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A Comparative Study to Evaluate the Efficacy and Safety of Azilsartan and Olmesartan in Stage 1 Hypertension

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Abstract

Background: Hypertension is sustained elevation of systemic arterial pressure. Hypertension is defined as systolic blood pressure >130mmHg and diastolic blood pressure >80mmHg according to AHA-2017 guidelines. **Aim:** To evaluate the efficacy and safety of azilsartan and olmesartan in stage 1 hypertension patients. **Methods:** This study was carried out in a tertiary care teaching hospital (in Punjab in northern India) consisted of 100 patients of newly diagnosed stage 1 hypertension as per the guidelines of 7th report of Joint national committee on Prevention, Detection, Evaluation and treatment of high blood pressure. The patients were enrolled in study following the inclusion and exclusion criteria after taking informed consent. The patients were subjected to thorough history, physical examination and relevant investigation. 50 patients were put on azilsartan (group 1) 40mg/80mg and 50 patients on olmesartan (group 2) 20mg/40mg for the treatment of stage 1 hypertension. The patients were followed at weekly intervals for 8 weeks. The patients were monitored for response to treatment by recording their blood pressure and doses were increased if the response is suboptimal after two weeks. Adverse effects of both the drugs were noted and compared. Data thus obtained was analyzed statistically to compare the efficacy and safety of azilsartan and olmesartan. **Results:** There was a gradual significant reduction in SBP and DBP in both the groups at 2 weeks, 4 weeks, 6 weeks, and 8 weeks after the treatment. On Comparison of fall in SBP and DBP between Group 1 and Group 2 at different time intervals the difference in SBP and DBP reduction between azilsartan and olmesartan was not statistically significant. Drug side effects like diarrhea, dizziness, headache and rashes were reported. There was a significant increase in side effects with olmesartan as compared to azilsartan. **Clinical Signifance:** Azilsartan is a new drug as compared to Olmesartan. So this study will help to compare and evaluate their efficacy and side effects in treatment of stage 1 hypertensive patients. It will help to promote the rational use of drugs. **Conclusions:** Both Azilsartan and Olmesartan were equally effective in reducing systolic and diastolic blood pressure but Azilsartan was tolerated better with fewer incidences of side effects as compared to Olmesartan.

Keywords:- Azilsartan, Drug Efficacy, Hypertension, Olmesartan.

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INTRODUCTION

Hypertension is one of the most important public health problem. It is a silent killer of mankind. It is common, asymptomatic, readily detectable, usually easily treatable and often leads to lethal complications if left untreated.[1]

Hypertension is one of those disorders which can be prevented by non- pharmacological measures especially by primordial prevention before its appearance as signs and symptoms in the body. The general measures that can be employed include: relief of stress, dietary management, regular aerobic exercises, weight reduction (as needed) and control of other risk factors leading to atherosclerosis. Modifications of lifestyle are a better approach to prevent the occurrence of hypertension.[2]

Hypertension is one of the leading risk factors for ischemic heart disease, stroke, heart failure, and renal dysfunction. Thus, management of hypertension should be targeted not only for BP control but also for the reduction of overall cardiovascular and renal morbidity and mortality.[3]

The angiotensin II receptor blockers (ARBs) represent a newer class of antihypertensive agents. Their mechanism of action differs from that of the angiotensin-converting enzyme (ACE) inhibitors, which also affect the renin-angiotensin system. The ARBs were developed to overcome several of the deficiencies of ACE inhibitors.[4]

The ARBs mechanism of action, selective inhibition of angiotensin II by competitive antagonism of the angiotensin II receptors has been speculated to reduce adverse effects and possibly improve clinical efficacy. ARBs displaces angiotensin II from the angiotensin II receptor and produce their blood pressure lowering effects by antagonizing angiotensin II-induced vasoconstriction, aldosterone release, catecholamine release, arginine vasopressin release, water intake, and hypertrophic response.[5]

Azilsartan is a new angiotensin receptor blocker. Azilsartan lowers blood pressure by blocking the action of angiotensin II at the AT1 receptor, a hormone that contracts blood vessels and reduces water excretion through the kidneys.[6]

Olmesartan is a non-peptide angiotensin II receptor antagonist. The drug acts by selectively blocking angiotensin II type 1 receptor sites in vascular smooth muscle, thereby inhibiting the vasoconstrictor effects of angiotensin II.[7]

Hypertension is a risk factor and may associate with several disorders or conditions. Many drugs are reported to be effective in treating hypertensive patients with different disorders or conditions. The present study was designed to evaluate and compare the efficacy and safety of Azilsartan and Olmesartan in stage 1 hypertension.

MATERIAL AND METHODS

This observational prospective study was carried out on 100 patients of newly diagnosed stage 1 hypertension as per the guidelines of 7th report of joint national committee on prevention, detection, evaluation and treatment of high blood pressure in a tertiary care teaching hospital situated in northern region of Punjab in north India. Informed and written consent was obtained from every

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participating patient and study was cleared by ethical committee of our institute.

Patient of either sex 18 – 65 years of age with newly diagnosed stage 1 hypertension that was systolic blood pressure 140-159 mmHg and Diastolic blood pressure 90-99 mmHg that were not have taken any anti-hypertensive treatment previously were included in this study. Patients with associated DM, CAD, LVF, chronic renal and liver failure, pregnancy and lactating women were excluded from this study. Those who fulfilled the selection criteria were explained the purpose of the study. 50 patients were put on the drug Azilsartan (group 1) 40/80mg dose and 50 patients were put on the drug Olmesartan (group 2) 20/40mg dose. To obtain uniform reading and to avoid instrumental errors, all readings were recorded by the same sphygmomanometer. Blood Pressure was recorded both in the supine and sitting position. Postural change in Blood Pressure was also noted. The bladder of the sphygmomanometer was inflated quickly to a pressure of 20 mm Hg above the systolic level, as recognized by the disappearance of the radial pulse. Korotkoff sound I was be taken as systolic blood pressure and Korotkoff sound V was taken as diastolic blood pressure.

Patients fulfilling the following requirements prior to recording the BP were included in the study:-

1) No caffeine for the preceding hour.
2) No smoking for the preceding 30 minutes.
3) No exogenous adrenergic stimulants e.g. phenylepherine in nasal decongestants.
4) Quiet and warm setting.

A number of recordings: at least two recordings were taken at interval of 10 minutes. If the readings varied by more than 5 mm hg, additional reading was taken until two readings were closed.

Patients were put on drug treatment with Azilsartan or Olmesartan after thorough history, clinical examination and relevant investigations. 50 patients were put on Azilsartan and 50 put on Olmesartan for the treatment of Hypertension. Azilsartan was started as 40 mg and Olmesartan as 20 mg in the morning. BP was recorded daily in the morning in the ward patients and weekly in the OPD patients. The patients were followed up at weekly intervals for 8 weeks. The dose was escalated if the response shown by the patients after two weeks was suboptimal. The appearance of side effects i.e dizziness, headache, angioedema, diarrhoea, cough, rash on clinical examination, and increase in serum creatinine by doing laboratory investigations were observed. A data was prepared on the basis of information and was analyzed statistically for antihypertensive effects and side effects of Azilsartan and Olmesartan.

RESULTS

[Figure 1] shows the mean age of patients in group 1 is 47.84 and the mean age of patients in group 2 is 43.60 years. Patients in group 1 were significantly older than the patients in group 2. [Figure 2] shows Amongst 50 patients included in group 1, 58% were males and 42% were females. In group 2, 52% were males and 48% were females. There was no significant difference in gender distribution in between both the groups. [Table 1 & 2] shows that the difference in SBP and DBP reduction between azilsartan and olmesartan were not significant at different time intervals. [Table 3] shows that in total 5 patients had side effects in group 1

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and 10 patients had side effects group 2. Drug side effects like diarrhea, dizziness, headache and rashes were reported. There was a significant increase in side effects with olmesartan as compared to azilsartan. [Table 4]

shows that the difference in serum creatinine levels between azilsartan and olmesartan was not significant.

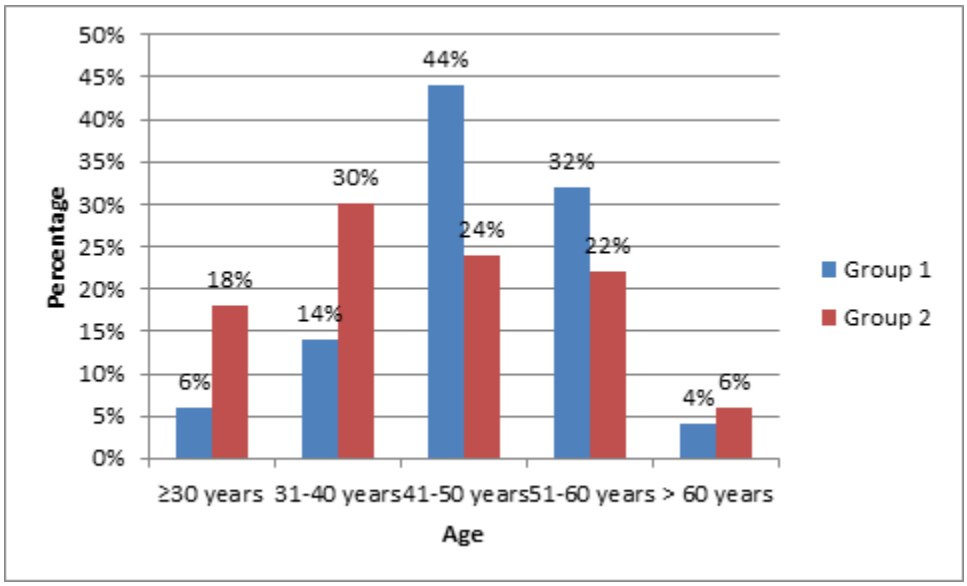

Figure 1: Age distribution

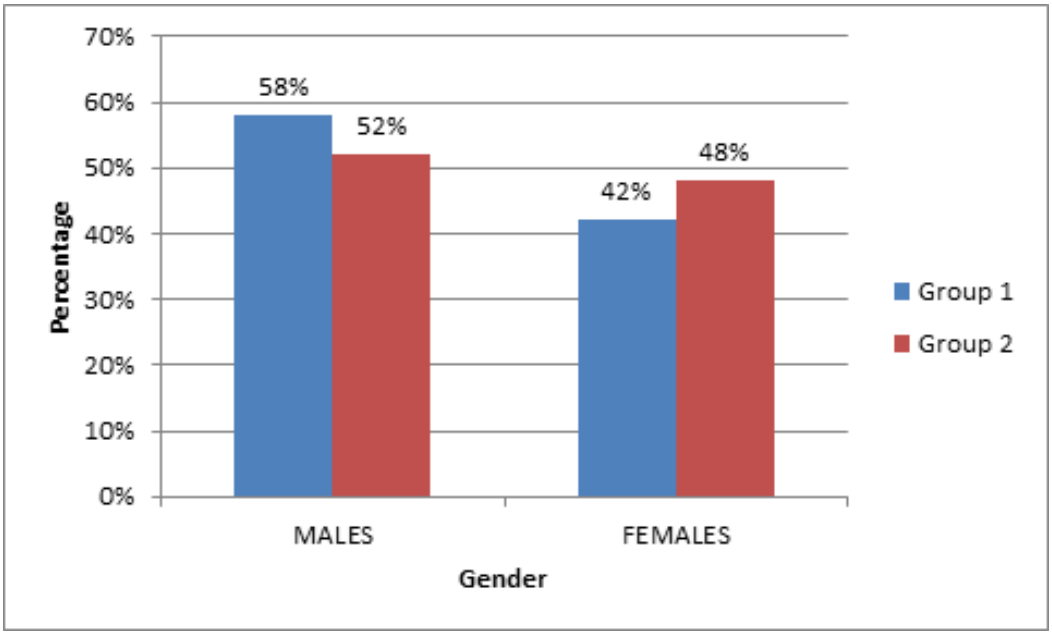

Figure 2: Gender distribution

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Table 1: Comparison of fall in SBP between group 1 and group 2 at different time intervals

Time intervals	0 weeks (Mean±SD)	2 weeks (Mean±SD)	4 weeks (Mean±SD)	6 weeks (Mean±SD)	8 weeks (Mean±SD)
Group 1	149±5.55	146.28±5.72	144.4±4.49	141.64±4.25	137.44±4.16
Group 2	148.64±5.07	146.44±5.66	143.12±3.9	140.16±3.47	138.32±3.71
P value (T TEST)	0.73	0.88	0.13	0.05	0.26

Table 2: Comparison of fall in DBP between group 1 and group 2 at different time intervals

Time intervals	0 weeks (Mean±SD)	2 weeks (Mean±SD)	4 weeks (Mean±SD)	6 weeks (Mean±SD)	8 weeks (Mean±SD)
Group 1	94.12±2.78	91.68±3.13	89.44±2.13	88.2±2.83	85.06±2.65
Group 2	94±2.79	92±2.88	89.52±2.72	87.96±3.71	86.68±3.37
P value (T TEST)	0.82	0.59	0.87	0.71	0.69

Table 3: Side effects from group 1 and group 2

Side effects	Group 1 (50)		Group 2 (50)		P value (Fishers exact test)
	Number of Patients	Percentage	Number of Patients	Percentage	
Diarrhea	1	2%	0	0	0.0001
Dizziness	2	4%	4	8%	
Rash	2	4%	2	4%	
Headache	0	0	4	8%	

Table 4: Comparison of serum creatinine in group 1 at different time intervals

Time intervals	0 weeks	2 weeks	4 weeks	6 weeks	8 weeks	P value (ANOVA)
Serum creatinine (Mean±SD)	0.69±0.34	0.71±0.33	0.76±0.34	0.84±0.26	0.75±0.29	0.13

DISCUSSION

The mean age of patients in the present study in group 1 (Azilsartan) was 47.84 ± 9.61 years and the mean age of patients in group 2 was 43.80 ± 11.70 years. The age was comparable in the two groups (p>0.05). So there was no significant difference in both groups as far as age is concerned [Table 1]. Patients in group 1 were significantly older than the patients in group 2. Sezai A et al (2016),[8] in their study compared azilsartan and olmesartan, and they reported that the overall mean age of patients in both the groups was 68.8 years which was older compared to the present study.

Shiga Y et al (2017),[9] compared the efficacy and safety of azilsartan to those of olmesartan in a prospective randomized clinical trial. They reported that the mean age of patients in the Azilsartan group was 72 years and the mean age of patients in the olmesartan group was 70 years which was older compared to the present study.

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Zaman ZA et al (2017),[10] conducted a study to compare the efficacy and tolerability of once-daily treatment of the new angiotensin type1 receptor blocker (ARB) Azilsartan with Olmesartan and Candesartan. They reported that the mean age of patients in azilsartan was 51 years and olmesartan was 52 years which was comparable to the present study.

In the present study in group 1, 58% were males and 42% were females. In group 2, 52% of patients were males and 48% were females. Although male preponderance was seen in our study this was statistically not significant as the p-value was >0.05. So there was no significant difference in gender distribution between both the groups. Similar results were reported by Sezai A et al, Shiga Y et al, and Zaman ZA et al in their studies.[8,9,10]

There was a gradual significant reduction in SBP and DBP in group 1 (azilsartan) and group 2 (olmesartan) at 2 weeks, 4 weeks, 6 weeks, and 8 weeks but the difference in SBP and DBP reduction between azilsartan and olmesartan was not significant statistically (p>0.05).

Shiga Y et al in their study concluded that the depressor effect of azilsartan was not different from that of olmesartan.[9]

White WB et al, Zannad F et al and Sica D et al in their studies reported that Azilsartan in clinically approved doses as azilsartan has been shown to lower 24-hour BP in hypertensive patients significantly more than the maximum approved dose of olmesartan, the latter being considered by some to be one of the most potent ARBs for lowering BP.[11,12,13]

Similar results were shown by Zaman A et al,[10] in their study who reported that all drugs reduced both systolic blood pressure (SBP) and Diastolic blood pressure (DSP) significantly, but the reduction in SBP and DSP with azilsartan (80mg) was significantly greater than with other drugs. The difference in BP reduction between azilsartan (40mg) and olmesartan (40mg) was not significant but both azilsartan (40mg) and olmesartan (40mg) were significantly more effective than candesartan (12mg).

In group 1 (Azilsartan) Side effects like diarrhea, dizziness and rashes were present in 3 patients at 2 weeks. Rash was present in one patient at 4 weeks and dizziness was presents in one patient at 6 weeks.

In group 2 (Olmesartan) rash was present in 1 patient at 2 weeks. Rash was present in one patient at 4 weeks; dizziness and headache were both present in 4 patients at 4 weeks.

In total 5 patients had side effects in group 1 and 10 patients had side effects in group 2. There was a statistically significant increase in side effects with olmesartan as compared to azilsartan.

Zaman ZA et al (2017),[10] in their study reported that Azilsartan had similar safety and tolerability profile compared to olmesartan and candesartan. The most common adverse effects such as headache, dyslipidemia, and dizziness were comparable to present study.

Bhosle DS et al (2018),[14] compared the efficacy and safety of AZL 40mg in patients of stage-I HTN. Adverse effects such as Upper respiratory tract inflammation, Gastroenteritis,

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headache, dizziness, and fatigue were reported with azilsartan similar to the present study.

Bhajni E et al (2020),[15] compared the efficacy, safety, and cost-effectiveness of AZL 40-80 mg in patients of stage-I HTN. Adverse effects such as nasopharyngitis, upper respiratory tract infection, gastroenteritis, headache, dizziness, and fatigue were reported with azilsartan which was comparable to the present study.

In group 1 there was no significant difference in the levels of serum creatinine at different intervals that is 0 weeks, 2 weeks, 4 weeks, 6 weeks and 8 weeks. In group 2 there was no significant difference in the levels of serum creatinine at different intervals that is 0 weeks, 2 weeks, 4 weeks, 6 weeks and 8 weeks. The difference in serum creatinine levels between azilsartan and olmesartan was not significant. It was observed that in both the groups the mean levels of serum creatinine were increased at the end of 8 weeks when compare to 0 weeks.

Sezai A et al (2016),[8] in their study compared the serum creatinine levels between azilsartan and olmesartan and they reported that there were no significant differences between the two groups which were comparable to the present study.

Shiga y et al (2017),[9] compared the safety and efficacy of Azilsartan and Olmesartan in patients with essential hypertension. Serum creatinine in the Azilsartan group significantly increased after 3 months as compared to the olmesartan group.

Kakio y et al (2017),[16] compared the practical efficacy of azilsartan and olmesartan. There were no significant differences in renal function between the two groups which were comparable to the present study.

CONCLUSIONS

Both Azilsartan and Olmesartan were equally effective in reducing systolic and diastolic blood pressure but Azilsartan was tolerated better with less incidence of side effects as compared to Olmesartan. It can be concluded that 40-80mg of Azilsartan once a day is as effective as 20-40mg of Olmesartan once a day in the treatment of stage 1 hypertension. However further studies with more patients are needed to establish the efficacy and safety of Azilsartan and Olmesartan.

Limitations of the study

We recognize the some limitations of our study. The present study was a single center study and hence not reflects the wider population of this region. Further studies with more patients are needed to establish the efficacy and safety of Azilsartan and Olmesartan.

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