

고지혈증 환자에서 Simvastatin 투여 효과

정명호 · 차광수 · 박종철 · 서정평 · 박주형
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= Abstract =

Clinical Effects of Simvastatin in Patients with Hypercholesterolemia

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Background : To evaluate the clinical efficacy of Simvastatin, a HMG-CoA reductase inhibitor, we observed the changes of clinical characteristics and lipid profiles after Simvastatin administration in patients with hypercholesterolemia.

Methods and Results : Simvastatin 10mg was given once daily for 12 weeks in 35 patients (60 ± 6.0 years ; 14 male, 21 female) with hypercholesterolemia. High density lipoprotein-cholesterol (HDL-C) was increased from 38 ± 10 to 45 ± 9mg/dl (p < 0.05). Simvastatin significantly decreased total cholesterol (TC) from 235 ± 15 to 181 ± 21mg/dl (23.0%), low-density lipoprotein cholesterol (LDL-C) from 164 ± 19 to 104 ± 18mg/dl (36.5%), TC/HDL-C from 7.0 ± 2.0 to 4.4 ± 1.1, LDL-C/HDL-C from 4.9 ± 1.7 to 2.5 ± 0.8 (p < 0.01 respectively). Apo B was decreased by 31% (119 ± 19 to 87 ± 15mg/dl), apo B/A₁ ratio was decreased by 41% (1.2 ± 0.2 to 0.7 ± 0.2) and lipoprotein(a) decreased by 12% (33 ± 22 to 29 ± 17), while apo A₁ was increased by 25% (104 ± 18 to 130 ± 23mg/dl, p < 0.01 respectively). No patients complained of chest pain, but two had skin rashes. Creatine kinase and creatinine were not changed in all patients.

Conclusions : Simvastatin is an effective and well tolerated cholesterol lowering agent in patients with hypercholesterolemia.

KEY WORDS : Simvastatin · Hypercholesterolemia · Apolipoprotein · Lipoprotein(a).

서 론 (LDL - C) 가가
(TC) 가, 가

1 - 4)

. 45 , 55
 5 - 10)
 fibric acid , 가 , 55
 , (nicotinic acid), (bile 65 가 (1)
 acid - binding resin), probucol, , 가
 TC 20% , 1 10 , 140/90mmHg
 4,5). fibrate probucol ,
 (HDL - C) , HDL - C 35mg/dl ,
 가 , (body mass index)가 29
 niacin (kg/m²) , 70
 (resin) 18 , ,
 가 , ,
 11). ,
 HMG CoA reduc - (TG) 500mg/dl
 tase 가 I, IV V , ,
 ,
 Lovastatin Pravastatin , (ileal bypass),
 12 - 18). Simvastatin Lovastatin ,
 가 HMG CoA reductase , HMG - CoA reductase ,
 가 fibric acid
 10,19,20), ,
 가 . 60 ± 6.0
 가 14 , 가 21 .
 Simvastatin
 , 1 Simvastatin 10mg 12
 .
 연구 대상 및 방법
 1. 대 상
 1996 7 12
 35
 , National Cholesterol Education Pr -
 ogram Adult Treatment Panel Guidelines II(NCEP
 ATP II) 21). ,
 TC 가 240mg/dl 210mg/dl dewald LDL - C . Apo
 2가 A1, apo B Lp(a) Behring Nephelometer 100
 . Hitachi 747
 TC ,
 TG glycerol - 3 - phosphate
 , HDL - C dextran sulfate - MgCl₂
 , Frie -
 Apo

Analyzer , Simvastatin 2 117 ± 22mg/dl, 4
 102 ± 17mg/dl, 8 97 ± 15mg/dl, 12
 104 ± 18mg/dl
 (p<0.01).

3. 통 계

paired t test Wilco -
 xon Signed Rank test p value
 가 0.05 .

결 과

1. 혈청 지질의 변화(Fig. 1)

1) 혈청 총콜레스테롤(TC)치의 변화

Simvastatin TC 235 ± 15mg/dl , Si -
 mvastatin 2 185 ± 21mg/dl, 4
 175 ± 21mg/dl, 8 174 ± 19mg/dl, 12
 181 ± 21mg/dl
 (p<0.01).

2) 저밀도지단백 콜레스테롤(LDL-C)의 변화

Simvastatin LDL - C 164 ± 19mg/dl

3) 고밀도지단백 콜레스테롤(HDL-C)의 변화

Simvastatin HDL - C 39 ± 10mg/dl
 , Simvastatin 2 41 ± 8mg/dl, 4
 45 ± 9mg/dl, 8 45 ± 7mg/dl, 12
 45 ± 9mg/dl 4
 가 (p<0.01).

4) 중성지방(TG)의 변화

Simvastatin TG 162 ± 62mg/dl , Si -
 mvastatin 2 141 ± 47mg/dl, 4
 141 ± 52mg/dl, 8 159 ± 68mg/dl, 12
 162 ± 76mg/dl

5) TC/HDL-C비

Simvastatin TC/HDL - C 7.0 ± 2.0
 , Simvastatin 2 5.1 ± 1.2, 4

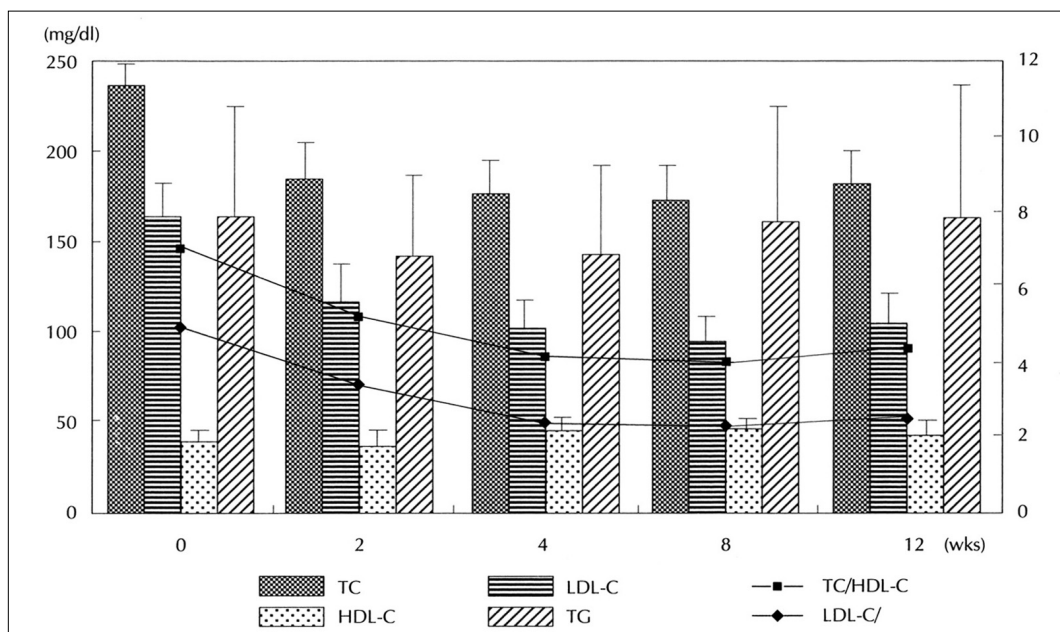


Fig. 1. Changes in total cholesterol(TC), LDL-C(low density lipoprotein-Cholesterol), HDL-C(high density lipoprotein-cholesterol), TG(triglyceride), ratio of TC/HDL-C and LDL-C/HDL-C at baseline, 2, 4, 8 and 12 weeks after Simvastatin treatment. Simvastatin decreased TC, LDL-C, TC/HDL-C, LDL-C/HDL-C and increased HDL-C.

4.1 ± 0.9, 8 4.0 ± 0.8, 12 4.4 ± 1.1

(p<0.01).

6) LDL-C/HDL-C의 비

Simvastatin LDL - C/HDL - C 4.9 ±
1.7 , Simvastatin 2 3.3 ± 1.1, 4
2.4 ± 0.7, 8 2.2 ± 0.5, 12
2.5 ± 0.8

(p<0.01).

2. 혈청 아포지단백(apo)과 LP(a)의 변화(Fig. 2)

1) Apo A₁의 변화

Simvastatin apo A₁ 104 ± 18mg/dl
, Simvastatin 2 112 ± 20mg/dl,
4 121 ± 20mg/dl, 8 117 ± 15mg/
dl, 12 130 ± 23mg/dl
4 12 가 (p<

0.01).

2) Apo B의 변화

Simvastatin apo B 119 ± 19mg/dl ,

Simvastatin 2 94 ± 22mg/dl, 4
88 ± 20mg/dl, 8 85 ± 19mg/dl, 12
87 ± 15mg/dl

(p<0.01).

3) Apo B/A₁비의 변화

Simvastatin apo B/A₁ 1.2 ± 0.2 ,
Simvastatin 2 0.9 ± 0.2, 4 0.8
± 0.2, 8 0.7 ± 0.2, 12 0.7 ± 0.2

(p<0.01).

4) Lipoprotein(a)의 변화

Simvastatin LP(a) 33 ± 22mg/dl ,
Simvastatin 2 32 ± 21mg/dl, 4
31 ± 21mg/dl, 8 28 ± 17mg/dl, 12
29 ± 17mg/dl 8 12

(p<0.05).

3. 기타 임상병리 검사 소견

Simvastatin Simvastatin 2 , 4 ,
8 12 7.3 ±

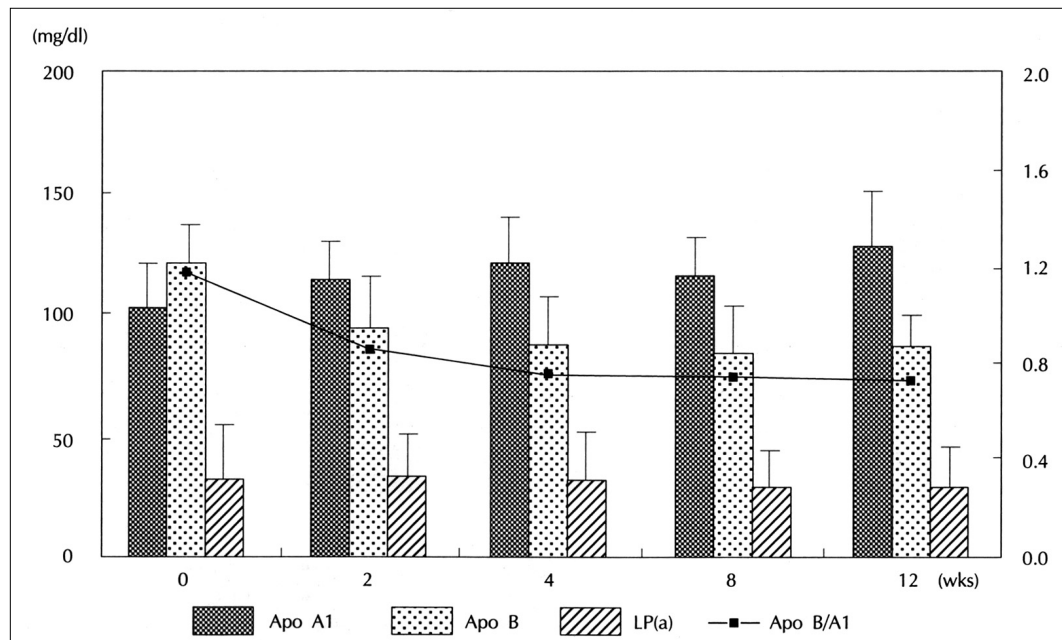


Fig. 2. Changes in apo A₁, apo B, lipoprotein(a) [Lp(a)] and ratio of apo B/A₁ at baseline, 2, 4, 8 and 12 weeks after Simvastatin treatment. Simvastatin decreased apo B, Lp(a), apo B/A₁ and increased apo A₁.

1.6, 6.8 ± 1.2 , 6.4 ± 1.2 , 6.6 ± 1.1 , $6.8 \pm 1.3 \times 10^3 / \text{mm}^3$, 13.4 ± 0.9 , 13.0 ± 1.0 , 13.0 ± 0.9 , 13.1 ± 1.0 , $13.3 \pm 1.0 \text{g/dl}$, 38.4 ± 2.8 , 37.0 ± 2.7 , 37.5 ± 2.6 , 37.8 ± 2.7 , $38.3 \pm 2.9\%$, 251 ± 14 , 269 ± 39 , 238 ± 40 , 239 ± 39 , $235 \pm 31 \times 10^3 / \text{mm}^3$, AST 25 ± 5 , 24 ± 5 , 25 ± 6 , 29 ± 7 , $30 \pm 8 \text{U}$, ALT 25 ± 9 , 29 ± 11 , 26 ± 10 , 32 ± 14 , $36 \pm 16 \text{U}$, Alkaline Phosphatase 83 ± 18.9 , 87.9 ± 21.5 , 86.9 ± 20.0 , 91.5 ± 27.5 , $85.7 \pm 23.9 \text{U}$, 0.9 ± 0.1 , 0.8 ± 0.2 , 0.8 ± 0.2 , $0.8 \pm 0.2 \text{mg/dl}$, 103 ± 16 , 103 ± 14 , 107 ± 16 , 101 ± 8 , $108 \pm 2 \text{mg/dl}$, 85 ± 29 , 82 ± 34 , 106 ± 45 , 98 ± 35 , $95 \pm 34 \text{mg/dl}$, 0.9 ± 0.2 , 1.0 ± 0.2 , 0.9 ± 0.2 , $0.9 \pm 0.2 \text{ mg/dl}$

8).

HDL - C
(reverse cholesterol transport)
24 - 26)

4. 부작용

8,27,28)

2
1
가

(endothelium - derived relaxing factor : EDRF),
(prostacyclin), EDHF (endothelium - derived hyperpolarization factor), endothelin

고 안

가
apo B, Lp(a)
22)
TC
1 - 4)

EDRF,
(tissue plasminogen activator : t - PA),
(heparin sulfate)

가 EDRF (agonist)
(acetylcholine)
(paradoxical contraction) 32)

8,23)

33)

t - PA가
(plasminogen activator inhibitor)

(adhesion molecule)가 가
34 - 40)

Simvastatin Lp(a)
가

Simvastatin

Simvastatin HMG CoA reductase
, TC, LDL - C, apo B, LP(a)
HDL - C, apo A₁ 가

4S 10,41,42), CARE , MAAS(Multicenter Anti -
atheroma Study) 48) Simvastatin
가

HMG CoA reductase 가

43,44)

HMG CoA reductase 요 약

HMG -

CoA mevalonate 연구배경 :

(LDL receptor) HMG CoA redu -
가 LDL - C , ctase 가

Simvastatin , Simvastatin Lovast -
11 - 19) atin 가 HMG CoA reductase
가

Simvastatin 가

2 , 가

가 Lovastatin 방 법 :

Mevalothin 12 - 18) 1996 7 12

12 Simvastatin

TC 23.0% 25% 35

4S study , LDL - 60 ± 6.0

C 36.5% , 35% 4S study 가 14 , 가 21 . Simvastatin
, HDL - C 18.4% 가 8% 가 4S , , TC, TG, HDL - C,
가 10) A₁(apo A₁), B(apo B), (a)

apo B Simvastatin 12 (Lp(a))
31% , Sweany 45) 27.8% , , ,
Ose 46) 17.9% (creatine kinase), Si -
, apo A₁ 25% mvastatin 1 (10mg) , Si -
가 , Ose 46) 7.8% 가 mvastatin 2, 4, 8, 12

Lp(a) Simvastatin 12.0% 결 과 :

, Slunga 47) 가 Lp(a)가 1) : TC LDL - C Simvasta -
가 tin , HDL - C Sim -

2) (apo) LP(a) : Apo A₁
Simvastatin 4 12
가 , apo B Apo B/A₁ Simvastatin
(p<0.01). LP(a) Sim -
vastatin 8 12
(p<0.05).

3) :

1 1 1 1

1 1 1

2

4) :

1 2

가

Simvastatin

LDL - C, apo B, LP(a) HDL - C, apo A₁ 가 .

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