Lercanidipine, Enalapril, and Their Combination in the Treatment of Elderly Hypertensive Patients

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Introduction

Several trials have shown that hypertensive patients whose blood pressure (BP) is brought under control (< 140/90 mmHg) have significantly fewer cardiovascular events than patients whose BP remains uncontrolled [1]. However, despite the availability of multiple antihypertensive drugs, BP is difficult to control, especially systolic BP and in elderly patients [2]. In most clinical trials aimed at controlling BP, more than two antihypertensive drugs are almost always required. The importance of combination therapy has been emphasized in current guidelines [3]. Adding a second antihypertensive drug may be a better option in non-controlled patients than switching to a different drug or increasing the dose of the first compound.

Aim

In this study, we tested the hypothesis that combination therapy with lercanidipine [4], a lipophilic dihydropyridine calcium antagonist with long duration of action, and enalapril [5] is more effective than either drug alone in reducing 24-h systolic BP in hypertensive elderly patients.

Methods

Patients aged 60–85 years with an office systolic BP (SBP) of 160–179 mmHg, an office diastolic BP (DBP) < 110 mmHg and a mean daytime SBP > 135 mmHg

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were included in the study. Patients with severe hypertension, diabetes mellitus, or prior cardiovascular events were excluded because the study design involved the administration of placebo for 4 weeks.

This was a randomized, double-blind, placebo-controlled, four-way crossover study, balanced for first-order carry-over. Four centers participated, two in Finland and two in Spain. After a 2-week run-in period, eligible patients were randomly assigned to receive a 4-week treatment with placebo (P); lercanidipine 10 mg (L); enalapril 20 mg (E); and a combination of the two drugs (L/E). All patients were scheduled to receive one of the four treatments. Double-blind medications were taken once-daily in the morning. At the end of each treatment period, office trough (24 ± 2 h post-dose) sitting blood pressure was measured. A 24-h ambulatory blood pressure monitoring (ABPM) was obtained on the last day of drug intake.

The primary efficacy parameter was the mean reduction in 24-h SBP of active treatment vs placebo. The 24-h SBP was chosen as the primary efficacy variable since the mean 24-h BP is the most solid information provided by ABPM.

Results

Of the 103 patients who were screened, 75 patients (40 males, 54%) with a mean age of 66 years were randomized to the study. Of these 75 patients, 71 received P, 69 L, 70 E and 72 L/E. The intention to treat (ITT) population consisted of 72 patients of which 62 patients completed the four ABPMs foreseen after randomization. Mean seated office BP was 168/92 mmHg. Mean baseline 24-h SBP was 151 mmHg. The administration of P, L, E and L/E was associated with a mean 24-h SBP of 144, 137, 133, and 127 mmHg, respectively (Fig. 1). Compared to the mean 24-h SBP reduction observed with P, active antihypertensive therapy significantly decreased the mean 24-h SBP by a mean of 8.2 (L), 12.9 (E), and 17.9 (L/E) mmHg ($p < 0.0001$ compared to 24-h SBP with P). Office BP values were similarly reduced. A seated SBP < 140 mmHg was recorded in 11% (P), 18% (L), 23% (E), and 48% (L/E) of the patients, and a seated BP < 140/90 mmHg in 8% (P), 18% (L), 19% (E), and 45% (L/E) of the patients.

Two patients on P and two on L/E were withdrawn from the study. Adverse events were recorded in 9% (P), 12% (L), 16% (E), and 14% (L/E) of the patients.

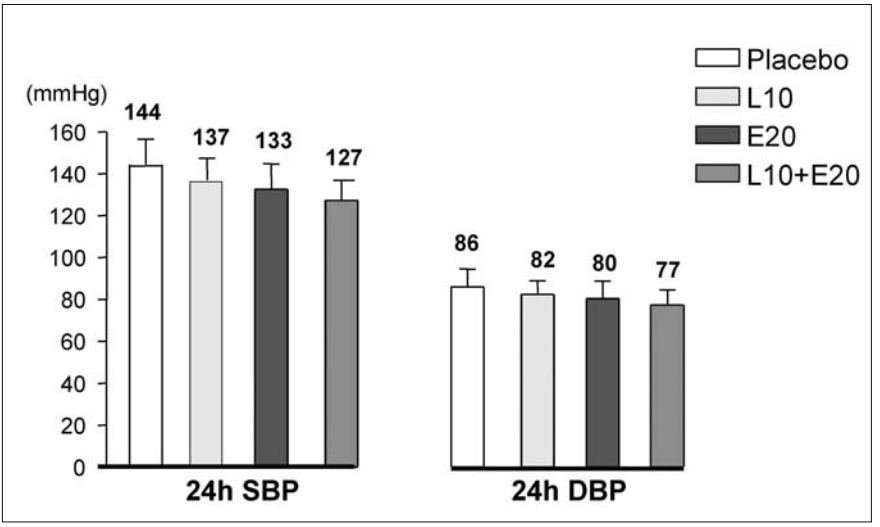

Fig. 1. Mean 24-h blood pressure. *SBP*, Office systolic blood pressure; *DBP*, office diastolic blood pressure; *L*, Lercanidipine (10 mg); *E*, enalapril (20 mg)

Conclusions

This study showed that in elderly hypertensive patients combination therapy with L/E is significantly more effective than either placebo or the two monotherapies in reducing ambulatory and clinic systolic and diastolic BP. The finding that combination therapy with enalapril and lercanidipine decreased 24-h BP by a mean of 17.9/9.2 mmHg supports the JNC 7 recommendation to initiate therapy with two agents in patients whose BP is > 20 mmHg above the SBP goal or > 10 mmHg above the DBP goal [3]. In fact, combination therapy with L and E was associated with a BP < 140/90 mmHg in 45% of the patients and monotherapy with L or E in < 20% of the patients. Since a prompt reduction of BP values is associated with a significant reduction in the number of cardiovascular events [6], the achievement of BP values < 140/90 mmHg within a 4-week period may be of substantial benefit.

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