Original Article

A Comparative Study of Morning & Evening Doses of Telmisartan in Patients of Hypertension in A Tertiary Care Hospital; A Prospective Observational Study

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ABSTRACT

Background: Hypertension is a major global health issue that elevates the risk of cardiovascular diseases, particularly in India, where a significant portion of adults is affected, resulting in high morbidity and mortality. Despite advancements in treatment, effective management strategies are still needed. This study focuses on telmisartan, an angiotensin II receptor blocker (ARB) commonly used for essential hypertension, examining the effects of administering it in the evening versus the morning to improve blood pressure control and patient adherence by aligning with the body's natural circadian rhythms.

Materials & Methods: A prospective observational study was conducted involving 340 newly diagnosed hypertensive patients. Participants were randomly assigned to receive telmisartan either in the morning or evening. Blood pressure measurements and laboratory investigations were performed at baseline and follow-ups (1, 4, and 12 weeks).

Results: The evening dosing group showed significantly greater reductions in both systolic and diastolic blood pressure compared to the morning group ($P<0.05$). Additionally, the evening group had better adherence rates. Clinical parameters, including sodium and potassium levels, were also assessed, showing significant differences in electrolyte levels but no notable changes in urea or creatinine.

Conclusion: Administering telmisartan in the evening provides significant advantages, including better blood pressure control and adherence to treatment, while aligning with the body's circadian rhythms. This timing should be considered when prescribing telmisartan for hypertension management.

Keywords: Hypertension, Telmisartan, Angiotensin II receptor blockers, Evening dosing, Blood pressure control, Circadian rhythm.

INTRODUCTION

Hypertension is a growing global health issue and a significant risk factor for cardiovascular diseases such as arrhythmia, stroke, and valvular heart disease.[1] In India, the Great India Blood Pressure Survey reported 234 million adults with hypertension, leading to 98,912 deaths and over 2.5 million disability-adjusted life-years in 2017 due to hypertensive heart disease. [2] Poor control of hypertension contributes to increased healthcare costs and resource utilization.

Despite its serious consequences, awareness, treatment, and control of hypertension in India remain inadequate. [3] Several guidelines, including the 2014 Eighth Joint National Committee, 2017 ACC, 2018 ESC/ESH, and 2019 Indian Guidelines on Hypertension–IV, provide recommendations for the definition, classification, evaluation, and management of hypertension.[4-7]

Angiotensin II receptor blockers (ARBs) are recommended as first-line therapy for hypertension by various guidelines.[6,7] Multiple observational studies have confirmed ARBs as effective both as monotherapy and in combination with other antihypertensive drugs. [8-10] ARBs work by selectively blocking the effects of angiotensin II, a potent vasoconstrictor, making them highly effective and well-tolerated for blood pressure management.[11]

Telmisartan is a widely preferred ARB in India, chosen by 73% of physicians as a first-line treatment for essential hypertension.[8] It is an orally active, long-acting angiotensin II receptor antagonist with a half-life of 20 to 30 hours, selectively inhibiting the angiotensin II AT1 receptor without affecting other cardiovascular systems. [12] The optimal effect is achieved at a daily dose of 80 mg, with side effects similar to placebo.[13]

Telmisartan has demonstrated efficacy in lowering blood pressure in clinical trials and real-world studies in Indian patients.[14,15] Some studies also suggest taking telmisartan in the evening due to higher ARB sensitivity at that time.

Previous anecdotal studies have compared the antihypertensive efficacy of valsartan when taken either in the morning or at bedtime by hypertensive patients over a 3-month period. Significant blood pressure (BP) reduction was achieved regardless of administration time.[16] However, valsartan taken at bedtime was more effective in improving the sleep time-relative BP decline, decreasing nocturnal BP, and increasing the percentage of patients with controlled BP. [16,17] These results are particularly significant because studies have shown that nighttime BP is a stronger predictor of cardiovascular outcomes than daytime BP.[18-20]

It remains unclear whether this time-dependent efficacy applies to all ARBs or is specific to valsartan, which has a peak effect 4-6 hours after morning dosing. Telmisartan, with a longer half-life (24 hours), may exhibit different efficacy based on administration time. This prospective observational study aims to compare the efficacy of telmisartan as monotherapy in hypertension when administered in the morning versus the evening. The study will evaluate the antihypertensive effect of telmisartan (20 mg, 40 mg, and 80 mg) at both times of day, as well as assess its safety and tolerability in hypertensive patients.

MATERIALS AND METHODS

After approval from the institutional ethical committee, this prospective observational study was conducted in the Department of Pharmacology, MGM Medical College and M.Y. Hospital, Indore and 340 patients with Newly diagnosed Hypertension (both males & females) attending the Medicine OPD of M.Y Hospital, Indore and qualifying the inclusion criteria were enrolled in the study. A pre informed written consent was taken from all the patients before enrollment.

Inclusion Criteria

- Newly diagnosed Male and Female patients with Hypertension according to JNC 8 CRITERIA:
  - STAGE I (SBP 140-159mm Hg and DBP 90-99mmHg).
  - STAGE II (SBP >160mmHg and DBP >100mmHg)
- Age range 18yrs-60yrs
- Patients willing to give written informed consent.

Exclusion Criteria

- Severe hypertension (SBP:>=180mmHg and DBP >=120mmHg), hypertensive emergency, hypertensive urgency
- Pregnant and lactating females.
- Patients with any other co-morbidities.
- Patient with more than one anti-hypertensive drugs.

Methodology

All patients were randomly allocated into two groups depending upon time of dosage of Telmisartan i.e., odd (morning) & even (evening) basis.

After taking pre-informed written consent from the patient, a pre-structured proforma was used to collect the desired baseline data. At first visit, data regarding demographic profile, dietary habits and intake of abusive substances like nicotine and alcohol was obtained.

Baseline Blood pressure was measured with Mercury (conventional) sphygmomanometer (Morning v/s evening) before giving Telmisartan. On subsequent visits (0, 1 week,4 weeks & 12 weeks) following information was assessed: Blood Pressure changes after giving Telmisartan (20/40/80) in sitting position with Mercury (conventional) sphygmomanometer (Morning v/s evening)

Laboratory investigations i.e., Sodium (Na+), Potassium (K+), Urea, Creatinine, BMI & Age were done before and after treatment.

Data was collected on a predesigned proforma and analyzed by appropriate statistical tests.

Statistical Analysis

The data was coded and entered into Microsoft Excel 2010, and analyzed using both Excel 2010 and SPSS 20.0 for Windows. Descriptive analysis was conducted on the population, with categorical or dichotomous variables expressed as absolute values and percentages. These were compared using Pearson's chi-square test. Continuous variables with normal distribution were presented as mean (± SD) and compared using the Student's T-test or ANOVA test. The correlation between two quantitative variables was determined using Karl Pearson's or Spearman's coefficient of correlation. A chi-square test was used to assess associations between variables, with a p-value of less than 0.05 considered statistically significant.

RESULTS

Demographic Profile:

Age: In our study, the largest proportion of patients (38.8%) were in the 45-55 age group, followed by 35.9% in the 35-45 age range, 15.3% in the 25-35 age group, while the 55-65 age group had the fewest patients at 10%. The mean age in the morning dosing group was slightly higher compared to the evening group, though this difference was not statistically significant (54.69 ± 8.62 vs 54.85 ± 7.92; P=0.515; Chi-Square test). (Table 1)

Gender: The study had a higher proportion of males [193 (56.8%)] compared to females [147 (43.2%)], with a male-to-female ratio of 1.3:1. There was no statistically significant difference in gender distribution between the study groups (P=0.913; Chi-Square test). (Table 1)

Weight, Height & BMI: The Student T-Test revealed significant differences in weight, height, and BMI (P<0.05) between the study groups, but no statistically significant differences were found in mean weight (73.68 vs. 72.66; P=0.233), height (162.78 vs. 162.78; P=0.632), or BMI (27.75 vs. 27.66; P=0.202) between the morning and evening groups. Thus, both groups were comparable regarding these parameters. (Graph 1)

Hemodynamic parameters:

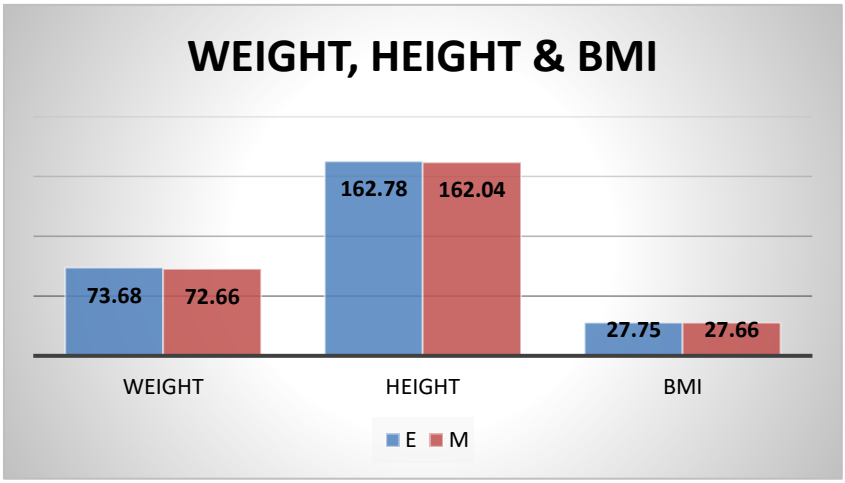
SBP: The study found a significant difference in mean systolic blood pressure (SBP) between the morning and evening groups at follow-ups of 1, 4, and 12 weeks (P<0.05; Student T-Test). In the morning group, SBP decreased from a baseline of 160.17 ± 7.752 to 127.18 ± 4.785 after 1 week, while the evening group dropped from 159.93 ± 7.683 to 120.84 ± 2.581. The evening group showed a greater reduction in SBP compared to the morning group across all follow-up intervals, with significant mean differences observed at 1 week (39.09 ± 8.158 vs. 32.99 ± 8.751; P=0.000), 4 weeks (38.34 ± 8.225 vs. 32.12 ± 8.754;

P=0.000), and 12 weeks (38.76 ± 7.947 vs. 32.19 ± 8.400; P=0.000). Overall, taking the medication in the evening resulted in a significantly better reduction in SBP. (Graph 2)

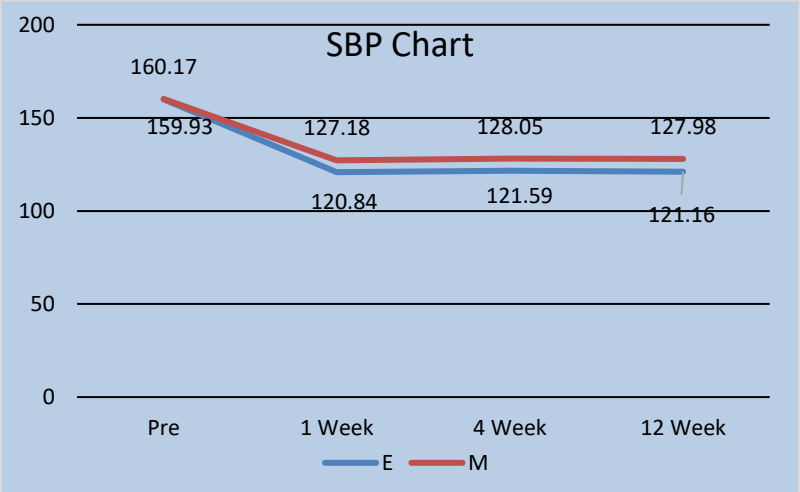
DBP: A statistically significant difference in mean diastolic blood pressure (DBP) between morning and evening dosing groups at 1, 4, and 12 weeks (P<0.05). The morning group showed a reduction in DBP from a baseline of 89.91 ± 3.363 to 80.41 ± 1.190 after one week, while the evening group decreased from 90.41 ± 3.719 to 80.09 ± 0.525. The evening group consistently demonstrated greater reductions in DBP at all follow-ups, with significant differences noted at 1 week (10.33 ± 3.735 vs. 9.50 ± 3.435; P=0.034), 4 weeks (10.34 ± 3.787 vs. 9.26 ± 3.719; P=0.000), and 12 weeks (10.40 ± 3.722 vs. 9.43 ± 3.452; P=0.013). Therefore, evening administration of the medication was associated with better DBP reduction compared to morning dosing. (Graph 3)

Table 1: Distribution of study participants depending upon demographic parameters

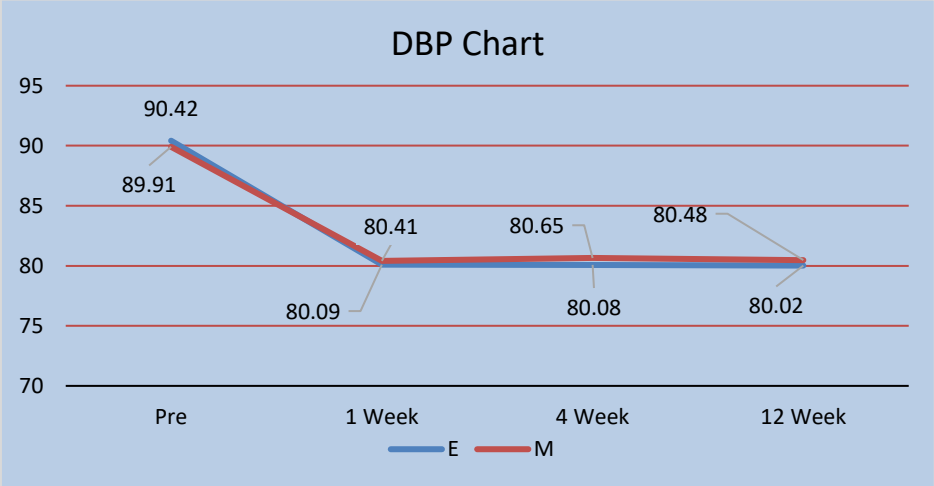
Parameter	Group E (N=170)	Group M (N=170)	Total (N=340)	P value
	No of patients (%)	No of patients (%)	No of patients (%)	
Age				
25-35 years	29 (17.1%)	23 (13.5%)	52 (15.3%)	0.515 (NS)
35-45 years	62 (36.5%)	60 (35.3%)	122 (35.9%)	
45-55 years	60 (35.3%)	72 (42.4%)	132 (38.8%)	
55-65 years	19 (11.2%)	15 (8.8%)	34 (10%)	
Gender				
F	73 (42.9%)	74 (43.5%)	147 (43.2%)	0.913 (NS)
M	97 (57.1%)	96 (56.5%)	193 (56.8%)	



Graph 1: Comparison of Mean value of Weight, Height and BMI between two study groups



Graph 2: Comparison of Mean SBP value at Different Duration between two study groups



Graph 3: Comparison of Mean value of Different Duration between two study groups

Table 2: Comparison of Mean value of Clinical Parameters for Kidney function tests (Sodium, Potassium, Urea and Creatinine) between two study groups

Parameters	Group	N	Mean	Std. Dev	T Test	P Value	Result
Sodium	M	170	140.918	2.9501	2.742	0.006	Sig
	E	170	140.006	3.1763			
Potassium	M	170	4.343	0.6879	3.654	0.000	Sig
	E	170	4.066	0.7106			
Urea	M	169	27.20	8.0838	0.610	0.543	Non-Sig
	E	170	26.62	9.4583			
Creatinine	M	170	1.180	0.3441	-0.862	0.389	Non-Sig
	E	170	1.835	9.8937			

Clinical Parameters for Kidney function tests (Sodium, Potassium, Urea and Creatinine): Morning mean values for sodium (140.92 ± 2.95) and potassium (4.34 ± 0.69) levels were significantly higher compared to evening values (sodium: 140.01 ± 3.18; potassium: 4.07 ± 0.71; P=0.000). However, there were no statistically significant differences between the morning and evening groups for urea (27.20 ± 8.08 vs. 26.62 ± 9.46; P=0.543) and creatinine levels (1.18 ± 0.34 vs. 1.84 ± 9.89; P=0.389). (Table 2)

DISCUSSION

Telmisartan has demonstrated effectiveness in lowering blood pressure in Indian patients with hypertension through clinical trials and real-world studies, with recommendations suggesting evening administration due to enhanced sensitivity to angiotensin receptor blockers (ARBs) at that time.[14,15] Prior research has highlighted differences in pharmacokinetics and pharmacodynamics among various classes of blood pressure medications, including ARBs, which could affect their efficacy based on the time of day they are taken.

Previous studies comparing the antihypertensive effects of valsartan indicated that while significant blood pressure reduction occurred regardless of administration time, taking it at bedtime resulted in better nocturnal blood pressure control and an increased proportion of patients achieving controlled blood pressure. This is significant because nighttime blood pressure is often a better predictor of cardiovascular outcomes than daytime readings.[21,22]

The current study enrolled 340 newly diagnosed hypertensive patients to assess the optimal timing for administering Telmisartan (20mg, 40mg, or 80mg) to maximize its antihypertensive effect. Consistent with earlier findings, evening dosing of Telmisartan significantly enhanced the sleep time–relative blood pressure decline, particularly in patients classified as non-dippers. This circadian variation in blood pressure is influenced by several factors, including autonomic nervous system activity and the renin-angiotensin-aldosterone system, which exhibits marked circadian patterns in hormone levels. Clinical studies have shown that evening dosing of angiotensin-converting enzyme inhibitors also leads to improved nocturnal blood pressure control and a more favorable circadian blood pressure profile.

In our study, the largest patient demographic (38.8%) fell within the 45-55 age group, followed by 35.9% in the 35-45 age group, and 15.3% in the 25-35 age range. The smallest cohort consisted of patients aged 55-65 years (10%). The

mean age was slightly higher in the evening group (54.85 ± 7.92 years) compared to the morning group (54.69 ± 8.62 years), though this difference was not statistically significant (P=0.515). These findings are consistent with Hermida *et al.* [23], who reported a mean age of 46.4 ± 12.0 years, and with Poulter NR *et al.* [24], who noted a mean age of 61.8 ± 10.3 years among 103 patients. Similarly, Agarwal A *et al.* [25], found a mean age of 48.23 years, further supporting the comparability of our results.

In our study of 340 patients, a higher proportion were male, with 193 (56.8%) compared to 147 (43.2%) females, resulting in a male-to-female ratio of 1.3:1. This distribution aligns with the findings of Hermida *et al.* [23], who reported 114 men and 101 women in their study. Similarly, Poulter NR *et al.* [24] noted that 56% of their 103 recruited patients were male, with a mean age of 62 years and 44% being female. Furthermore, 92% of patients in Poulter's study completed all three 24-hour recordings.

In our study, there were no statistically significant differences in weight, height, and BMI between the morning and evening groups. The mean weight in the morning group was slightly lower (73.68 ± 7.808) than in the evening group (72.66 ± 7.905; P=0.233). The mean height was slightly higher in the morning group (162.78 ± 9.168) compared to the evening group (162.04 ± 12.097; P=0.632). The mean BMI was also marginally higher in the morning group (27.75 ± 4.215) than in the evening group (27.66 ± 4.005; P=0.840). These findings are consistent with those of Hermida *et al.*[23], who reported similar non-significant comparisons for mean height (164.2 ± 10.0 vs. 164.9 ± 10.7; P=0.649), weight (73.4 ± 15.6 vs. 76.4 ± 16.0; P=0.176), and BMI (27.1 ± 4.2 vs. 28.0 ± 4.7; P=0.098).

The study revealed a statistically significant reduction in both systolic blood pressure (SBP) and diastolic blood pressure (DBP) among patients taking medication in the evening compared to those taking it in the morning, across all follow-up periods (1 week, 4 weeks, and 12 weeks; P<0.05). In the morning group, baseline SBP decreased from 160.17 ± 7.752 to around 127.98 ± 4.045, while in the evening group, it dropped from 159.93 ± 7.683 to 121.16 ± 2.320. Similarly, baseline DBP in the morning group fell from 89.91 ± 3.363 to 80.48 ± 1.163, whereas the evening group experienced a decline from 90.41 ± 3.719 to 80.02 ± 0.216. These findings suggest that evening dosing is more effective in achieving lower blood pressure levels than morning dosing, highlighting the importance of timing in antihypertensive treatment.

A study by Hermida *et al.* [23], demonstrated that telmisartan effectively lowers blood pressure in both morning and evening doses, with greater effectiveness observed in bedtime administration. Bedtime valsartan treatment also significantly reduced urinary albumin excretion, largely due to decreased nocturnal blood pressure and increased relative blood pressure decline during sleep. Additionally, a reduction in plasma fibrinogen was linked to improved nighttime blood pressure profiles. These results, consistent with our findings, highlight the clinical importance of timing in antihypertensive therapy. Notably, non-dipping of nocturnal blood pressure is associated with increased risks of end-organ injury and cardiovascular events, suggesting that nighttime blood pressure is a better predictor of cardiovascular mortality than daytime or overall, 24-hour measurements.

The comparison of clinical parameters between morning and evening study groups revealed significantly higher mean values for sodium (140.918 ± 2.9501 vs. 140.006 ± 3.1763) and potassium (4.343 ± 0.6879 vs. 4.066 ± 0.7106; p < 0.000) in the morning group. However, no significant differences were found for urea (27.20 ± 8.0838 vs. 26.62 ± 9.4583; p = 0.543) and creatinine (1.180 ± 0.3441 vs. 1.835 ± 9.8937; p = 0.389). Similar findings were reported by Hermida *et al.*[23], who noted comparable serum values for various parameters, including glucose and creatinine, at baseline and after treatment. Agarwal *et al.*[25], observed significant improvements in clinical parameters after three months of telmisartan treatment, including reductions in 24-hour urinary protein, serum creatinine levels, and blood pressure, alongside an increase in glomerular filtration rate (GFR). These results align with the present study, suggesting that evening administration of telmisartan may offer various benefits for specific individuals.

Hence, it can be concluded that taking telmisartan or Telmastran in the evening offers several benefits, including improved blood pressure control during sleep, reduced daytime side effects, better medication compliance due to established routines, and effective management of morning hypertension by ensuring adequate drug levels in the bloodstream when blood pressure typically rises.

This study on telmisartan's timing for hypertension has limitations, including a small sample size, short duration, and lack of control groups, which affect the reliability of results. Patient variability and measurement methods introduce additional challenges, limiting the generalizability of findings and insights into long-term effects. To improve understanding, future research must employ rigorous study design and statistical analysis.

CONCLUSION

The findings of this study suggest that administering telmisartan in the evening offers significant advantages for patients with essential hypertension, particularly in terms of better nocturnal blood pressure control and improved adherence to treatment regimens. Bedtime dosing aligns with the body's natural circadian rhythms, effectively mitigating morning hypertension and enhancing overall cardiovascular protection. Given the comparable efficacy of bedtime administration to morning dosing while offering additional benefits, this timing should be considered when prescribing telmisartan for hypertension management.

Ethical approval: Written informed consent was obtained from the subjects before enrolling in the study. Confidentiality of patient information was maintained.

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REFERENCES

1. Kjeldsen SE. Hypertension and cardiovascular risk: general aspects. Pharmacol Res. 2018;129:95–9.
2. Ramakrishnan S, Zachariah G, Gupta K, Shivkumar Rao J, Mohanan PP, Venugopal K, et al. Prevalence of hypertension among Indian adults: results from the great India blood pressure survey. Indian Heart J. 2019;71:309–13.
3. Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, et al. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. J Hypertens. 2014;32:1170–7.
4. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311:507–20.
5. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/ AHA/ AAPA/ ABC/ ACPM/ AGS/ APhA/ ASH/ ASPC/ NMA/ PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/ American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71: 1269–324.
6. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39:3021–104.
7. AoPo I. Indian guidelines on hypertension-IV 2019. J Assoc Physicians India. 2019;67:8–46.
8. Ramakrishnan S, Ingole S, Dey A, Jain R. Management of hypertension: Insights into prescribing behavior with focus on angiotensin receptor blockers. J Pract Cardiovasc Sci. 2017;3:22–7.
9. Gupta R, Malhotra A, Malhotra P. Study of prescribing pattern of drugs used in the treatment of hypertension in a tertiary care teaching hospital in North India: an observational study Int J Res. Med Sci. 2018;6:2380–4.
10. Romday R, Gupta AK, Bhambani P. An assessment of antihypertensive drug prescription patterns and adherence to joint national committee-8 hypertension treatment guidelines among hypertensive patients attending a tertiary care teaching hospital. Int J Res Med Sci. 2016;4:5125–33.
11. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, Rocella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42: 1206–1252.
12. Gadge P, Gadge R, Paralkar N, Jain P, Tanna V. Effect of telmisartan on blood pressure in patients of type 2 diabetes with or without complications. Perspect Clin Res. 2018;9:155–60.
13. Prikryl P, Cornélissen G, Neubauer J, Prikryl P Jr, Karpisek Z, Watanabe Y, Otsuka K, Halberg F. Chronobiologically explored effects of Telmisartan. Clin Exp Hypertens. 2005 Feb-Apr;27(2-3):119-28.
14. Kalikar M, Nivangune KS, Dakhale GN, Bajait CS, Sontakke SD, Motghare VM, et al. Efficacy and tolerability of olmesartan, telmisartan, and losartan in patients of stage i hypertension: a randomized. Open-label Study J Pharmacol Pharmacother. 2017;8:106–11.
15. Arif AF, Kadam GG, Joshi C. Treatment of hypertension: postmarketing surveillance study results of telmisartan monotherapy, fixed dose combination of telmisartan? hydrochlorothiazide/amlodipine. J Indian Med Assoc. 2009;107:730–3.
16. Hermida RC, Calvo C, Ayala DE, Domı´nguez MJ, Covelo M, Ferna´ndez JR, Mojo´n A, Lo´pez JE. Administration-time-dependent effects of valsartan on ambulatory blood pressure in hypertensive subjects. Hypertension. 2003;42:283–290.
17. Hermida RC, Calvo C, Ayala DE, Ferna´ndez JR, Covelo M, Mojo´n A, Lo´pez JE. Treatment of non-dipper hypertension with bedtime administration of valsartan. J Hypertens. 2005;23:1913–1922.
18. Hermida RC, Calvo C, Ayala DE, Mojo´n A, Rodrı´guez M, Chaya´n L, Lo´pez JE, Fontao MJ, Soler R, Ferna´ndez JR. Administration time dependent effects of valsartan on ambulatory blood pressure in elderly hypertensive subjects. Chronobiol Int. 2005;22:755–776.
19. Staessen JA, Thijs L, Fagard R, O Brien ET, Clement D, de Leeuw PW, Mancia G, Nachev C, Palatini P, Parati G, Tuomilehto J, Webster J, for the Systolic Hypertension in Europe (Syst-Eur) trial investigators. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. JAMA. 1999;282: 539–546.
20. Dolan E, Stanton A, Thijs L, Hinedi K, Atkins N, McClory S, Den Hond E, McCormack P, Staessen JA, O'Brien E. Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin outcome study. Hypertension. 2005;46:156–161.

21. Lemmer B. Cardiovascular chronobiology and chronopharmacology. In: Touitou Y, Haus E, eds. Biologic Rhythms in Clinical and Laboratory Medicine. Berlin, Germany: Springer-Verlag; 1992: 418–427

22. Angeli A, Gatti G, Masera R. Chronobiology of the hypothalamic-pituitary-adrenal and renin-angiotensin-aldosterone systems. In: Touitou Y, Haus E, eds. Biologic Rhythms in Clinical and Laboratory Medicine. Berlin, Germany: Springer-Verlag; 1992: 292–314

23. Hermida RC, Ayala DE, Fernández JR, Calvo C. Comparison of the efficacy of morning versus evening administration of telmisartan in essential hypertension. Hypertension. 2007 Oct;50(4):715-22.

24. Poulter NR, Savopoulos C, Anjum A, Apostolopoulou M, Chapman N, Cross M, Falaschetti E, Fotiadis S, James RM, Kanellos I, Szigeti M, Thom S, Sever P, Thompson D, Hatzitolios AI. Randomized Crossover Trial of the Impact of Morning or Evening Dosing of Antihypertensive Agents on 24-Hour Ambulatory Blood Pressure. Hypertension. 2018 Oct;72(4):870-873.

25. Agrawal A, Kamila S, Reddy S, Lilly J, Mariyala MS. Effect of telmisartan on kidney function in patients with chronic kidney disease: an observational study. J Drug Assess. 2016 Nov 4;5(1):24-28.

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