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Original Research Article

The Long-Term Effects of Olmesartan Combined Amlodipine among Hypertensive Patients in a Tertiary Care Hospital – A Retrospective Study

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Abstract

Introduction: Hypertension, commonly known as high blood pressure, stands as a pervasive global health concern, often referred to as the "silent killer" due to its asymptomatic nature. The management of hypertension is critical to prevent cardiovascular complications and other associated health risks. This study aimed to observe the long-term effects of olmesartan combined with amlodipine among hypertensive patients. ***Methods:*** This was a retrospective observational study conducted in the Department of Medicine, Popular Medical College Hospital, Dhaka, Bangladesh during the period from January, 2023 to December, 2023. In our study, we included 210 hypertensive patients who were divided into three groups: Group A -Patients who received Olmesartan (OM 40 mg), Group B -Patients who received Amlodipine (AML 5 mg), and Group C -Patients who received the combination of Olmesartan (OM 40 mg) and Amlodipine (AML 5 mg). ***Result:*** We found the mean age was 52.8 ± 11.3 years. Most of our patients were male (68.10%). The majority of patients in Group B had ≤140⁄90 mmHg blood pressure than the other groups at the end of our study. Patients with ≤130⁄85 mmHg, were higher in Group A. Patients with ≤130⁄80 mmHg blood pressure during the last week of the study were highest in Group C. Drowsiness/dizziness, headache, nausea/vomiting, and stomach /abdominal pain were the most common side effects. ***Conclusion:*** In our study, we discovered that Olmevas AM (OM/AML) 40/5 mg was more effective at decreasing blood pressure than either OM (Olmesartan) 40 mg or AML (Amlodipine) 5 mg. There were no unexpected or unusual safety concerns found with OM/AML combo therapy.

Keywords: OM (Olmesartan), AML (Amlodipine), Hypertension, Long-term effects.

INTRODUCTION

Hypertension, commonly known as high blood pressure, stands as a pervasive global health concern, often referred to as the "silent killer" due to its asymptomatic nature [1]. The management of hypertension is critical to prevent cardiovascular complications and other associated health risks [2]. Among the various pharmacological interventions, the combination of olmesartan, an angiotensin II receptor blocker (ARB), and amlodipine, a calcium channel blocker, has gained attention as an effective approach to blood pressure control [3, 4]. This combination harnesses the complementary mechanisms of action of both classes of antihypertensive medications, aiming to provide comprehensive and sustained blood pressure regulation [5]. Hypertension is a global public health challenge affecting millions of individuals worldwide. The World Health Organization (WHO) estimates that over one billion people suffer from hypertension, contributing significantly to the global burden of cardiovascular diseases [6, 7]. Its insidious onset and the potential for severe complications such as stroke, heart attack, and renal failure underscore the importance of effective and long-term management strategies [8]. The multifactorial nature of hypertension often necessitates a combination of medications to achieve optimal blood pressure control. Olmesartan and amlodipine, each targeting different physiological pathways, are commonly prescribed in tandem to address the complex interplay of vasoconstriction, fluid retention, and sympathetic nervous system activation contributing to elevated blood

pressure [9, 10]. Olmesartan, as an ARB, acts by blocking the angiotensin II receptor, thereby inhibiting the vasoconstrictive and aldosterone-releasing effects of this hormone [11]. On the other hand, amlodipine exerts its effects by inhibiting calcium influx into vascular smooth muscle cells, leading to vasodilation. Combining these two medications aims to achieve a synergistic effect, providing more comprehensive blood pressure reduction than either agent alone [9]. Numerous clinical trials have investigated the efficacy of the olmesartan-amlodipine combination in hypertensive patients [12]. Results from these trials suggest that dual therapy is associated with a greater reduction in blood pressure compared to monotherapy with either olmesartan or amlodipine alone [13]. Moreover, the combination has demonstrated efficacy across diverse patient populations, including those with resistant hypertension and individuals with multiple comorbidities. Understanding the long-term safety profile and tolerability of any antihypertensive regimen is paramount in ensuring patient adherence and minimizing adverse effects [14, 15]. Studies assessing the combination of olmesartan and amlodipine have generally reported a favorable safety profile, with adverse events comparable to those observed with individual monotherapies [16]. However, ongoing pharmacovigilance and post-marketing surveillance remain essential to detect rare or late-emerging adverse effects [17]. Despite the accumulated knowledge on the short-term efficacy and safety of the olmesartan-amlodipine combination, gaps exist in understanding its long-term effects [18]. Longitudinal studies tracking patients over extended periods are needed to elucidate the sustained blood pressure control, cardiovascular outcomes, and potential side effects associated with prolonged use [19]. In conclusion, the combination of olmesartan and amlodipine represents a promising therapeutic approach for hypertensive patients, leveraging the synergistic effects of two distinct antihypertensive mechanisms. However, a comprehensive understanding of the long-term effects, including cardiovascular outcomes, safety, and tolerability, is crucial for informing evidence-based clinical practice [20]. This exploration aims to delve into the existing literature, identify research gaps, and shed light on the ongoing quest to optimize hypertension management for improved patient outcomes.

Objective of the study

The study's main objective was to observe the long-term effects of olmesartan combined with amlodipine among hypertensive patients.

METHODOLOGY & MATERIALS

This was a retrospective observational study and was conducted in the Department of Medicine, Popular Medical College Hospital, Dhaka, Bangladesh during the period from January, 2023 to December 2023. In our study, we included 210 hypertensive patients who came to receive treatment at our hospital's outdoor department of medicine. The patients were divided into three groups- Group A (Patients who received Olmesartan 40 mg), Group B (Patients who received Amlodipine 5 mg), and Group C (Patients who received the combination of Olmesartan 40 and Amlodipine 5 mg).

These are the following criteria to be eligible for enrollment as our study participants: a) Patients aged between 40 to 70 years; b)Patients with hypertension; c) Patients who received hypertensive medication ; d) Patients who received anti-hypertensive agents; e)Patients who were willing to participate were included in the study And a) Patients with uncontrolled DM & pregnancy; b) Patients with Coagulopathy; c) Patients with previous surgical history; d) Patients with allergy to the study medicines; e) Patients with any history acute illness (e.g., renal or pancreatic diseases, ischemic heart disease etc.) were excluded from our study.

In the present study, the patients received Olmevas AM 40/5 (Olmesartan 40 mg and Amlodipine 5 mg, manufactured by Popular Pharmaceuticals PLC). They received medications once daily for 8 weeks. After receiving our prescribed medicine, our patients were re-examined after 8th week, 12th week, 16th week, 20th week, 28th week, 40th week, and 52 weeks.

Statistical Analysis

All data were recorded systematically in preformed data collection form, and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS 21 (Statistical Package for Social Sciences) for Windows version 10. A probability value <0.05 was considered as a level of significance. Ethical Review Committee of Popular Medical College Hospital, Dhaka, Bangladesh approved the study.

RESULT

Table 1: Baseline characteristics of our study subjects

Baseline	N=210	P (%)	P-value
Mean age (years)	52.8 ± 11.3		0.486
Gender			
Male	143	68.10	
Female	67	31.90	
Smoking	184	87.62	

Baseline	N=210	P (%)	P-value
History of hypertension	121	57.62	
History of asthma	87	41.43	
History of COPD	74	35.24	
BMI (kg/m^2)	27.67±4.24		0.614
Heart Rate (per minute)	76.0 ± 11.9		0.474
Systolic blood pressure (mm Hg)	155.24 ± 20.78		0.641
Diastolic blood pressure (mm Hg)	95.94 ± 11.69		0.162
Comorbidities			
DM	189	90.00	
Dyslipidemia	118	56.19	

Table 1 shows the baseline characteristics of our patients. We found the mean age was 52.8 ± 11.3 years. Most of our patients were male (68.10%) compared to female (31.90%). Among our patients, 87.62% were smokers and 57.62% had a history of hypertension. The mean BMI was 27.67±4.24 kg/m^2, heart rate was 76.0 ± 11.9 beats /min. At baseline, the mean SBP and DBP were 155.24 ± 20.78 and 95.94 ± 11.69 respectively. As comorbidity, we found DM (90%) and dyslipidemia (56.19%) in our patients.

Table 2: Distribution of our study patients by mean seated blood pressure

Time point	Blood pressure	Group A (N=70)	Group B (N=70)	Group C (N=70)	P-value
At 8th week	SeSBP (mmHg)	154.0 ± 10.2	153.0 ± 10.4	152.5 ± 11.1	**0.742**
	SeDBP (mmHg)	98.1 ± 8.8	97.7 ± 8.1	96.7 ± 6.1	
At 12th week	SeSBP (mmHg)	153.2 ± 7.4	153.0 ± 8.4	151.0 ± 10.4	**0.674**
	SeDBP (mmHg)	97.1 ± 6.8	97.4 ± 5.8	97.6 ± 7.1	
At 16th week	SeSBP (mmHg)	153.0 ± 6.7	153.2 ± 6.4	151.1 ± 8.4	**0.021**
	SeDBP (mmHg)	96.2 ± 5.7	96.7 ± 4.1	95.7 ± 5.3	
At 20th week	SeSBP (mmHg)	150.8 ± 7.6	150.0 ± 8.4	151.0 ± 8.4	**0.074**
	SeDBP (mmHg)	95.7 ± 3.8	95.7 ± 4.1	95.1 ± 3.4	
At 28th week	SeSBP (mmHg)	148.0 ± 7.4	149.0 ± 7.1	147.0 ± 8.4	**0.042**
	SeDBP (mmHg)	94.1 ± 2.9	94.7 ± 3.8	94.7 ± 4.1	
At 40th week	SeSBP (mmHg)	143.8 ± 10.2	144.0 ± 10.4	143.0 ± 11.4	**0.034**
	SeDBP (mmHg)	94.2 ± 3.8	94.7 ± 4.1	94.1 ± 4.1	
At 52 week	SeSBP (mmHg)	133.0 ± 10.4	134.0 ±9.4	132.0 ± 11.4	**0.014**
	SeDBP (mmHg)	94.1 ± 3.8	94.7 ± 4.1	94.2 ± 3.1	

SeDBP =Seated diastolic blood pressure; SeSBP =Seated systolic blood pressure

Table 2 shows the mean blood pressure of our patients. In the 8th week, the mean SeSBP was 154.0 ± 10.2,153.0 ± 10.4, and 152.5 ± 11.1 mmHg in Groups A, B & C respectively. The mean SeDBP was 98.1 ± 8.8, 97.7 ± 8.1 & 96.7 ± 6.1 mmHg in Groups A, B & C respectively. At 52 week, the mean SeSBP decreased to 133.0 ± 10.4, 134.0 ±9.4 & 132.0 ± 11.4 mmHg in Group A, B & C respectively, and the mean SeDBP also decreased to 94.1 ± 3.8, 94.7 ± 4.1 & 94.2 ± 3.1 mmHg in Group A, B & C respectively.

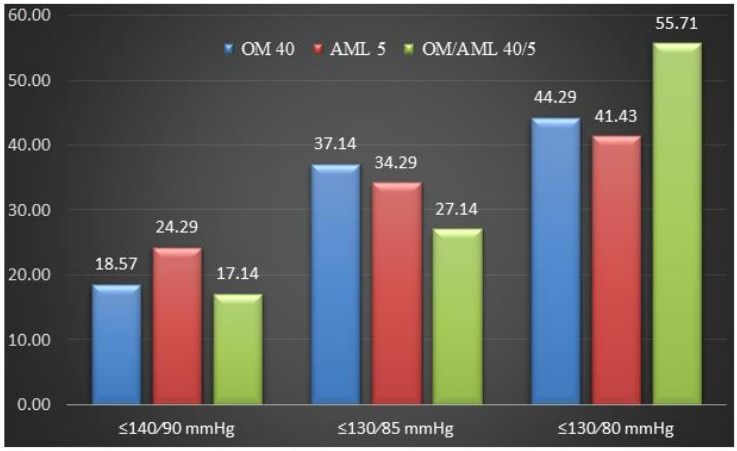

Figure 1: Distribution of our study patients by blood pressure at the end of our study

Figure 1 shows the blood pressure of our patients at 52 weeks of the study. We found the majority of patients in AML 5 group had ≤140⁄90 mmHg blood pressure than the other groups at the end of our study. Patients who had ≤130⁄85 mmHg, were higher in OM 40 group. Patients having ≤130⁄80 mmHg blood pressure during the last week of the study were highest in OM/AML 40/5 mg group.

Table 3: Distribution of our patients by side effects & adverse events

Side effects	Group A	Group B	Group C
Drowsiness/ Dizziness	10 (14.29%)	6 (8.57%)	2 (2.86%)
Flatulence	2 (2.86%)	1 (1.43%)	1 (1.43%)
Headache	3 (4.29%)	2 (2.86%)	0
Nausea/Vomiting	3 (4.29%)	2 (2.86%)	1 (1.43%)
Constipation	2 (2.86%)	0	1 (1.43%)
Stomach/Abdominal pain	2 (2.86%)	2 (2.86%)	0
Adverse events			
Blood bilirubin increased	1 (1.43%)	-	0
Blood cholesterol increased	0	-	1 (1.43%)
Blood triglycerides increased	0	-	1 (1.43%)
Blood creatine phosphokinase increased	1 (1.43%)	0	1 (1.43%)
White blood cell count decreased	-	1 (1.43%)	0
Aspartate aminotransferase increased	-	3 (4.29%)	0
Alanine aminotransferase increased	2 (2.86%)	2 (2.86%)	0

In Table 3 we showed the side effects & adverse events of our patients. The majority of patients had drowsiness/dizziness in Group A (14.29%) than in Group B (8.57%) & Group C (2.86%). Followed by headache and nausea/vomiting both were 4.29% in Group A, and 2.86% in Group B while in Group C only 1 patient got nausea and no side effects of headache. Group C didn't get any stomach or abdominal pain as a side effect but both Group B & C found 2.86% of our patients. In Group A, 4 adverse events were found, and in Group B 6 events were found while in Group C only 3 cases were found.

DISCUSSION

In the present study, we showed the efficacy and safety of a 40/5 mg fixed-dose combination of OM/AML in our patients with mild to moderate hypertension in a tertiary care hospital. Patients with type 2 diabetes, high body mass index, mild to severe hypertension, and patients over the age of 60 have all been demonstrated to benefit from fixed-dose OM/AML combos safely and effectively.

In terms of lowering both SeDBP and SeSBP, we discovered that the fixed-dose combination of 40/5 mg OM/AML was considerably more successful than monotherapy with either component. Furthermore, a greater number of our patients met their blood pressure goals using combination therapy than through monotherapies.

Several studies found fixed-dose OM/AML combinations as safe and effective in subgroups such as blacks, patients over the age of 65, patients with type 2 diabetes, patients with a high body mass index, and those with severe hypertension [21-25]. Furthermore, a titrate-to-goal study of this combination reported that combinations as high as 10/40 mg OM/AML were well tolerated with few adverse effects. [26] The results observed with OM/AML combination therapy in this study are consistent with the results from similar studies evaluating fixed-dose OM/AML combinations [27-30]. Several studies evaluated ARB/AML combinations are also consistent with our findings [31, 32].

After 8 weeks, the mean SeSBP significantly reduced to 152.5 ± 11.1 mmHg from baseline in OM/AML 40/5 mg group. The mean SeDBP also reduced to 96.7 ± 6.1 mmHg in OM/AML 40/5 mg group than the other two groups. Zhu *et al*., reported the mean reduction of trough SeSBP/SeDBP was about 13.8/11.6 mmHg in OM/AML 20/5 mg group, and 10.5/9.6 mmHg in OM 40 mg group, and their second study they mentioned the mean reduction of trough SeSBP/SeDBP was about 14.6/11.9 mmHg in OM/AML 20/5 mg group, and 9.1/7.7 mmHg in AML 5 mg group after the completion of 8-week treatment [27].

In our study, the most common side effects were drowsiness/dizziness, headache, nausea/vomiting, and stomach /abdominal pain. We found 4, 6 & 3 adverse events in OM 40 mg, AML 5 mg and OM/AML 40/5 mg group respectively. Ball *et al*., discovered that olmesartan/HCTZ patients reported upper respiratory tract infections, flushed faces, and dizziness more frequently than placebo users. [33] According to multiple case reports and research studies, the most well-known serious adverse event associated with olmesartan is sprue-like enteropathy [34-36]. Rubio-Tapia *et al*., first reported that 22 olmesartan recipients with chronic diarrhea could recover after discontinuing the medication [37]. Watery diarrhea, nausea, weight loss, and abdominal pain are the typical signs of olmesartan-induced enteropathy, and these symptoms can go away when the drug is stopped. Studies on pathology revealed

distinct inflammatory alterations in the intestinal mucosa, including villous blunting and nearly total villous atrophy of the mucosa in the small intestine [29, 36–38].

Long-term studies examining the effects of antihypertensive medication categories on cardiovascular morbidity and mortality provide another opportunity to assess combination therapy, as each class of drugs has effects on the cardiovascular system beyond just decreasing blood pressure. For individuals who have mild to moderate hypertension, high blood pressure-reducing ability is likely not necessary, even though it is vital when treating severe hypertension. On the other hand, the extra blood pressure reductions brought about by combination therapy are clinically significant and may result in notable improvements in cerebrovascular and cardiovascular outcomes. There is a correlation between small reductions in blood pressure and decreased risk of stroke, heart attacks, and mortality.

The current investigation has demonstrated that combination therapy combining OM and AML provides extra antihypertensive efficacy for patients with mild to moderate hypertension who have not responded to either medication used alone. Consequently, these patient's blood pressure was successfully regulated by an OM/AML 40/5 mg fixed-dose combo pill. For individuals with hypertension, this combination is anticipated to provide more therapeutic advantages than monotherapy.

Many studies have shown that the combination of olmesartan and amlodipine reduced inflammatory markers and increased insulin sensitivity more than either drug alone. This combination can be extremely helpful for hypertensive individuals who experience a variety of symptoms [30, 39, 41].

Limitations of the study

Our study was a single-center study. We took a small sample size due to our short study period. After evaluating these patients, we follow up with them for only one year, and after that, we do not know any other possible interference that may happen in the long term with these patients.

CONCLUSION AND RECOMMENDATIONS

In our study, we discovered that Olmevas AM (OM/AML) 40/5 mg was more effective at decreasing blood pressure than either OM 40 mg or AML 5 mg. There were no unexpected or unusual safety concerns found with OM/AML combo therapy. We found that Olmevas AM (OM/AML) 40/5 mg had more long-term effects than OM (Olmesartan) 40 mg or AML (Amlodipine) 5 mg among patients with mild to severe essential hypertension.

So further study with a prospective study design including a larger sample size needs to be done to validate and evaluate our findings.

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Conflict of Interest: None declared

Ethical Approval: The study was approved by the Institutional Ethics Committee

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