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A comparative study of efficacy and safety of drugs in stage I hypertensive patients attending cardiac OPD at tertiary care hospital

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Abstract

To study the efficacy and safety profile of Azilsartan 40 mg and Olmesartan 40 mg in stage I systemic Hypertension among patients attending cardiac OPD in a tertiary care center. All patients with stage I systemic hypertension of either sex, aged 20-65 years, with blood pressures of >140/90 mmHg or diabetes mellitus attending the cardiac outpatient. After initial screening, diagnosed cases of essential hypertension were randomly allocated to either group 1 (Tablet Azilsartan 40 mg or group 2 (Tablet Olmesartan 40 mg). The patients were advised to report for follow-up for review on the 4th, 8th, 12th, and 24th week.The mean decrease in the systolic blood pressure in both groups was statistically significant with a P value of <0.0000001. Both drugs controlled blood pressure at similar proportions. However, the mean of SBP and DBP for the Azilsartan group was lower than the Olmesartan Group. Both drugs were tolerated well, and no significant adverse effects were noted during the study.

Keywords: Hypertension; Olmesartan; Azilsartan; Hospital

1. Introduction

Hypertension is the most powerful risk factor for the cardiovascular diseases and the final purpose of antihypertensive treatment is to reduce morbidity and mortality of cardiovascular disease associated with hypertension. Blood pressures (BPs) usually follow a distinct circadian rhythm, characterized by a nocturnal decline during sleep of 10%–30%, followed by a moderate-to marked increase coinciding with the time of awakening [1]. Morning hypertension is an important clinical condition that is closely related to cardiovascular disease and is a significant predictor of target organ damage [2]. To control morning BPs, well-tolerated antihypertensive agents with long durations of action are required. Hypertension is defined as either a sustained systolic blood pressure greater than 140 mm Hg or a sustained diastolic blood pressure greater than 90 mm Hg, according to the Joint National Committee (JNC VIII) on hypertension. Hypertension is one of the leading risk factors for ischemic heart disease, stroke, heart failure, and renal dysfunction. According to WHO data, the overall prevalence of raised blood pressure in adults aged 25 and over was around 40% in 2008 [3]. According to Indian literature, the prevalence of Hypertension among Indians aged 25 and over is 29.8%. Significant differences in hypertension prevalence were noted between rural and urban parts [27.6% (23.2–32.0) and 33.8% (29.7–37.8); P=0.05]. Thus, the management of hypertension should be targeted not only for BP control but also for the reduction of overall cardiovascular and renal morbidity and mortality; in these settings, the lack of medical success is one of the many reasons triggering the development of new antihypertensive agents [4]. Several antihypertensives are available, like ACE inhibitors and angiotensin II receptor blockers (ARB). Blockade of the renin-angiotensin system with ACE inhibitors has provided effective treatment of these conditions; however, some of the adverse effects of ACE inhibitors appear to be unrelated to angiotensin II blockade. For example, cough and angioedema are due to other effects of ACE inhibition, such as the degradation of bradykinins and prostaglandins. In general, ARBs are well tolerated. None of the drugs reviewed has a specific, dose-dependent adverse effect. Because cough is seen as

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a class effect of ACE inhibitors, studies with ARBs have specifically addressed this concern. The frequency of cough is significantly lower in patients taking ARBs than in patients taking ACE inhibitors. Angiotensin receptor blockers (ARB) are more selective angiotensin blockers and have the potential for complete inhibition of angiotensin than ACE inhibitors. Nowadays, ARBs are the most commonly used antihypertensive drugs [5]. Azilsartan is a new ARB; it is potent and has a higher affinity for and slower dissociation from AT 1 receptor than other ARBs. Olmesartan is another ARB widely prescribed drug by practitioners.Olmesartan belongs to the angiotensin II receptor blocker (ARB) family of drugs, which also includes telmisartan, candesartan, losartan, valsartan, and irbesartan. ARBs selectively bind to angiotensin receptor 1 (AT1) and prevent the protein angiotensin II from binding and exerting its hypertensive effects, which include vasoconstriction, stimulation and synthesis of aldosterone and ADH, cardiac stimulation, and renal reabsorption of sodium, among others. Overall, olmesartan's physiologic effects lead to reduced blood pressure, lower aldosterone levels, reduced cardiac activity, and increased excretion of sodium [6].

Olmesartan also affects the renin-angiotensin aldosterone system (RAAS), which plays an important role in hemostasis and regulation of kidney, vascular, and cardiac functions. Pharmacological blockade of RAAS via AT1 receptor blockade inhibits negative regulatory feedback within RAAS, which is a contributing factor to the pathogenesis and progression of cardiovascular disease, heart failure, and renal disease. In particular, heart failure is associated with chronic activation of RAAS, leading to inappropriate fluid retention, vasoconstriction, and ultimately a further decline in left ventricular function. ARBs have been shown to have a protective effect on the heart by improving cardiac function, reducing afterload, increasing cardiac output and preventing ventricular hypertrophy and remodeling [7].

Olmesartan is commonly used for the management of hypertension and Type 2 Diabetes-associated nephropathy, particularly in patients who are unable to tolerate ACE inhibitors. ARBs such as olmesartan have been shown in a number of large-scale clinical outcomes trials to improve cardiovascular outcomes including reducing risk of myocardial infarction, stroke, the progression of heart failure, and hospitalization.Like other ARBs, olmesartan blockade of RAAS slows the progression of diabetic nephropathy due to its renoprotective effects [8].

Hence this study was taken up to study the efficacy and safety profile of both drugs. Azilsartan is a selective blocker of angiotensin-1 (AT1) receptors that prevents angiotensin II binding, resulting in vasodilation and a decrease in the effects of aldosterone because of the presence of such receptors in the vascular smooth muscle and the adrenal gland [9]. Azilsartan is a recently approved ARB and appears more efficacious in reducing BP than other ARBSs with a similar safety and tolerability profile. Many clinical trials have been conducted. comparing the efficacy of Azilsartan with other ARBs and ACE inhibitor Ramipril. Azilsartan has pleiotropic effects with antiproliferative effects within vascular-endothelial cells compared to other ARBs. Pleiotropic effects are attributable to Azilsartan's inverse agonistic properties. Azilsartan also suppresses angiotensin II-mediated plasminogen activator inhibitor type 1, causing increased collagen deposition, thus stabilizing atherosclerotic plaque. The trials have shown Azilsartan to be more effective in reducing the mean 24 h systolic BP compared to its counterparts. This study compares the efficacy and safety of newer ARB Azilsartan with Olmesartan.

2. Materials and methods

All patients with stage I systemic hypertension of either sex, aged 20-65 years, with blood pressures of>140/90 mmHg and/or diabetes mellitus attending the cardiac outpatient and meeting the inclusion criteria were enrolled in the study. Patients with a history of hypersensitivity or allergy to Azilsartan or Olmesartan, impaired kidney function test confirmed by serum creatinine level>2 mg/dl, impaired liver function test such as SGOT or SGPT>two times standard limit, asthma, pregnant and lactating women, those who have received other antihypertensive treatment, non-compliant patients, and those who are unwilling to give informed consent are excluded from the study. After the selection of patients, they were examined by the consultant physician to rule out Grade I Essential hypertension. Systolic and diastolic blood pressure was measured in the right arm, in a sitting posture, by the auscultatory method using a standard sphygmomanometer. [10] The pressure at which the sounds are first heard is taken as the systolic pressure, and the pressure at which the sounds disappear is taken as the diastolic pressure. Two blood pressure recordings are taken at an interval of 15 min by the same physician. After initial screening, the demographic data, family history, past medical history, findings of physical examination, and clinical examination were recorded in the case report form. Diagnosed cases of essential hypertension were randomly allocated to either group 1 (to receive tablet Azilsartan 40 mg or group 2 (to receive tablet Olmesartan 40 mg).

2.1. Group A

50 patients with stage I hypertension in one group received Azilsartan 40 mg once daily for 6 months.

2.2. Group O

50 patients with stage I hypertension in one group received Olmesartan 40 mg once daily for 6 months. All patients were instructed to take the tablet orally once a day in the morning with a glass of water. The patients were advised to report for follow-up for review on the 4th, 8th, 12th, and 24th week [11]. On each visit, blood pressure was recorded. Blood sugar, urine analysis, renal function test, liver function test, and ECG were assessed before starting the treatment. The patients were instructed to report immediately if they developed any adverse effects such as postural dizziness, nasopharyngitis, etc.

2.3. Study Design

This study is an observational study that is being carried out prospectively in the outpatient departments.

2.4. Inclusion Criteria

All patients with stage I systemic hypertension of either sex, aged 20-65 years, with blood pressures of>140/90 mmHg and/or diabetes mellitus attending the cardiac outpatient department at ACSR General Hospital and meeting the inclusion criteria were enrolled in the study [12].

2.5. Exclusion Criteria

Patients with a history of hypersensitivity or allergy to Azilsartan or Olmesartan, impaired kidney function test confirmed by serum creatinine level>2 mg/dl, impaired liver function test such as SGOT or SGPT>two times standard limit, asthma, pregnant and lactating women, those who have received other antihypertensive treatment, non-compliant patients, and those who are unwilling to give informed consent are excluded from the study [13].

2.6. Statistical methods

The data was entered and analyzed using Microsoft Excel 2010. Descriptive and inferential statistical analyses were used in the present study. Results on continuous measurements were presented on mean±SD (Min-Max), and results on categorical measures were presented in Number (%). Significance was assessed at a 5% level of significance. ANOVA test was used to compare intragroup variables [14].

3. Results and discussion

The evaluate the efficacy and safety profile of Olmesartan 40 mg and Azilsartan 40 mg in stage I Hypertension among patients attending cardiac OPD in a tertiary care center [Table 1].

Table 1 The age distribution

Age group	Group A	Percentage	Group O	Percentage
41-49 y	21	38	18	39
51-59 y	16	35	21	38
61-69 years	13	27	11	23
Total	50	100	50	100
mean±SD	49.56±9.4 y		50.15±8.69 y	

In the study population, among the A group, 39% belonged to the age group of 41-49 y, followed by 51-59 y (38%) and 61-69 y (23%). Among the O group, 38% belonged to 51-59 y, followed by (39%) of 41-49 y, and 61-69 y (23%) [Figure 2 & Table 1].

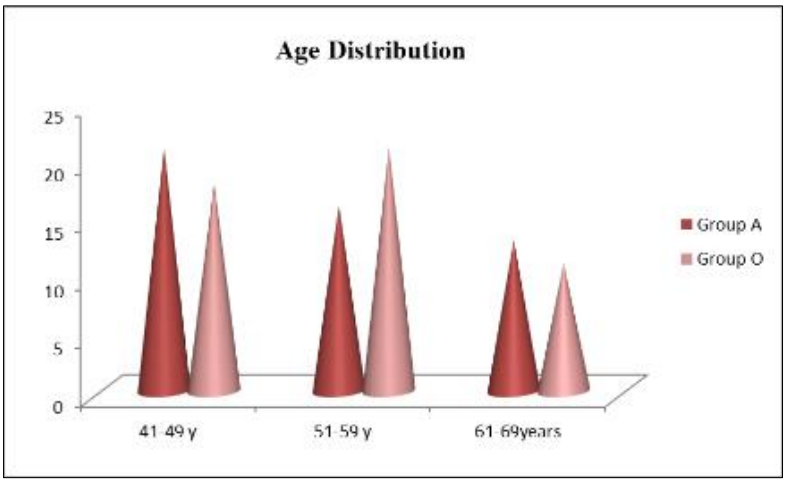

Figure 2 The age distribution

Table 2 Gender distribution

Gender	Group	azilsartan Percentage	Group	Olmesartan Percentage
Males	30	61	41	81
Females	20	39	9	19
Total	50	100	50	100

In the study population, among the O group, 61% were males, and 39% were females. Among the T group, 81% were males, and 19% were females [Figure 4 & Table 3].

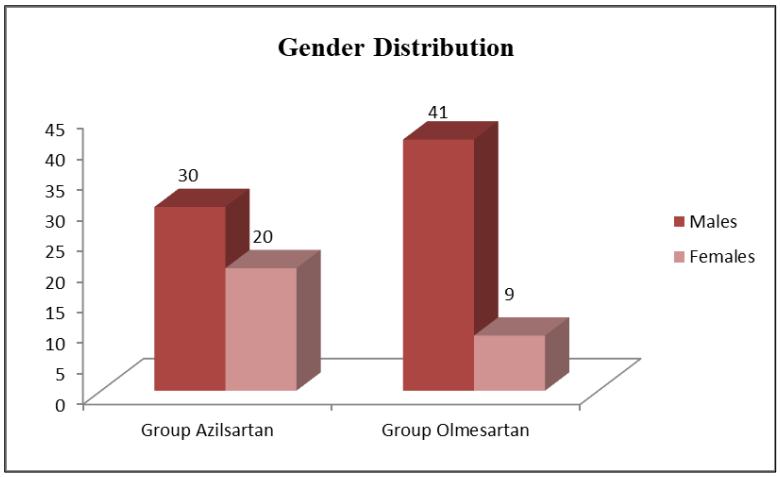

Figure 3 The gender distribution of the study population

Table 3 The mean values of parameters

Parameter	Group Azilsartan		Group Olmesartan		P value
	Mean	Standard Deviation	Mean	Standard Deviation	
Height in cms	165.2	6.25	157.4	8.1	T=1.74, P=0.08
Weight in kgs	64.8	10.52	70.9	6.9	T=-0.48, P=0.6
BodyMass Index in kg/m2	26.54	3.55	30.56	3.96	T=-1.36, P=0.17

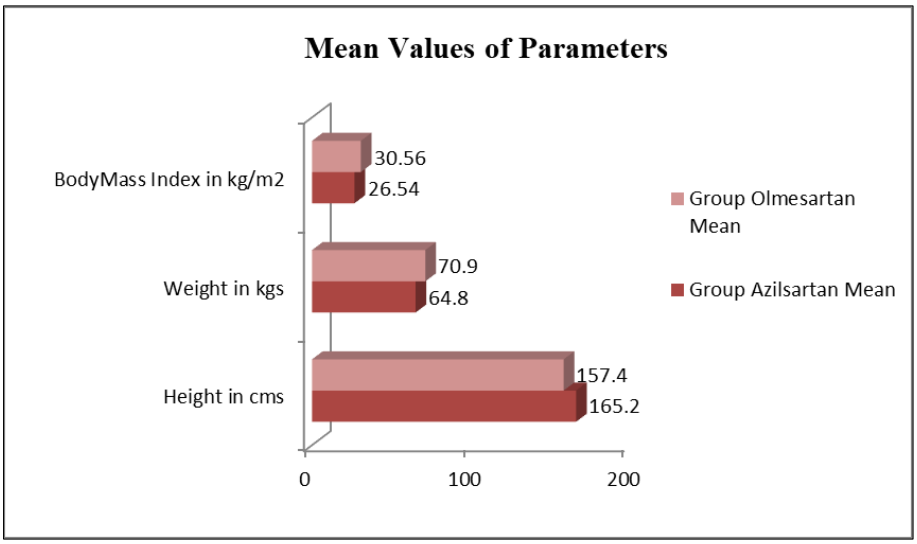

Figure 4 The mean values of parameters

In the study population, among the A group, the mean height was 165.2±6.25 cm. Among the O group, the mean height was 157.4±8.1 cm. No statistically significant difference was observed between the mean heights of both groups. In the study population, among the Azilsartan group, the mean weight was 64.8±10.52 kgs. Among the Olmesartan group, the mean weight was 70.9±6.9 kgs. No statistically significant difference was observed between the groups' mean weights. In the study population, the Azilsartan group, the mean BMI was 26.54 kg/m2. The Olmesartan group's mean BMI was 30.56±3.96 kg/m2. No statistically significant difference was observed between the mean BMI of the groups [Figure 6 & Table 5].

Table 4 The mean blood pressure values

Baseline Parameter	Group Azilsartan		Group Olmesartan	
	Mean	Standard Deviation	Mean	Standard Deviation
Systolic Blood pressure in mmHg	149.37	5.19	148.57	4.88
Diastolic Blood pressure in mmHg	93.37	4.15	93.20	3.92

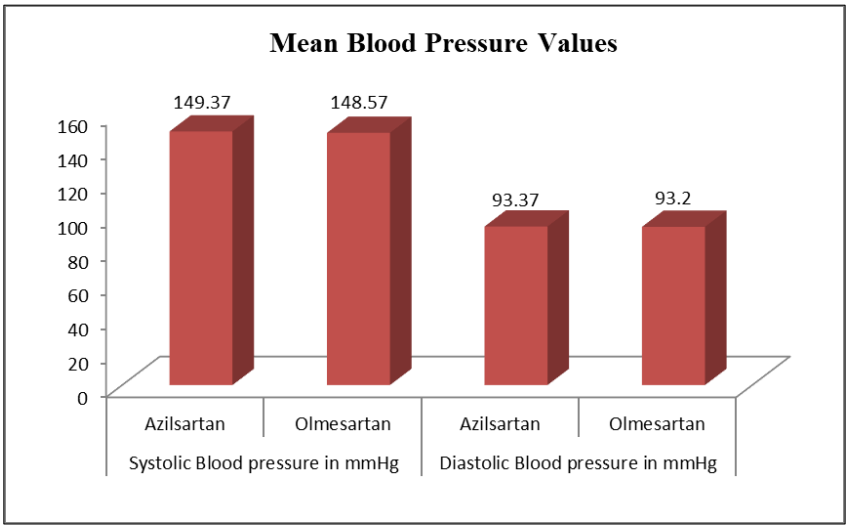

Figure 5 The mean blood pressure values of Baseline Parameters

Table 5 The mean blood pressure values in 4th week

Blood pressure in 4thweek	Group Azilsartan		Group Olmesartan	
	Mean	Standard Deviation	Mean	Standard Deviation
Systolic Blood pressure in mmHg	144.35	5.37	142.21	5.29
Diastolic Blood pressure in mmHg	91.53	4.31	91.51	4.21

In the study population, among the Azilsartan group, the mean systolic blood pressure in 4th week was 144.35±5.37 mm Hg. The mean diastolic blood pressure was 91.53±4.31 mm Hg. Among the Olmesartan group, the mean systolic blood pressure in 4th week was 142.21±5.29 mm Hg. The mean diastolic blood pressure was 91.53±4.31 mm Hg [Figure 8 & Table 9].

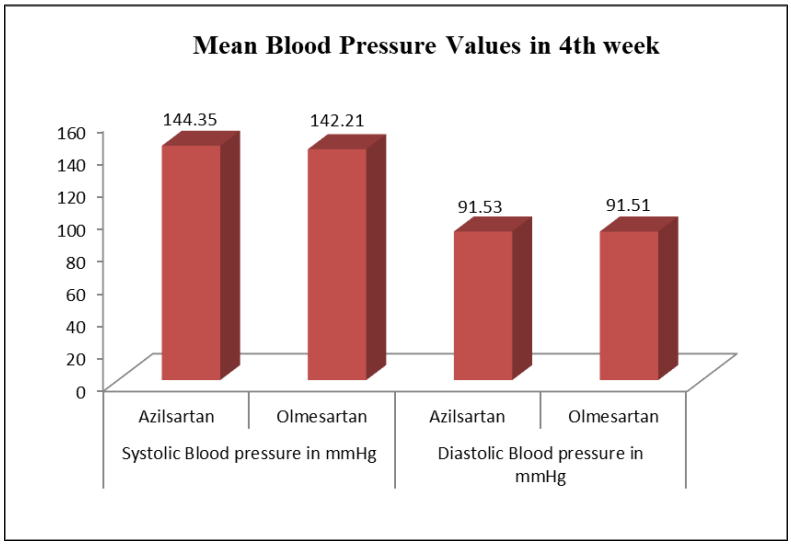

Figure 6 The mean blood pressure values in 4th week

Table 6 The mean blood pressure values in the 8th week

Blood pressure in 8thweek	Group Azilsartan		Group Olmesartan	
	Mean	Standard Deviation	Mean	Standard Deviation
Systolic Blood pressure in mmHg	138.29	4.51	138	3.2
Diastolic Blood pressure in mmHg	86.50	3.41	85.06	2.21

In the study population, among the Azilsartan group, the mean systolic blood pressure in the 8th week was 138.29±4.51 mm Hg. The mean diastolic blood pressure was 86.50±3.41 mm Hg. Among the Olmesartan group, the mean systolic blood pressure in the 8th week was 138±3.2 mm Hg. The mean diastolic blood pressure was 86.06±2.21 mm Hg [Figure 10 & Table 11].

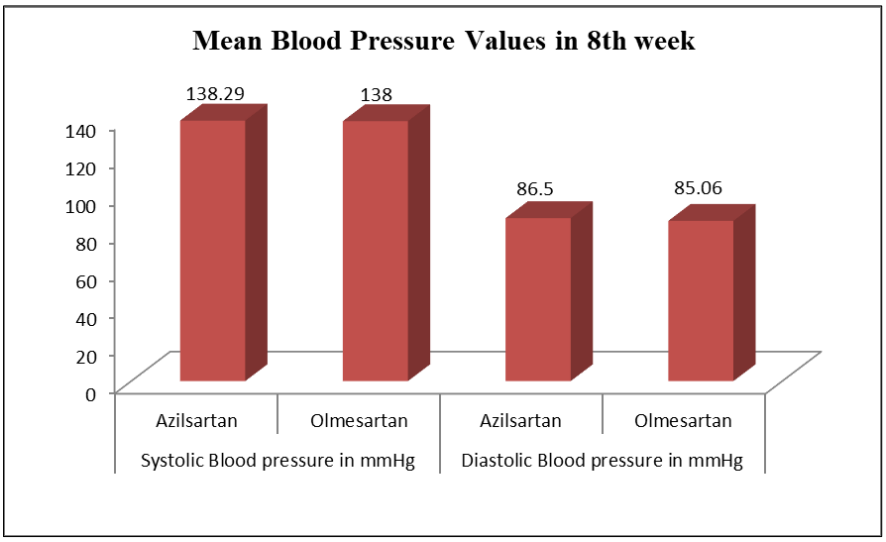

Figure 7 The mean blood pressure values in 8th week

Table 7 The mean blood pressure values in the 12th week

Blood pressure in 12thweek	Group Azilsartan		Group Olmesartan	
	Mean	Standard Deviation	Mean	Standard Deviation
Systolic Blood pressure in mmHg	132.67	5.1	128.41	6.2
Diastolic Blood pressure in mmHg	83.53	1.67	85.21	3.21

In the study population, among the Azilsartan group, the mean systolic blood pressure in the 12th week was 132.67±4.1 mm Hg. The mean diastolic blood pressure was 83.53±2.67 mm Hg. Among the Olmesartan group, the mean systolic blood pressure in the 12th week was 128.41±6.2 mm Hg. The mean diastolic blood pressure was 85.21±3.21 mm Hg [Figure 12 & Table 13].

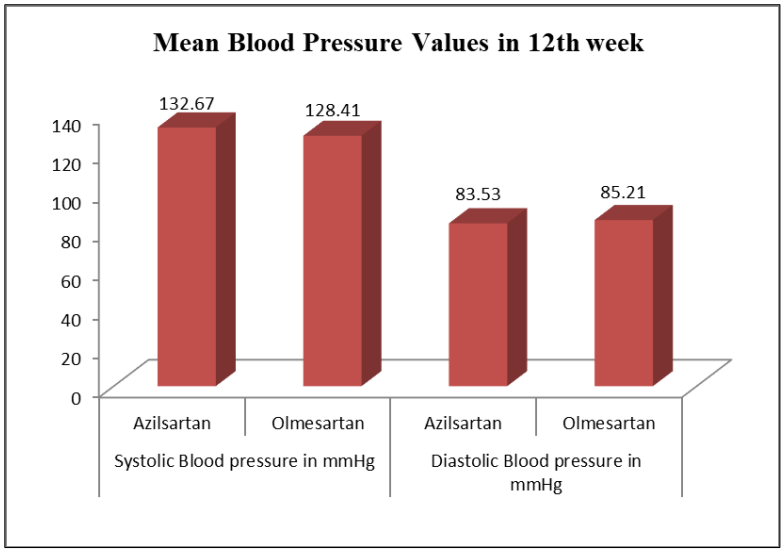

Figure 8 The mean blood pressure values in 8th week

Table 8 The mean blood pressure values in the 24th week

Blood pressure in 24thweek	Group Azilsartan		Group Olmesartan	
	Mean	Standard Deviation	Mean	Standard Deviation
Systolic Blood pressure in mmHg	120	5.2	124	3.9
Diastolic Blood pressure in mmHg	81.01	3.1	82	6.21

In the study population, among the Azilsartan group, the mean systolic blood pressure in the 24th week was 120±5.2 mm Hg [Figure 13 & Table 15]. The mean diastolic blood pressure was 81.01±3.1 mm Hg. Among the Olmesartan group, the mean systolic blood pressure in the 24th week was 124±3.9 mm Hg. The mean diastolic blood pressure was 82±6.21 mm Hg.

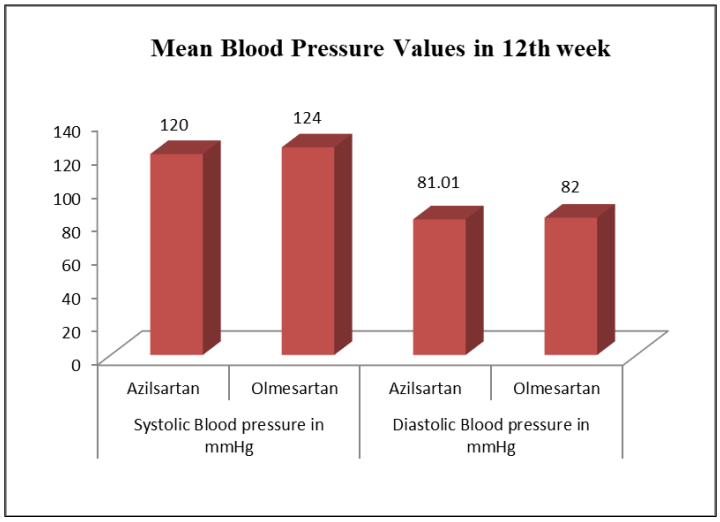

Figure 9 The mean blood pressure values in 12th week

Table 9 The mean blood pressure values at various intervals

S. No	Parameter	Systolic blood pressure (mmHg)			
		Group azilsartan	ANOVA P value	Group Olmesartan	ANOVA P value
1	Baseline	149.37±5.19	<0.0000001	148.57±4.88	<0.0000001**
2	4th week	144.35±5.37	(Highly significant)	142.21±5.29	(Highly significant)
3	8th week	138.29±4.51		138±3.2	
4	12th week	132.67±5.1		128.41±6.2	
5	24th week	120±5.2		124±3.9	

In the study population, among the Azilsartan group, the baseline means systolic blood pressure was 149.37±5.19, which decreased to 120±5.2 mm Hg at the end of the study period [Figure 16 & Table 17]. The difference between the SBP at various intervals is statistically significant, with a P value of <0.0000001.

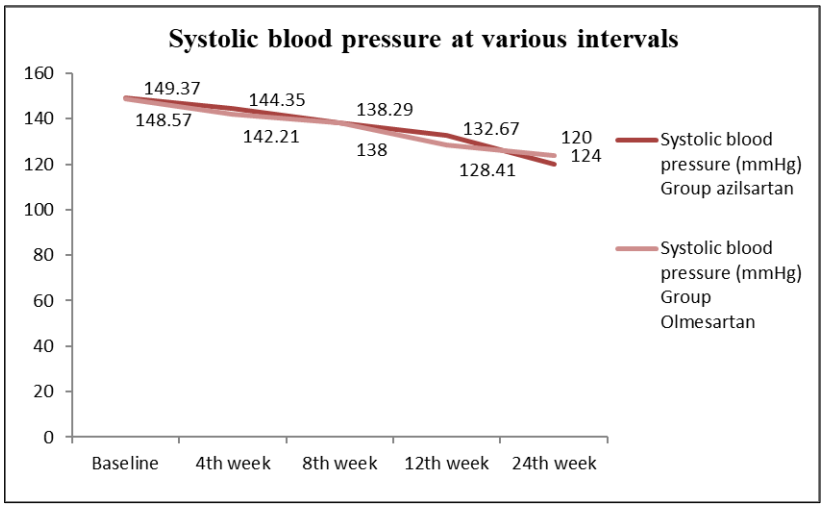

Figure 10 The systolic blood pressure at various intervals

Table 10 The mean blood pressure values at various intervals

S. No	Parameter	Diastolic blood pressure (mmHg)			
		Group azilsartan	ANOVA P value	Group Olmesartan	ANOVA P value
1	Baseline	91.37±4.15	<0.0000001	91.20±2.92	<0.0000001**
2	4th week	90.53±3.31	(Highly significant)	90.51±3.21	(Highly significant)
3	8th week	86.50±3.41		87.06±3.21	
4	12th week	81.53±2.67		82.21±4.21	
5	24th week	80±2.1		81±5.21	

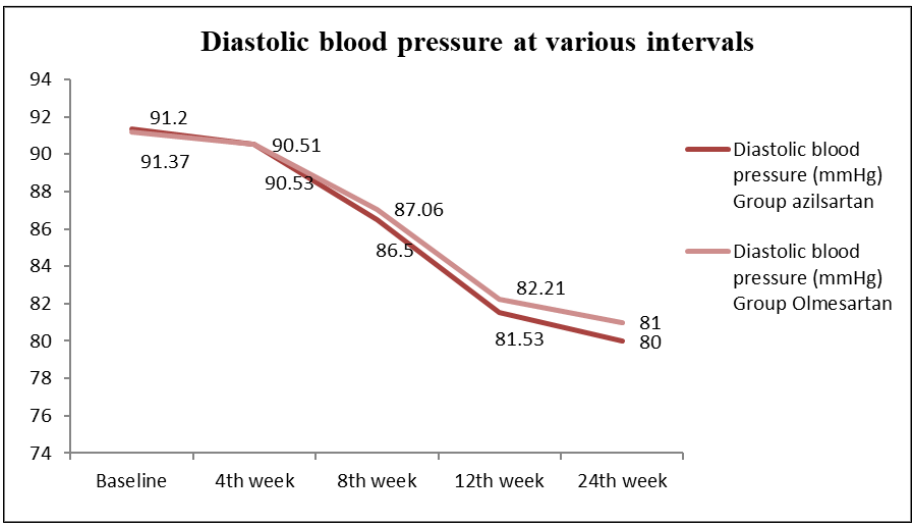

Figure 11 The diastolic blood pressure at various intervals

In the study population, among the Azilsartan group, the baseline means diastolic blood pressure was 91.37±4.15, which decreased to 80±2.1 mm Hg at the end of the study period [Figure 18, 20 & Table 19]. The difference between the DBP

at various intervals is statistically significant, with a P value of <0.0000001. Among group Olmesartan, the baseline means diastolic blood pressure was 91.20±2.92 mmHg which decreased to 81±5.21 mm Hg at the end of the study period. The difference between the DBP at various intervals is statistically significant, with a P value of <0.0000001.

Table 11 The adverse drug reactions/side effects

Adverse drug reactions	Group azilsartan	Percentage	Group Olmesartan	Percentage
Present	5	13	8	15
Absent	43	87	42	85
Total	50	100	50	100

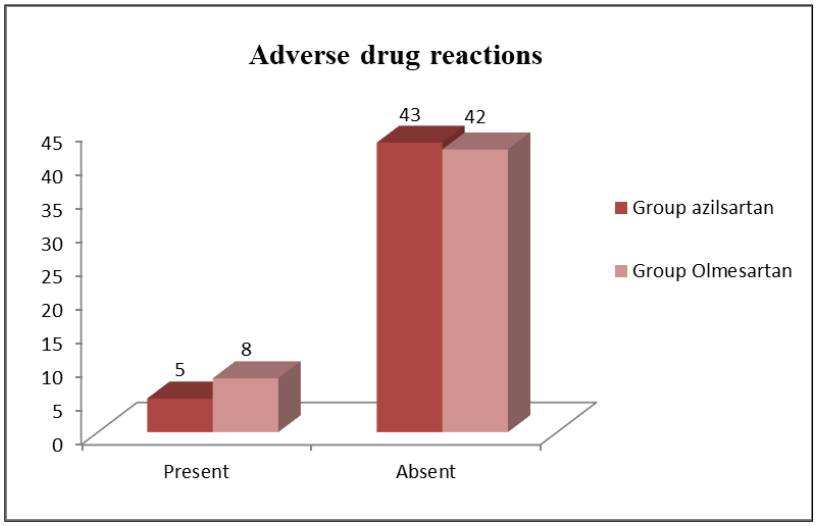

Figure 12 Adverse drug reactions among the study population: In Group A and O

In the study population, among the Azilsartan group, 12% had experienced adverse effects of the drugs. Among the Olmesartan group, 14% had experienced adverse effects from the drugs [Figure 22 & Table 21].

Table 12 The types of adverse drug reactions/side effects

Adverse drug reactions/Side effects	Group azilsartan	Percentage	Group Olmesartan	Percentage
Headache	2	32.33	1	13.28
Nausea	1	17.66	2	29.56
Fatigue	2	17.66	3	42.84
Dizziness	1	32.33	1	15.28
Total	6	100.00	7	100.00

In the study population, among the Azilsartan group, only 2 patients reported headache and Fatigue. Whereas dizziness, nausea and fatigue were reported by one patient each figure 12. Among the Olmesartan group, 3 patients reported fatigue and 2 reported nausea. Headache and dizziness were reported by one patient each as shown in table 23 Figure 24.

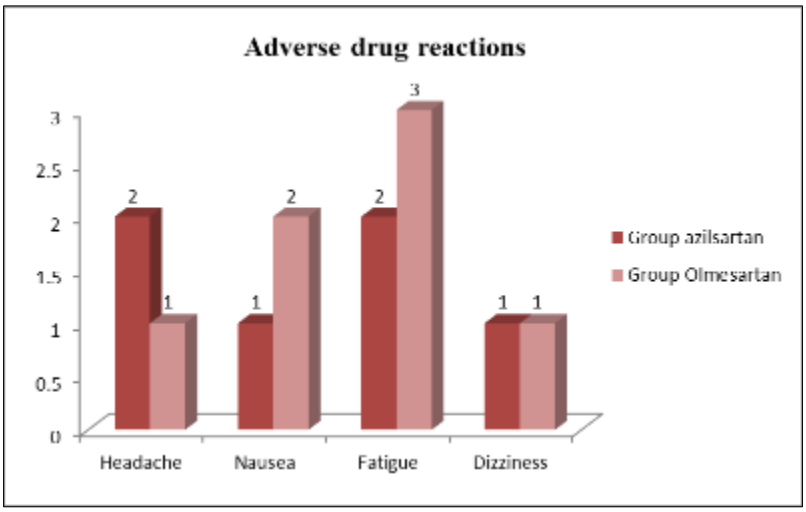

Figure 13 Adverse drug reactions among the study population: Among Group A and O

4. Conclusion

The present study was conducted to evaluate the efficacy and safety profile of Olmesartan 40 mg and Azilsartan 40 mg in stage I Hypertension patients. Both drugs controlled blood pressure at similar proportions. However, the mean of SBP and DBP for the Azilsartan group was lower than the Olmesartan Group. Both drugs were tolerated well, and no significant adverse effects were noted during the study. Both drugs are equally safe and efficacious, but Azilsartan can be considered superior in terms of efficacy.

Compliance with ethical standards

Acknowledgments

We want to thank Dr. Yerikala Ramesh sir, for supporting and guiding us in writing of research article.

Disclosure of conflict of interest

The authors declare that this study has no conflict of interest.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors'.

Statement of informed consent

Informed consent was not obtained from all individual participants included in the study.

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