Efficacy and Safety of Atorvastatin 10 mg Every Other Day in Hypercholesterolemia

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Abstract

Objectives : The authors sought to evaluate the safety and efficacy of atorvastatin administered every other day in patients with hypercholesterolemia.

Background : Statins have efficacy in lowering cholesterol and reducing cardiovascular events but their cost is a major disadvantage. Atorvastatin is the most potent statin and has a long half-life. Therefore, atorvastatin given on alternate days may be reasonable and cost effective, particularly in hypercholesterolemia patients.

Method and Result : Sixty patients with hypercholesterolemia despite diet therapy were enrolled into the study. They received atorvastatin 10 mg every other day before bedtime. Duration of treatment was 8 weeks. A lipid profile was determined as baseline, at 4 weeks and again at 8 weeks. Atorvastatin every other day significantly reduced total cholesterol (TC), triglyceride (TG), and LDL-c *versus* baseline. The TC, TG, and LDL-c levels were lower by 23 per cent, 8 per cent, and 30 per cent. Increase in HDL-c level was not statistically significant. Three patients had drug side effects. One patient had increased serum transaminase and one patient had increased serum muscle enzyme. The other one had somnolence.

Conclusions : In hypercholesterolemia patients, atorvastatin 10 mg every other day is safe and effective in lowering TC, TG, with LDL-c and a slight increase in HDL-c.

Key word : Atorvastatin, Hypercholesterolemia, Efficacy

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Statin has been proven to be effective in lowering cholesterol, preventing coronary heart disease in asymptomatic individuals[1,2] and preventing recurrent events in coronary heart patients [3,4]. Due to the efficacy, statin should be the drug of choice for hyperlipidemia treatment but usage is limited due to the cost. Atorvastatin is very potent with the longest half-life[5,9]. Plasma half-life of Atorvastatin is 14 hours and hydroxy-methylglutaryl coenzyme A (HMG-CoA) inhibitory half-life is 30 hours[9]. Ten-milligrams of atorvastatin daily can reduce total cholesterol by 28 per cent, low-density lipoprotein cholesterol by 37 per cent, triglyceride by 10-20 per cent and increases high-density lipoprotein cholesterol by 4-8 per cent[5-8]. The objective was to determine the efficacy and safety of atorvastatin 10 mg administered every other day in patients with hypercholesterolemia.

METHOD

Study Design

Patients aged 40 to 70 years who met lipid inclusion criteria. The inclusion criteria were: total cholesterol (TC) 213-310 mg/dl, low-density lipoprotein cholesterol (LDL-c) 100-190 mg/dl, and triglycerides 400 mg/dl or less. The exclusion criteria were: secondary hypercholesterolemia, unstable angina, planned coronary artery bypass graft or coronary angioplasty, acute myocardial infarction less than 6 months, congestive heart failure, impaired hepatic and renal function, and hypersensitivity to HMG-CoA reductase inhibitors. Participants were given dietary advice for 4 weeks. After that a 12-hour fasting blood was drawn and was sent to the central laboratory for lipid analysis. If serum lipid met the inclusion criteria, the patient would be assigned to treatment with atorvastatin 10 mg every other day at bedtime for 8 weeks and a second blood test for lipid analysis was done.

Statistics

Statistical analysis was performed by SPSS software. Continuous normally distributed data were expressed as mean ± SD and were compared by Student's *t*-test. A 2-side p value < 0.05 was to be considered statistically significant.

RESULTS

From July 1999 to November 2000, 67 patients were recruited, only 60 patients fulfilled the entry criteria and complied with the dietary advice. Seven patients were excluded because their cholesterol levels were at NCEP guidelines. Patients and lipid profiles after diet control period are shown in Tables 1 and 2. After 8 weeks of therapy with atorvastatin 10 mg every other day, total cholesterol was reduced on average by 23 per cent, LDL-c by 30 per cent, and triglycerides by 8 per cent, whereas high-density lipoprotein cholesterol (HDL-c) rose by 2 per cent (Table 3). Three patients had adverse events, 1abnormal liver profile, 1 increasing muscle enzyme, and 1somnolence. One patient withdrew from the study due to somnolence.

DISCUSSION

This study demonstrated that atorvastatin 10 mg every other day reduced LDL-c by approxi-

Table 1. Baseline characteristics of the patients.

	N=60	%
Male	28	47
Age, year	55 ± 11	
Hypertension	32	53
Coronary heart disease	14	23
Diabetes mellitus	9	15
Other therapy		
Aspirin	31	52
Beta-blockers	14	23
ACE inhibitors	16	27
Calcium antagonists	15	25

Table 2. Lipid components after diet control.

	-4 weeks (n=60)	0 week (n=60)	P
Total cholesterol (mg/dl)	271 ± 35	269 ± 39	0.52
Triglyceride (mg/dl)	160 ± 72	183 ± 32	0.67
HDL-c (mg/dl)	52 ± 13	54 ± 12	0.82
LDL-c (mg/dl)	176 ± 32	178 ± 35	0.06

Table 3. Lipid components after treatment.

	0 week (n=51)	8 week (n=51)	P
Total cholesterol (mg/dl)	270 ± 41	206 ± 36	< 0.001
Triglyceride (mg/dl)	191 ± 140	155 ± 86	0.01
HDL-c (mg/dl)	54 ± 12	55 ± 13	0.10
LDL-c (mg/dl)	177 ± 36	121 ± 34	< 0.001

mately 30 per cent and total cholesterol approximately 23 per cent. The results from the multicenter placebo-controlled trial in which atorvastatin 10 mg was given daily reduced LDL-c by approximately 34 per cent and total cholesterol by approximately 27 per cent[6-10].

It appears that atorvastatin has a long duration of action (20 to 30 hours with active metabolites) and is lipophilic[5,9]. Other statins have a maximum half-life of about 3 hours. From an animal study[11], atorvastatin appears to be a tissue-selective inhibitor of HMG-CoA reductase, with primary action in the liver. Atorvastatin enters the membrane of the endoplasmic reticulum (where HMG-CoA reductase resides) in hepatocytes (the site of cholesterol synthesis). By inhibiting HMG-CoA reductase, atorvastatin reduces hepatic cholesterol synthesis and promotes an upregulation of hepatic LDL receptors and hepatic apoB/E receptors[11]. Due to the long duration of action, atorvastatin limits the availability of cholesterol for assembly apoB-containing lipoproteins in the liver.

Poor compliance is the major problem when prescribing the medication every other day but from this study, it was found that patients were able to comply very well with the regimen. After three patients who had abnormal liver function, muscle enzyme, and somnolence stopped the drug, their abnormal laboratory tests and somnolence were improved.

This regimen can save costs by half by giving atorvastatin 10 mg every other day which was able to reduce LDL-c by 30 per cent and total cholesterol by 23 per cent.

It was concluded that atorvastatin 10 mg every other day is effective and may be comparable to an equivalent dose administered every day in reducing LDL-c and total cholesterol in patients with hypercholesterolemia.

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การศึกษาประสิทธิภาพและความปลอดภัยในการใช้ยาอะทอวาสแตติน 10 มก. วันเว้นวันในผู้ป่วยไขมันในเลือดสูง

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Statin เป็นกลุ่มยาลดระดับคลอเรสเตอรอลที่มีประสิทธิภาพ สามารถลดระดับคลอเรสเตอรอลได้ 28% ระดับแอล.ดี.แอลได้ 37% ระดับไตรกลีเซอไรด์ได้ 10–20% และสามารถเพิ่มระดับ เอช.ดี.แอล ได้ 4–8% ซึ่งสามารถลดอุบัติการของโรคหลอดลเอดหัวใจได้ทั้งในคนที่เคยหรือไม่เคยมีอาการมาก่อน

วัตถุประสงค์ : เพื่อศึกษาถึงประสิทธิภาพและความปลอดภัยของยา Atorvastatin 10 มก. วันเว้นวัน

วิธีการและผลการศึกษา : ทำการศึกษาผู้ป่วยระดับคลอเรสเตอรอลสูง 60 รายที่ไม่สามารถลดได้โดยการควบคุมอาหาร ให้ยาอะทอวาสแตติน 10 มก. วันเว้นวันก่อนนอนเป็นเวลา 8 สัปดาห์ วัดระดับของไขมันในเลือดก่อนและหลังได้รับยา พบว่า สามารถลดระดับ คลอเรสเตอรอล, ไตรกลีเซอไรด์ และ แอล.ดี.แอล ได้ 23%, 8% และ 30% ผลข้างเคียงมีระดับของเอนไซม์กล้ามเนื้อและเอนไซม์ตับเพิ่มขึ้นอย่างละ 1 ราย ส่วนอีก 1 ราย มีอาการง่วงซึม

สรุป : ยา อะทอวาสแตติน 10 มก. วันเว้นวันสามารถลดระดับไขมันในเลือดได้อย่างมีประสิทธิภาพและปลอดภัย

คำสำคัญ : ไขมันในเลือดสูง, อะทอวาสแตติน, วันเว้นวัน

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