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Comparison of Fixed-Dose Combinations of Amlodipine/Losartan Potassium/Chlorthalidone and Amlodipine/Losartan Potassium in Patients With Stage 2 Hypertension Inadequately Controlled With Amlodipine/Losartan Potassium: A Randomized, Double-blind, Multicenter, Phase III Study

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ABSTRACT

Purpose: The goal of this study was to compare the efficacy and safety of fixed-dose combinations of amlodipine/losartan potassium/chlorthalidone (A/L/C) and A/L in Korean patients with stage 2 hypertension inadequately controlled by A/L.

Methods: This study was an 8-week, randomized double-blind, multicenter, phase III clinical trial. Three hundred forty volunteer patients with stage 2 hypertension were randomized to receive A/L/C or A/L. The primary end point was a change in sitting systolic blood pressure (SitSBP) after 8 weeks of treatment. As secondary end points, the change in SitSBP after 2 weeks of treatment and the change in sitting diastolic blood pressure (SitDBP) were compared between treatment groups. All patients were assessed for adverse events, clinical laboratory data, and vital signs.

Findings: Of 330 patients from 33 medical centers, 328 patients who had available efficacy data were analyzed. After 8 weeks of double-blind treatment, the mean (SD) changes in SitSBP at 8 weeks were −16.4 (0.9) mm Hg and −6.9 (1.0) mm Hg in the A/L/C and A/L groups, respectively. A/L/C had a statistically superior blood pressure–lowering effect compared with that of A/L (mean [SD] difference, 9.5 [1.3] mm Hg; $P < 0.001$). The mean (SD) change in SitDBP at 8 weeks was significantly greater with A/L/C (−8.0 [0.6] mm Hg) than with A/L (−3.6 [0.6] mm Hg) ($P < .001$). In terms of the mean (SD) change in SitDBP at 2 weeks compared with baseline, A/L/C (−5.9 [0.5] mm Hg) was statistically different from A/L (−2.9 [0.5] mm Hg) ($P < .001$). Mean (SD) SitSBP change from baseline to week 2 was −13.2 (0.9) and −5.5 (0.9) in the A/L/C and A/L groups, respectively, with a statistically significant blood pressure–lowering effect ($P < 0.001$). The number of participants who achieved target blood pressure at week 8 was significantly higher in the A/L/C group (93 patients [55.7%]) than in the A/L group (48 [29.8%]) ($P < 0.001$). Adverse drug reactions were observed in 23 patients (7.0%), and the incidence of dizziness was significantly higher in the A/L/C group than in the A/L group (4.8% vs 0.6%, $P = 0.037$) There were no serious adverse events associated with the study drugs.

Implications: The results of this study suggest that A/L/C had a significantly increased blood pressure–lowering efficacy compared with that of A/L and had a good safety profile. ClinicalTrials.gov identifier: NCT02916602. (*Clin Ther.* 2017;▮:▮▮▮–▮▮▮)

Key words: amlodipine, chlorthalidone, hypertension, losartan, single-pill combination.