

# Efficacy and Safety of Azilsartan Medoxomil and Telmisartan in Hypertensive Patients: A Randomized, Assessor-Blinded Study

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## Abstract

**Background:** Few studies have compared the safety and efficacy of azilsartan medoxomil (AZL-M) and telmisartan in hypertensive patients, especially using ambulatory blood pressure monitoring (ABPM).

**Objective:** The objective of this study was to compare the efficacy and safety profile of AZL-M and telmisartan in hypertensive patients using ABPM and clinic blood pressure (BP) monitoring.

**Materials and Methods:** This prospective, randomized, open-label, blinded endpoint, parallel-arm study included 700 patients, aged 18–70 years, with clinic and 24-h mean ambulatory systolic BP (SBP) of 150–180 mmHg and 130–170 mmHg, respectively. They were randomized equally into two groups: Group A received AZL-M 40 mg and Group T received telmisartan 40 mg; the dose was force titrated to 80 mg after 2 weeks if the response rate was not achieved. BP (clinical and ambulatory) was measured after 12 weeks and compared with baseline measurements.

**Results:** AZL-M significantly reduced the 24-h mean ambulatory SBP (Group A:  $112.74 \pm 7.58$  mmHg; Group T:  $113.96 \pm 8.52$  mmHg;  $P < 0.0001$ ) and diastolic BP (Group A:  $71.39 \pm 5.89$  mmHg; Group T:  $67.29 \pm 6.79$  mmHg;  $P < 0.0001$ ) compared with telmisartan at week 12. The clinic SBP significantly decreased in Group A at weeks 4 ( $-30.69 \pm -0.33$  mmHg) and 12 ( $-39.69 \pm -1.09$  mmHg) (for both,  $P = 0.0001$ ). Dose titration was done in 99 and 128 patients from Group A and Group T, respectively ( $P = 0.012$ ). Headache was the most common adverse drug reaction (Group A: 21; Group T: 27) and fatigue the least.

**Conclusion:** This study found that AZL-M has greater antihypertensive efficacy than telmisartan, with comparable side effects. In addition, ABPM was shown to be a feasible method for such studies.

**Keywords:** Adverse drug reaction, ambulatory blood pressure monitoring, azilsartan medoxomil, hypertension, telmisartan

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## INTRODUCTION

Cardiovascular diseases caused approximately 17.9 million deaths worldwide in 2016, nearly one-third of all deaths.<sup>[1]</sup> Notably, hypertension-related complications alone account for nearly 7.5 million deaths every year.<sup>[2]</sup> In fact, 40.6% of cerebrovascular disease cases and 34.7% of ischemic heart disease cases are attributable to hypertension.<sup>[3]</sup> Between 2005 and 2015, there was a 10.5% increase in the total death rate attributable to hypertension, whereas there was a 37.5% increase in the number of deaths directly caused by hypertension.<sup>[4]</sup>

Early detection, proper management and efficient control of hypertension help to prevent several complications that may or may not be life-threatening but do affect the quality of life, such as elevated risk of heart disease, kidney failure, stroke, blindness, cognitive impairment, aneurysms and hemorrhage. Despite the availability of various antihypertensive treatments, hypertension remains inefficiently controlled; only about <70% of patients receiving treatment successfully achieve blood pressure (BP) goals.<sup>[5-7]</sup>

Drugs modulating the renin–angiotensin–aldosterone system, most commonly angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), are most often prescribed for treating hypertension because of their high efficacy and low side effect profile with a tolerability similar to that of placebo.<sup>[8-11]</sup> Telmisartan is a US Food and Drug Administration (FDA)-approved drug for the treatment of hypertension. It is an orally active, safe, long-acting ARB, with the longest half-life (24 h) compared with all other hypertension drugs.<sup>[12-14]</sup> Azilsartan medoxomil (AZL-M), previously known as TAK-491, is the eighth ARB to achieve the US FDA approval for the treatment of hypertension. It is a prodrug, which, after oral administration, is hydrolyzed into bioactive moiety azilsartan (TAK-536), and has a half-life of 11 h.<sup>[15,16]</sup>

Few studies have compared the safety and efficacy of AZL-M and telmisartan in hypertensive patients.<sup>[17,18]</sup> However, based on an extensive Medline search, no such comparative study was found to have been conducted using ambulatory BP monitoring (ABPM). Therefore, this study aimed to compare the efficacy and safety of AZL-M and telmisartan using ABPM and clinic BP monitoring, when administered in equal doses. As currently there is no evidence suggestive of either drug being superior to the other, the authors hypothesize that both the drugs have a similar antihypertensive effect, and thus the study is an equivalence study.

## MATERIALS AND METHODS

### Study design and participants

This prospective, randomized, open-label, blinded endpoint, parallel-arm study was conducted at Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India, from November 2017 to October 2018 after obtaining the ethical approval from the Institutional Ethical Committee (TMMC/IEC/2017/62) on September 11, 2017.

A sample size of 674 patients was determined to be sufficient to achieve an approximately 90% power with a two-sided significance level of 5%. Considering the possibility of dropouts, a total of 700 individuals (both male and female), aged 18–70 years, with hypertension, i.e., with a clinic systolic BP (SBP) of  $\geq 150$ – $\leq 180$  mmHg (Stage 2) and a 24-h mean ambulatory SBP of  $\geq 130$ – $\leq 170$  mmHg,<sup>[19]</sup> were included in the study from the inpatient and outpatient departments of the hospital. All patients voluntarily provided written informed consent before inclusion in the study.

Patients with suspected or known secondary hypertension, severe diastolic hypertension (seated diastolic BP [DBP]  $> 115$  mmHg), clinically significant kidney dysfunction (estimated glomerular filtration rate of  $< 30$  mL/min/1.73 m<sup>2</sup>), history of major cardiovascular events in the past 6 months, type 1 diabetes mellitus or poorly controlled type 2 diabetes mellitus (hemoglobin A1c  $> 8\%$ ), hyperkalemia, significant hepatic abnormalities, suspected or known renal artery stenosis, as well as special populations such as night-shift workers, women of childbearing potential not using any contraception and pregnant/nursing women were excluded from the study.

Before enrollment, clinical investigations such as serum potassium level, kidney function test, glomerular filtration rate, liver function test, glycosylated hemoglobin, and electrocardiography were performed to ensure subject eligibility, followed by recording their demographic data including age, weight, height, sex, and body mass index (BMI).

### Randomization

After enrollment, participants were randomly divided into two groups (Group A and Group T) in a 1:1 ratio. Simple randomization was performed using the chit-pull randomization technique. A total of 700 paper chits marked either A or T (350 each) were put in a box, and each participant drew a chit from the box to determine the group. During the entire process, no chit was replaced in the box. Participants in Group A were to receive AZL-M 40 mg and those in Group T were to receive telmisartan 40 mg.

## Implementation

Patient enrollment, randomization and intervention assignment were performed by three authors: a cardiologist, a physician and a medical intern. None of these were later involved in the data analysis. The study's outcome assessor, a consultant interventional cardiologist with a clinical experience of >20 years, as well as both the principal investigators who performed data analysis were blinded to the randomization sequence.

## Intervention

At week 0 (baseline), participants in Group A and Group T were administered an oral daily dose of AZL-M 40 mg and telmisartan 40 mg, respectively. At week 2, the proportion of responders (defined as the participant whose clinic SBP achieved a target of <140 mmHg or reduction by 20 mmHg from baseline and/or whose clinic DBP achieved a target of <90 mmHg or reduction by 10 mmHg from baseline) was evaluated. Individuals who failed to show adequate response were allocated to dose titration from 40 mg to 80 mg, in case of both the drugs. The titrated dose was then continued until week 12.

At week 4, clinic BP was again monitored, and any nonresponders would have been excluded from the study at this time because of the failure of drug efficacy and to ensure fewer drugs induced toxicity in participants at higher dose. At the final follow-up (week 12), clinic BP was recorded, and ABPM was performed. Change in clinic BP and 24-h mean ambulatory BP was observed when compared with baseline.

At each follow-up, participants were assessed for adverse drug reactions (ADRs) using open-ended questions. The data were recorded on a questionnaire-based ADR monitoring form based on the WHO monitoring guidelines; this form elicits data regarding patient demographics, past medical history, present drug treatment, description and assessment of ADR.<sup>[20]</sup> In addition, the subject could spontaneously report an event throughout the study. The Naranjo Scale was used to determine ADR. All ADR events were categorized as serious and nonserious based on if it resulted in termination of participation from the study. The participants were also allowed to voluntarily withdraw their consent at any stage of the study after informing of the same.

## Outcomes and measurements

Change in 24-h mean SBP (at week 12) was the primary endpoint, which was assessed using ABPM. Changes in clinic BP and 24-h mean DBP at week 12 were taken as a secondary endpoint along with the

proportion of responders (as defined previously). Safety endpoints included incidence of adverse events and its outcome (i.e., discontinuation from the study). There were no changes in the outcome measurements after commencement of the study.

ABPM was performed at baseline and at week 12 using an ambulatory BP monitor (Meditech ABPM-05; Meditech Ltd., Budapest, Hungary). The baseline ambulatory BP was recorded during the 24-h period prerandomization, and then, at week 12, it was performed 24 h after administration of final dose of the respective drug. In each case, BP was measured at intervals of 20 min between 6 am and 10 pm and then after every 40 min between 10 pm and 6 am. The minimum quality control criteria for ABPM included a monitoring period of 24 h, a minimum of 80% of successful means of the total number of means to be recorded (mean = single event of BP recording), no consecutive hours without any valid BP reading and no more than two nonconsecutive hours without any valid BP reading.

Clinic BP was measured at baseline and at each follow-up (weeks 2, 4 and 12 after administration of the first dose of drug) using an automated sphygmomanometer (Omron HEM 705-CP, Vernon Hills, IL). After 24 h of the last study drug intake at 12 weeks, monitoring was performed in duplicates at an interval of 5 min and the average was recorded.

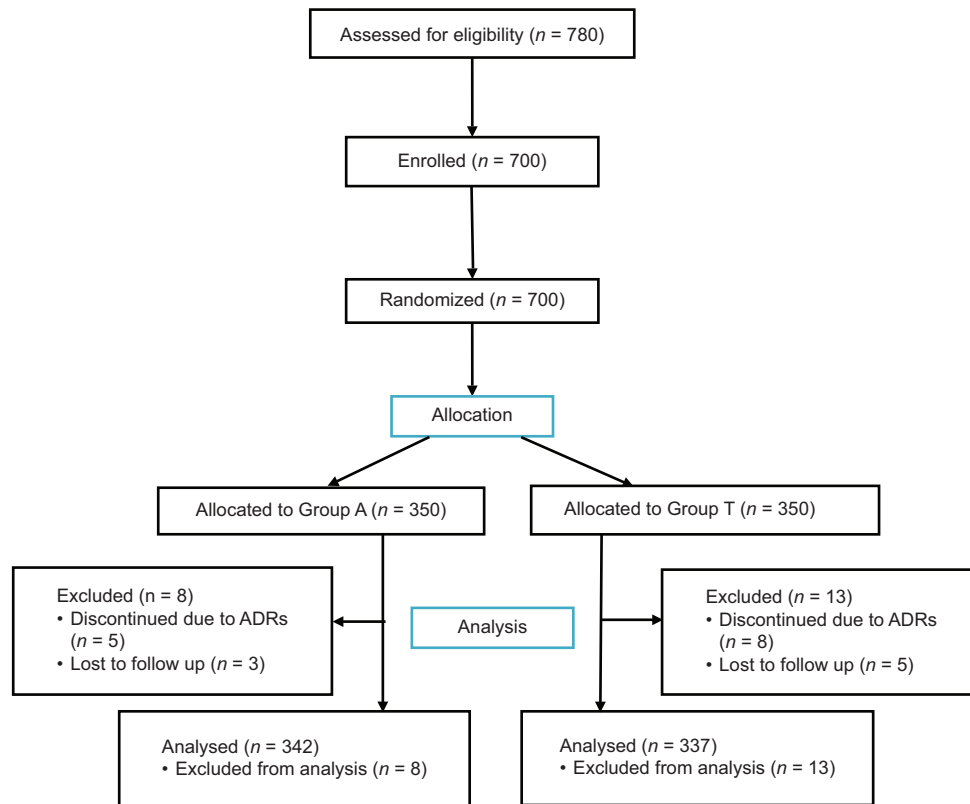
## Statistical analysis

Statistical analysis was performed using SPSS (version 20.0; SPSS Inc., Chicago, IL, USA). According to the type of data, it was either represented as mean  $\pm$  standard deviation or as frequency (percentage). The parametric data were analyzed using unpaired Student's *t*-test, and comparison was made between the two groups according to a stepwise testing procedure for controlling type 1 error. The test was two-sided, and results were exhibited as 95% confidence intervals and *P* value at a 5% level of significance.

## RESULTS

### Participants

From November 2017 to October 2018, 700 patients who met the inclusion criteria after assessment were enrolled in this study. These patients were equally randomized into two groups (350 each) to receive the respective treatment. However, 21 patients (8 from Group A and 13 from Group T) were subsequently either lost to follow-up or opted for voluntary withdrawal, and thus the final analysis included 679 patients [Figure 1].



**Figure 1:** CONSORT flow diagram of the study patients

There was no significant difference between the baseline data of both the groups in terms of age, gender distribution, BMI, clinic SBP and DBP and 24-h mean SBP and DBP ( $P > 0.05$ ) [Table 1]. The baseline clinic SBP for Group A and Group T was  $158.12 \pm 7.67$  and  $158.80 \pm 5.97$  mmHg, respectively ( $P = 0.19$ ), whereas the baseline clinic DBP was  $96.52 \pm 10.28$  and  $97.68 \pm 9.11$  mmHg, respectively ( $P = 0.11$ ). The baseline 24-h mean SBP for Group A and Group T was  $138.12 \pm 10.22$  and  $137.52 \pm 8.74$  mmHg, respectively ( $P = 0.40$ ), whereas the 24-h mean DBP was  $82.56 \pm 8.86$  and  $83.44 \pm 8.11$  mmHg, respectively ( $P = 0.17$ ) [Table 1].

### Intervention outcomes

At 12 weeks of treatment, there was a significant change from baseline data in the 24-h mean ambulatory SBP between the two groups (change in Group A =  $-25.38 \pm -2.64$ ; change in Group T =  $-23.56 \pm -0.22$ ) ( $P < 0.0001$ ). Similarly, a significant decrease in the 24-h mean ambulatory DBP was observed in Group A ( $-11.17 \pm -2.97$ ) compared with Group T ( $-16.15 \pm -1.32$ ) ( $P < 0.0001$ ) [Figure 2].

A statistically insignificant change was observed in clinic SBP at week 2 in comparison with baseline (change in Group A =  $-19.58 \pm 5.11$ ; change in Group T =  $-19.98 \pm 5.68$ ) ( $P = 0.33$ ). However, Group A showed a statistically

**Table 1: Demographic characteristics of the randomized patients at baseline**

Variables	Group A	Group T	P
Age (years)	$50.56 \pm 14.98$	$49.64 \pm 13.56$	0.39
Sex, n (%)			
Male	196 (56)	203 (58)	0.59
Female	154 (44)	147 (42)	
BMI (kg/m <sup>2</sup> )	$25.64 \pm 2.84$	$25.39 \pm 2.83$	0.24
Clinic BP (mmHg)			
SBP	$158.12 \pm 7.67$	$158.80 \pm 5.97$	0.19
DBP	$96.52 \pm 10.28$	$97.68 \pm 9.11$	0.11
24-h mean BP (mmHg)			
SBP	$138.12 \pm 10.22$	$137.52 \pm 8.74$	0.40
DBP	$82.56 \pm 8.86$	$83.44 \pm 8.11$	0.17

Group A – Treated with azilsartan medoxomil; Group T – Treated with telmisartan; BP – Blood pressure; SBP – Systolic BP; DBP – Diastolic BP; BMI – Body mass index

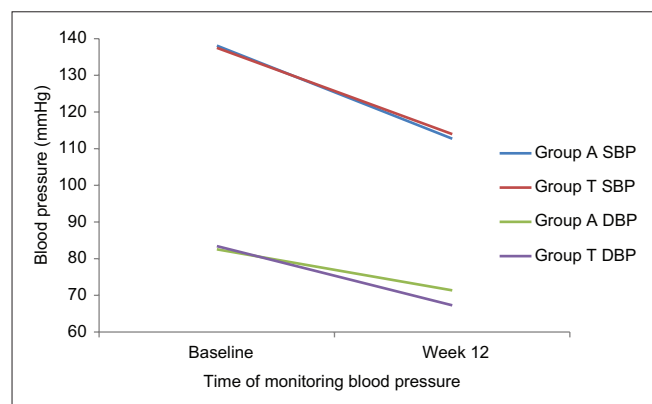
significant change from baseline in clinic SBP at week 4 (change in Group A =  $-30.69 \pm -0.33$ ; change in Group T =  $-32.34 \pm -0.21$ ) ( $P < 0.0001$ ) and week 12 (change in Group A =  $-39.69 \pm -1.09$ ; change in Group T =  $-36.84 \pm 1.07$ ) ( $P < 0.0001$ ) [Table 2 and Figure 3].

For clinic DBP, the results of both the groups were comparable at week 2 (change in Group A =  $-14.89 \pm -3.26$ ; change in Group T =  $-15.14 \pm -0.11$ ) ( $P = 0.16$ ) and week 12 (change in Group A =  $-24.69 \pm -2.57$ ; change in Group T =  $-24.51 \pm -2.88$ ) ( $P = 0.39$ ). However, a significant decrease in clinic DBP was seen between Group

**Table 2: Changes from baseline in clinic systolic blood pressure**

Variables (mmHg)	Group A (n = 342)	Group T (n = 337)	P
Baseline clinic SBP	158.12 ± 7.67	158.80 ± 5.97	0.19
Change from baseline clinic SBP at week 2	-19.58 ± 5.11	-19.98 ± 5.68	0.33
Change from baseline clinic SBP at week 4	-30.69 ± -0.33	-32.34 ± -0.21	<0.0001*
Change from baseline clinic SBP at week 12	-39.69 ± -1.09	-36.84 ± 1.07	<0.0001*

\*Statistically significant difference between groups ( $P < 0.05$ ). Group A – Treated with azilsartan medoxomil; Group T – Treated with telmisartan; SBP – Systolic blood pressure



**Figure 2:** Changes in the mean 24-hour ambulatory systolic blood pressure and diastolic blood pressure between Group A and Group T

A ( $-20.04 \pm -4.42$ ) and Group T ( $-20.85 \pm -4.18$ ) at week 4 ( $P = 0.01$ ) [Table 3].

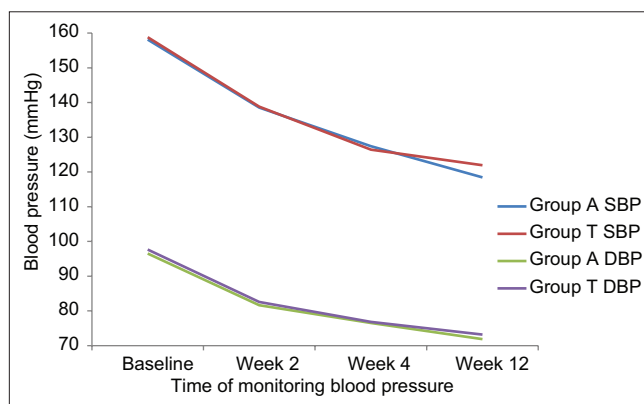
### Adverse drug reactions

In total, 92 (26%) participants from Group A and 111 (32%) from Group T complained of ADRs ( $P = 0.11$ ). Headache was found to be the most commonly occurring ADR in Group A (22.8%), followed by orthostatic hypotension (17.4%), muscle spasm (16.3%), nausea (15.2%), cough (13%), fatigue (8.7%) and dizziness (6.5%). Group T presented a similar trend, with headache being the most commonly reported ADR (24.3%) and fatigue (7.8%) being the least. A comparison of various ADRs between the two groups revealed insignificant results ( $P > 0.05$ ).

A total of 5 (0.01%) participants from Group A and 8 (0.02%) from Group T opted for voluntary withdrawal due to ADRs; however, the results were found to be insignificant. Comparable results were found for the number of patients lost to follow-up during the study: 3 (<0.01%) from Group A and 5 (0.01%) from Group T ( $P = 0.96$ ). A significant difference was noted between the groups in terms of number of participants who required dose titration (Group A = 99; Group T = 128;  $P = 0.012$ ) [Table 4]. There were no nonresponders at week 4 in either group.

### DISCUSSION

With progressing age, a notable decline is seen in the plasma renin activity along with a small decrease in



**Figure 3:** Changes in the mean clinic systolic blood pressure and diastolic blood pressure between Group A and Group T

circulating angiotensin II and an increase in angiotensin type 1 receptor density.<sup>[21]</sup> However, in the present study, an insignificant difference was noted in the mean age of all study participants in either group. Thus, age of the participants did not affect the results, despite the wide range included.

Using the 24-h mean ambulatory SBP rather than the mean clinic SBP as a primary efficacy endpoint is a unique facet of this study. The inclusion criteria of the present study specify a 24-h mean SBP of >130 mmHg, above which it is considered as elevated and is clinically significant.<sup>[22,23]</sup> An increase in the sample size is required in any clinical hypertension study due to the greater changeability of SBP both with clinic and home measurements, which are relative to DBP.<sup>[24]</sup> Using ABPM greatly decreases this requirement of sample size, being functional to compare antihypertensive drugs, while assessing the time-course change in BP due to the drug. In case of middle-aged and elderly people, ABPM has better reproducibility as compared to clinic BP monitoring, and this typically reduces the sample size requirement by 30%–50% for demonstrating similar effects.<sup>[24,25]</sup>

In the present study, compared with baseline values, improvements in the 24-h mean ambulatory SBP and DBP at week 12 were significantly better among those treated with AZL-M than telmisartan, thereby indicating that AZL-M had better efficacy. In terms of 24-h mean ambulatory SBP, Bakris *et al.*<sup>[26]</sup> found that treatment with

**Table 3: Changes from baseline in clinic diastolic blood pressure**

Variables (mmHg)	Group A (n = 342)	Group T (n = 337)	P
Baseline clinic DBP	96.52 ± 10.28	97.68 ± 9.11	0.11
Change from baseline clinic DBP at week 2	-14.89 ± -3.26	-15.14 ± -0.11	0.16
Change from baseline clinic DBP at week 4	-20.04 ± -4.42	-20.85 ± -4.18	0.01*
Change from baseline clinic DBP at week 12	-24.69 ± -2.57	-24.51 ± -2.88	0.39

\*Statistically significant difference between groups ( $P < 0.05$ ). Group A – Treated with azilsartan medoxomil; Group T – Treated with telmisartan; DBP – Diastolic blood pressure

**Table 4: Adverse drug reaction evaluation and requirement for dose titration**

Variables	Group A, n (%)	Group T, n (%)	P
Total adverse events	92 (26)	111 (32)	0.11
Headache	21 (22.8)	27 (24.3)	0.80
Orthostatic hypotension	16 (17.4)	18 (16.2)	0.82
Nausea	14 (15.2)	18 (16.2)	0.84
Fatigue	8 (8.7)	9 (7.8)	0.88
Muscle spasm	15 (16.3)	17 (15.3)	0.85
Dizziness	6 (6.5)	9 (8.1)	0.67
Cough	12 (13)	13 (11.7)	0.77
Patients discontinued due to adverse events	5 (0.01)	8 (0.02)	0.96
Patients lost to follow-up	3 (<0.01)	5 (0.01)	0.96
Requirement for dose titration	99 (29)	128 (38)	0.012*

\*Statistically significant difference between groups ( $P < 0.05$ ). Group A – Treated with azilsartan medoxomil; Group T – Treated with telmisartan

azilsartan resulted in insignificantly higher reductions than with olmesartan. Similarly, White *et al.*<sup>[27]</sup> found that a decrease in the 24-h mean ambulatory DBP was significantly higher in those treated with AZL-M than those treated with valsartan or olmesartan. Therefore, this study adds to the current literature showing that AZL-M is more effective than various ACEIs for improving 24-h ambulatory SBP and DBP.

In the current study, treatment with AZL-M was found to result in a significantly better change from baseline clinic SBP at weeks 4 and 12 than those treated with telmisartan. No similar findings are available for a direct comparison between the two investigational drugs; however, in a study conducted by Zhu *et al.*,<sup>[28]</sup> it was found that telmisartan leads to a significant reduction in clinic SBP at week 8 compared with losartan. Interestingly, the current study found that at week 4, a significant decrease in clinic DBP was observed between the study groups. This indicates that both the drugs are equally effective in reducing the clinic DBP in hypertensive patients. However, several studies suggest that treatment with AZL-M reduces clinic DBP significantly more than other ARBs. One such study was conducted by White *et al.*,<sup>[29]</sup> who found that in hypertensive patients with type 2 diabetes or prediabetes, AZL-M resulted in a significant decrease in clinic DBP compared with both olmesartan and valsartan at their highest approved clinical.

A meta-analysis conducted by Zhao *et al.*<sup>[30]</sup> concluded that in patients with essential hypertension, AZL-M causes

more reduction in BP assessed at office than olmesartan. However, the findings of a meta-analysis conducted by Takagi *et al.*<sup>[31]</sup> involving 5422 hypertensive patients suggest that telmisartan reduces clinic BP more than valsartan. As both the meta-analyses depicted contrary results, the current study was conducted to compare the antihypertensive efficacy of AZL-M versus telmisartan and found better control in both clinic and ambulatory BP with AZL-M.

In the present study, a comparable number of participants had ADRs. However, the events were mild in severity, with headache being the most commonly occurring ADR, followed by orthostatic hypotension, muscle spasm, nausea, cough, fatigue and dizziness in both the groups. There was an insignificant difference between the type of ADRs in patients treated with AZL-M and telmisartan. In the literature, Sica *et al.*<sup>[32]</sup> found similarity in terms of adverse event reporting among patients treated with AZL-M and valsartan: 65.4% of patients treated with AZL-M 40 mg, 65.3% patients treated with AZL-M 80 mg and 59.2% of patients treated with valsartan 320 mg complained of adverse events, with headache being the most common, followed by dizziness and urinary tract infection.

The number of participants who opted for voluntary withdrawal because of ADRs was low and comparable between both the groups in this study. In addition, an insignificant proportion of participants were lost to follow-up during the study. These findings were supported by a pooled analysis conducted by White *et al.*,<sup>[29]</sup> who concluded that the safety and tolerability profile of AZL-M was similar to that of valsartan, olmesartan and placebo.

In the present study, a significant difference was observed between the two groups in terms of number of participants requiring dose titration. Participants in Group A required less dose escalation, thereby exhibiting that AZL-M has a better antihypertensive effect at a lower dose than telmisartan. In a meta-analysis by Smith *et al.*,<sup>[33]</sup> where the titration to response toward dose of telmisartan and losartan was compared, it was concluded that a lesser number of patients on treatment with telmisartan required dose titration than those on losartan.

In the current study, all ABPM reporting was done by a single cardiologist, which decreased the chances of interobserver variability. The observer bias in measurement of BP by auscultatory method was completely eliminated using ABPM. In addition, a correlation was established and highlighted between BP monitoring by ABPM and mercury sphygmomanometer in terms of BP values with anthropometric variables.

At all recorded time intervals, a subtle difference was found in BP reduction between the two drugs. For instance, at week 12, the difference of reduction in the mean 24-h ambulatory SBP and DBP between Groups A and T was  $-1.22$  and  $4.1$  mmHg, respectively. Similarly, the difference of reduction in clinic SBP and DBP at week 12 between the two groups was  $-3.53$  and  $-1.34$  mmHg, respectively. The numerical differences were small, but it does not undermine the strength of the conclusion.

Although the participants in this study were treated with the drugs for a short duration of 3 months, the findings of the study suggest that long-term treatment with AZL-M may be feasible, as minimal adverse events may result in enhanced medication adherence. However, longer duration studies are required to further validate the current study findings. Moreover, the use of two BP measurement techniques (i.e., clinic monitoring and ABPM) results in internal validation of the study data. In addition, the findings of the study demonstrate that using ABPM (as the primary endpoint for efficacy) is feasible and promotes a better understanding of pharmacodynamic behavior of the studied drugs.

Physical status of patients while using the ABPM device is a matter of consideration. The device must be relatively positioned at the level of the heart while monitoring BP and must stay in that position for the entire 24-h monitoring period. However, in certain cases, patients did not take care of that and 3.3 (average) means out of the total means were unsuccessful, which were considered as clinically insignificant and did not affect the study results.

## CONCLUSION

Using clinic monitoring and ABPM, the present study found that AZL-M has greater antihypertensive efficacy than telmisartan, with comparable side effects. This suggests that AZL-M may enhance BP control in patients with hypertension. In addition, AZL-M was found to elicit a better response rate compared to telmisartan. However, longer duration studies are required to further validate the findings of this study.

## Ethical considerations

This study was approved by the Institutional Ethical Committee of Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India, on September 11, 2017 (TMMC/IEC/2017/62). The study was conducted in adherence with the guidelines of the Declaration of Helsinki, 2013. Signed informed consent was obtained from all patients before inclusion in the study.

## Peer review

This article was peer-reviewed by two independent and anonymous reviewers.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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