13.8 mg/dL apo E HDL apo  
(p = 0.004). A - 1 , apo B  
, 4 12%  
, 2 apo E  
Hong <sup>28)</sup> 4

<sup>29)32-37)</sup> 2, 4 (glucose intolerance)  
 가  
 2/2, 2/4, 4/4 가 Hong <sup>28)</sup>  
 3/3 가 LDL 가  
 2 가 (chylomicron) VLDL  
 remnant  
<sup>38)</sup>  
 가  
 가  
 apo E 가  
<sup>29)</sup> 4 allele 가 apo E 4  
 가 5 40% 가  
<sup>43)</sup> 4 가 4/4 가  
 Hardy - Weinberg  
 2가 7%, 3가 80%  
 4가 13%  
 Kim, <sup>9)39)</sup> Oh <sup>40)</sup>  
 apo E 3/3가 (Fig. 3),  
 64% 가 , 3/4 2/3  
 Kim  
 3/4  
 LDL  
<sup>29)41)42)</sup> 가  
 apo E Ryu <sup>44)45)</sup> Apo E genotype  
 2가 가 HDL  
 fat diet( 39%, 15%, American 435  
 mg/day) NCEP ( 30%, 가  
 10%, 300 mg/day) Apo E alle  
 , apo E 4 2/3, 3/3, 3/4 HDL  
 LDL 가 가 가  
 2/2, 2/4, , 4/4  
 lacto - ovo vegetarian ,  
 4/4  
 LDL , Lp(a) 가

150 (B ) . , A

가 , , lacto - ovo - vegetarian . B

가 . Apo E

HDL 12

3/4 LDL 가

가 , LDL , Lp(a) 가

apoE 3/3 64.1%

가 3/4 20.7%, 2/3 11.8%

2/2 4/4 1.3%

2/4 0.6%

가 .

2 0.067,

3 0.80, 4 0.133 , 2

0.078, 3 0.796, 4 0.126 .

요 약

연구배경 :

3/4 LDL

가 가 (p<0.05). apo E

3/4 ,

LDL 가 (p<0.01).

결 론 :

lipid profile

가 , LDL 가 가

apo E 3/4

가 , lipoprotein(a)( Lp(a)), apo E

가

방 법 :

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35

중심 단어 : Apolipoprotein E . .

154 (A )



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