International Journal of Basic & Clinical Pharmacology
Sharma D et al. Int J Basic Clin Pharmacol. 2023 Nov;12(6):805-809
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20233190

Original Research Article

Comparison of efficacy of azilsartan with olmesartan in patients of hypertension: randomized controlled trial

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Received: 14 July 2023
Revised: 12 September 2023
Accepted: 13 September 2023

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ABSTRACT

Background: Azilsartan and olmesartan are members of ARBs, used in the management of hypertension. Objective was to evaluate efficacy of azilsartan with olmesartan in patients of hypertension.
Methods: A randomized, prospective, open label, comparative study was carried out in Pharmacology and Medicine department at Dr. RPGMC Kangra at Tanda, HP. The study stretched over one year and blood pressure was monitored at first, third and sixth month**.** Out of 69 patients, 35 patients in group A were prescribed tablet azilsartan 40 mg/day and 34 patients in group B patients were prescribed tablet olmesartan 20 mg/day. Tablet chlorthalidone 12.5 mg/day was add on in both the groups. Data was presented as mean±SD. Student's t test was used and p value <0.05 was considered significant.
Results: In group A, systolic blood pressure (SBP) values improved from baseline of 153±10 mmHg to 111±18 mmHg ($p<0.001$) at 3 months and 109±6.1 mmHg ($p<0.001$) at 6 months and diastolic blood pressure (DBP) values from baseline of 87±7 mmHg to 67.1±4.6 mmHg ($p<0.001$) at 3 months and 67.6±2.5 mmHg ($p < 0.001$) at 6 months. In group B, SBP values improved from baseline of 154±8.5 mmHg to 127±3.6 mmHg ($p<0.001$) at 3 months and 123±4 mmHg ($p<0.001$) at 6 months and DBP values from baseline of 85±6.5mm Hg to 75.7±3.3 mmHg ($p<0.001$) at 3 months and 73±3.3 mmHg ($p<0.001$) at 6 months. On intergroup comparison improvement in hypertension was better in azilsartan group ($p<0.001$).
Conclusions: The study concluded that azilsartan is significantly better than olmesartan in controlling the hypertension.

Keywords: Azilsartan, Olmesartan, Chlorthalidone hypertension

INTRODUCTION

Hypertension is one of the leading risk factors for ischemic heart disease, stroke, heart failure, and renal dysfunction.[1] 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.[2] Drugs targeting the renin-angiotensin-aldosterone system (RAAS) are cornerstone of the management of hypertension. Four classes of molecules make it to the list of RAAS blockers: angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), mineralocorticoid receptor antagonist, and direct renin inhibitors (DRI). Aldosterone antagonists are primarily reserved for resistant hypertension, whereas major trials of DRI did not meet their primary end points. Hence, RAAS modulators in daily practice of hypertension include ACEi and ARB. Because of a favorable side effect profile, many practitioners choose ARB over ACEi as first-line therapy.[3] ARBs act via inhibiting the angiotensin II type 1 receptor and decreasing RAAS-associated adverse effects. The first ARB which was approved for hypertension was losartan, way back in 1986. Till March

2018, Food and Drug Administration (FDA) approved 8 ARBs for various indications. In chronological order the list includes losartan, valsartan, candesarten, irbesartan, eposartan, telmisartan, olmesartan, and azilsartan, being the latest addition.[4] Azilsartan medoxomil is a prodrug which is hydrolysed in the gastrointestinal tract before getting absorbed in the system. After oral administration, bioavailability of azilsartan medoxomil is approximately 60% with peak plasma concentration reached within 1.5 to 3 hours.[5] Olmesartan blocks the vasoconstrictor effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in vascular smooth muscle. Olmesartan medoxomil is rapidly and completely bioactivated by ester hydrolysis to olmesartan during absorption from the gastrointestinal tract. The absolute bioavailability of olmesartan is approximately 26%. After oral administration, the peak plasma concentration of olmesartan is reached after 1 to 2 hours. Food does not affect the bioavailability of Olmesartan.[6] More than two-thirds of hypertensive individuals are inadequately controlled on mono therapy. It is recommended to initiate treatment with a combination of a rennin angiotensin system (RAS) blocker with a calcium channel blocker (CCB) or thiazide / thiazide-like diuretic. Most diabetic hypertensive individuals are treated with RAAS inhibitors and most guidelines recommend adding a calcium channel blocker or diuretic as add-on therapy.[7] Hypertensive patients are prone to fluid retention and are at significant risk of developing heart failure or renal impairment.[8] Such patients are also likely to benefit from the volume control and/ or natriuresis provided by diuretics.[9] Chlorthalidone is a thiazide-like diuretic used for the treatment of hypertension and for management of edema caused by conditions such as heart failure or renal impairment.[10] There is no such comparative study conducted in our set up in patients of hypertension. Hence, we want to find out which drug was more efficacious in our scenario.

METHODS

The study was a randomized, prospective, open label, comparative interventional study. The present study was carried out in Department of Pharmacology, Department of Medicine, Dr. R.P.G.M.C. Kangra at Tanda, Himachal Pradesh, after approval by institutional ethics committee. The study population was the consenting adult patients of hypertension. The study was undertaken during the period April 2020 to October 2021.

Inclusion and exclusion criteria

The study included all diagnosed consenting adult patients of either gender of hypertension (BP >140/90 mmHg). Exclusion criteria Not willing to give written informed consent. Patients with kidney disease, Congestive heart failure NYHA classes II-IV, Recent major cardiovascular events (<6 months prior to randomization), Pregnant females and known hypersensitivity to drugs.

As shown in consort diagram, 75 patients were assessed on the basis of eligibility criteria. 5 patients were excluded on the basis of exclusion criteria and 70 patients were randomized in 2 groups. 35 patients in group A were given tab azilsartan + chlorthalidone and 35 patients in group B were given tab olmesartan + chlorthalidone. One patient in group B was lost to follow up. 35 patients in group A and 34 patients in group B were analyzed.

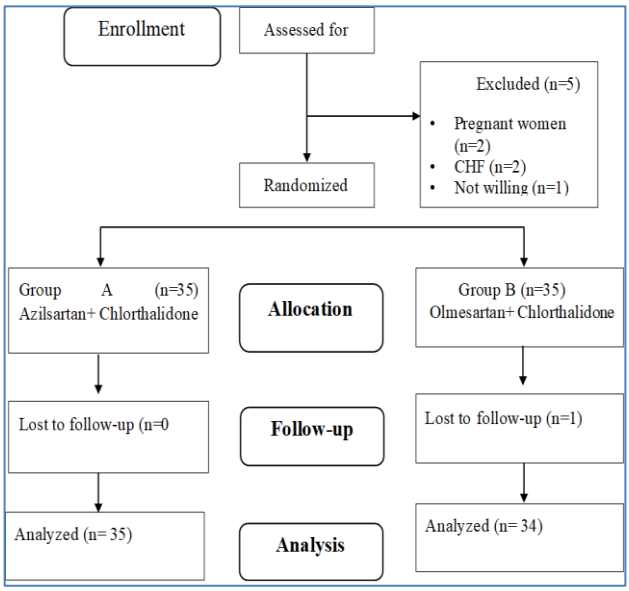

Figure 1: Consort diagram.

Table 1: Description of both the groups.

Group A	Group B
Azilsartan 40 mg once a day in morning+ Chlorthalidone 12.5mg once a day in morning	Olmesartan 20 mg once a day in morning+ Chlorthalidone 12.5mg once a day in morning.

Study duration

Total duration was one year and blood pressure was monitored at the end of first, third and sixth month after initiating the treatment. Detailed history of the patients was elicited, clinical examination was done. Once diagnosed, the patients were informed about the study through the patient information sheet in their own language and were allowed to understand thoroughly about the study and related aspects. After a written informed consent, the participants were assigned to either group A or B, based on computer generated random numbers through simple randomization technique.

Statistical analysis

Categorical data was expressed as frequency and percentages and analyzed by using Chi square test. Quantitative variables were expressed as mean±SD and percentages. Student's t-test was used for comparing

continuous variables between the two groups, p value <0.05 was considered significant.

Measurements of outcome

On completion of 6 month of intervention the outcome was assessed on the basis of improvement of blood pressure in patients.

RESULTS

As shown in (Table 2), in group A and B, majority of patients were > 60 years of age group. 21(60%) patients in group A and 16 (47%) in group B were males. 14 (40%) patients in group A and 18 (53%) in group B were females. 24 (69%) patients in group A and 20 (59%) patients in group B had family history of hypertension. 15 (43%) patients in group A and 16 (47%) patients in group B had family history of diabetes. 17 (49%) patients in group A and 16 (47%) patients in group B had history of smoking. 13 (37) patients in group A and 9 (26%) patients in group B had history of alcohol intake.

Table 2: Baseline characteristics.

Parameters	Group A (N=35) Frequency (%)	Group B (N=34) Frequency (%)	P value
Age (years)			
31-40	0	2 (6)	0.412
40- 50	1 (3)	2 (6)	
50-60	10 (29)	7 (21)	
>60	24 (69)	23(68)	
Gender			
Male	21 (60)	16 (47)	0.281
Female	14(40)	18 (53)	
Family H/O Hypertension	24 (69)	20 (59)	0.400
Family H/O Diabetes	15 (43)	16(47)	0.726
Smoker	17 (49)	16 (47)	0.900
Alcoholic	13(37)	9 (26)	0.342
Mean body mass index (BMI)	25.05±1.82	25.83±2.73	0.167

Systolic blood pressure (SBP)

As shown in (Table 3), there was progressive significant improvement in systolic blood pressure in both the groups. In group A, values improved from baseline of 153±10 mmHg to 125±12 mmHg (p<0.001) at 1 month; 111±18 mmHg (p<0.001) at 3 months; 109±6.1 mmHg (p<0.001) at 6 months. In group B, values improved from baseline of 154±8.5 mmHg to 131±7.4 mmHg (p<0.001) at 1 month; 127±3.6 mm Hg (p<0.001) at 3 months; 123±4 mmHg (p<0.001) at 6 months. Moreover, group A had significantly greater improvement in comparison to group B at 1-month (125±12 mmHg vs.131±7.4 mmHg; p<0.009, 3 months (111±18 mmHg vs. 127±3.6 mmHg; p<0.001) and at 6 months (109±6.1 mmHg vs. 123 ±4 mmHg; p<0.001). As shown in (Figure 2), there was progressive significant improvement in systolic blood pressure in both the groups. In group A, values improved from baseline of 153±10 mmHg to 125±12 mmHg at 1 month; 111±18 mmHg at 3 months; 109±6.1 mmHg at 6 months. In group B, values improved from baseline of 154±8.5 mmHg to 131±7.4 mmHg at 1 month; 127±3.6 mmHg at 3 months; 123±4 mmHg at 6 months. Moreover, group A had significantly greater improvement in comparison to group B at 1-month (125±12 mmHg vs.131±7.4 mmHg), at 3 months (111±18 mmHg vs. 127±3.6 mmHg and at 6 months (109±6.1 mmHg vs. 123±4 mmHg).

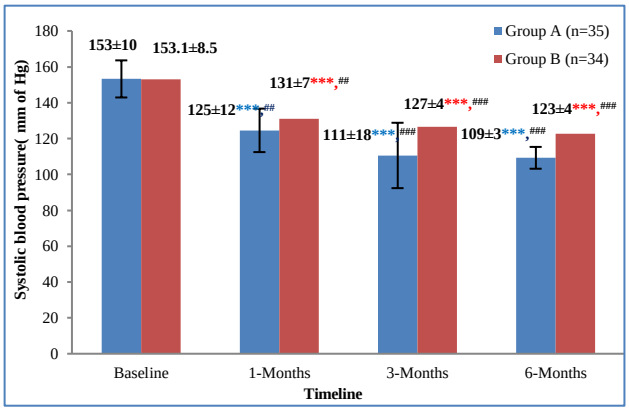

Figure 2: Improvement of systolic blood pressure in two groups.

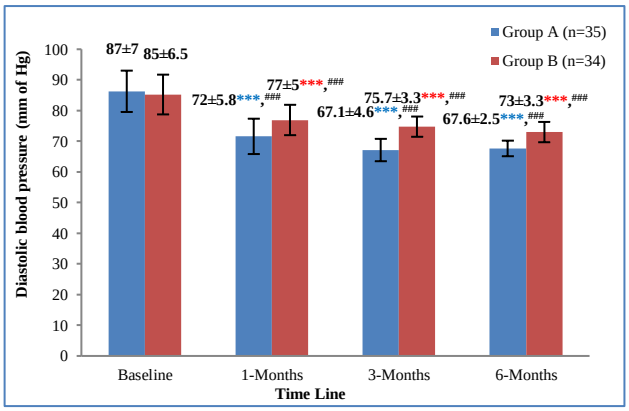

Figure 3: Improvement of diastolic blood pressure in two groups.

Diastolic blood pressure (SBP)

As shown in (Table 4), there was progressive significant improvement in diastolic blood pressure in both the groups. In group A, values improved from baseline of 87±7 mmHg to 72±5.8 mmHg (p<0.001) at 1 month; 67.1±4.6 mmHg (p<0.001) at 3 months; 67.6±2.5 mmHg (p<0.001) at 6 months.

Table 3: Improvement of systolic blood pressure in two groups.

SBP	Group A (N=35)	Group B (N=34)	P value# Intergroup
Baseline	153±10	153.1±8.5	0.931
1 Month	125±12*	131±7.4*	0.009#
3 Months	111±18*	127±3.6*	<0.001#
6 Months	109±6.1*	123±4*	<0.001#
P value Intra group	Baseline vs. 1 month <0.001*	Baseline vs. 1 month <0.001*	
	Baseline vs. 3 month <0.001*	Baseline vs. 3 month <0.001*	
	Baseline vs. 6 month <0.001*	Baseline vs. 6 month <0.001*	

Data expressed as mean±SD, # Un paired student t-test (Intergroup comparison), *Paired student t-test (Intra group comparison)

Table 4: Improvement of diastolic blood pressure in two groups.

SBP	Group A (N=35)	Group B (N=34)	P value# Intergroup
Baseline	87±7	85±6.5	0.512
1 Month	72±5.8*	77±5*	<0.001#
3 Months	67.1±4.6*	75.7±3.3*	<0.001#
6 Months	67.1±2.5*	73±3.3***	<0.001#
P value Intra group	Baseline vs. 1 month <0.001*	Baseline vs. 1 month <0.001*	
	Baseline vs. 3 month <0.001*	Baseline vs. 3 month <0.001*	
	Baseline vs. 6 month <0.001*	Baseline vs. 6 month <0.001*	

Data expressed as mean±SD, # Un paired student t-test (Intergroup comparison), *Paired student t-test (Intra group comparison)

In group B, values improved from baseline of 85±6.5 mmHg to 77±5 mmHg (p<0.001) at 1 month; 75.7±3.3 mmHg (p<0.001) at 3 months; 73±3.3 mmHg (p<0.001) at 6 months. Moreover, group A had significantly greater improvement in comparison to group B at1 month (72±5.8 vs.77±5 mmHg; p<0.001) at 3 months (67.1±4.6 vs. 75.7±3.3 mmHg; p<0.001) and at 6 months (67.6±2.5 vs.73±3.3 mmHg; p<0.001). As shown in (Figure 3), diastolic blood pressure in group A improved from baseline of 87±7mm Hg to 72±5.8 mmHg at 1 month; 67.1±4.6 mmHg at 3 months; 67.6±2.5 mmHg at 6 months. In group B, values improved from baseline of 85±6.5mm Hg to 77±5mm Hg at 1 month; 75.7±3.3mmHg at 3 months; 73±3.3 mmHg at 6 months. Moreover, group A had significantly greater improvement in comparison to group B at 1 month (72±5.8 vs.77±5 mmHg), at 3 months (67.1±4.6 vs. 75.7±3.3 mmHg and at 6 months (67.6±2.5 vs.73±3.3 mmHg).

DISCUSSION

Angiotensin receptor blockers (ARBs) are recommended as the initial choice of treatment in hypertension patients. Previous trials have evaluated and compared the effect of ARBs in such patients with respect to control of blood pressure. Similar observations have been made by Domenic et al, Takagi et al, White William et al, Weber et al, Sinha et al regarding improvement of systolic and diastolic blood pressure.[11-15] A study by Domenic et al,

observed that there were greater SBP and DBP reductions throughout the 24-hour interval, as well as greater target BP achievement, with all 6 doses of AZL-M/CLD relative to their respective monotherapy components.[11] A study by William et al compared the effects of AZI-M with those of OLM and valsartan (VAL).[13] It revealed that 80 mg of AZI-M resulted in a minor reduction in mean SBP over 24 hours compared to the maximum clinically approved doses of OLM (40 mg) and VAL (320 mg), without a significant increase in adverse effects. A study by Shubhadeep et al showed that azilsartan 40 mg and 80 mg were noninferior to telmisartan 40 mg in reducing SBP and DBP, and 24 hour mean ambulatory SBP and DBP.[15] In addition, patients in the azilsartan 80 mg group has shown slightly better reduction in SBP than azilsartan 40 mg and Telmisartan 40 mg. In our study, we compared the efficacy of azilsartan with olmesartan in hypertensive patients. Both azilsartan and olmesartan resulted in a significant improvement in SBP and DBP from baseline in this study. Moreover, azilsartan showed significantly greater improvement of blood pressure in comparison to olmesartan over 6 month of period in the study.

Limitations

Limitation of current study were; this study being post graduate thesis, the follow-up could not be extended beyond 6 months. Follow-up for longer duration would have added more evidence about efficacy of our drugs.

CONCLUSION

It was concluded that both the study drugs have shown significant improvement blood pressure but azilsartan

showed a statistically significant improvement than olmesartan in terms of normalizing systolic and diastolic blood pressure.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. High Blood Pressure Facts. Available at: https://blogs.cdc.gov/global/2015. Accessed on 24 July 2022.
2. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. Available at: https://www.nhlbi.nih.gov/files/docs/guidelines/jnc7full.pdf. Accessed on 24 July 2022.
3. Timmer PB, Duncia JV, Carini DJ. Discovery of losartan, the first angiotensin II receptor antagonist. J Hum Hypertens. 1995;9(5):S3-18.
4. Dahlöf B, Devereux RB, Kjeldsen SE. Cardiovascular morbidity and mortality in the losartan intervention for endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet. 2002; 359(9311):995-1003.
5. Sica D, White WB, Weber MA. Comparison of the novel angiotensin II receptor blocker azilsartan medoxomil vs. valsartan by ambulatory blood pressure monitoring. J Clin Hypertens. 2011;13(7):467-72.
6. Drugs used in blood pressure. Available at: https://www.accessdata.fda.gov. Accessed on 24 July 2022.
7. Grossman A, Grossman E. Blood pressure control in type 2 diabetic patients. Cardiovasc. Diabetol. 2017; 16(1):1-5.
8. Bahtiyar G, Gutterman D, Lebovitz H. Heart failure: a major cardiovascular complication of diabetes mellitus. Curr Diab Rep. 2016;16:116.
9. Lin JJ, Chang HC, Ku CT, Chen HY. Hydrochlorothiazide hypertension treatment induced metabolic effects in type 2 diabetes: a metaanalysis of parallel-design RCTs. Eur Rev Med Pharmacol Sci. 2016;20:2926-34.
10. Shahin MH, Johnson JA. Mechanisms and pharmacogenetic signals underlying thiazide diuretics blood pressure response. Curr Opin Pharmacol. 2016; 27:31-7.
11. Sica D, Bakris GL, White WB, Weber MA, Cushman WC, Huang P, et al. Blood pressure–lowering efficacy of the fixed-dose combination of azilsartan medoxomil and chlorthalidone: a factorial study. J Clini Hypertens. 2012;14(5):284-92.
12. Takagi H, Mizuno Y, Niwa M, Goto SN, Umemoto T. A meta-analysis of randomized controlled trials of azilsartan therapy for blood pressure reduction. Hypertens Res. 2014;37(5):432-7.
13. White WB, Cuadra RH, Lloyd E, Bakris GL, Kupfer S. Effects of azilsartan medoxomil compared with olmesartan and valsartan on ambulatory and clinic blood pressure in patients with type 2 diabetes and prediabetes. J Hypertens. 2016;34(4):788.
14. Weber MA, Sever P, Juhasz A, Roberts A, Cao C. A randomized trial of the efficacy and safety of azilsartan medoxomil combined with chlorthalidone. J Renin Angiotens Aldos Sys. 2018;19(3):147.
15. Sinha S, Chary S, Thakur P, Talluri L, Reddy VK, Agarwal M, et al. Evaluation of the Efficacy and Safety of Azilsartan in Adult Patients with Essential Hypertension: A Randomized, Phase-III Clinical Study in India. J Assoc Phys India. 2021;69(2):35-9.

Cite this article as: Sharma D, Sood A, Kansal D, Kapoor D, Sharma A. Comparison of efficacy of azilsartan with olmesartan in patients of hypertension: randomized controlled trial. Int J Basic Clin Pharmacol 2023;12:805-9.