Lovastatin and Coadministered Antihypertensive/Cardiovascular Agents

James L. Pool, Charles L. Shear, Maria Downton, Harold Schnaper, Sandra Stinnett, Carlos Dujovne, Reagan H. Bradford, and Athanassios N. Chremos

Hypertension and hypercholesterolemia frequently coexist and may require concomitant drug treatments. The efficacy and safety profile of lovastatin given in the presence of antihypertensive medication was evaluated using patient subgroups identified in the Expanded Clinical Evaluation of Lovastatin (EXCEL) Study. The EXCEL study examined 8,245 patients with moderate hypercholesterolemia randomly assigned either to a group treated with lovastatin (20–80 mg daily) or to a group given placebo for 48 weeks. After adjustment for patient characteristics, pairwise comparisons were made between patients taking no antihypertensive agents (n=3,772) and those taking either calcium antagonists (n=446), selective ß1-adrenergic receptor blockers (n=326), nonselective ß-adrenergic receptor blockers (n=219), potassium-sparing diuretics (n=187), thiazide diuretics (n=126), or angiotensin converting enzyme inhibitors (n=171). The placebo-corrected dose-dependent effect of lovastatin on the percent change from baseline in low-density lipoprotein cholesterol was not attenuated in any subgroup and was slightly enhanced in the calcium antagonist subgroup (−29% to −44%, p=0.06) when compared with patients taking no antihypertensive agents (−24% to −40%); this difference, however, was only of borderline significance. Patterns of lovastatin-induced increase in high-density lipoprotein cholesterol and decrease in triglycerides were not consistently different among the subgroups. Examination of mean changes in serum transaminases, mean changes in creatine kinase, and the proportion of patients discontinuing therapy for clinical adverse experiences did not indicate the presence of an interaction. In conclusion, there was no evidence for an attenuation of the lovastatin-induced changes in lipids and lipoproteins or of an alteration in the safety profile of lovastatin when administered concurrently with commonly used antihypertensive agents. (Hypertension 1992;19:242–248)

KEY WORDS • hypercholesterolemia • essential hypertension • lipids • antihypertensive therapy

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Hypertension and hypercholesterolemia are major risk factors in the pathogenesis of coronary heart disease (CHD).1 These two risk factors coexist in patients more frequently than would be expected by chance alone,2,3 and a syndrome of dyslipidemic hypertension has been identified.4 The National Health and Nutrition Examination Survey II found that 40% of persons with hypertension have elevated total cholesterol levels (240 mg/dl or more).5 Certain classes of antihypertensive agents have adverse effects on plasma concentrations of lipids and lipoproteins.5 These adverse lipid changes may be partially responsible for the less than anticipated reduction in incidence of CHD associated with antihypertensive treatment.6

With the advent of the potent and well-tolerated 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors,7 pharmacological therapy for hypercholesterolemia has become more prevalent.8 As a result, it will be commonplace for hypertensive patients who have high total and low density lipoprotein (LDL) cholesterol levels to be coadministered an HMG-CoA reductase inhibitor and antihypertensive agents. It is therefore important to evaluate potential interactions between these compounds. In this report, the efficacy and safety profile of lovastatin in the presence of antihypertensive medication was evaluated using patient subgroups identified in the Expanded Clinical Evaluation of Lovastatin (EXCEL) Study.9

Methods

Details of the study design, methods, baseline patient characteristics,9 and basic results10–13 of the EXCEL study have been presented elsewhere. In summary, the EXCEL study evaluated the efficacy and safety profiles of lovastatin using a diet- and placebo-controlled, randomized, double-blind design. After a minimum of 4 weeks on a cholesterol-lowering diet, 8,245 patients with moderate hypercholesterolemia (total cholesterol 6.21–7.76 mmol/l [240–300 mg/dl]; LDL cholesterol 4.14
Excluded from the analyses were antihypertensive medication classes with a patient size of less than 100. These included α-adrenergic receptor blockers, β-adrenergic receptor blockers with intrinsic sympathomimetic activity, agents primarily exhibiting central nervous system activity, loop and other diuretics, and primary vasodilators (n=244). Also excluded from analyses were patients taking more than one class of the above mentioned medications (n=1,998), those who had stopped taking medication or switched medication classes during the course of the trial (n=444), or those with no postrandomization lipid determinations (n=57).

Statistical Analyses

Efficacy analyses. Modification of the efficacy profile of lovastatin by the use of a concurrent antihypertensive agent was assessed using separate linear statistical models for LDL cholesterol, high density lipoprotein (HDL) cholesterol, and triglycerides. The percent change from baseline for each efficacy parameter was used as the dependent variable in each of the models. Treatment group was included as an independent variable in each model as were patient characteristics (covariates) previously identified as statistically important in altering lovastatin-induced changes in lipids.14 The patient characteristics included in those analyses consisted of baseline demographic, medical, biochemical, and health habit descriptors; treatment observations were also evaluated and included weight change, change in self-reported dietary compliance, self-reported study drug compliance, and self-reported fasting at the time of a lipid/lipoprotein measurement. The current analyses built on those previous statistical models14 by altering their structure to include the additional effects for antihypertensive agents. Antihypertensive agent subgroups were included using "modular" coding of the design matrix in which the general intercept was eliminated from the model and was replaced by antihypertensive group-specific treatment terms. Deviations from means coding (effect coding) were used for treatment effects and for the (k-1) levels of each categorical covariate. Continuous covariates were centered at their mean values.

Since previous analyses identified race-by-treatment interactions,14 inclusion of data for nonwhites would have required such an interaction term in the models. Substantial problems with multicollinearity arising from the disparity in sizes of the racial groups (96% were white) would have resulted. In addition, for nonwhites classification by race and hypertensive treatment group led to very small cell sizes and, therefore, very low power to detect interactive drug effects. Consequently, only the data for white patients with active treatment period lipid/lipoprotein measurements (n=4,892) were considered in the efficacy analyses.
The validity of the statistical models was assessed with standard diagnostic techniques to assess multicollinearity in the regressors and effects of hyperinfluential observations. The models were found to be robust with respect to these potential problem areas and were retained for computation of estimates of the treatment means for each antihypertensive subgroup.

These models were used to test whether an antihypertensive agent enhanced or decreased the effect of lovastatin on LDL cholesterol, HDL cholesterol, or triglycerides. Specifically, statistical tests were performed to assess the extent that the lovastatin effect in each of the six antihypertensive agent subgroups differed from the lovastatin effect in the no antihypertensive agent subgroup. Means, adjusted to average values of covariates, were computed for each combination of antihypertensive agent subgroup and treatment (dose) group. Linear combinations of these adjusted means were used to test hypotheses. For each of the six antihypertensive subgroups, the overall antihypertensive agent subgroup-by-treatment interaction was tested to assess whether the four placebo-adjusted treatment effects in a specific antihypertensive agent subgroup were the same as the corresponding four effects in the no antihypertensive agent subgroup. Since this overall interaction test contained four degrees of freedom, it was partitioned into four more directed, one-degree-of-freedom components. Each of these four components was evaluated by comparing separately the six antihypertensive agent subgroups with the no antihypertensive agent subgroup. Since this overall antihypertensive agent subgroup-by-treatment interaction assessed the equivalence of the placebo-adjusted treatment effect, averaged over the four lovastatin doses; 2) the linear component of the antihypertensive agent subgroup-by-treatment interaction assessed the equivalence of the straight line component of the lovastatin dose-response relation; 3) the quadratic component of the antihypertensive agent subgroup-by-treatment interaction assessed the equivalence of the curvature (quadratic) component of the lovastatin dose–response relation; and 4) comparison of the 40-mg/day regimens component of the antihypertensive agent subgroup-by-treatment interaction assessed the equivalence of the difference between the effect of the 40-mg once daily dose and the 20-mg twice daily dose.

Safety analyses. Safety analyses centered on identifying differences among subgroups in the two laboratory abnormalities known to be associated with lovastatin therapy: increased serum transaminases (alanine aminotransferase [ALT] and aspartate transaminase [AST]) and creatine phosphokinase (CPK) levels. The mean difference in the change from baseline to the end of therapy for the no antihypertensive agent subgroup versus each of the six monotherapy subgroups was calculated for these laboratory parameters. Differences in which the 95% confidence interval did not overlap zero were considered statistically significant. Whites and nonwhites were included in these analyses. In addition, as a screening procedure to identify other potential tolerability differences among subgroups, the proportion of patients discontinuing therapy due to clinical adverse experiences in each of the six antihypertensive agent subgroups was compared with that of the no antihypertensive agent subgroup by using the Cochran-Mantel-Haenszel test and stratifying by treatment group.

Results

Patient Subgroup Characteristics

Baseline demographic and laboratory characteristics of the subgroups are shown in Table 1. The average age of patients was 57 years; patients taking antihypertensive agents were from 1 to 6 years older than those not taking medication. All subgroups were predominantly white; however, greater proportions of nonwhites and women were represented in the two diuretic subgroups than in the other subgroups. A history of CHD was reported in a majority of patients taking calcium antagonists (77%) or β-blockers (53%) compared with 19% or less of patients in the other subgroups. Hypertension was reported as a preexisting condition in only 34–64%
of patients in the calcium antagonist or β-blocker
subgroups compared with 83% or more of the patients
in the other subgroups taking antihypertensive agents.
The hypertension and CHD history differences among
the monotherapy subgroups probably reflect the indica-
tions for which these agents were primarily prescribed.

At baseline, average levels of LDL cholesterol and
triglycerides were similar among the subgroups,
whereas HDL cholesterol was increased among the two
diuretic subgroups, indicative of the greater proportion
of women in these two subgroups.

**Lipids and Lipoproteins**

For patients in the no antihypertensive agent sub-
group, a dose-dependent decrease in LDL cholesterol
was observed, ranging from 24% at 20 mg once daily to
40% at 40 mg twice daily (after correcting for placebo)
in the lovastatin treatment groups (Table 2). A slightly
greater decrease was also seen in the subgroup taking ACE inhibitors; the placebo-corrected
dose-dependent mean percent reduction for these pa-
tients ranged from 29% to 47% in the lovastatin treat-
ment groups (p = 0.071 for overall treatment interac-
tion). A major contributor to the enhanced decrease
found in the ACE inhibitor subgroup was the unexpected
ly large (3.9%) increase in LDL cholesterol for its
placebo group. No consistent differences in LDL cho-
esterol reduction were noted in the other subgroups.

The structure of the antihypertensive agent sub-
group-by-treatment interaction was partitioned into the
four components described in "Methods": 1) averaged-
over-dose component, 2) linear component, 3) quad-
artic component, and 4) comparison of 40-mg/day
regimens component. For LDL cholesterol, the aver-
aged-over-dose component was highly significant
(p = 0.005) for the calcium antagonist subgroup, margin-
ally significant (p = 0.09) for the ACE inhibitor sub-
group, and not significant (p > 0.60) for the other sub-
groups. The linear and quadratic components were
nonsignificant (p > 0.20), indicating that the marginal
enhancement in the calcium antagonist and ACE inhib-

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**Table 2. Low-Density Lipoprotein Cholesterol: Adjusted Mean Percent Change From Baseline for Antihypertensive Agent Subgroups by Lovastatin Treatment Group**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo</th>
<th>20 qpm</th>
<th>40 qpm</th>
<th>20 bid</th>
<th>40 bid</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No antihypertensive agents</td>
<td>+0.9(672)</td>
<td>-23.0(692)</td>
<td>-29.8(720)</td>
<td>-33.0(713)</td>
<td>-39.4(721)</td>
<td></td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>+1.2(71)</td>
<td>-27.4(82)</td>
<td>-32.6(87)</td>
<td>-36.9(73)</td>
<td>-43.2(116)</td>
<td>0.060</td>
</tr>
<tr>
<td>Selective β-blockers</td>
<td>-0.2(75)</td>
<td>-24.2(57)</td>
<td>-29.9(64)</td>
<td>-34.9(67)</td>
<td>-42.6(48)</td>
<td>0.631</td>
</tr>
<tr>
<td>Nonselective β-blockers</td>
<td>-0.0(42)</td>
<td>-23.9(45)</td>
<td>-31.5(42)</td>
<td>-34.2(44)</td>
<td>-38.4(36)</td>
<td>0.836</td>
</tr>
<tr>
<td>Potassium-sparing</td>
<td>+0.2(30)</td>
<td>-24.4(35)</td>
<td>-28.6(27)</td>
<td>-32.0(32)</td>
<td>-40.5(38)</td>
<td>0.795</td>
</tr>
<tr>
<td>Diuretics</td>
<td>-0.0(20)</td>
<td>-24.0(18)</td>
<td>-29.9(18)</td>
<td>-36.3(19)</td>
<td>-38.4(17)</td>
<td>0.786</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>+3.9(28)</td>
<td>-25.1(29)</td>
<td>-28.5(39)</td>
<td>-35.3(38)</td>
<td>-42.9(28)</td>
<td>0.071</td>
</tr>
</tbody>
</table>

Values are adjusted for covariates (see text and Reference 14). qpm, Once daily in the evening; bid, twice daily,
morning and evening; ACE, angiotensin converting enzyme.

*Comparison with no antihypertensive agents group. Test is for overall antihypertensive agent subgroup-by-
treatment interaction (degrees of freedom equal 4).

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**Table 3. High-Density Lipoprotein Cholesterol: Adjusted Mean Percent Change From Baseline for Antihypertensive Agent Subgroups by Lovastatin Treatment Group**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo</th>
<th>20 qpm</th>
<th>40 qpm</th>
<th>20 bid</th>
<th>40 bid</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No antihypertensive agents</td>
<td>+1.5(660)</td>
<td>+6.4(678)</td>
<td>+6.0(706)</td>
<td>+7.9(699)</td>
<td>+9.2(706)</td>
<td></td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>+0.3(67)</td>
<td>+5.3(81)</td>
<td>+7.7(78)</td>
<td>+7.2(73)</td>
<td>+9.3(114)</td>
<td>0.480</td>
</tr>
<tr>
<td>Selective β-blockers</td>
<td>+2.4(75)</td>
<td>+5.3(56)</td>
<td>+6.5(65)</td>
<td>+6.7(66)</td>
<td>+9.6(47)</td>
<td>0.797</td>
</tr>
<tr>
<td>Nonselective β-blockers</td>
<td>+0.0(42)</td>
<td>+3.4(44)</td>
<td>+4.2(42)</td>
<td>+7.7(43)</td>
<td>+9.9(36)</td>
<td>0.669</td>
</tr>
<tr>
<td>Potassium-sparing</td>
<td>+4.7(28)</td>
<td>+6.9(35)</td>
<td>+10.1(26)</td>
<td>+11.2(32)</td>
<td>+9.6(38)</td>
<td>0.594</td>
</tr>
<tr>
<td>Diuretics</td>
<td>+3.2(20)</td>
<td>+8.7(18)</td>
<td>+12.5(18)</td>
<td>+9.7(19)</td>
<td>+7.7(17)</td>
<td>0.376</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>+2.2(28)</td>
<td>+2.4(27)</td>
<td>+9.6(39)</td>
<td>+10.6(37)</td>
<td>+8.9(27)</td>
<td>0.095</td>
</tr>
</tbody>
</table>

Values are adjusted for covariates (see text and Reference 14). qpm, Once daily in the evening; bid, twice daily,
morning and evening; ACE, angiotensin converting enzyme.

*Comparison with no antihypertensive agents group. Test is for overall antihypertensive agent subgroup-by-
treatment interaction (degrees of freedom equal 4).
TABLE 4. Triglycerides: Adjusted Mean Percent Change From Baseline for Antihypertensive Agent Subgroups by Lovastatin Treatment Group

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo</th>
<th>20 qpm</th>
<th>40 qpm</th>
<th>20 bid</th>
<th>40 bid</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No antihypertensive agents</td>
<td>+5.9(675)</td>
<td>-7.3(692)</td>
<td>-10.8(721)</td>
<td>-14.0(714)</td>
<td>-17.5(722)</td>
<td>. . .</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>+12.5(71)</td>
<td>-8.5(82)</td>
<td>-14.8(81)</td>
<td>-14.8(73)</td>
<td>-15.0(116)</td>
<td>0.101</td>
</tr>
<tr>
<td>b-Selective b-blockers</td>
<td>+7.5(76)</td>
<td>-4.6(57)</td>
<td>-11.9(65)</td>
<td>-10.7(66)</td>
<td>-16.5(48)</td>
<td>0.886</td>
</tr>
<tr>
<td>Nonselective b-blockers</td>
<td>+11.7(43)</td>
<td>-6.4(45)</td>
<td>-14.0(42)</td>
<td>-13.1(44)</td>
<td>-17.7(36)</td>
<td>0.578</td>
</tr>
<tr>
<td>Potassium-sparing diuretics</td>
<td>+9.5(30)</td>
<td>-9.5(35)</td>
<td>-12.2(27)</td>
<td>-8.8(32)</td>
<td>-12.4(38)</td>
<td>0.586</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>+1.5(20)</td>
<td>-6.7(18)</td>
<td>-5.8(18)</td>
<td>-19.0(19)</td>
<td>-15.1(17)</td>
<td>0.673</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>+3.1(28)</td>
<td>+2.6(29)</td>
<td>-9.8(39)</td>
<td>-7.6(39)</td>
<td>-19.6(28)</td>
<td>0.192</td>
</tr>
</tbody>
</table>

Values are adjusted for covariates (see text and Reference 14). qpm, Once daily in the evening; bid, twice daily, morning and evening; ACE, angiotensin converting enzyme.

*Comparison with no antihypertensive agents group. Test is for overall antihypertensive agent-subgroup-by-treatment interaction (degrees of freedom equal 4).

Safety Analyses

In the no antihypertensive agent subgroup, patients' serum ALT levels decreased 2.0 units/l from baseline in the placebo group and increased 4.7 units/l in the lovastatin 40 mg twice daily group. The differences in mean change from baseline between the no antihypertensive agent subgroup and each monotherapy subgroup were similar for the placebo and lovastatin 40 mg twice daily treatment groups as indicated by the 95% confidence intervals, which overlapped zero in all instances except one (placebo patients in the thiazide diuretic subgroup) (Figure 2). Similar results were obtained for AST (data not shown).

In the no antihypertensive agent subgroup, the difference in mean change from baseline to end of therapy in CPK between the placebo and 40 mg twice daily groups was 9 units/l. This pattern was similar in most of the other subgroups, except for the much higher difference in the calcium antagonist and potassium-sparing diuretic subgroups (39 units/l and 35 units/l, respectively). However, all 95% confidence intervals for the differences between each monotherapy subgroup and the no antihypertensive agent subgroup overlapped zero, indicating no significant differences (Figure 3).

In the no antihypertensive agent subgroup, the percent of patients discontinuing therapy due to clinical...
adverse experiences ranged from 3.5% in the placebo group to 5.0% in the lovastatin 20 mg once daily group (Table 5). For the calcium antagonist subgroup, there was a tendency for decreasing discontinuations with increasing dose. No other subgroup showed a pattern of discontinuation that was consistently different from that of the no antihypertensive agent subgroup, and no statistically significant differences were detected.

**Discussion**

The analyses presented here from the EXCEL study of patients with moderate hypercholesterolemia document no attenuation in the lipid-altering efficacy of lovastatin when administered to patients being treated concurrently with frequently administered antihypertensive agents. Moreover, there appears to be no clinically important deterioration in the safety and tolerability profiles of lovastatin when taken with these antihypertensive agents. The recent absence of an effect on lovastatin is important when considering previously identified adverse effects of certain classes of antihypertensive agents on serum lipids and the less than expected reduction in CHD incidence that has been found in treated hypertensive patients.36,18,19

About 60 million adults in the United States have hypertension; a similar number have blood cholesterol levels above 240 mg/dl and may be considered candidates for medical intervention.3 Thus, millions of patients in the United States are likely to be treated concurrently with these agents. Unfortunately, there is currently a paucity of data on possible interactions between antihypertensive and cholesterol-lowering drugs. Interactions that are known to occur or are theoretically plausible include an attenuation of LDL cholesterol lowering with concomitant use of bile acid sequestrants and thiazide diuretics20; interference with the hypotensive action of several antihypertensive drugs when used concomitantly with nicotinic acid, aspirin, or nonsteroidal anti-inflammatory agents3; and a potential adverse effect of thiazide diuretics on hyperglycemia when given concurrently with nicotinic acid.3

The findings presented here should be interpreted conservatively since a number of limitations exist. The question addressed and the analyses performed were post hoc in nature and should be considered exploratory. The use of nonrandomized subgroups may have introduced potential confounding factors into the comparisons, although this was minimized for the efficacy

### Table 5. Patients Discontinuing the Study Because of Clinical Adverse Experiences for Antihypertensive Therapy Subgroups by Lovastatin Treatment Group

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo</th>
<th>20 qpm</th>
<th>40 qpm</th>
<th>20 bid</th>
<th>40 bid</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No antihypertensive agents</td>
<td>25 (3.5)</td>
<td>37 (5.0)</td>
<td>29 (3.8)</td>
<td>28 (3.7)</td>
<td>38 (4.9)</td>
<td>...</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>8 (10.1)</td>
<td>6 (7.1)</td>
<td>2 (2.4)</td>
<td>1 (1.3)</td>
<td>0 (0.0)</td>
<td>0.706</td>
</tr>
<tr>
<td>β-Selective β-blockers</td>
<td>0 (0.0)</td>
<td>2 (3.3)</td>
<td>6 (9.1)</td>
<td>0 (0.0)</td>
<td>1 (2.0)</td>
<td>0.248</td>
</tr>
<tr>
<td>Nonselective β-blockers</td>
<td>2 (4.3)</td>
<td>5 (10.9)</td>
<td>3 (7.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0.765</td>
</tr>
<tr>
<td>Potassium-sparing diuretics</td>
<td>0 (0.0)</td>
<td>1 (2.6)</td>
<td>3 (9.1)</td>
<td>1 (2.6)</td>
<td>2 (4.9)</td>
<td>0.769</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>1 (3.4)</td>
<td>1 (3.7)</td>
<td>1 (4.5)</td>
<td>1 (4.0)</td>
<td>1 (4.3)</td>
<td>0.922</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>0 (0.0)</td>
<td>3 (10.0)</td>
<td>1 (2.3)</td>
<td>3 (7.5)</td>
<td>1 (3.4)</td>
<td>0.710</td>
</tr>
</tbody>
</table>

qpm, Once daily in the evening; bid, twice daily, morning and evening; ACE, angiotensin converting enzyme.

*Comparison with no antihypertensive agents group.
analyses through statistical adjustment. The sample sizes in the subgroups varied widely, from 3,772 patients taking no antihypertensive medication to 126 patients taking thiazide diuretics; only one fifth of these numbers of patients were in each specific treatment group of the various subgroups. This wide variation in subgroup size led to differential ability to detect differences in the efficacy and safety parameters analyzed. For example, in Tables 2-4 the study had a power of 0.80 to detect a difference of size 4.9% (calcium antagonist subgroup) to 9.1% (thiazide diuretic) for LDL cholesterol, 5.6% (calcium antagonist and β-selective β-blocker subgroups) to 10.2% (thiazide diuretic subgroup) for HDL cholesterol, and 11.6% (calcium antagonist and β-selective β-blocker subgroup) to 21.6% (thiazide diuretic subgroup) for triglycerides. Finally, patients on multiple concurrent therapies for hypertension were excluded from these analyses to simplify data interpretation; therefore, a lack of effect on the efficacy and tolerability of lovastatin in these cases should not be inferred.

A slight enhancement in the reduction of LDL cholesterol, which was of borderline significance, was found in association with lovastatin when coadministered with calcium antagonists or ACE inhibitors. Further analyses of these effects suggested that the enhancement of the LDL cholesterol lowering found in the calcium antagonist subgroup consisted of a uniform and highly significant (p=0.005) effect when averaged across lovastatin dose groups, whereas the marginally significant findings in the ACE inhibitor subgroup were not uniform across dose and largely were influenced by the unexpected increase in the placebo group. Although these findings require validation as noted above, the additional lowering in LDL cholesterol found with calcium antagonists was small (3–5%) relative to the 24–40% lowering found with lovastatin alone. Assuming the effect observed was not spurious, potential biological mechanisms underlying an enhancement of the lovastatin effect in the presence of calcium antagonists are unknown.

In summary, with the previously mentioned limitations, the use of lovastatin concurrently with prevalent classes of antihypertensive agents appears to result in no major variation in the efficacy and safety profiles seen with lovastatin alone.

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References


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