

**Original Paper**

# Changes in Central Aortic Pressure, Endothelial Function and Biomarkers in Hypertensive African-Americans with the Cardiometabolic Syndrome: Comparison of Amlodipine/Olmesartan versus Hydrochlorothiazide/Losartan

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## Key Words

Cardiometabolic syndrome · African-Americans · Compliance · Inflammation · Hypertension

## Abstract

Sixty-six self-identified African-American subjects with stage 1 and 2 hypertension and characteristics of the cardiometabolic syndrome were treated with amlodipine/olmesartan (A/O) versus losartan/hydrochlorothiazide (L/H) for 20 weeks in an open-label, active comparator fashion. Subjects not meeting a blood pressure (BP) value of <125/75 mm Hg on either regimen at week 14 were placed on additional or alternative therapy. After 20 weeks of therapy, systolic BP was reduced by  $34.6 \pm 4.2$  mm Hg in the A/O group and by  $27.0 \pm 4.1$  mm Hg in the L/H group ( $p = 0.012$  A/O vs. L/H). Diastolic BP was reduced by  $16.9 \pm 2.0$  mm Hg in the A/O group and by  $12.3 \pm 2.0$  mm Hg in the L/H group ( $p = 0.022$  A/O vs. L/H). There was a substantial increase in endothelial function of 44 and 103% in the L/H and A/O groups, respectively ( $p < 0.005$  A/O vs. L/H). Central aorta augmentation pressure was significantly reduced by 42% with the A/O treatment, and a smaller, significant reduction of 28% was observed with the L/H treatment ( $p = 0.034$  A/O vs. L/H). There was a reduction in sIL-6 levels of 20 and 33%, a reduction in serum leptin levels of 22 and 40%, and an increase in serum adiponectin of 19 and 46% in the L/H and A/O groups, respectively ( $p < 0.005$  A/O vs. L/H for each biomarker). Treatment with A/O after 14 weeks reduced pulse wave velocity by 22% ( $p = 0.011$  time comparison), whereas L/H treatment had no significant effect. Our findings suggest that, in addition to effective BP reduction, A/O differentially regulates markers of inflammation and obesity, thereby potentially providing greater vascular protection.

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## Introduction

The prevalence of hypertension is highly variable among populations worldwide. In the United States, there is a disproportionate burden of this disease and its complications in African-Americans [1]. African-Americans have the highest prevalence of hypertension in the world, at a level that is significantly higher than that in individuals of African origin living outside the United States [2]. According to the 2003–2004 National Health and Nutrition Examination Survey (NHANES), the prevalence of hypertension is 39.1% in African-Americans and 28.5% in white Americans [3]. The increased prevalence of hypertension in African-Americans has been attributed to both genetic and environmental factors [4]. Additionally, hypertension is usually observed at a younger age in African-Americans and results in more severe disease complications. This leads to a higher hypertension-related mortality rate – 49.9% for African-American men and 40.6% for African-American women, compared to 17.9% for the overall US population in 2004 [1].

Diagnosis and treatment of obese patients with hypertension require that health-care providers address the additional issues of glucose intolerance and dyslipidemia. Ethically sensitive strategies to promote therapeutic lifestyle changes, specifically increased physical activity and reduced dietary intake resulting in weight loss, are not as well defined. A sedentary lifestyle and poor cardiorespiratory fitness are not only associated with the cardiometabolic syndrome but could actually be considered features of it. These issues are significant in the health of African-American individuals, who experience greater difficulty in blood pressure (BP) control, encounter increased hypertensive and diabetic complications, and have higher levels of obesity [5].

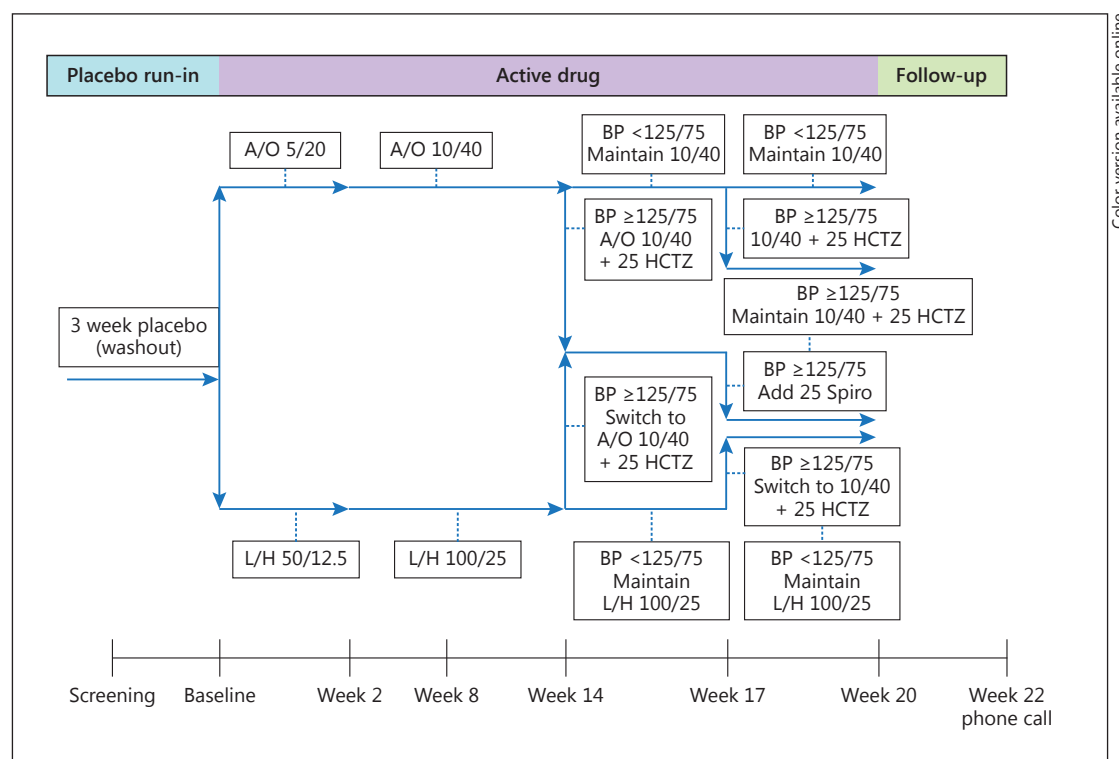
Growing evidence suggests that the regulation of adipose tissue may represent an important link between increased insulin resistance, hypertension and obesity – all key factors in the cardiometabolic syndrome [6–8]. Furthermore, increased angiotensin II activity within adipose tissue is associated with increased levels of the hormone leptin and reduced levels of adiponectin [9, 10]. Adiponectin levels are inversely correlated with visceral obesity, insulin resistance and hyperlipidemia [11, 12], and increased markers of adiponectin have been associated with a decreased risk in coronary heart disease in diabetic men [13]. In endothelial cells, adiponectin decreases the activity of inflammatory genes such as adhesion molecules [14]. Leptin is an adipocyte-specific hormone that plays a central role in the regulation of body weight [15]. Leptin, produced predominantly by subcutaneous adipocytes, is present at higher concentrations in obese individuals [16].

This study evaluates the effects of a comparison between amlodipine/olmesartan (A/O) and losartan/hydrochlorothiazide (L/H) therapy in hypertensive African-Americans with the cardiometabolic syndrome. We included the cardiometabolic syndrome as a criteria for this study as approximately 30% of African-Americans are obese [3], a substantial component of hypertensive patients.

## Methods

### *Subjects*

African-American men and women between the ages of 18 and 75 years (mean age 50.0) with stage I or II hypertension and meeting the NCEP/ATP III criteria for the cardiometabolic syndrome were enrolled in the study. Subjects were excluded if they had any of the following: inadequately controlled diabetes mellitus (with a glycosylated hemoglobin >8.0%); active coronary heart disease, cerebrovascular disease, peripheral vascular disease or renovascular disease; known history of cirrhosis; history of chronic renal failure requiring dialysis or significant renal dysfunction (defined as serum creatinine >3.5 mg/dl not receiving continuous renal replacement therapy), or a mental condition rendering the subject unable to understand the scope and



**Fig. 1.** The AMORE Study: protocol and timeline.

possible consequences of the study. Women of childbearing age were required to use an acceptable method of birth control. All patients were informed about the purpose of this study, and written informed consent was obtained from all subjects. Complete confidentiality for each subject was provided throughout the study process.

#### Study Design and Treatment Duration

This was a prospective, randomized, parallel-group, open-label, blinded-end point, active comparator, multicenter, 20-week titration study on the efficacy and safety of A/O versus L/H therapy in African-American subjects with hypertension and the cardiometabolic syndrome. After screening, patients were observed during a 3-week placebo run-in period. The subjects were then excluded from the study if their systolic BP exceeded 180 mm Hg and/or their diastolic BP exceeded 110 mm Hg during the run-in period. Otherwise, subjects were randomized 1:1 to either A/O 5 mg/20 mg or L/H 50 mg/12.5 mg once daily for 2 weeks and then titrated to A/O 10 mg/40 mg or L/H 100 mg/25 mg once daily for 12 weeks. Subjects meeting a BP goal of <125/75 mm Hg after 14 weeks were maintained on their current regimen for an additional 6 weeks (fig. 1). Subjects not meeting the BP goal of <125/75 mm Hg on either regimen at week 14 were placed on A/O 10/40 plus hydrochlorothiazide (HCTZ) 25 mg (10/40/25) for the remainder of the study. BP is reported as intent-to-treat analysis. Therefore, data are analyzed based on the initial treatment intent and not the eventual treatment that the patients received. Pill counts were obtained at each visit to determine compliance. The study protocol was approved by the institutional review board prior to its implementation.

Changes in brachial systolic and diastolic BP, central aortic pressure and endothelial function were the co-primary end points of the study. Brachial BP was measured at baseline and at each study visit in a sitting position from the nondominant arm as a mean of 3 consecutive measurements at 5-min intervals using an Omron sphygmomanometer.

#### Measurement of Central Aortic Blood Pressure and Pulse Wave Velocity

Radial artery applanation tonometry was used to measure central aortic pressure, pulse wave analysis and pulse wave velocity (PWV) in patients using SphygmoCor equipment and software (AtCor Medical,

Itasca, Ill., USA) [17, 18]. Radial artery applanation tonometry measurements were obtained immediately following two measurements of brachial BP on the subject's dominant arm while the patient was in a seated position. The PWV measurements were taken at baseline and during visits at weeks 14 and 20. By measuring the peripheral pressure pulse wave, BP in the ascending aorta (central aortic systolic BP) was determined, providing information about a subject's degree of arterial stiffness and cardiac performance. PWV is a direct measure of aortic stiffness and has been shown to be a risk factor in a number of cardiovascular-related diseases. The carotid-femoral PWV measured in this study was determined by the mechanical properties of the aorta and a portion of the carotid artery, both of which are elastic arteries.

#### *Brachial Artery Reactivity Measured by Ultrasonography for Determining Endothelial Function*

We determined the endothelium-dependent, flow-mediated dilation of the brachial arteries from two-dimensional ultrasound images according to established and validated methodologies at baseline and at week 14. Images were obtained with a Hewlett Packard 8-mHz linear array transducer and an HP Image Point ultrasound system (HP, Andover, Mass., USA) [19]. Each triggered event consisted of 3 sequential frames. This yielded a total of 12 images to be analyzed. The intima-media interface was chosen for both the near wall and the far wall of the artery. A linear portion of the vessel was analyzed. Measurements from the 12 frames were averaged. The end point of measurement was the percent change in diameter in response to reactive hyperemia or nitroglycerin.

#### *Measurement of Biomarkers of Inflammation and Obesity*

Plasma samples were drawn at baseline and at week 20. The samples were centrifuged and stored at  $-80^{\circ}\text{C}$  until ready for analysis. An aliquot was drawn, and an enzyme immunoassay (Cayman Chemical, Ann Arbor, Mich., USA) for the markers soluble adiponectin and leptin was performed on each sample in triplicate. A total of 50  $\mu\text{l}$  of serum was used for analysis, and enzyme immunoassay was performed as previously described [14]. The levels of these biomarkers were determined on a plate reader at an optical density of 420 nm. We found no interference of olmesartan, losartan, amlodipine, or HCTZ or its metabolites in these assays.

#### *Statistical Analysis*

All values are presented as the mean  $\pm$  standard deviation for continuous variables and as the percentage of total patients for categorical variables. The independent sample t test and analysis of variance (ANOVA) were used for comparison of continuous and categorical variables, respectively. A p value of  $<0.05$  was considered statistically significant, and all p values were two-sided. Calculations were performed with SPSS software (version 10.0, SPSS, Chicago, Ill., USA).

## Results

### *Study Demographics*

A total of 115 subjects were screened, of which 66 patients were randomized. The reason for the lower-than-expected randomization rate was that during the placebo run-in period, there was a substantial number of subjects whose systolic BP exceeded 180 mm Hg and/or whose diastolic BP exceeded 110 mm Hg. Of the randomized subjects, 50 patients (19 males and 31 females) completed the 20-week study. At week 14, 8 patients in the L/H treatment group did not meet the BP goal of  $<125/75$  mm Hg and were switched to A/O 10/40 plus HCTZ 25 mg (10/40/25) for the remainder of the study. Additionally, 12 patients in the A/O group did not meet the BP goal of  $<125/75$  mm Hg at week 14, and HCTZ was added to the treatment regimen for these patients for the remainder of the study. All patients met the BP goal at 20 weeks of treatment. Unwillingness to continue was the main reason for dropping out of the study. The follow-up of all patients was 100% complete. Table 1 shows patient characteristics and baseline demographics for those who completed the study. Table 2 demonstrates the changes in urine and serum biomarkers of oxidation, inflammation and renal function between the study groups.

**Table 1.** Demographics and metabolic parameters of hypertensive African-Americans with the cardiometabolic syndrome

|                          |              |
|--------------------------|--------------|
| Women, %                 | 61.5         |
| Age, years               | 50.0 ± 12.5  |
| Systolic BP, mm Hg       | 148.8 ± 14.3 |
| Diastolic BP, mm Hg      | 90.4 ± 8.2   |
| BMI                      | 36.4 ± 5.3   |
| Total cholesterol, mg/dl | 189.2 ± 36.7 |
| LDL cholesterol, mg/dl   | 124.5 ± 35.5 |
| HDL cholesterol, mg/dl   | 52.0 ± 14.2  |
| Triglycerides, mg/dl     | 123.3 ± 63.9 |
| Glucose, mg/dl           | 93.8 ± 14.5  |
| Creatinine, mg/dl        | 0.9 ± 0.1    |
| Bilirubin, mg/dl         | 0.5 ± 0.2    |

Data are means ± SD, unless otherwise indicated. BMI = Body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

**Table 2.** Measurement of serum and urine biomarkers

|                                    | L/H         |             | A/O         |             |
|------------------------------------|-------------|-------------|-------------|-------------|
|                                    | baseline    | 14 weeks    | baseline    | 14 weeks    |
| PAI-1, ng/ml                       | 245 ± 42    | 196 ± 33*   | 271 ± 35    | 189 ± 29*   |
| Creatinine, mg/dl                  | 0.9 ± 0.2   | 1.0 ± 0.2   | 1.0 ± 0.2   | 1.0 ± 0.3   |
| Cystatin C, mg/l                   | 0.83 ± 0.12 | 0.79 ± 0.16 | 0.79 ± 0.19 | 0.82 ± 0.14 |
| HOMA-IR index                      | 2.3 ± 0.4   | 2.1 ± 0.5   | 2.5 ± 0.4   | 1.9 ± 0.3*  |
| Urine protein: creatinine, mg/mmol | 22.6 ± 4.9  | 20.8 ± 3.8  | 18.0 ± 4.1  | 20.3 ± 3.4  |
| Urine isoprostane, pg/ml           | 155 ± 51    | 170 ± 46    | 137 ± 32    | 145 ± 30    |

HOMA-IR = Homeostasis model assessment for insulin resistance; PAI-1 = plasma activator inhibitor-1.

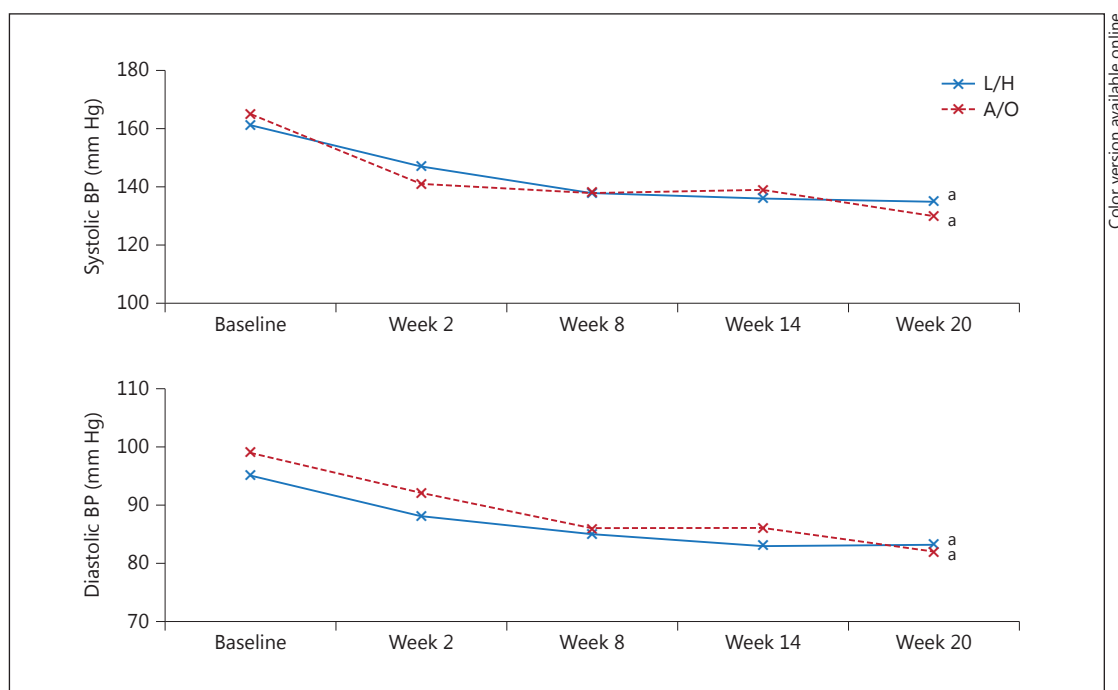
\*  $p < 0.05$ , significantly different from baseline.

### Analysis of Blood Pressure with the Two Treatment Groups

Figure 2 displays the systolic and diastolic BP of patients in the A/O versus L/H treatment groups. By 14 weeks of treatment, BP had reduced significantly in both groups and was further lowered at week 20. In the A/O group, there was a reduction in systolic BP of  $34.6 \pm 4.2$  mm Hg and in diastolic BP of  $16.9 \pm 2.0$  mm Hg (baseline: 165/99 mm Hg; 14 weeks: 140/86 mm Hg; 20 weeks: 130/82 mm Hg). In comparison to the A/O group, there was a less significant reduction in systolic BP of  $27.0 \pm 4.1$  mm Hg and in diastolic BP of  $12.3 \pm 2.0$  mm Hg (baseline: 162/97 mm Hg; 14 weeks: 137/84 mm Hg; 20 weeks: 135/84 mm Hg) at 20 weeks of treatment in the L/H group. The 20-week changes in systolic ( $p = 0.012$  A/O vs. L/H) and diastolic BP ( $p = 0.022$  A/O vs. L/H) were statistically significant from baseline in both treatment groups.

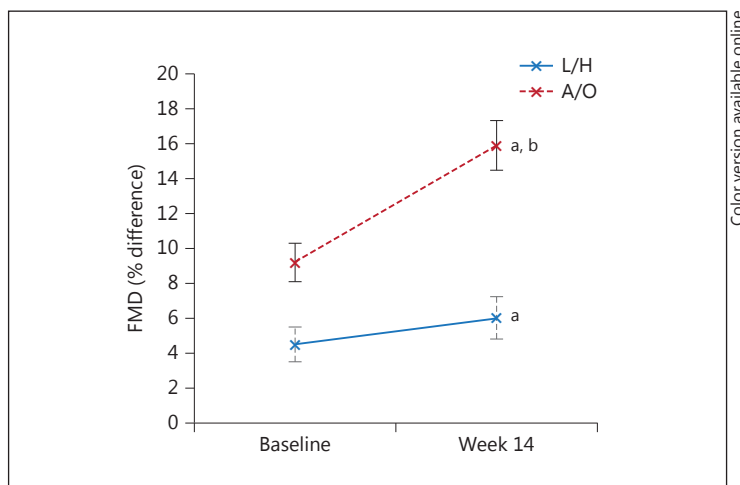
### Changes in Endothelial Function in Response to A/O versus L/H Therapy

Concomitant with the reduction in BP, both treatment groups indicated a significant improvement in endothelial function (fig. 3). The L/H group had an increase in endothelial function of 44% at 14 weeks of therapy ( $p < 0.001$  vs. baseline). There was a more substantial increase in endothelial function in the A/O group of 103% versus baseline at 14 weeks of therapy ( $p < 0.005$  vs. baseline;  $p < 0.005$  vs. L/H).



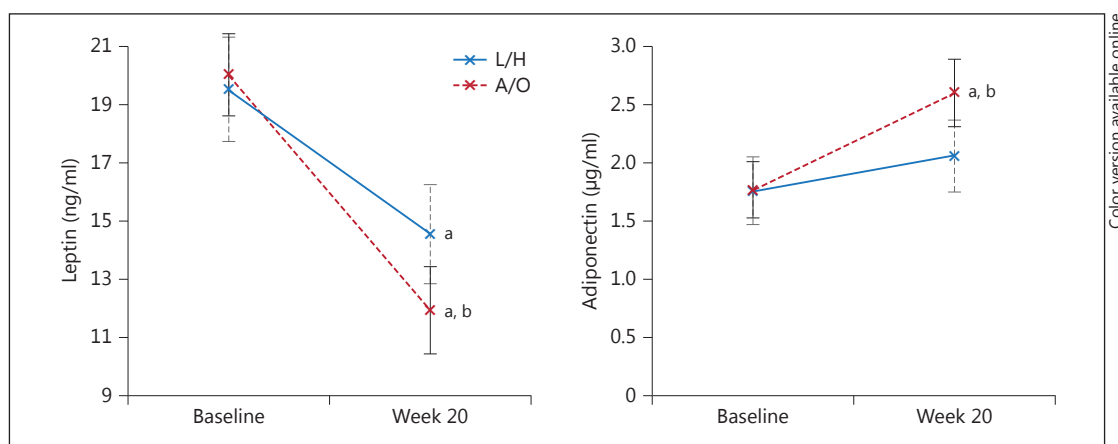
**Fig. 2.** Effect of A/O versus L/H on systemic BP. <sup>a</sup>  $p < 0.005$ : the difference between baseline and 20 weeks (time comparison).

**Fig. 3.** Effect of A/O versus L/H on flow-mediated dilation (FMD). Patients were randomized to either A/O or L/H for a 14-week period, and additional therapy as indicated was given thereafter. Flow-mediated dilation studies using high-resolution ultrasound (detailed in the Methods section) were performed at baseline and at 14 weeks of therapy. <sup>a</sup>  $p < 0.005$ : the difference between baseline and 20 weeks (time comparison). <sup>b</sup>  $p < 0.005$ : the difference between L/H and A/O (group comparison).

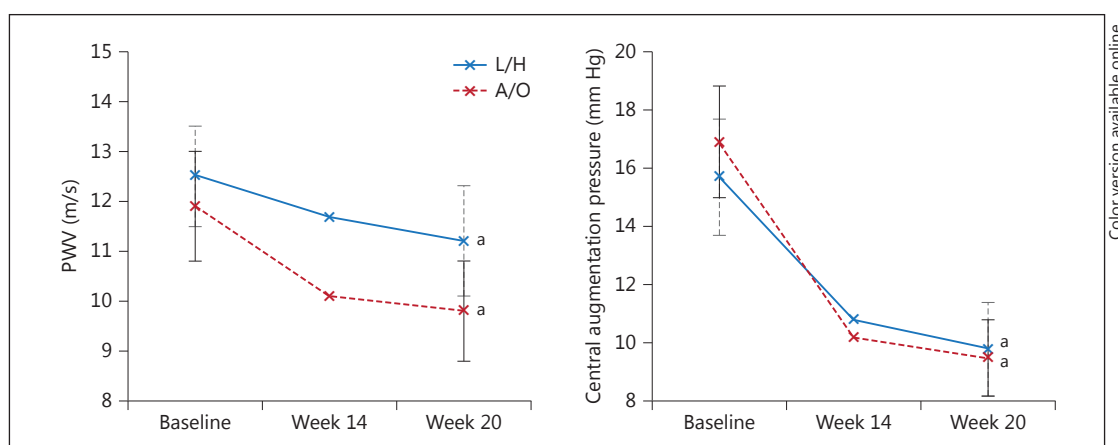


#### Effects of A/O versus L/H Therapy on Serum Leptin and Adiponectin

Figure 4 shows the levels of serum biomarkers at baseline and at week 20 in both treatment groups. To determine the modulating effects of A/O versus L/H treatment on circulating molecule expression in the vasculature, serum leptin levels were measured as a marker of inflammation and obesity. Both treatment groups showed a reduction in serum leptin. There was a reduction in leptin of 22% in the L/H group ( $p = 0.045$  vs. baseline) and a further reduction in leptin of 40% in the A/O group ( $p = 0.006$  vs. baseline;  $p = 0.031$  vs. L/H). To determine the effects of antihypertensive therapy on circulating markers of obesity, levels of serum adiponectin were measured. Following treatment with L/H, there was a nonsignificant



**Fig. 4.** Effect of A/O versus L/H on serum soluble biomarkers. Patients were randomized to either A/O or L/H for a 14-week period, and additional therapy as indicated was given thereafter to 20 weeks of treatment. Using the ELISA technique, soluble serum levels of leptin, IL-6 and adiponectin were performed at baseline and at 20 weeks of therapy. <sup>a</sup>  $p < 0.005$ : the difference between baseline and 20 weeks (time comparison). <sup>b</sup>  $p < 0.005$ : the difference between L/H and A/O (group comparison).



**Fig. 5.** Effect of A/O versus L/H on PWV and central aorta augmentation pressure. Patients were randomized to either A/O or L/H for a 14-week period, and additional therapy as indicated was given thereafter to 20 weeks of treatment. Radial artery applanation tonometry was used to measure central aortic pressure, pulse wave analysis and pulse wave velocity (PWV) in patients using SphygmoCor. <sup>a</sup>  $p < 0.005$ : the difference between baseline and 20 weeks (time comparison).

increase in serum adiponectin levels of 19%. However, treatment with A/O significantly increased serum adiponectin levels by 46% ( $p = 0.012$  vs. baseline;  $p = 0.027$  vs. L/H).

#### Effects of A/O versus L/H Therapy on Pulse Wave Velocity and Central Aorta Augmentation Pressure

The effects of A/O versus L/H therapy on parameters of arterial compliance and vascular stiffness were determined at baseline as well as at 14 weeks and 20 weeks of therapy (fig. 5). After 14 weeks, treatment with A/O reduced PWV by 22% ( $p = 0.011$  time comparison), whereas L/H treatment had no significant effect. Central aorta augmentation pressure, a

predictor of cardiovascular risk, was significantly reduced ( $p < 0.005$  time comparison) with A/O by 42% and less effectively with L/H by 28% ( $p = 0.034$  A/O vs. L/H). Similar results were observed at the 20-week time point.

## Discussion

Though medical treatment has been effective in the treatment of hypertension, its incidence continues to be high, particularly in African-American patients [20, 21]. This study shows a substantial benefit of A/O combination therapy in hypertensive African-American patients with the cardiometabolic syndrome. In comparison to the L/H group, in the A/O group, systolic and diastolic BP reductions were significant and a higher number of patients were able to reach normotensive BP levels with therapy.

This was an intent-to-treat study, and at week 14, L/H patients who were not meeting BP goals were switched to the A/O group and HCTZ was added. Those patients who were in the A/O group and did not meet BP goals were additionally treated with HCTZ. Eight patients in the L/H group achieved the BP goal only after being switched to the A/O group. It can be speculated that, if these patients had not been switched over, the BP difference between the L/H and A/O groups would have been even more pronounced at 20 weeks of treatment. In the A/O group, 12 patients required HCTZ at week 14 to meet BP goals. The recent TRINITY study [22] provides evidence that the further addition of HCTZ to amlodipine and olmesartan is well tolerated and may be necessary for some patients, especially diabetics, to reach BP goals.

In this study, we confirmed the differential effects of therapy on biomarkers of inflammation and obesity. Moreover, we showed that the A/O treatment had selectively more powerful effects on affecting these levels than the L/H treatment.

More recently, research has focused on potential differences in arterial wall function between African-Americans and Caucasians and their impact on vascular homeostasis [20, 23]. Studies have demonstrated reduced NO-mediated vasodilation of forearm resistance vessels to mental stress and endothelium-dependent and -independent pharmacological and physiological stimuli [24]. In this observation, flow-mediated dilation was significantly lower in age-matched African-Americans than in Caucasians (4.8 vs. 8.9%, respectively;  $p < 0.0001$ ), and nitroglycerin-mediated dilation was also significantly lower in African-Americans than in Caucasians (11 vs. 15%, respectively;  $p < 0.0002$ ). Thus, healthy African-American males and females show reduced endothelium-dependent and -independent responsiveness of blood vessels in than Caucasians. Body mass index has been shown to be inversely correlated with endothelium-independent responses [20]. These findings expand our understanding of racial differences in vascular function and indicate a mechanistic explanation for the increased incidence and severity of cardiovascular disease observed in African-Americans. This diminished response to vasodilators may result in a decreased pattern of hemodynamic reactivity that leads, in the long term, to increased vascular tone and hypertension. Importantly, the impact of the metabolic syndrome demonstrates progressive impairment of flow-mediated dilation with increasing exposure to risk factors for the metabolic syndrome [25].

Proinflammatory mechanisms are thought to be a hallmark of the cardiovascular disease process, notably in disease states such as hypertension. These findings are often exacerbated by the increasing prevalence of obesity worldwide. Obesity is frequently accompanied by high plasma levels of nonesterified fatty acids that cause insulin resistance in skeletal muscles and overload the liver with lipids, producing fatty liver and atherogenic dyslipidemia [25]. Fat accumulation in the liver may also stimulate hepatic cytokine production and lead to higher levels of proinflammatory markers. Taken together, the abnormal proinflammatory

state leads to a worsening of metabolic control, abnormal vascular function and, eventually, cardiovascular and renal diseases [8, 13].

Multiple pharmacological agents are approved in the United States for the treatment of hypertension and by differing mechanisms of action. Often, single-drug therapy does not adequately lower BP, and combination therapies are prescribed [26]. The combination of amlodipine and olmesartan has been shown to result in a significant BP lowering as compared to either amlodipine or olmesartan alone [27–29]. Additionally, the antioxidative and anti-inflammatory-mediated mechanisms of action observed with the combination of olmesartan and amlodipine may be beneficial in reducing the progression of insulin resistance, diabetes mellitus and cardiovascular diseases [30–33].

Lifestyle changes, including an increased prevalence of obesity and the metabolic syndrome, contribute to the incidence of hypertension [34, 35]. At the environmental level, barriers to healthy lifestyles include lack of access to exercise facilities at work or in the community, lack of bicycle and walking paths as well as high traffic and crime in urban settings that prevent access to safe walking areas. For individual African-Americans, overall perceived and real barriers to engage in exercise and healthy diets may outweigh perceived positive outcomes of total lifestyle changes, underscoring the importance of individual effective problem solving to reduce barriers and information to influence outcome [36, 37].

#### *Limitations of the Study*

Our investigation was a single-center, short-term study (20 weeks of therapy) to determine the potential mechanisms by which combination therapy with amlodipine and olmesartan may be effective in a high-risk African-American population with hypertension and the cardiometabolic syndrome. This was an open-label study; all study patients received treatment, and there was no control group. Because of the lack of a BP control, we cannot discount the fact that the beneficial effects observed with the two treatment groups may be in part a result of BP reduction. Furthermore, the present findings do not clearly demonstrate the cause(s) for the more powerful anti-inflammatory and antioxidant effect observed in the A/O group. It could result from the differences between the two angiotensin receptor blockers (olmesartan vs. losartan), the difference between a calcium channel blocker (amlodipine) and a diuretic (HCTZ), and/or a more significant BP reduction in the A/O group. Any combination of the above reasons constitutes a plausible explanation. Due to the small sample size, we were not able to evaluate differences among various subsets within our study population. The subjects in our study are at significant risk for the development of cardiovascular and renal disease and its related complications. The placebo run-in period demonstrated a substantial number of subjects who failed achieving the BP goal because of a significant rise in BP off antihypertensive therapy. Therefore, these results may not be applicable to lower-risk populations.

#### **Conclusions**

As many as 30% of adult African-Americans are obese and may have characteristics of the metabolic syndrome (a constellation of factors including obesity, hypertension, dyslipidemia and diabetes) [34]. These findings imply that the use of a combination therapy with an angiotensin receptor antagonist and a calcium channel blocker in hypertensive African-Americans with the cardiometabolic syndrome results in significant BP reduction as well as positive vascular changes, thereby protecting against the development of cardiovascular and renal disease. The long-standing problem of hypertension in African-Americans is exacerbated with the growing incidence of obesity and the subsequent cardiometabolic syndrome.

Therefore, it is probable that this type of therapy would have significant effects in treating BP and components of the cardiometabolic syndrome. Proinflammatory mechanisms are important in the pathogenesis of cardiovascular disease. The findings in the present study suggest, in part, the mechanisms by which the utilization of amlodipine and olmesartan (with or without concomitant therapy) may be beneficial in the prevention of cardiovascular and concomitant renovascular diseases. The pharmacological combination of olmesartan and amlodipine has powerful anti-inflammatory effects within the vasculature plus the ability to reduce arterial stiffness. Long-term outcome studies should be considered to determine the utility of these agents in the primary prevention of cardio- and renovascular diseases in this high-risk African-American population.

### Acknowledgements

The authors wish to thank Ibis Bridges, Michelle Binns, Sumona Banik, and Sujana Bhaheetharan for their excellent technical assistance throughout the course of the study.

### Disclosure Statement

This study was supported by an unrestricted grant from Daiichi Sankyo, Inc. to Drs. Khan and Ferdinand, and the study drugs (amlodipine/olmesartan and losartan/HCTZ) were provided by Daiichi Sankyo, Inc. The other authors have no conflicts of interest to disclose regarding this study or the preparation of the manuscript.

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