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Original Research Article

A prospective comparative efficacy of azilsartan and telmisartan in hypertensive patients

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ABSTRACT

Background: Hypertension (HT) is defined as either a sustained systolic blood pressure of greater than 140 mmHg or a sustained diastolic blood pressure of greater than 90 mmHg, according to joint national committee (JNC VIII) on hypertension.
Methods: A prospective, open, randomized parallel group comparative study of AZL versus telmisartan was done in patients of stage-I HT. The study included 80 patients, 40 in each group (group I and group II) coming to the Department of Pharmacology, Mahatma Gandhi Medical College and Research Institute, Pillayarkuppam, Pondicherry from January 2016 to December 2017. The study was conducted over 8 weeks. Group-I, patients received azilsartan 40-80 mg per day in divided doses and group-II, patients received telmisartan 40-80 mg per day in divided doses according to severity of hypertension.
Results: Patients receiving AZL 40 mg and telmisartan 40 mg showed a significant fall ($p<0.05$) in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at 4 weeks and 8 weeks, when compared to baseline. The difference in SBP and DBP between group I (AZL) and II (telmisartan) was statistically significant at 4 weeks ($p<0.05$) and was highly significant at 8 weeks ($p<0.001$). Adverse effects such as nasopharyngitis, upper respiratory tract infection, gastroenteritis, headache, dizziness, and fatigue were reported with both drugs.
Conclusions: Reduction of BP with AZL was more as compared to telmisartan at 4 weeks and 8 weeks. Safety and tolerability were similar in both groups.

Keywords: Telmisartan, Azilsartan, SBP, DBP

INTRODUCTION

Hypertension is defined as either a sustained systolic blood pressure of greater than 140 mmHg or a sustained diastolic blood pressure of greater than 90 mmHg, according to joint national committee (JNC VIII) on hypertension.[1] Although many patients may not have symptoms but chronic hypertension can lead to heart disease and stroke, the top two causes of death in the world. Hypertension is also an important risk factor in the development of chronic kidney disease.[2]

Effective control of blood pressure in patients with hypertension is required to produce a maximum reduction in clinical cardiovascular events and expert consensus guidelines advocate BP levels <140/90 mmHg in patients lacking target organ involvement and <130/80 mmHg in patient with diabetes mellitus, heart disease, or kidney disease.[3] Angiotensin II appears to exert a central role in both the pathophysiology of essential hypertension and arteriosclerosis- associated hypertension6 and insulin resistance. Angiotensin receptor blockers are more selective blockers of angiotensin and have the potential

for complete inhibition of angiotensin than ACE inhibitors. Among the angiotensin receptor blockers telmisartan has favorable pharmacokinetic profile, has longest plasma half-life and is the commonly prescribed ARB.[4] After clinical introduction of losartan in 1995, US Food and Drug Administration (FDA) approved azilsartan medoxomil as the 8th ARB for the treatment of hypertension in 2018.[5] Azilsartan was discovered by modifying the tetrazole ring present in candesartan. Azilsartan has been shown to be effective in reducing BP when administered orally as either the ester prodrug azilsartan medoxomil or as the primary compound.[6] The aim of this study was to compare safety and efficacy of newer ARB azilsartan with telmisartan.

METHODS

The present study was conducted by the Department of Pharmacology, Mahatma Gandhi Medical College and Research Institute, Pillayarkuppam, Pondicherry, India from January 2016 to December 2017.

Total 80 patients with HT were evaluated after having fulfilled the inclusion and exclusion criteria, in the parallel group, comparative, randomized, prospective and open labelled study.

Inclusion criteria

Inclusion criteria were new patients with HT i.e., not on any antihypertensive therapy. Adult males and females of age 21 years or more.

Exclusion criteria

Exclusion criteria were patients already on anti-hypertensives. Patients who were hyper-sensitivity to AZL or telmisartan. Women who were pregnant, lactating or were planning to get pregnant. Evidence of severe renal disorder. Patients with hepatic insufficiencies. Patients who were not willing or were not able to comply with the proceedings of the study. Patients with severe bradycardia, cardiogenic shock, heart block, sick sinus syndrome, decompensated HF, bronchial asthma, hypothyroidism, hyperthyroidism, CVA, CAD.

Patients were randomly allocated into 2 groups from time to time i.e., 40 cases in each group. The study was conducted over 8 weeks. The study protocol was approved by institutional ethics committee.

A written informed consent was taken from patients after explaining them about study drugs. Patients in group I were given AZL 40 mg once daily and subsequent titration was carried out up to maximum recommended dose of 80 mg/d depending on therapeutic response.

Patients in group II were given telmisartan 40mg once daily and subsequent titration was carried out up to maximum dose of 80 mg/d depending on therapeutic response. BP was measured on day 0, 4th week and then on 8th week.

Following base line investigations were carried out at the commencement of treatment hemoglobin (Hb), total leucocyte count (TLC), differential leucocyte count (DLC), fasting blood sugar (FBS), blood urea, uric acid, serum creatinine, serum electrolytes, liver function test (LFT), lipidogram, echocardiography (ECG) and urine routine examination (R/E). At the end of the treatment the investigations were repeated and compared with the previous ones. Adverse effects as reported by patients were recorded and compared. For cost-effectiveness analysis, mean cost of drugs in both the treatment groups was calculated for 8 weeks, by noting the maximum retail price (MRP) of all the study drugs.

Effectiveness was calculated as mean change in mean blood pressure (MBP) from baseline to 8 weeks in both the treatment groups. Data was statistically analyzed using t-test. The results were eventually tabulated and graphically represented.

RESULTS

A total of 80 patients with stage-I HT were enrolled in the study and were randomly allocated into 2 groups i.e. 40 cases in each group. There were 19 (47.5%) males and 21 (52.5%) females in group I and 21 (52.5%) males and 19 (47.5%) females in group II. Statistical analysis showed that the difference between the 2 groups was not significant.

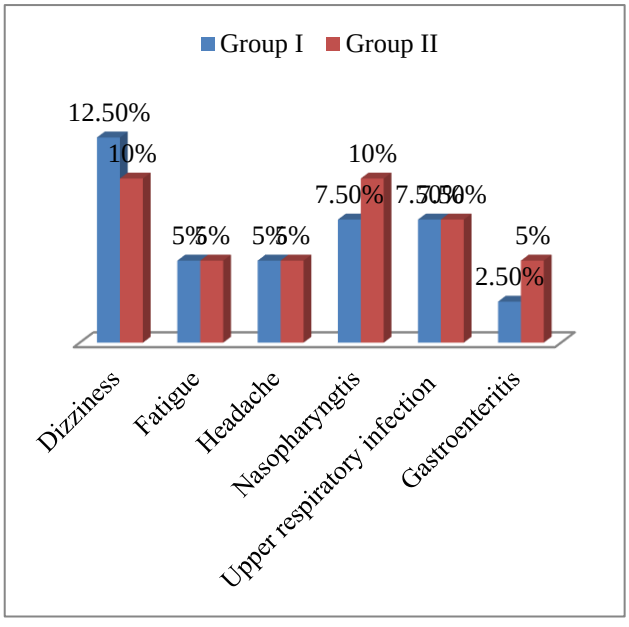

Figure 1: Comparison of adverse events in group I and group II.

The mean age in group I was 54.83 (8.12) years and the mean age in group II was 54.63 (8.95) years. Maximum number of individuals was in age group of 46-55 years.

Table 1: SBP at different visits in group I and group II.

Time intervals	Groups	N	Mean	SD	SE mean	Mean difference	T test	P value
Baseline	Group I	40	149.00	3.87	0.60	0.45	0.515	0.608
	Group II	40	149.45	3.95	0.62			
After 4 weeks	Group I	40	137.89	2.71	0.43	1.55	2.254	0.027
	Group II	40	139.35	3.40	0.54			
After 8 weeks	Group I	40	132.00	1.81	0.29	3.3	5.607	0.001
	Group II	40	135.30	3.25	0.51			

Table 2: DBP at different visits in group I and group II.

Time intervals	Groups	N	Mean	SD	SE mean	Mean difference	T test	P value
Baseline	Group I	40	91.20	1.86	0.28	0.8	1.894	0.062
	Group II	40	92.00	1.93	0.29			
After 4 weeks	Group I	40	85.20	1.86	0.31	0.85	2.089	0.040
	Group II	40	86.05	1.78	0.28			
After 8 weeks	Group I	40	80.70	1.32	0.21	2.5	6.337	0.001
	Group II	40	83.20	2.11	0.33			

Table 3: Mean blood pressure in group I and group II.

Group	MBP ±SD (baseline)	MBP ±SD (8 weeks)	Mean difference	T test	P value
Group I	110.42±1.91	96.90±1.75	13.54±0.17	12.011	0.001
Group II	110.07±1.75	100.00±1.21	10.10±0.61		

Table 4: Cost effectiveness analysis.

Parameters	Group I	Group II	Difference in cost C1-C2	Difference in effectiveness	ICER
Cost (Rs)	414.40±14.73	352.70±12.51	61.60±2.23	3.43±0.44	17.96
Fall in MBP (mmHg)	13.53±0.17	10.10±0.61			

Statistically, there was no significant difference in mean age of both the groups.

Table 1 shows, that in group I, the mean SBP prior to treatment was 149.00±3.87 mmHg but after treatment, the SBP reduced to 137.80±2.71 mmHg, and 132.00±1.81 mmHg at 4th week and 8th week respectively. The reduction in SBP was found to be statistically significant $p<0.001$ at 4th week and 8th week of therapy on comparing with the baseline readings. In the telmisartan-treated group, the mean SBP prior to treatment was 149.45±3.95 mmHg. After treatment, the SBP reduced to 139.35±3.41 mmHg and 135.30±3.25 mm Hg at 4th week and 8th week respectively. The reduction in the mean SBP was found to be statistically significant $p<0.001$ at 4th week and 8th week of therapy when compared with the baseline readings.

On comparing the mean SBP in patients on AZL and telmisartan at baseline, 4 and 8 weeks, the mean difference at baseline was 0.45 mmHg, at 4 weeks was 1.55 mmHg and mean difference at 8 weeks was 3.3 mmHg.

DISCUSSION

HT plays a major role in causing CVD and it is a leading cause of stroke, MI, HF and kidney disease. While the benefits of BP reduction have been well documented, the majority of patients of HT remain with poorly controlled BP. In developing countries, the high rate of undetected and untreated cases of hypertension is a major concern.[7] Since, HT is a chronic condition and its treatment is life long, it is important to ensure that the patient is compliant to antihypertensive therapy.

Some of the major factors contributing to poor patient compliance are medication costs, side effects of the drugs and poor quality of life.[8] Multiple classes of antihypertensive drugs are available for clinical management of hypertension like diuretics, beta blockers, alpha blockers, calcium channel blockers (CCB),

angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonist, centrally acting sympatholytic and vasodilators.[9]

AZL is a new ARB which was discovered by modifying the tetrazole ring of candesartan. In the present study, we have observed that both azilsartan 40 mg once daily and telmisartan 40 mg once daily are effective agents in reducing both SBP and DBP throughout the study period when measured at the baseline with 4th and 8th week in stage-I hypertension. When efficacy of azilsartan was compared with telmisartan, we found that azilsartan was more effective than telmisartan in reducing SBP and DBP.[10]

The MBP in group I at baseline was 110.43 (2.87) and at 8 weeks was 96.90 (3.07). The MBP in group II at baseline was 110.10 (2.85) and at 8 weeks was 100.00 (3.11). Mean difference was 13.53 in group I and 10.10 in group II, which was statistically significant on comparing the two groups. There was more lowering of blood pressure in group I (AZL group).[11]

White, Weber and Sica (2011) conducted a randomized trial on 1291 patients, whose mean age was 56 years and baseline mean SBP was 145 mmHg. AZL-M at 80 mg was more efficacious than valsartan at 320 mg and olmesartan at 40 mg.

There was greater lowering of mean SBP with AZL i.e., 14.3 mmHg as compared to 10.0 mmHg with valsartan and 11.7 mmHg with olmesartan. It demonstrates that AZL-M at its maximal dose has higher efficacy than both olmesartan and valsartan at their maximal, approved doses without increasing the incidence of adverse events.[12]

CONCLUSION

Though AZL and telmisartan belong to the same anti-hypertensive drug class i.e. ARBs and effectively reduce SBP and DBP, AZL is a better choice as compared to telmisartan in my study because it caused more statistically significant decrease in BP with a similar safety and tolerability profile as telmisartan. So, prevents future cardiovascular complications. However, the anti-hypertensive effects of azilsartan in hypertensive patients with serious comorbidities remain to be determined, as we have excluded patients having any comorbidities. Another limitation of this study is its limited sample size and short duration, as well as the follow ups could have more to look for the long-term adverse effects of azilsartan as not much studies have been done on it.

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

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