

고콜레스테롤혈증환자에서 Atorvastatin의 유효성 및 안전성에 관한 연구

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Efficacy and Safety of Atorvastatin in Patients with Hypercholesterolemia

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ABSTRACT

Background : Previous studies indicated that a recently approved synthetic HMG-CoA reductase inhibitor, atorvastatin, reduces LDL cholesterol and triglyceride. To assess the efficacy on the level of serum LDL cholesterol and other lipoprotein fractions and its safety, we investigated 59 patients for lipid and side effect profile. **Method** : In patients with hypercholesterolemia, who showed 12-hours fasting serum LDL cholesterol >145 mg/dl and <250 mg/dl and triglyceride levels <400 mg/dl were enrolled to diet therapy for 4 weeks. After 4 weeks of diet therapy, serum lipid profile were reevaluated and patients with LDL cholesterol 130 mg/dl were as-signed to receive 10 mg dose of atorvastatin once daily for 4weeks. After 4 weeks of drug therapy, serum lipid profile were rechecked, if showed LDL cholesterol level 130 mg/dl, assigned to receive 20 mg dose of atorva-statin once daily until 8 weeks. **Result** : Of the 59 patients were assigned to receive atorvastatin therapy, 52 pati-ents completed the study. Among lipid profiles, total cholesterol, triglyceride, LDL-cholesterol and apolipoprotein B levels showed significant reduction with mean reduction rate of 28%, 13%, 38%, 32% respectively after 4 weeks and 31%, 13%, 41% and 34% respectively after 8 weeks. HDL-Cholesterol and lipoprotein (a) level did not show significant change after 8 weeks of therapy. Nine patients had mild adverse events, such as elevated ALT, epigastric pain, insomnia, thumb pain, postural hypotension, palpitation and constipation. Only three patie-nts of fifty-nine withdrew from the study due to adverse events related to drug treatment. **Conclusion** : The atorvastatin was highly effective and generally well tolerated with an acceptable safety profile in patients with primary hypercholesteleemia. (Korean Circulation J 1999;29(2):928-936)

KEY WORDS : Hypercholesterolemia · Atorvastatin..

서 론

(LDL - cholesterol)

: 1999 1 25

: 1999 9 1

: , 442 - 721

5

: (0331) 219 - 5712 · : (0331) 219 - 5708

1)

가,

가 가 1998 2 1998 7
가 가²⁾ 18 80
National cholesterol education pro-gram(NCEP)³⁾ 12 400 mg/dl
Friedewald⁶⁾ LDL -
cholesterol 가 145 mg/dl 250 mg/dl
LDL - cholesterol 가 160
mg/dl
가 2 LDL - cholesterol 130
mg/dL LDL -
cholesterol 100 mg/dL
HMG - CoA
TSH
1.5
A1C 가 10%
BUN 가 30 mg/dl
creatinine 2.0 mg/dl
aspartate transaminase(AST) alanine tran-
saminase(ALT)가 1.5
, creatine phosphoki-
nase(CPK)가 3
CPK가
HMG - CoA 10mg 160 m mHg
HMG - CoA 95 mmHg
, 3
⁵⁾
Atorvastatin FDA

LDL - cholesterol
HMG - CoA
atorvastatin 10 mg/day 20 mg/day 8
LDL - cholesterol
가

재료 및 방법

대 상

임상 실험 방법

8
4
AST, ALT, alk-
aline phosphatase(ALP), lactate dehydrogenase
(LDH), CPK, total protein, albumin, total bilibubin,

BUN, glucose, TSH, 가
A1c, hCG 4
2 (Fig. 1).
total cholesterol, triglyceride, 유효성 평가
HDL - cholesterol, apolipoprotein B 가 8
lipoprotein(a) 4, 52 8 LDL - chols -
8 12 - lead 130 mg/dl 가 65%
8 4 가
5) 8 LDL - cholesterol
130 mg/dl (%)
가 4 LDL - cholesterol 가
130 mg/dl (%),
4 8 LDL - cholesterol
(%, 4 8 total chole -
sterol, triglyceride, HDL - cholesterol,
apolipoprotein B (%)
안전성 평가
LDL - cholesterol, , , , ,
LDL - chole -
sterol 가 145 mg/dl
4 AST ALT가 ([+
1.5 CPK 가 3 2x]/3)
4 , , 4 , 8
AST, ALT (myopa -
thy) 가 4 10
transaminase 2
3 (%)
4 10 CPK 2
10
(%)
가
가 가

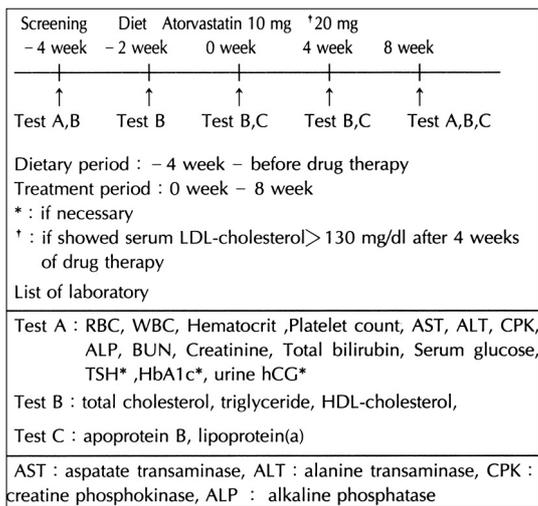


Fig. 1. The schedule of clinical trial and the list of laboratory test.

통 계 가 59
 ± , SPSS (13.5%) 4 20 mg 7
 가 (86.5%) 10 mg 45
 (%)
 parameter paired t - test AN - 262 ± 29 mg/dl, 158 ± 71
 OVA 0.05 mg/dl, HDL - cholesterol 50 ± 13 mg/dl, LDL -
 cholesterol 181 ± 25 mg/dl 4
 260 ± 26 mg/dl,
 152 ± 61 mg/dl HDL - Cholesterol 48 ± 11 mg/
 dl, LDL - Cholesterol 181.9 ± 24 mg/dl, apoli -
 poprotein B 137 ± 18 mg/dl, Lipoprotein(a) 21
 ± 17 mg/dl

결 과

대상환자의 임상적 특징
 114
 4 48
 가 20% 7 10 20% 4 , 1 , 3 , 2 ,
 21 , 10% 가 3
 38
 20% 59 유효성 평가
 50 ± 11 52 8 LDL - choles -
 가 3 , ALT 88.4% 10 mg
 가 2 , 가 2 41 (79%) 20 mg 5
 52 8
 가 52 182 ± 29 mg/dl 4 110 ± 21 mg/dl

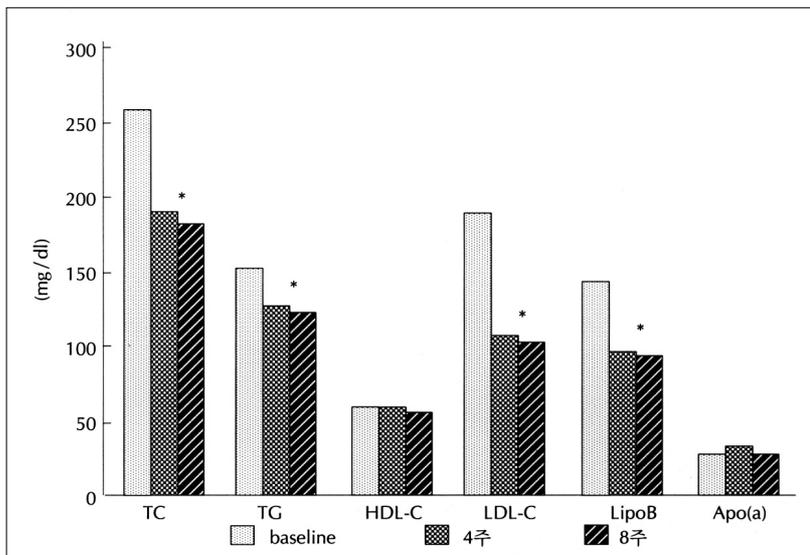


Fig. 2. The change of lipid profile during atorvastatin therapy.
 *p<0.01, baseline vs 4 weeks or 8 weeks, TC : Total cholesterol, TG : Triglyceride, HDL-C : high density lipoprotein-cholesterol, LDL-C : low density lipoprotein-cholesterol, LipoB : lipoprotein B, Apo(a) : apolipoprotein A1.

39% , 8 106 ± 19 mg/dl 41% (p<0.01, Table 1). 260 ± 26 mg/dl 4 184 ± 22 mg/dl 28% 8 177 ± 19 mg/dl 31% (p<0.01). 152 ± 61 mg/dl 4 126 ± 55 mg/dl 13% 8 123 ± 47 mg/dl 13% (p<0.05). HDL - cholesterol 48 ± 11 mg/dl 4 48 ± 13 mg/dl 가 , 8 46 ± 10 mg/dl . Apolipoprotein B 137 ± 18 mg/dl 4 91 ± 22 mg/dl dl 32% 8 89 ± 17 mg/dl 34% (p<0.01). Lipoprotein(a) 21 ± 17 mg/dl dl 4 23 ± 22 mg/dl, 8 21 ± 21 mg/dl (Figs. 2 and 3). LDL/HDL - cholesterol 3.9 ± 0.9 8 2.3 ± 0.8 40% (p<0.01).

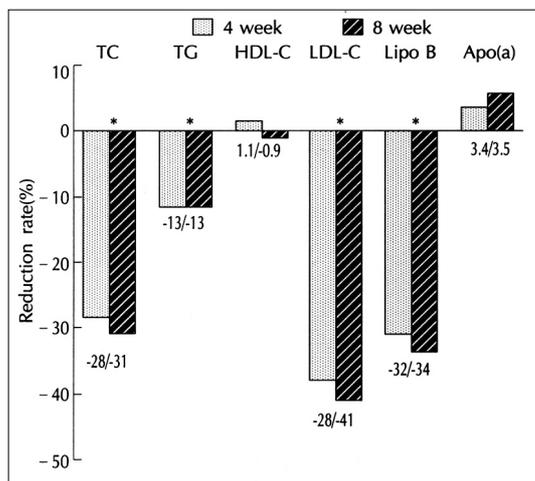


Fig. 3. The mean reduction rate of lipid profiles by atorvastatin as a time. *p<0.01, baseline vs 4 weeks or 8 weeks, TC : Total cholesterol, TG : Triglyceride, HDL-C : high density lipoprotein-cholesterol, LDL-C : low density lipoprotein-cholesterol, LipoB : lipoprotein B, Apo(a) : apolipoprotein A1.

안정성 평가 , , , hemoglobin, hematocrit ALT, albumin, total bilirubin, BUN, creatinine, uric acid, fasting glucose, Na, K, Cl, Ca, P 23 ± 6 IU/L 4 24 ± 6 IU/L, 8 23 ± 6 U/L , ALT 24 ± 9 U/L 4 27 ± 11 U/L, 8 26 ± 11 U/L . CPK 109 ± 66 U/L 4 99 ± 39 U/L, 8 98 ± 46 U/L .

Table 1. The change of lipid profile during treatment (Mean ± SD) (mg/dl)

	Baseline	4 week	8 week
Total cholesterol	260 ± 26	184 ± 22*	177 ± 19*
Triglyceride	152 ± 61	126 ± 52	123 ± 68
HDL-cholesterol	48 ± 11	48 ± 13	46 ± 10
LDL-cholesterol	181 ± 24	110 ± 21*	106 ± 19*
Apolipoprotein B	137 ± 18	91 ± 22*	89 ± 17*
lipoprotein(a)	21 ± 17	23 ± 22	21 ± 21

*p<0.01, baseline vs 4 weeks or 8 weeks

Table 2. Summary of clinical adverse effects to atorvastatin

Adverse event(s)	n = 9	dose
Musculoskeletal disorders		
Myalgia	1	10 mg
Gastrointestinal disorders		
Constipation	1*	20 mg
Epigastric pain	1	10 mg
Gastric fullness	1*	10 mg
Abnormal laboratory finding		
ALT elevation	2(1*)	10 mg
Others symptoms		
Insomnia	1*	10 mg
Postural hypotension	1	10 mg
Palpitation	1	10 mg

* ; No. of adverse effect related to Atorvastatin

9
가

5 5
ALT 1 , 1 ,
1 , 1 , 가 1
ALT ALT
가 1
ALT 가

4 4 1

1 4 ALT
가 , 1
ALT 가

1 1

(Table 2).

고 안

HMG - CoA hydroxymethylglu -
taryl CoA(HMG - CoA) (mevalonic acid)
HMG - CoA

LDL 가

⁵⁾⁷⁾ HMG CoA
lovastatin simvastatin LDL cholesterol
가 20% 30%
⁸⁾ atorvastatin 2.5 mg
80 mg LDL - cholesterol 가
25% 61% 가
LDL - cholesterol 90%가
2 ⁹⁾
CURVES ¹⁰⁾ atorvastatin 20 mg, 40
mg LDL - cholesterol
46%, 51% HMG CoA
LDL - cholesterol
가
Atorvastatin

atorvastatin 10mg simvastatin 40 mg
LDL - cholesterol

가

simvastatin 40 mg atorvastatin 40 mg

8
가 simva -
statin 가
atorvastatin

가
24 creatinine
statin atrovastatin simava -
¹¹⁾
atorvastatin

HMG CoA
가 HMG CoA

가 simvastatin 1.9 , pr -
avastatin 3 20 30
¹²⁾¹³⁾

HMG CoA
atorvastatin 10 mg 20 mg
LDL - cholesterol
8 가 41% ato -
rvastatin 10 mg 16 LDL - cholest -
erol 37% ^{14 - 16)}
가 lovastatin
20 mg 12 , pravastatin 10 mg 8 sim -
vastatin 40 mg 12 LDL - cholesterol
36%, 33%, 39% ^{17 - 19)}

HMG CoA
atorvastatin LDL - ch -
olesterol
atorvastatin 10 mg 20 mg
가 31%
atorvastatin 10 mg
20 mg 27%
30% ^{13 - 16)}

atorvastatin 10 mg simvastatin 20 mg . Atrovastatin 80 mg

40 mg 가 14% 가 ⁹⁾

¹⁵⁾ simvastatin 40 mg LDL/HDL - cholesterol 가

12 가 27% 3.9 ± 0.9 8 2.3 ± 0.8 40%

¹⁹⁾ atorvastatin 10 mg 20 mg sim - statin 10 mg 20 mg LDL - cholesterol/HDL -

vastatin 40 mg cholesterol 가 32%, 43%

. Atrovastatin 20

mg 80 mg 4

32% 46% ⁶⁾ 가 LDL/HDL - cholesterol 3 가

가 atorvastatin 40 mg ⁴⁾ atorvastatin

¹⁰⁾ atorvastatin

10 mg 16 atorvastatin 10%

17% ¹³⁾¹⁴⁾ ,

13% ¹³⁾ ,

¹⁷⁻¹⁹⁾ lovastatin, pravastatin simv -

astatin 11% 15%

¹⁰⁾¹¹⁾¹⁵⁾ atorvastatin 가 AST ALT가 3 4

가 HMG CoA ² ³ CPK 가 가

⁹⁻¹³⁾ ALT , ,

. Ato - , , 가

rvastatin HDL - cholesterol 가 12% ¹⁰⁾

가 가 ⁹⁾ 가 HDL -

HMG CoA 가 HDL -

cholesterol 가 가 ALT 1 ,

. atorvastatin 8 1 . Atrovastatin

HDL - cholesterol (Blood - brain barrier)

가 ¹⁰⁾ 가

apolipoprotein B 가 137 ± 1

18 mg/dl atorvastatin . Atrovastatin ¹⁰⁾ 가

10 mg 4 32%, 8 34%

atorvastatin 10mg 6 apo -

lipoprotein B 33% ²⁰⁾ HMG CoA

lovastatin pravastatin apolipo -

protein B 16% 20% ¹⁴⁾¹⁵⁾ sterol 가 130 mg/dl LDL - chole -

가 . Apolipoprotein B 4% LDL - 41%

가

²¹⁾ atorvastatin apolipoprotein B . 8

lipoprotein(a) ato -

rvastatin 10 mg 20 mg 8

가 ALT 가

요 약 ALT 가 1, 1

연구배경 : HMG CoA atorvastatin
 Atorvastatin HMG - CoA
 HMG - CoA

LDL - ator -

cholesterol

atorvastatin 10 mg/day 20 mg/day 8

LDL - cholesterol 가

재료 및 방법 : LDL - cholesterol 가

145 mg/dl 250 mg/dl

4 atorvastatin 10 mg 1

, 4 LDL - cholesterol

130 mg/dl 10 mg/day 8

, 130 mg/dl 20 mg/day 8

결 과 :

52 8 LDL - cholest -

erol 가 130 mg/dl 46

88.4% . LDL - cholesterol 4

39% , 8 41%

(p<0.01).

4 28% 8

31% (p<0.01).

4 13%

, 8 13%

(p<0.05). HDL - cholesterol 8

. Apolipoprotein B

4 32%

8 34% (p<0.01).

Lipoprotein(a) 8

. LDL/HDL - cholesterol

3.9 ± 0.9 8 2.3 ± 0.8

40% (p<0.01).

ALT 가

결 론 : HMG CoA atorvastatin

중심 단어 : Atorvastatin..

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