

LDL-콜레스테롤 상승 환자에 대한 Atorva-statin의 유효성 및 안전성에 대한 연구

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Efficacy and Safety of Atorvastatin in Patients with Elevated LDL-cholesterolemia

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ABSTRACT

Background and Objectives : HMG-CoA reductase inhibitors have been used for a decade to lower LDL cholesterol levels and to improve cardiovascular diseases and clinical outcomes. This study was designed to evaluate the clinical efficacy and safety profiles of atorvastatin, a new HMG-CoA reductase inhibitor, in patients with elevated LDL-cholesterolemia. **Material and Methods :** Eighty three patients who had high 12-hour fasting serum LDL-cholesterol level (≥ 145 mg/dl and ≤ 250 mg/dl) and serum TG level less than 400 mg/dl were enrolled. After completing an 4 week dietary phase, 50 patients who still had LDL-C ≥ 145 mg/dl and TG ≥ 400 mg/dl were assigned to receive atorvastatin 10 mg once daily for 4 weeks. After 4 weeks, the dose was continued for 4 weeks in each individual if serum LDL-cholesterol was maintained below 130 mg/dL. For each individual whose serum LDL-cholesterol was above 130 mg/dL, the dose was doubled (20 mg/day) and administered for 4 weeks. Serum AST, ALT and CPK were also measured in addition to blood chemistry tests for lipid profiles at 4 and 8 weeks for safety assessment. **Results :** 1) The total study population who completed the whole protocol was composed of 46 patients (23 male, 23 female, mean age 54 years). 2) At 4 weeks, the reduction by mean percent change from the baseline in LDL-cholesterol was -44.8% (from 182.3 ± 3.4 mg/dl to 99.7 ± 2.9 mg/dl). The fixed goal of LDL-cholesterol less than 130 mg/dl was achieved by 95.8%. 3) At 4 weeks, the mean percent change from the baseline in TC, TG, HDL-C, LDL/HDL-C and ApoB were -32.3%, -17.4%, +9.6%, -48.5% and -36.6%, respectively. 4) At 8 weeks, the mean percent change from the baseline in LDL-cholesterol was -43.0% (from 182.3 ± 3.4 mg/dl to 103 ± 2.4 mg/dl). The fixed goal of LDL-cholesterol less than 130 mg/dl was achieved by 91.3% of the whole patients. 5) At 8 weeks, the mean percent change from the baseline in TC, TG, HDL-C, LDL/HDL-C and ApoB were -31.3%, -22.6%, +13.7%, -48.8% and

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-35.9%, respectively. 6) No serious side effects were observed during the whole period. **Conclusion** : Atorvastatin is highly effective and safe in modulating lipid profiles favorably (lower LDL-Cholesterol, lower TG, elevate HDL-Cholesterol), in patients with serum lipid abnormality. (**Korean Circulation J 1999;29(12):1309-1316**)

KEY WORDS : Atorvastatin · LDL cholesterol · Hypercholesterolemia.

서 론

TG가 400 mg/dl 83

6) 4

lipoprotein - cholesterol, (low density LDL - C) mg/dl 4 , LDL - C 가 145

가 LDL - C 가 250 mg/dl 가 4

가 20% 4 LDL - C

1-3) mg/dl 250 mg/dl TG가 400 mg/dl

dl 50 가

가

HMG - CoA(3 - Hydroxy - 3 - Methyl Glutaryl - Coenzyme A)

lovastatin, simvastatin, pravastatin, fluvastatin . HMG - CoA

atorvastatin LDL - C 가 HMG - , 80 18

CoA (triglyceride, TG) TSH 1

4-5) 4 1.5 (TSH>5.5 μ IU/mL),

LDL - cholesterol 가 HbA1c가 10%

atorvastatin type ,

가 (BUN 30 mg/dl) crea-

대상 및 방법

ALT가 1.5 ,

(hyperbilirubinemia) ,

대 상 CPK 가 3

1998 3 10 CPK , (body mass index)가

12

AST

Friedewald LDL - C 가 30 ,

145 mg/dl 250 mg/dl 12 3

가 95 mmHg 20 mg 8
160 mmHg , (Fig. 1)
3 , ,
 , ,
가
 ,
가

유효성 평가
가 8
LDL - C 130 mg/dl
(%)
4 8 LDL - C (<130 mg/dl)
(%), 4 8
LDL - C (%), 4
8 total cholesterol(TC), TG, high de-
nsity lipoprotein - cholesterol(HDL - C), apolipop-
rotein B(Apo B), LDL - C/HDL - C (%)

방 법

4
(I, II, III)(Table 1)
가
atorvastatin 10 mg 4
4 , 8
Atorvastatin 10 mg 4
LDL - C 가 130 mg/dl
10 mg 8
, 130 mg/dl

안전성 평가
가 (0 , 4 ,
8) AST, ALT, creatinine phosphokinase(CPK)
가
(4 10 2 가
3) (%) 4 10
2 CPK가
10 (%)

통 계
(mean ± s.e)
SAS(version 6.1)
, paired t - test, ANOVA

Table 1. The list of laboratory tests

Test I : TC, TG, HDL-C, LDL-C, Apo B
Test II : AST, ALT, ALP, CPK, BUN, Fasting blood glucose,
Creatinine
Test III : Hemoglobin, Hematocrit, RBC, WBC, Platelet
TC : Total cholesterol TG : Triglyceride
HDL-C : High density lipoprotein cholesterol
LDL-C : Low density lipoprotein cholesterol
Apo B : Apolipoprotein B
ALP : Alkaline phosphatase
CPK : Creatitine phosphokinase

-4wks	-2wks	Baseline	4wks	8wks
Diet	Diet	Drug 10 mg	Drug 10 mg or Drug 20 mg	
Lab I, II, III			Lab I	Lab I, II, III

Fig. 1. Schedule and drug dosage.

결 과

대상환자

Atorvastatin 50
가
1 (1/50, 2%) ,
가 3 (3/50, 6%)
가 가 46 . 4
LDL - C 가 130 mg/dl 20 mg
2 (2/46, 4.3%) ,

Table 2. The changes of lipid profiles during treatment

		- 4 week	- 2 week	0 week	4 week	8 week
LDL-C	mg/dl	186.50 ± 3.37	183.36 ± 3.92	182.19 ± 3.41	99.74 ± 2.90	103.00 ± 2.37
TC	mg/dl	269.20 ± 3.69	262.57 ± 4.69	259.74 ± 3.63	175.04 ± 2.97	177.89 ± 3.02
HDL-C	mg/dl	51.00 ± 1.59	48.89 ± 1.67	46.07 ± 1.38	50.09 ± 1.73	52.02 ± 1.74
TG	mg/dl	158.46 ± 9.21	151.57 ± 8.29	157.41 ± 7.95	126.07 ± 8.64	114.35 ± 6.10
L/H-C		3.83 ± 0.14	3.92 ± 0.14	4.11 ± 0.14	2.12 ± 0.11	2.07 ± 0.08
ApoB	mg/dl			139.06 ± 2.58	87.45 ± 2.19	88.54 ± 1.04

Values are mean ± standard error L/H-C : LDL-C/HDL-C

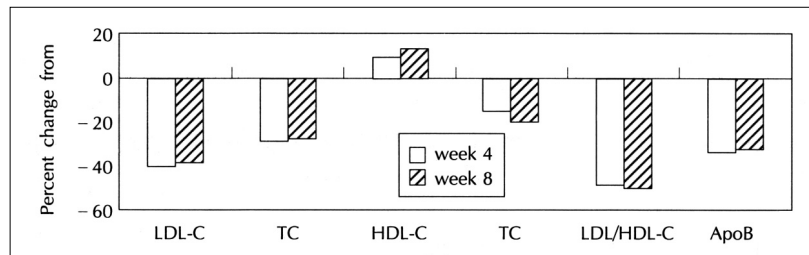


Fig. 2. Mean percent changes of serum lipid level during treatment.

10 mg 44 (44/46, 95.7%)
 54 (54.7 ± 1.4) (: 34, :
 73) 23 : 23 .
 유효성 46 , 4 LDL - C
 가 130 mg/dl 44
 95. 6% , 8 LDL - C 130
 mg/dl 42 91.3%
 LDL - C 182.3 ± 3.4
 mg/dl , 4 LDL - C 99.7 ± 2.9
 mg/dl 0 4 LDL - C
 - 44.8 ± 1.6% (p<
 0.05) 8 LDL - C 103 ± 2.4 mg/dl
 0 8 LDL - C - 43.0
 ± 1.4% (p<0.05, Table
 2, Figs. 2 and 3). 4 TC, TG,
 HDL - C, Apo B, LDL/HDL - C
 - 32.3 ± 1.3%, - 17.4 ± 4.6%, 9.6 ± 2.9%, - 36.6 ±
 1.6%, - 48. 5 ± 1.8%
 (p<0.05), 8 TC,
 TG, HDL, Apo B, LDL/HDL - C
 - 31.3 ± 1.0%, - 22.6 ± 4.1%, 13.7 ± 2.8%, - 35.9
 ± 1.3%, - 48.8 ± 1.6%

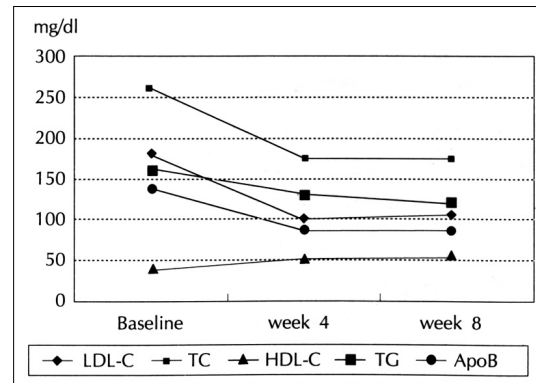


Fig. 3. Changes of serum lipid levels with atorvastatin therapy.

(p<0.05, Table 2, Figs. 2 and 3).

약제의 안전성

ALT, AST가 3
 (0%), CPK가
 10
 (0%). 8
 3 , 2 , 2 , 1

고 찰

atorvastatin 37% lovastatin
29% TC TG
statin atorvastatin
16-19) atorvastatin
HDL - C statin 가
1%
가 2%
6-8)
15% 9)
LDL - C
HMG - CoA
10-12) HMG - CoA
가 가
가 HMG - CoA
(mevalonic acid)
(LDL rece -
ptor) 가 가
LDL - C VLDL
lovastatin, pra -
vastatin, simvastatin, fluvastatin ato -
rvastatin atorvastatin lovastatin
simvastatin prodrug fluvastatin
pravastatin (active drug)
가 4) Atrovastatin
LDL - C 10 mg 80
mg 25% 60% LDL - C
13) Atrovastatin statin
LDL - C
HMG - CoA
14) atorvastatin
statin 15)
simvastatin LDL
atorvastatin LDL - C 가 VLDL LDL
46% simvastatin 27% atorvastatin
15-17) pravastatin atorva - 20 80
statin 35%, pravastatin 25% pravastatin mg 26% 46% TG 가
18) Lovastatin 21) 8

23% atorvastatin 10 20 mg fenofibrate 300 mg, 300 3000 mg atorva - stin TC, LDL - C, Apo B fenofibrate, ²²⁾ TG HDL - C fe - nofibrate LDL - C TG HMG - CoA

가 , atorvastatin TG atorvastatin 8 atorvastatin TC 259.7 mg/dl 177.8 mg/dl 31% LDL - C 182.2 mg/dl 103.0 mg/dl 43% TG 23% HDL - C 13% 가 stin

TC 20% 35% , LDL - C 27% 46% , TG 가 11% atorvastatin stin LDL - C 가 , TG Atorvastatin ²³⁻²⁶⁾ (, , ,) , , stin ⁴⁾ , 5 (3 , 2) , 1 , 2 atorvastatin ALT, AST 가 3 CPK가 10 Atorvastatin ato - ravastatin

2% 가 , stin .⁵⁾ 가 , , , 0.7% 가 3 16 . Atorvastatin stin 가 0.7% , 1% simvastatin, 1.1% fluvastatin, 1.9% lovastatin, 1.3% prava - stin ²⁷⁻²⁸⁾

요 약

연구배경 : 가 HMG - CoA atorvastatin 가 .

방 법 : 12 LDL - C 가 145 mg/dl 250 mg/dl TG가 400 mg/dl(4.5 mmol) 4 . 4 12 LDL - C 가 145 mg/dl 250 mg/dl TG가 400 mg/dl(4.5 mmol) atorvastatin 10 mg 4 Atorvastatin 10 mg 4 LDL - C 가 130 mg/dl 20 mg 8 .

결 과 : 1) 46 (: =23 : 23, 54) . 2) 4 , LDL - C 가 130 mg/dl 44 95.6% 8 42 91.3% . 3) (182.3 ± 3.4 mg/dl) 4 (99.7 ± 2.9 mg/dl) LDL - C - 44.8 ± 1.6% (p<0.05), 8 (103 ± 2.4 mg/dl) LDL - C - 43.0 ± 1.4% (p<0.05).

4) 4 TC, TG, HDL, Apo B,
LDL/HDL - C - 32.2 ± 1.3%,
- 17.4 ± 4.6%, 9.6 ± 2.9%, - 36.6 ± 1.6%, - 48.5 ± 1.
8% (p<0.

05), 8 TC, TG, HDL, Apo B, LDL/ HDL - C
- 31.3 ± 1.0%, - 22.6 ± 4.1%,
13.7 ± 2.8%, - 35.9 ± 1.3%, - 48.8 ± 1.6%
(p<0.05).

5) ALT/AST가 3
(0%) CPK가
10
(0%).

6) 8
3, 2, 2, 1

결 론 :

atorvastatin
가

중심 단어 : Atorvastatin · LDL -

감사문

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