Research Article

The Journal of Hypertension

Clinical effectiveness and safety of amlodipine/losartan-based single-pill combination therapy in patients with hypertension: Findings from real-world, multicenter observational databases.

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Received Date : May 02, 2024
Accepted Date : May 04, 2024
Published Date : June 04, 2024

ABSTRACT

To increase patient adherence to medication and clinical effectiveness, a number of single-pill combinations (SPCs) have been launched. Nevertheless, there is a paucity of empirical data on the efficacy of these SPCs in treating hypertension. In patients with hypertension, this study assessed the safety and real-world clinical effectiveness of amlodipine/losartan-based SPC treatments. From the databases of three tertiary hospitals in Korea, a total of 15, 538 patients receiving amlodipine/losartan-based SPCs—amlodipine + losartan (AL), amlodipine + losartan + rosuvastatin (ALR), and amlodipine + losartan + chlorthalidone (ALC)—were chosen. Target blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C) achievement rates were the effectiveness endpoints. Laboratory parameters were used to evaluate safety. PDC, or the proportion of medication days covered, was used to define drug adherence. The three groups all achieved the objective blood pressure goal at a rate that was above 90%. Despite the fact that many patients in the AL and ALC groups were on statins, the ALR group's goal LDL-C achievement rate was noticeably greater than that of the AL and ALC groups. With the exception of serum uric acid level and incidence rate of new-onset hyperuricemia, which were significantly lower in the AL and ALR groups than in the ALC group, safety endpoints did not differ significantly across the groups. Every group had a PDC greater than 90%. Amlodipine/losartan-based SPC therapy showed good target BP accomplishment rates in actual hypertensive patients. In particular, the target LDL-C goal accomplishment rate was higher for the rosuvastatin-combination SPC than for the other SPCs. The drug adherence of the three amlodipine/losartan-based SPC was very good.

Keywords : amlodipine, chlorthalidone, losartan, rosuvastatin, single-pill combination

INTRODUCTION

The number of people with hypertension is predicted to rise steadily and reach 1.56 billion globally by 2025.1 There are currently over 12 million hypertension patients in Korea, yet only 9 million of them use antihypertensive medications, and only 6.5 million of them see a doctor on a regular basis for therapy.2. Maintaining proper blood pressure (BP) in patients receiving treatment for hypertension—that is, systolic blood pressure (SBP) < 140 mmHg or diastolic blood pressure (DBP) < 90 mmHg—while they are having medication is a difficult problem. To reach their desired blood pressure, many hypertension patients need to take at least two antihypertensive medications.3. Of the patients receiving therapy for hypertension in Korea, 16.1% are taking three or more ntihypertensive medications, while 43.2% of patients are using two antihypertensive meds.2. Also, the majority of patients with By 2025, there will be 1.56 billion hypertensive individuals worldwide, according to forecasts of the number of cases rising gradually.1. In Korea, there are currently over 12 million people with hypertension; however, only 9 million of them take antihypertensive drugs, and only 6.5 million of them regularly visit a doctor for therapy.2. It can be challenging to keep patients' blood pressure (BP) within the recommended range while they are taking medication for hypertension, which is systolic blood pressure (SBP) < 140 mmHg or diastolic blood pressure (DBP) < 90 mmHg. Many patients with hypertension require the use of at least two antihypertensive drugs in order to achieve their target blood pressure.3. In Korea, 16.1% of patients undergoing treatment for hypertension take three or more antihypertensive drugs, and 43.2% of patients use.

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METHODS

Study Design

This study was retrospective, observational, cohort, and multicenter. Utilizing the Common Data Model (CDM) database of three tertiary institutions in Korea (Korea University Anam Hospital, Korea University Guro Hospital, and Korea University Ansan Hospital) under the Observational Medical Outcomes Partnership (OMOP), this study was conducted. The OMOP CDM schema, which is being used to standardize hospital electronic health records (EHRs) into the OMOP CDM database (https://github.com/OHDSI/CommonDataModel/), is provided by the Observational Health Data Sciences and Informatics cooperation. The ICD-10 coding system is utilized in Korea for diagnosis, and OMOP-CDM offers a unique concept ID that is linked to the code. The OMOP-CDM concept ID, which is translated to the ICD-10 code, was thus used to examine the data. Specific OMOP-CDM concept IDs were included in the supporting documentation. The OMOP-CDM.

All patients (n = 15 538) who had at least one prescription for an amlodipine/losartan-based SPC were included in the safety analysis.

The efficacy analysis comprised 13 239 patients in total. after excluding individuals (n = 2245) who had been taken combination medications containing amlodipine and losartan for less than four weeks. Only the re-prescription data were included for patients who received amlodipine/losartan-based SPCs following a "pill-vacation" of more than a year.

Efficacy Assessment

The effectiveness of amlodipine was evaluated using blood pressure and lipid profiles, which included total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides. based on losartan SPCs. Following a minimum of five minutes of relaxation in a seated position, blood pressure was taken using an automated sphygmomanometer in a quiet location. After having their blood pressure taken, patients were told not to smoke, drink alcohol, or take caffeine for 30 minutes. The earliest measurements of blood pressure and lipid profiles taken between 28 and 90 days following the first prescription were the short-term effectiveness objectives. When evaluating long-term efficacy, blood pressure and lipid profile measures taken at least ninety days following the initial prescription were used. The average of all measured blood pressure readings was utilized for the analysis if blood pressure was taken twice on the same day. The percentage of patients who reached the target blood pressure (SBP < 140) was called the target blood pressure attainment rate.

Safety Assessment

The amlodipine/losartan-based SPCs were shown to be safe based on BP and laboratory results. SBP less than 90 mmHg was classified as hypotension. A serum potassium level of less than 3.0 mmol/L was considered hypokalemia. Higher than 6.5 mg/dL serum uric acid was considered hyperuricemia. Impaired fasting glucose level was defined as plasma glucose level while fasting > 100 mg/dL. An rise in serum creatinine level (> 0.4 mg/dL) from baseline was considered a renal adverse event. An individual's urine protein level was considered to be "worsening" if the urine protein dipstick test result increased by more than one. The urine protein dipstick test was used to evaluate proteinuria.

RESULTS

Displays the study participants' baseline characteristics. The study population had a mean age of 63.3 ± 13.7 years, with 56.7% of the participants being male. various baseline features were found in each group, indicating that certain patients were favored to be in various therapy groups. Compared to the other two groups, the ALR group had a greater mean age. In the AL group, poor lifestyle choices, such as drinking and smoking, were more prevalent. Heart-related conditions (dyslipidemia, heart attacks, coronary artery diseas. or TIA) were more common in the 3-drug combination pill groups (ALC and ALR groups) than in the AL group, along with a higher body mass index. Furthermore, compared to the other two groups, chronic renal disease was seen less frequently in the ALR group. Prior to the initiation of amlodipine/losartan-based SPCs, more than 50% of the patients in all groups were taking antihypertensive drugs; the ALC group had the greatest percentage of these individuals. By comparison, the ALR group (rosuvastatin combination group) had the lowest percentage of patients who had been receiving antilipidemic drugs prior to beginning amlodipine/losartan-based SPCs. In the three-drug combination pill groups (ALC and ALR), patients took a significantly fewer total number of pills.

For the short-term efficacy study, the mean follow-up period was 49.2 days, whereas for the long-term analysis, it was 330.0 days. During the short-term efficacy analysis, both SBP and DBP showed substantial reductions (−9.7 mmHg for SBP and −5.9 mm g for DBP, p <.05) (Figure 2). The long-term study showed that the reduction in blood pressure from the short-term analysis (−8.5 mm Hg for SBP and −5.9 mm Hg for DBP, p <.05) persisted. The ALC group had the highest baseline SBP and DBP of all the groups; hence, even though their BP decreased the most during the short-term efficacy study, their SBP remained higher than that of the other two groups. Notably, these variations were lessened and targeted throughout the long-term efficacy analysis. The three groups'

BP achievement rates were comparable, which could be explained by the ALC group's notable BP-lowering impact. In summary, the long-term efficacy investigation revealed that the target blood pressure attainment percentage of amlodipine/losartan-based SPCs was 93.4%.

Displays the PDC for the amlodipine/losartan-based SPCs. Every group had a PDC of at least 90%. The range of drug exposure was 233–422 days on average. Interestingly, PDC was considerably lower in the two-drug combination group (AL group) compared to the three-drug combination groups (ALC and ALR groups; p <.05). Additionally, the 2-drug combination group (AL group) had a smaller proportion of patients with PDC > 80% than the 3-drug combination groups (ALC and ALR groups; 85.6%, 90.5%, and 93.2%, respectively; p <.05).

DISCUSSION

The purpose of this study was to evaluate the safety and effectiveness profiles of amlodipine/losartan-based SPCs in hypertension patients in a real-world clinical context. Using data from electronic health records, this is the first and largest real-world long-term observational study of the three amlodipine/losartan based SPCs. We discovered many clinical viewpoints for hypertension patients from this investigation. Initially, compared to the two-drug combination pill group (AL group), the three-drug combination pill groups (ALC and ALR groups) showed a reduced overall pill burden and higher treatment adherence. Comparing the three-drug combination pill groups to the two-drug combination pill group, the total pill number was less than 1. In comparison to the two-drug combination group, the PDC in the three-drug combination groups was higher (95.0% vs. 90.7%).

Second, despite having differing baseline characteristics, all three groups treated with amlodipine/losartan based SPCs achieved comparable excellent BP control. For each of the three groups, the target BP attainment rates exceeded 90%. Third, the ALR group of SPC that took statins showed the biggest improvements in controlling dyslipidemia. In the ALR group, the target LDL-C attainment rate was the highest at 89.1%. Secondly, the safety profiles of all three groups were strong. During long-term assessment, the goal blood pressure achievement rate of amlodipine/losartan-based SPCs was almost 90%, which is presumably higher than the average blood pressure control rate of patients receiving medication in Korea (71%), who have hypertension.14 Surprisingly, only 70% to 85% of people receiving treatment for hypertension have regulated blood pressure in wealthy nations like Canada, Germany, and the United States.15 These results point to a reduction in pill load associated with amlodipine/losartan-based SPC therapy for hypertensive patients currently on multidrug therapy, which may promote medication compliance. Prior research has demonstrated that higher medication adherence and hypertension control are linked to taking fewer medications.16, 17 Additionally, a recent systematic review with 44 research found that SPC enhances medication adherence.

There are various restrictions on our investigation. First, the missing values led to the exclusion of a large number of patients. Given that older patients or those with cardiovascular problems may be less resistant to medical testing, participants examined in this study may be at increased risk for cardiovascular disease. Second, there was a substantial difference in the baseline characteristics of the three groups. This difference could be attributed to prescription indication differences or patient and physician preferences. Patients with greater blood pressure were administered ALC by doctors, and those with increased cardiovascular risk were prescribed ALR.

As a result, there might have been a bias in selection. After controlling for baseline characteristics, multivariate logistic regression analysis revealed that ALR would be an independent predictor of the target LDL-C attainment (odd ratio 2.32, 95% confidence interval 1.09–4.93, p =.03). But still describing the three amlodipine/losartan-based SPCs' clinical effectiveness, safety, and medication adherence is more important than making comparisons between them. The real-world clinical data of the three distinct SPCs in the current study will be able to precisely identify the strengths and weaknesses of each SPC and further improve the quality of clinical treatment for patients with hypertension, as there are various clinical spectrums of hypertensive patients.

CONCLUSION

This is the first long-term real-world observational research of three amlodipine/losartan-based SPCs, as far as we are aware. SPC therapy based on amlodipine and losartan showed good target blood pressure accomplishment rates. When compared to other SPCs, the rosuvastatin combination SPC had a higher target LDL-C goal accomplishment rate. The three amlodipine/losartan-based SPCs demonstrated outstanding drug adherence, good safety, and good efficacy. The current study's overall conclusions will offer direction for reinterpreting the specific clinical applications of SPC in individuals with multiple medication-taking hypertension.

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