Weekly Versus Daily Dosing of Atorvastatin

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Twenty-four consecutive patients of a single family physician who had achieved NCEP-II goal levels of low-density lipoprotein cholesterol (LDL-C) on a daily atorvastatin dose of 10 mg for at least 6 months were invited to switch to 20 mg weekly. Mean LDL levels for the 22 patients who completed the trial had been reduced by 43% from baseline on 10 mg daily ($P < .05$) and were reduced by 22% from baseline on the seventh day following the last weekly dose of 20 mg ($P < .05$). Total cholesterol to high-density lipoprotein cholesterol (TC/HDL-C) ratios were reduced by 31% and 17%, respectively (both $P < .05$) and triglycerides by 20% and 10% (both $P < .05$).

■ KEY WORDS Atorvastatin; weekly dosing; hyperlipidemia; cost-effectiveness. (*J Fam Pract 2002; 51:365-366*)

Atorvastatin is a potent antihyperlipidemic but is quite expensive, costing up to $700 for a 1-year supply of 10-mg tablets in retail pharmacies. Weekly dosing has the potential to lower costs and increase convenience while maintaining a similar effect on lipids. The active metabolites have a serum half-life of 11 to 57 hours,[1-4] acting on a target that responds slowly to intervention. Furthermore, atorvastatin demonstrates prolonged inhibition of HMG-CoA reductase compared with other statins, presumably because of longer residence of the drug or its metabolites in the liver.[5] Two abstracts of meeting presentations have reported efficacy for alternate-day dosing on small patient samples,[1,2] but no reported attempts have been made to test longer dosing intervals. The purpose of this pilot study was to investigate the effect of weekly dosing of atorvastatin on patients who were currently well controlled on daily doses of the drug.

METHODS

Selection of Patients

Twenty-four consecutive patients presenting for routine follow-up in a private clinical practice whose LDL-C levels exceeded National Cholesterol Education Program (NCEP-II) guidelines[6] on 2 occasions and who had successfully met their goals on 10 mg atorvastatin daily were offered a 12-week trial of 20 mg atorvastatin weekly. All 24 patients gave written informed consent, although one changed his mind and never altered his dosing and another experienced headaches after taking the first 20-mg dose and reverted to a regimen of 10 mg daily.

Study Protocol

Study participants were instructed verbally and in writing to make no special efforts to change their lifestyle as a result of their involvement. The potential skewing effect of such efforts on research was explained. If they were already intending to alter their diet or exercise levels, this was acceptable. They were to take atorvastatin at the usual time of day on a day of the week that seemed most convenient. If they forgot a dose, it was to be taken the next day. Compliance with weekly dosing was assessed at each contact by explicit questioning. Fasting chemical and lipid profiles were available on patients' charts; for purpose of analysis, the last profile before initiation of any statin therapy was used as the pretreatment baseline and the last profile on 10 mg atorvastatin daily as the treatment baseline. Profiles were repeated with the patient fasting on the seventh day after the last 20-mg dose before that dose was repeated.

TABLE 1
BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS

Characteristic	Number
Male / female	12 / 10
Comorbidity	
Hypertension	9
Type 2 diabetes mellitus	4
Hepatitis C	1
Coronary artery disease	2
Smoking	2
Mean age in years (range)	54 (42–72)

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TABLE 2

RESPONSE OF LIPID PARAMETERS TO DAILY AND WEEKLY DOSING WITH ATORVASTATIN

	Pretreatment	10 mg Daily	20 mg Weekly
LDL-C mg/dL	178	101 *†	138 *
HDL-C mg/dL	46	46	48
Triglycerides mg/dL	174	139 *	157 *
Total cholesterol mg/dL	259	175 *†	218 *
Total cholesterol/HDL-C ratio	5.8	4.0 *†	4.8 *
AST U/L	28	28	22

* P < .05 vs pretreatment. † P < .05 vs 20 mg weekly.
Conversion factors:
LDL-C, HDL-C, TC: (mg/dL) x (.026) = SI mmol/L
Triglycerides: (mg/dL) x (.011) = SI mmol/L
AST denotes aspartate aminotransferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SI, Système Internationale.

Statistical Analysis

The data were analyzed with repeated measures ANOVA followed by a Student–Newman–Kuels post hoc test to determine differences between specific treatments. Differences with a 2-tailed *P* value of less than .05 were considered statistically significant.

RESULTS

Baseline Characteristics

Table 1 presents the baseline characteristics of participants. The average age was 54 years (range 42 to 72 years). There were 12 men and 10 women. Thirteen subjects had comorbid conditions (9 hypertension, 4 type 2 diabetes, 1 hepatitis C, 2 coronary artery disease, and 2 tobacco use).

Cholesterol Reduction

Results for LDL-C, HDL-C, triglycerides, TC, TC/HDL-C ratio, and aspartate aminotransferase (AST) are summarized in Table 2. LDL levels fell 43% and 22%, respectively, on daily and weekly dosing; HDL-C levels were essentially unchanged; triglycerides fell 20% and 10%; TC, 33% and 16%; TC/HDL-C, 31% and 17%; and AST, 0% and 21%.

Adverse Reactions

The only reported adverse reaction from doubling the dose of atorvastatin was headache in the patient who dropped out for that reason. No attempt was made to repeat the higher dose to see if this reaction was replicable. No subjects reported myalgias. The mean AST actually dropped on weekly dosing. One patient who had hepatitis C and was in clinical remission experienced a fall in pretreatment AST on daily dosing and a further reduction on weekly dosing.

DISCUSSION

With pharmaceutical costs leading medical inflation, a current challenge for clinicians is to alter the cost-benefit ratio of prescriptions to the advantage of patients. Weekly dosing, as has recently been approved for alendronate sodium (Fosamax) and fluoxetine hydrochloride (Prozac), is one approach to this problem. In this preliminary study, weekly dosing of 20 mg atorvastatin resulted in a 22% reduction of LDL-C, measured on the seventh day after dosing. This regimen represents an approximately 80% reduction in yearly cost compared with that of a regimen of 10 mg daily.

Since this study did not investigate the pattern of LDL-C reduction in the interval between doses, further research is needed to delineate the area under the curve and the impact on clinical outcomes before conclusions may be drawn regarding the effectiveness of weekly dosing.

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