A Prospective Comparative Study of Efficacy and Pleiotropic Effect of Telmisartan versus Enalapril in Hypertensive Patients with Dyslipidaemia in a Tertiary Care Hospital in Visakhapatnam

Supriya Sanke[1], Chitra Karuppiah[2], Hema Sundar Rao Dumpala[3], Sai Vishnu Vardhan Allu[4], Syamala Shanthi Kumari Bonela[5]

[1, 2, 3, 4, 5] Department of Pharmacology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India.

ABSTRACT

BACKGROUND

Hypertension is a silent killer, an asymptomatic chronic disorder if left untreated which results in major health problems. Goal of treatment is to decrease the morbidity and mortality associated with cardiovascular and cerebrovascular complications of hypertension when it is associated with dyslipidaemia. The renin angiotensin system plays an important role in the regulation of blood pressure and in the pathogenesis of hypertension. Telmisartan is an ARB (angiotensin receptor blocker) and Enalapril is an ACE inhibitor. The purpose of this study is to compare the efficacy of Telmisartan with Enalapril in patients of essential hypertension with dyslipidaemia, and to observe the effects of Telmisartan and Enalapril on blood lipid levels of these patients.

METHODS

This is a prospective, randomized, comparative and open label study conducted among 70 patients who were included in the study and were divided in to two groups. Group A - consisting of 35 patients receiving Telmisartan 40 mg, and Group B receiving Enalapril 5 mg orally once a day. Informed consent was obtained from all the patients. Follow up was done after 4, 8 and 12 weeks. Blood pressure was recorded at every visit and lipid profile was done at the time of enrolment and after 12 weeks of study period.

RESULTS

Baseline demographic attributes were comparable between both the groups including total cholesterol and low-density lipoprotein (LDL). The mean reduction in systolic and diastolic blood pressure (BP) after 12 weeks was highly significant (P value < 0.001) in both the groups but when mean reduction in SBP & DBP was compared, there was no significant difference (P > 0.05) between the drugs. Blood levels of total cholesterol, LDL, triglyceride had significantly reduced (P < 0.05) in Telmisartan group compared to Enalapril group after 12 weeks of follow up and mean high density lipoprotein (HDL) level significantly increased in Telmisartan group (P < 0.05) but no increment was seen in Enalapril group.

CONCLUSIONS

Telmisartan and Enalapril had comparable antihypertensive effect and significant reduction in blood pressure was seen after 12 weeks of therapy in both the groups. In addition, Telmisartan showed more beneficial effects on lipid profile when compared to Enalapril.

KEYWORDS

Hypertension, Dyslipidemia, Lipid Profile, Telmisartan, Enalapril

Corresponding Author:
Dr. Chitra Karuppiah,
 # 503, Kalyan Garden,
Naval Coastal Battery Down,
Maharanipeta, Visakhapatnam – 530002,
Andhra Pradesh, India.
E-mail: chitravk16@gmail.com

DOI: 10.18410/jebmh/2021/360

How to Cite This Article:
Sanke S, Karuppiah C, Dumpala HSR, et al. A prospective comparative study of efficacy and pleiotropic effect of telmisartan versus enalapril in hypertensive patients with dyslipidaemia in a tertiary care hospital in Visakhapatnam. J Evid Based Med Healthc 2021;8(23):1915-1921. DOI: 10.18410/jebmh/2021/360

Submission 06-02-2021,
Peer Review 15-02-2021,
Acceptance 21-04-2021,
Published 07-06-2021.

BACKGROUND

Hypertension or raised blood pressure is one of the leading risk factors for mortality and disability[1] due to its high prevalence and its association with increased risk of cardiovascular, cerebrovascular, and reno vascular diseases. The diseases caused and the possible complications make the therapy difficult. A study showed that India with a population of 1.32 billion contributes large part to this burden. The prevalence of hypertension in urban population is 33.8 % while that in rural population is 27.6 % and overall, it is 29.8 %.[2] High-income countries have begun to reduce hypertension in their populations through strong public health policies such as reduction of salt in processed food and widely available diagnosis and treatment that tackle hypertension and other risk factors together. There are significant health and economic gains attached to early detection, adequate treatment, and proper control of hypertension. Treating the complications of hypertension entails costly interventions such as cardiac bypass surgery, carotid artery surgery and dialysis, and this results in draining of individual and government budgets.

It is well-established that hypertension and dyslipidaemia are the two major contributing risk factors for cardiovascular and cerebrovascular diseases. Studies have consistently indicated that hypertension and hypercholesterolemia frequently coexist, causing what is known as dyslipidemic hypertension (DH).[3] The risk of CVD associated with concomitant hypertension and dyslipidaemia is more multiplicative than the sum of the individual risk factors.[4,5] This has been recognized in the recent treatment guidelines that emphasize the need to quantify a person's overall cardiovascular disorder (CVD) risk.[6,7] Activation of renin-angiotensin-aldosterone system (RAAS) is the primary etiologic event in the development of hypertension.[8] Chronic activation of RAAS is the crucial driver in the initiation and progression of cardiovascular disorders.[9,10,11] Angiotensin receptor blockers (ARB's) exert their antihypertensive action by inhibiting the binding of angiotensin 2 to angiotensin receptors. Among the ARB's Telmisartan is the topic of interest because of its beneficial effects on hypertension as well as lipid and glucose metabolism[12,13]

However, studies comparing Telmisartan and Enalapril in hypertensive patients with dyslipidaemia have variable conclusions. Telmisartan is available as 20, 40 and 80 mg oral tablets. Enalapril is available as 2.5, 5, 10, 20 & 40 mg tablets and 1 mg/ml and 2.5 mg/ml injections. Therefore, there was a need for the study to gain insight into the pleotropic effects of Telmisartan besides antihypertensive properties in Indian population.

Objectives

1. To compare the efficacy of Telmisartan with Enalapril in patients of essential hypertension with dyslipidaemia in controlling blood pressure.
2. To observe the effects of Telmisartan and Enalapril on lipid profile of these patients.

METHODS

This is a prospective comparative study conducted in the out-patient department of General Medicine, in King George Hospital, Visakhapatnam. This study was conducted from 1st September 2018 to 30th August 2019 for period of one-year. Totally 70 patients were included in the study.

Inclusion Criteria

- Patients with mild to moderate essential hypertension of either sex within the age group of 18 – 65 years were included in the study.
- They were either newly diagnosed patients and those who had discontinued antihypertensive medication voluntarily for more than 4 weeks.
- Who willingly gave the informed consent

Exclusion Criteria

- Patients on antihypertensive therapy other than Telmisartan and Enalapril.
- Patients of secondary hypertension
- Patients with impaired liver function defined as serum glutamic oxaloacetic transaminase (SGOT) or serum glutamic pyruvic transaminase (SGPT) > 2 times the normal limit
- Patients with impaired kidney function confirmed by serum creatinine > 2 mg/dl
- Pregnant and lactating females
- Patients with history suggestive of obstructive biliary disease, cholestasis or severe hepatic impairment
- Female patients of the child-bearing age group not using medically approved contraceptives

Institutional ethical committee clearance was obtained prior to the initiation of study. Informed consent was taken from all the patients after providing them with all necessary information about the study. Demographic details, personal history, and past medical history of the patient were recorded. All baseline clinical assessments including the following were done -

1. General examination
2. Systemic examination
3. Blood sugar levels
4. Lipid profile (TC, LDL, TG, HDL)
5. Serum potassium
6. Complete haemogram
7. Liver function tests (serum bilirubin, SGPT, SGOT)
8. Kidney function tests (serum creatinine, BUN)
9. Routine urine analysis
10. Thyroid profile (T3, T4, TSH)
11. 24-hour urinary metanephrine
12. 24-hour urinary cortisol

Sample Size Calculation

A pilot study was conducted among 10 members. The results were found to be $\mu_1 = 86.44$, $\mu_2 = 89.37$, $\sigma_1 = 3.61$ & $\sigma_2 =$

2.04, type I error ($\alpha = 0.01$) type II error (β = 0.10). The sample size was calculated by using this formula. So, the minimum sample required for this study is (n = 30), but we have collected 35 sample for better results.

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \times 2\sigma^2}{(\mu^1 - \mu^2)^2}$$

After baseline assessment, out of 70 patients 35 were started on treatment with Telmisartan 40 mg (Group - A) and 35 patients were put on Enalapril 5 mg. (Group B).

After the commencement of the treatment, follow-up was performed at 4, 8 and 12 weeks. At each visit, complete clinical examination was carried out and recording of systolic and diastolic blood pressure of each patient using a mercury sphygmomanometer by the auscultation method. The BP was recorded in a sitting position after 10 minutes of rest. The pressure at which the sounds were first heard was taken as the systolic pressure and the pressure at which the sounds disappeared was taken as the diastolic pressure. Safety was assessed in terms of both subjective and objective systemic adverse-effects. Subjective symptoms such as headache, dizziness, fatigue, back pain, dyspepsia, myalgia, pruritus, nausea and dry cough were assessed by questioning the patient at each visit. Objective signs like rash and hypotension checked. Lipid profile was repeated at 12 weeks of follow up.

Statistical Analysis

Data will be entered in MS - Excel and analysed by using statistical package for social sciences (SPSS) V22. Normality will be checked by using Kolmogorov Simonov test. Descriptive statistics will be represented with percentages, mean with SD. Independent t-test, paired t-test & chi-square test will be applied based on nature of the distribution. P < 0.05 will be considered as statistically significant.

RESULTS

Sl. No.	Parameter	Group A (Telmisartan) N = 35	Group B (Enalapril) N = 35	P Value Intergroup	Significance
1.	Age	45.42	46.9	0.102	NS
2.	Gender	16 males 19 females	18 males 17 females	0.632	NS
3.	Body mass index (BMI)	28.12	28.03	0.437	NS
4.	Systolic blood pressure (SBP)	151.6 ± 3.613	153.2 ± 3.88	0.090	NS
5.	Diastolic blood pressure (DBP)	93.77 ± 2.315	94.23 ± 2.102	0.390	NS
6.	Total cholesterol TC (mg/dl)	208.98 ± 5.71	211.07 ± 6.06	0.142	NS
7.	LDL (mg/dl)	137.12 ± 12.74	141.12 ± 10.70	0.160	NS
8.	TG triglycerides (mg/dl)	148.82 ± 9.73	146.36 ± 9.12	0.279	NS
9.	HDL (mg/dl)	41.611 ± 3.53	42.96 ± 2.26	0.06	NS

Table 1. Demographic and Baseline Clinical Characteristics of the 70 Patients

A total of 97 patients were screened of which 24 patients were not meeting the inclusion criteria. Balance 73 eligible patients were taken into the study among which 38 of them were on treatment with Telmisartan 40 mg/day and the rest of the patients (35) were on Enalapril 5 mg/day. Three patients from Group A were lost to follow up during the study period. Hence 35 patients in group A and 35 patients in group B were studied.

Baseline Profile

All parameters at base line were comparable as there is no statistically significant difference between the two groups except for triglycerides and HDL.

Systolic Blood Pressure

Intra Group Results

In group A, the base line mean SBP 151.66 ± 3.613 mmHg was reduced to 131.89 ± 2.166 mmHg at 4 weeks, 126.40 ± 2.316 mmHg at 8 weeks and 125.09 ± 2.3133 at 12 weeks of therapy with Telmisartan. In group B, the base line mean SBP 153.20 ± 3.88 was reduced to 131.54 ± 2.99 at 4 weeks, 127.31 ± 2.42 at 8 weeks and 124.46 ± 2.174 at 12 weeks of therapy with Enalapril. The reduction in mean SBP was statistically highly significant over 12 weeks of therapy in both the treatment groups.

Inter Group Results

There is no significant difference in mean SBP values when the two groups were compared at baseline and also at each subsequent follow ups. Intra group results of diastolic blood pressure: In group A, the base line mean DBP 93.77 ± 2.315 mmHg was reduced to 90.34 ± 1.781 mmHg at 4 weeks, 88.11 ± 1.676 mmHg at 8 weeks and 86.86 ± 1.39 at 12 weeks of therapy with Telmisartan. In group B, the base line DBP 94.23 ± 2.102 was reduced to 91.49 ± 2.442 at 4 weeks, 87.60 ± 1.802 at 8 weeks and 86.40 ± 1.519 at 12 weeks of therapy with Enalapril. The reduction in mean DBP was statistically highly significant over 12 weeks of therapy in both the treatment groups.

Diastolic Blood Pressure

There is no significant difference in mean DBP values when the two groups were compared at baseline and also at each subsequent follow-up.

Triglycerides

Intra Group Results

In-group A, baseline means triglyceride levels were 148.82 mg/dl and were reduced to 140.980 mg/dl. In group B, baseline mean triglyceride levels were 143.36 mg/dl and were reduced to 136.126 mg/dl. There is a significant difference between the baseline and after treatment values of mean triglycerides with 12 weeks of treatment in both the groups.

Groups	Baseline SBP	SBP 12 Weeks	P Value (Intra group)	Baseline DBP	DBP 12 Weeks	P Value (Intra Group)
Group A (Telmisartan)	151.66 ± 3.613	125.09 ± 2.133	< 0.0001	93.77 ± 2.315	86.86 ± 1.39	< 0.0001
Group B (Enalapril)	153.20 ± 3.88	124.46 ± 2.174	< 0.0001	94.23 ± 2.10	86.4 ± 1.51	< 0.0001
P Value (Inter Group)	0.09	0.226		0.39	0.194	

Table 2. Systolic and Diastolic Blood Pressure Values at Baseline and 12 Weeks

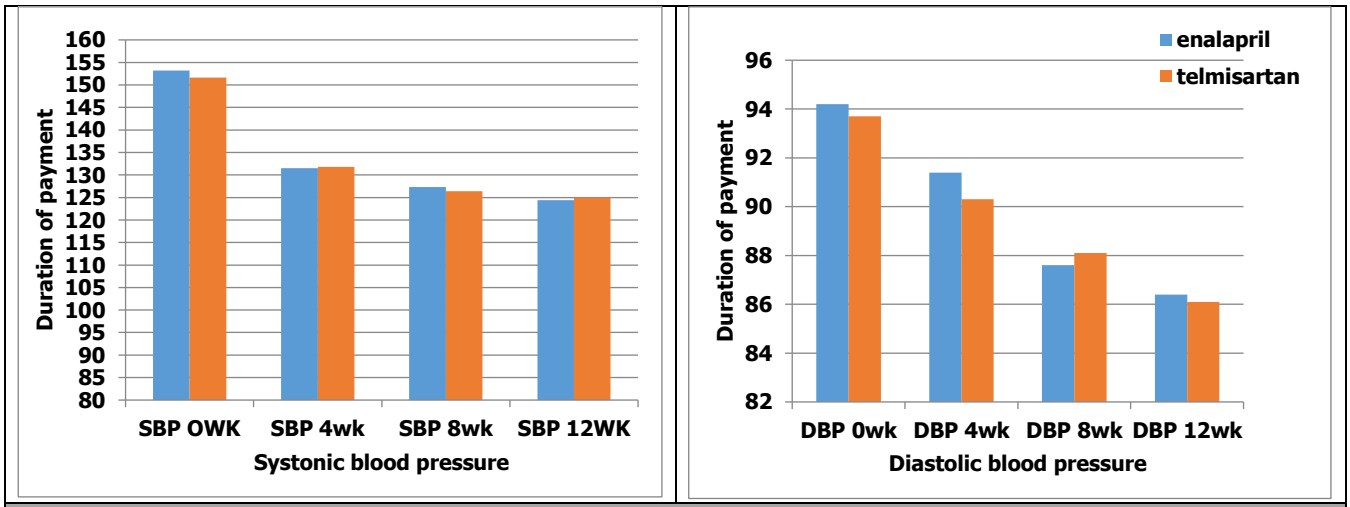

Figure 1. Systolic and Diastolic Blood Pressure Reduction in Both the Groups

Inter Group Results

At baseline, there is no significant difference between the two groups in their mean triglyceride levels implying that both are comparable. At the end of the follow up, i.e., at 12th week, there is a significant difference in their mean TG values. This infers that Telmisartan is more effectively reducing the triglyceride levels when compared to Enalapril.

Total Cholesterol

Intra Group Results

In group A, baseline total cholesterol mean values were 208.980 mg/dl and were reduced to 198.983 mg/dl. In group B, baseline total cholesterol mean values were 211.071 mg/dl and were reduced to 207.206 mg/dl. There is a significant difference between the baseline and after treatment values of mean total cholesterols with 12 weeks of treatment among the two groups.

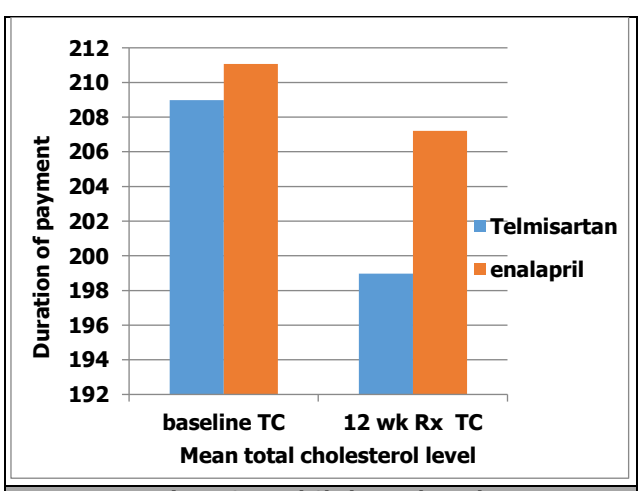

Figure 2. Total Cholesterol Levels Mean Values in Both the Groups

Inter Group Results

At baseline, there is no significant difference between the two groups in their mean total cholesterol levels. But at the end of the follow up, i.e. At 12th week, there is a significant difference. But Telmisartan is more effective in reducing the mean total cholesterol levels when compared to Enalapril

LDL Levels

Intra Group Results

A significant difference was observed in group A patients receiving Telmisartan in their LDL levels after 12 weeks of therapy. While in group B patients, there was no significant reduction.

Inter Group Results

At baseline, the two groups are comparable with respect to their means and at the end of follow up, there is significant difference in their LDL cholesterol values with a P value of 0.003 showing that, Telmisartan is effective in reducing mean LDL values when compared to Enalapril

HDL Levels

Groups	TG 0	TG 12	TC 0	TC 12	LDL 0	LDL 12	HDL 0	HDL 12
Group a (Telmisartan)	148.	143.	208.	198.	137	128.	41	43
Group b Enalapril)	140.	136.	211.	207.	141	137	42	42
P Value Inter Group	0.18	0.023	0.142	< 0.0001	0.160	0.003	0.04	0.67

Table 3. Lipoproteins Levels Measured in the Two-Treatment Groups at Baseline & after Treatment

Intra Group Results

In group A, baseline mean HDL levels were 41.61 mg/dl and were increased to 43.13 mg/dl. In group B, baseline mean HDL levels were 42.96 mg/dl and didn't change thereafter. There is a significant increase in HDL values in Telmisartan

group but in case of Enalapril group, there was no increment.

Inter Group Results

At baseline, the difference in mean HDL values was significant implying that the two groups were not comparable

DISCUSSION

Studies have consistently indicated that hypertension and hypercholesterolemia frequently coexist, causing what is known as dyslipidemic hypertension.[3] The risk of CVD associated with concomitant hypertension and dyslipidaemia is more multiplicative than the sum of the individual risk factors. This has been recognized in the recent treatment guidelines that emphasize the need to quantify a person's overall CVD risk.[6,7] Hence the goal of hypertension treatment is to decrease the morbidity and mortality associated with cardiovascular and cerebrovascular events. A reduction in systolic blood pressure of 5 mmHg has been associated in observational studies with mortality reductions of 14 % from stroke, 9 % from heart disease, and 7 % from other causes.[14]

The present study did comparative evaluation of effects of Telmisartan and Enalapril on BP, serum HDL and LDL levels. Though there are plenty of studies evaluating the effects of Telmisartan as well as Enalapril in patients with essential hypertension with dyslipidaemia, the baseline characteristics of study subjects, duration of evaluation and doses of Telmisartan and Enalapril varies from study to study. To get more conclusive opinion, the present study results are discussed with those studies having almost same doses of study drugs with almost similar duration of evaluation as that of present study.

Comparison of Systolic Blood Pressures in Group A & Group B

Intra Group Results

In group A, the base line mean SBP 151.66 ± 3.613 mmHg was reduced to 131.89 ± 2.166 mmHg at 4 weeks, 126.40 ± 2.316 mmHg at 8 weeks and 125.09 ± 2.3133 at 12 weeks of therapy with Telmisartan. In group B, the base line mean SBP 153.20 ± 3.88 was reduced to 131.54 ± 2.99 at 4 weeks, 127.31 ± 2.42 at 8 weeks and 124.46 ± 2.174 at 12 weeks of therapy with Enalapril. The reduction in mean SBP was statistically highly significant over 12 weeks of therapy in both the treatment groups.

Inter Group Results

There is no significant difference in mean SBP values when the two groups were compared at baseline and also at each subsequent follow-up. This result was in agreement with the studies of Raja M et al. Hannedouche T et al. (2001),[12] Pankaj Kumar et al. KS Podila et al.

Comparison of Diastolic Blood Pressures in Group A & Group B

Intra Group Results

In group A, the base line mean DBP 93.77 ± 2.315 mmHg was reduced to 90.34 ± 1.781mmHg at 4 weeks, 88.11 ± 1.676 mmHg at 8 weeks and 86.86 ± 1.39 at 12 weeks of therapy with Telmisartan. In group B, the base line DBP 94.23 ± 2.102 was reduced to 91.49 ± 2.442 at 4 weeks, 87.60 ± 1.802 at 8 weeks and 86.40 ± 1.519 at 12 weeks of therapy with Enalapril. The reduction in mean DBP was statistically highly significant over 12 weeks of therapy in both the treatment groups.

Inter Group Results

There is no significant difference in mean DBP values when the two groups were compared at baseline and also at each subsequent follow ups. This result was in agreement with the studies of Raja M et al.[15] Hannedouche T et al. (2001). Pankaj Kumar et al. KS Podila et al.

Comparison of Triglyceride Levels in Group A & Group B

Intra Group Results

In group A, baseline mean triglyceride levels were 148.82 mg/dl and were reduced to 140.980 mg/dl. In group B, baseline mean triglyceride levels were 143.36 mg/dl and were reduced to 136.126 mg/dl. There is a significant difference between the baseline and after treatment values of mean triglycerides with 12 weeks of treatment in both the groups.

Inter Group Results

At baseline, there is no significant difference between the two groups in their mean triglyceride levels implying that both are comparable. At the end of the follow up, i.e. At 12th week, there is a significant difference in their mean TG values. This infers that Telmisartan is more effectively reducing the triglyceride levels when compared to Enalapril. This result was in agreement with the studies of KS Podila et al. Spyridon Koulouris.

Comparison of Total Cholesterol Levels in Group A & Group B

Intra Group Results

In group A, baseline total cholesterol mean values were 208.980 mg/dl and were reduced to 198.983 mg/dl. In group B, baseline total cholesterol mean values were 211.071 mg/dl and were reduced to 207.206 mg/dl. There is a significant difference between the baseline and after treatment values of mean total cholesterols with 12 weeks of treatment among the two groups.

Inter Group Results

At baseline, there is no significant difference between the two groups in their mean total cholesterol levels. But at the end of the follow up, i.e. At 12th week, there is a significant difference. But Telmisartan is more effectively reducing the cholesterol mean total levels when compared to Enalapril.

This result was in agreement with the studies of Dongxiu Xu et al. Pervez et al. Jayapriya B et al.

Comparison of LDL levels in Group A & Group B

Intra Group Results

A significant difference was observed in group A patients receiving Telmisartan in their LDL levels after 12 weeks of therapy. While in-group B patients, there was no such significant reduction in levels of LDL cholesterol.

Inter Group Results

At baseline the two groups are comparable with respect to their means and at the end of follow up, there is significant difference in their LDL cholesterol values with a P value of 0.003 showing that, Telmisartan is effective in reducing mean LDL values when compared to Enalapril. This result was in agreement with the studies of Dongxiu Xu et al[16]. Suresh thota et al. Pervez et al. Jayapriya B et al.

Comparison of HDL Levels in Group A & Group B

Intra Group Results

In group A, baseline mean HDL levels were 41.61 mg/dl and were increased to 43.13 mg/dl. In group B, baseline mean HDL levels were 42.96 mg/dl and didn't change thereafter. There is a significant increase in HDL values in Telmisartan group but in case of Enalapril group, there is no increment.

Inter Group Results

At baseline, the difference in mean HDL values was significant implying that the two groups were not comparable. This result was in agreement with the studies of Dongxiu Xu et al.[16] Suresh thota et al. Pervez et al. Jayapriya B et al.

Limitations

- The present study has the limitation of relatively small number of patients with short duration.
- To establish conclusive results on the pleotropic effects of telmisartan beyond as an anti-hypertensive drug, longer study time and higher doses > 40 mg / day are required.

CONCLUSIONS

In hypertensive patients with dyslipidaemia, the aim is to control hypertension and maintain favourable lipid profile in order to minimize the cardiovascular, renovascular and cerebrovascular complications and improve the patient's prognosis. Clinicians all over the world are seeking more evidence for pleotropic effects of Telmisartan beyond blood pressure control. So, the present study demonstrated that both Telmisartan & Enalapril had comparable anti-hypertensive effect. In addition, Telmisartan showed more beneficial effects on lipid profile when compared to Enalapril. Thus, Telmisartan can be preferred in patients of essential hypertension with dyslipidaemia over Enalapril.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Gupta R, Mohan I, Narula J. Trends in coronary heart disease epidemiology in India. Ann Glob Health 2016;82(2):307-315.
[2] Anchala R, Kannuri NK, Pant H, et al. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness and control of hypertension. J Hypertens 2014;32(6):1170-1177.
[3] Kannel WB. Fifty years of Framingham study contributions to understanding hypertension. J Hum Hypertens 2000;14(2):83-90.
[4] Stamler J, Wentworth D, Neaton JD. Prevalence and prognostic significance of hypercholesterolemia in men with hypertension: prospective data on the primary screenees of the Multiple Risk Factor Intervention Trial. Am J Med 1986;80(2A):33-39.
[5] Castelli P, Anderson K. A population at risk. Prevalence of high cholesterol levels in hypertensive patients in the Framingham Study. Am J Med 1986;80(2A):23-32.
[6] Borghi C. Interactions between hypercholesterolemia and hypertension: implications for therapy. Curr Opin Nephrol Hypertens 2002;11(5):489-496.
[7] Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285(19):2486-2497.
[8] Hsueh WA, Wyne K. Renin-Angiotensin-aldosterone system in diabetes and hypertension. J Clin Hypertens (Greenwich) 2011;13(4):224-237. http://doi.wiley.com/10.1111/j.1751-7176.2011.00449.x
[9] Riberio-Oliveira A, Nogueira Al, Pereira RM, et al. The renin angiotensin system and diabetes. An update Vasc Health Risk Management 2008;4(4):787-803.
[10] Rizos CV, Elisaf MS, Liberopoulos EN. Are the plerotropic effects of Telmisartan clinically relevant? Curr Pharm Des 2009;15(24):2815-2832.
[11] Akhrass PR, McFarlane SI. Telmisartan and cardioprotection. Vasc Health Risk Management 2011;7:677-683. http://ovidsp.ovid.com/ovidweb.cgi?t=js&page=reference&D=emed11&news = N&AN=22140310.
[12] Kurtz TW. Treating the metabolic syndrome: Telmisartan as a peroxisome proliferator activated receptor – gamma activator. Acta Diabetol 2005;42(Suppl 1):39-16.

[13] Burnier M. Telmisartan: a different angiotensin II receptor blocker protecting a different population? J Int Med Res 2009;37(6):1662-1679.
[14] Whelton PK, He J, Appel LJ, et al. Primary prevention of hypertension: clinical and public health advisory from The National High Blood Pressure Education Program. JAMA 2002;288(15):1882-1888.
[15] Raja M, Shukla A, Mehani R, et al. Comparative study of Telmisartan and Ramipril as an antihypertensive in mild to moderate hypertension. National Journal of Physiology, Pharmacy and Pharmacology 2016;6(5):1.
[16] Dongxiu X, Junfa L, Cuiling J, et al. Effects of Telmisartan on hypertensive patients with dyslipidemia and insulin resistance. Journal of Geriatric Cardiology 2007;4(3):149-152.