Original Article

Comparative evaluation of Metoprolol and Telmisartan in hypertensive patients

Agarwal A[1], Chhabra MK[2], Walia R[3], Gupta PD[4]

[1]Dr Amrit Agarwal
Assisiant Professor, Pharmacology
Pacific Medical College and hospital
Udaipur, Rajasthan, India
dramrit2012@gmail.com

[2]Dr MK Chhabra
Reader, Pharmacology
Dr Harvansh Singh Judge Institute of Dental Sciences and Hospital
Chandigarh, India
kiranchhabra7@gmail.com

[3]Dr Rani Walia
Professor & Head, Pharmacology
hod.pharmacology@mmumullana.org

[4]Dr PD Gupta
Professor, Medicine
docgupta@gmail.com

[3,4]Maharishi Markandeshwar Institute of Medical Sciences & Research
Mullana, Ambala, India

Received: 15-02-2014
Revised: 20-04-2014
Accepted: 18-06-2014

Correspondence to:
Dr Amrit Agarwal
08295354731
dramrit2012@gmail.com

ABSTRACT

Background: *Epidemiological studies and clinical trials have shown that meticulous control of blood pressure is required in patients with hypertension to ensure decreased cardiovascular morbidity and mortality.*

Objective: *To compare the effect of Metoprolol and Telmisartan on blood pressure reduction and heart rate in patients of Stage I Hypertension.*

Material and Methods: *This was a prospective, randomized, open, parallel study conducted at the outpatient department of Medicine. Patients of either sex with Grade I Hypertension according to JNC VII, aged between 18-60 years were enrolled and followed up every 2 weeks from baseline till 12 weeks. Patients were randomly divided into two groups to receive tablet Metoprolol 50 mg (Group A, n=30) and Telmisartan 40 mg (Group B, n=30) once a day. Response to study treatments was evaluated in terms of decrease in Blood pressure and heart rate. Results were analysed using Student's 't' test.*

Results: *Baseline characters of both the groups were well balanced. Systolic Blood Pressure was reduced by 7.5 % from Metoprolol and 12.9% by Telmisartan and Diastolic Blood Pressure was reduced by 8.2% in group A and 13.6% in group B. Both the drugs leads to significant reductions (i.e. P <0.05) in systolic as wel as diastolic BP. Heart rate reduction was significant and was observed to be more with the Metoprolol group i.e. 15.2% reduction as compared to 9.1% reduction with Telmisartan.*

Conclusion: *Telmisartan is a better choice than Metoprolol in Indian Population for treating Grade I hypertension as it leads to greater reduction in Blood Pressure and less effect on Heart rate.*

Keywords: *Grade I Hypertension, metoprolol, telmisartan, systolic blood pressure, diastolic blood pressure, heart rate*

Introduction

Among the underdeveloped and developing countries including the South Asian countries (including India and Pakistan) Cardiovascular disease (CVD) is the most common contributor of morbidity and mortality. Amongst the cluster group of CVDs Hypertension (HTN) represents the most common cardiovascular risk factor, treatment of which significantly reduces the cardiovascular morbidity and mortality. [1]

Hypertension is defined as systemic blood pressure of 140/90 mmHg or more on two separate occasions measured at least one to two weeks apart.[2] It is classified according to JNC VII [2] as –

Normal → ≤ 120 and ≤ 80 (mm of Hg)
Pre-hypertensive → 120-139 and 80-89 (mm of Hg)
Stage I → 140-159 and 90-99 (mm of Hg)
Stage II → ≥160 and ≥100 (mm of Hg)

The prevalence of HTN increases with advancing age; for example, about 50% of people between the ages of 60 and 69 years old have HTN, and the prevalence is further increased beyond age of 70 years. [2] It is also associated with a number of serious conditions and accounts for 13.5% of all

premature deaths, 54% of all strokes and 47% of ischemic heart diseases. [3] It affects approximately one-third of the world's adult population and it is predicted to increase with 60% towards 2025. [4] Cardiovascular diseases caused 2.3 million deaths in India in the year 1990; this is projected to double by the year 2020. Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India. [5] Thus, a meticulous control of Blood Pressure needs to be achieved by the anti-hypertensive drugs. Amongst them, the most commonly prescribed ones are Beta-adrenergic receptor blockers which are recommended as first-line therapy for HTN by all Joint National Committees (JNCs) for the prevention, detection, evaluation, and treatment of high blood pressure (BP) from the first to the last JNC-7. [6] For this study, Metoprolol was chosen amongst the Beta-Blockers because of its broad use in clinical practice and favourable safety profile, including its safe use in diabetics, asthmatics and patients with renal impairment. It is recommended for the treatment of arterial hypertension and has been shown to be effective in reducing BP and Left Ventricular Hypertrophy. [7]Another popularly used drug among the antihypertensives is Telmisartan which was chosen for this study because, although Angiotensin converting enzyme inhibitors eg. Ramipril, were used on the forefront to treat HTN, Angiotensin Receptor Blockers were developed because of their similar efficacy and lower side effect profile (dry cough), it has also shown to be efficacious in high risk patients and has proved to lower the incidence of stroke and CVDs. Telmisartan proved to be effective when given in 24 hour dosage interval (due to their plasma half life i.e. 24hours), indicating better patient compliance. [7] *So* the aim of the study was to evaluate the antihypertensive efficacy and effect on heart rate in patients of Haryana, treated either with Metoprolol or Telmisartan.

Material and Methods

A prospective, randomized, open parallel group study of 12 weeks duration was conducted by the Department of Pharmacology in association with Department of Medicine from January 2012 to June 2013 at outpatient department of Medicine, M.M.I.M.S.R, Mullana, Ambala. The study protocol was approved before the commencement of the study by the Institutional Ethics Committee. Sixty patients of both the sexes within the age group 18 to 60 years after fulfilling the inclusion and exclusion criteria were enrolled and were divided into 2 groups. Group A patients received Metoprolol 50mg once a day for 12 weeks and Group B patients received Telmisartan 40mg once a day for 12 weeks. Patients with Stage I hypertension in the age group of 18-60 years of both sexes and who were willing to give written & informed consent were included. They were either newly diagnosed patients or were those who had discontinued antihypertensive medication voluntarily for more than 4 weeks. The following categories of patients were excluded from the study: patients on other antihypertensive therapy, patients of secondary hypertension, patients with impaired liver function defined as SGOT or SGPT >2 times the normal limit, patients with impaired kidney function (confirmed by serum creatinine >2 mg/dl), patients with history of drug allergy, alcohol intake, bronchial asthma, chronic obstructive pulmonary disease (COPD), peripheral

arterial disease and female patients who were pregnant or lactating.

Study Methodology

Patients were enrolled after informed and written consent as per the inclusion and exclusion criteria. Clinical evaluation of all the patients was done by measuring blood pressure and heart rate before administration of drug. Patients were randomly assigned to receive either Metoprolol or Telmisartan with 30 patients in each group. Group A patients received 50 mg of Metoprolol once a day orally for 12 weeks while group B patients received 40 mg of Telmisartan once a day orally for 12 weeks. After enrollment into the study, follow-up was performed after every 2 weeks till 12 weeks. At each visit, complete clinical examination was carried out, including a recording of systolic and diastolic blood pressure (BP) of each patient using a mercury sphygmomanometer by the auscultation method. The BP was recorded in a sitting position after 10 min 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. Following the same procedure BP will be recorded in supine position. Heart rate was also measured at each visit using the palpatory method. Investigations such as Renal function tests, Liver Function tests were performed during the first visit and after 12 weeks of the study period. The laboratory assessments of various parameters were carried out in the computerized clinical biochemistry laboratory of M.M.I.M.S.R. Hospital, Mullana. Chest X-Ray, ECG, USG Abdomen were done to satisfy the eligibility/ exclusion criteria. The primary efficacy end point included reduction in BP from baseline to week 12. Other end point included change in Heart rate before initiating the therapy and after 12 weeks of therapy.

Statistical analysis

For comparison between pre- and post treatments i.e. within the group, Student's paired 't' test was used. Difference between groups or independent variables were compared by Student's unpaired 't' test for normally distributed variables. Statistical analysis was performed using computer software - SPSS version 16.0. The level of significance was determined by probability value (p value). *P*-value <0.05 was taken as significant.

Results

Baseline characteristics

Baseline characteristics of patients with Stage I hypertension receiving Metoprolol 50 mg once daily (Group A, n=30) or Telmisartan 40 mg once-daily (Group B, n=30) were summarized in Table 1. There were no significant differences of baseline parameters i.e. the demographic as well as clinical parameters of Blood pressure and Heart rate between the groups. Changes of Blood pressure and Heart rate in detail from baseline to after 12 weeks therapy are presented in Table 2. There was a significant change in all the parameters at the end of twelve weeks. (p<0.001) When an intergroup comparison was made in the two study groups, there was no significant difference (p>0.05 NS) noted at baseline but at twelve weeks the values of all the three parameters, in between the groups show a significant difference i.e. p <0.05 **(Table 3)**

Table 1: Baseline characters of Group I & Group II

Characteristic	Group 1	Group II
Number of patients	30	30
Age Range (years) **Mean Age (years)**	28 - 60 44.2 ± 8.1	27 – 60 43.9 ± 9.6
Sex (Male / Female)	18/12	17 / 13
Systolic BP (mm. Hg)	148.2 ± 4.4	147.9 ± 5.5
Diastolic BP (mm. Hg)	94.6 ± 3.2	94.7 ± 2.9
Heart rate (Pulse/minute)	85.7 ± 2.1	86.8 ± 2.0

Table 2: Comparison of Systolic BP, Diastolic BP and Heart rate at Baseline and at 12 weeks in both the groups

Parameter	Mean ± SD Group I		Mean ± SD Group II	
	At Baseline	At 12 weeks	At Baseline	At 12 weeks
Systolic BP (mm. Hg)	148.2 ± 4.4	137.1± 3.8**	147.9 ± 5.5	129.3 ± 4.0**
Diastolic BP (mm. Hg)	94.6 ± 3.2	86.9 ± 3.3**	94.7 ± 2.9	81.2 ± 2.4**
Heart Rate (Pulse/minute)	85.7 ± 2.1	72.6 ± 1.9**	86.8 ± 2.0	78.8 ± 1.6**

***significant, **highly significant, *** very highly significant**

Table 3: Inter group comparison of Systolic BP, Diastolic BP and Heart rate at Baseline and at 12 weeks in both the groups

Parameter	Mean ± SD Baseline		Mean ± SD At 6 Weeks	
	Group I	Group II	Group I	Group II
Systolic BP (mm. Hg)	148.2 ± 4.4	147.9 ± 5.5	137.1 ± 3.8	129.3 ± 4.0*
Diastolic BP (mm. Hg)	94.6 ± 3.2	94.7 ± 2.9	86.9 ± 3.3	81.2 ± 2.4*
Heart Rate (Pulse/ minute)	85.7 ± 2.1	86.8 ± 2.0	72.6 ± 1.9	78.8 ± 1.6*

(*P value <0.05 i.e. there is significant differnce in BP and Heart Rate reduction when comparison is made in between the two drugs)

Percentage change in Systolic Blood Pressure before initiation of therapy to after 12 weeks of therapy is total reduction of 7.5 % by Metoprolol 50 mg and 12.9 % by Telmisartan 40 mg. (Figure 1)

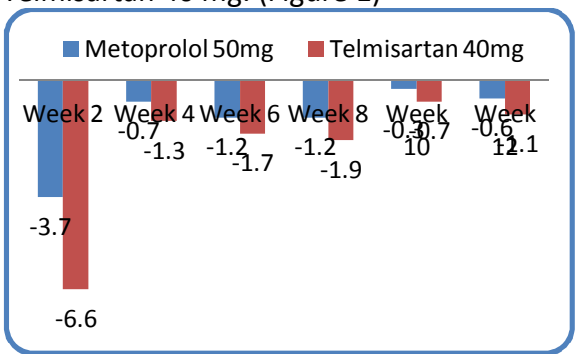

Fig.1 Comparison of Percentage Reduction in Systolic Blood Pressure of Group A and Group B

Total Change in Diastolic Blood Pressure after 12 weeks of therapy is 8.2% reduction in group A and 13.6% decrease in Diastolic BP in group B. (Figure 2)

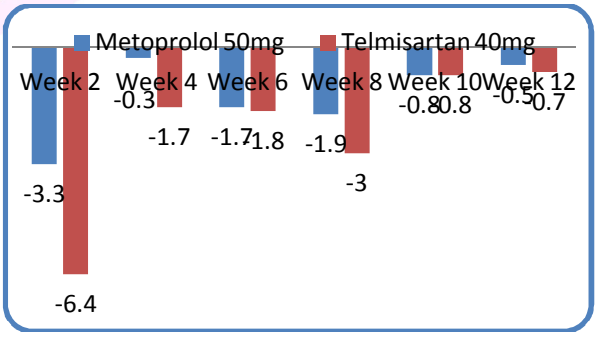

Fig. 2 Comparison of Percentage Reduction in Diastolic Blood Pressure of Group A and Group B

Heart rate reduction was significant and was observed to be more with the Metoprolol group i.e. 15.2% reduction as compared to 9.1% reduction with Telmisartan. (Figure 3)

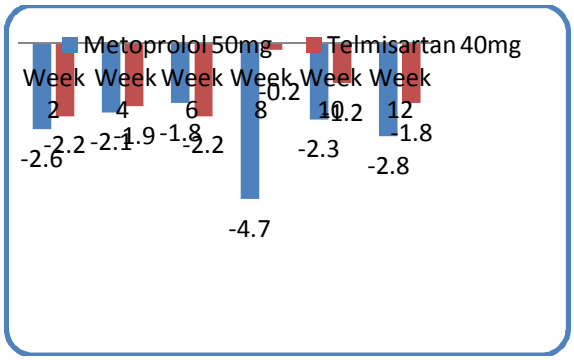

Fig. 3 Comparison of Percentage Difference in Heart Rate in Group A and Group B

Discussion

In the present prospective, randomized, comparative twelve week clinical trial two antihypertensive drugs Metoprolol (50 mg/day) orally for 12 weeks was administered to Group A (n=30 Patients) and Telmisartan (40 mg/day) orally for 12 weeks was administered to Group B (n=30 Patients) we found that both the drugs were effective in improving the various parameters of hypertension and caused reduction in BP and Heart rate.

When we compared the two drugs to determine the superiority of one therapy over the other; we found that Telmisartan is more effective in reducing both Systolic and Diastolic blood pressure while Metoprolol have more profound effect on reduction of heart rate than Telmisartan

Hypertension remains a major health problem being one of the leading causes of death and disability. Prevalence of hypertension among Indians is 26.78% in males and 27.65% in females. [8] Thus, a control of different components of Blood Pressure would serve the cause of reduced cardiovascular morbidity and mortality. One amongst these components is Systolic blood pressure. The mean systolic blood pressure in the Group A at baseline period was 148.2 ± 4.4 mm Hg which was significantly reduced ($p < 0.001$) at each time interval of 2 weeks and by end of the 12th week it was reduced to 137.1 ± 3.8 mmHg (Table 2) i.e. an average reduction of 11.11 mmHg which is comparable with the results obtained in a 12 weeks study done by Dahlof B et al, [9] compairing efficacy of Metoprolol and Felodipine in which Metoprolol showed a reduction of 11 mmHg in systolic blood pressure. Also a study done by Zachariah PK et al. [10] comparing efficacy of Lisinopril and Metoprolol showed 12 mmHg reduction in systolic blood pressure with Metoprolol group. This suggests that our trial have similar impact on the systolic blood pressure with Metoprolol as demonstrated by the study of Dahlof B et al and Zachariah PK et al. The mean systolic blood pressure in the Group B at baseline period was 147.9 ± 5.5 mmHg which was significantly reduced ($p < 0.001$) by end of the 12th week to 129.3 ± 4.0 mm Hg (Table 2) i.e. an average reduction of 19.07 mmHg. These results are comparable with those of studies done by Freytag F et al [11] which showed a reduction of 20.9 mm Hg in systolic BP with telmisartan. Also, a 12 weeks study done by Pramod B, Akat et al. [12] showed a reduction of 26.38 ± 10.98 mm Hg in systolic BP. The difference in the reduction in systolic BP in Telmisartan Group from baseline was significantly higher in the previous studies than our study. This could be attributed to differences in the patient profile as well as due to ethnic differences.

Diastolic blood pressure is another well established cardiovascular risk factor which was decreased from baseline to 12th week in group A (Metoprolol) from 94.6 ± 3.2 mm Hg to 86.9 ± 3.3 mm Hg i.e. an average reduction of 7.75 mmHg. (Table 2) ($p< 0.001$). These results are comparable with those of studies done by Dahlof B et al. [9] which showed a 8 mm Hg reduction of

diastolic BP and a reduction from 110 to 99 mm Hg (p less than 0.01) i.e. 12 mm Hg reduction of diastolic BP was observed by Zachariah PK et al.[10] In group B (Telmisartan) patients, average diastolic Blood Pressure reduction was observed to be 12.87 mm Hg i.e. from 94.7 ± 2.9 mm Hg (baseline) to 81.2 ± 2.4 mm Hg, after 12 weeks (Table 2). In a study conducted by Freytag F et al.[11] reductions in diastolic Blood Pressure was reported to be 14.4 mm Hg after 26 weeks of Telmisartan therapy. Also, a 12 weeks study done by Pramod B. Akat et al. [12] showed a reduction of 14 ± 2.98 mm Hg in diastolic BP. This difference may be attributed to the difference in the responses of the patients of different ethnic origins.

The third important parameter i.e. Heart rate in the Group A (Metoprolol) at baseline period was 85.7 ± 2.1 beats per min which was significantly reduced to 72.6 ± 1.9 beats per min. (Table 2), counting for an average reduction of 13 beats/minute. A study conducted by Pollare T et al. [13] showed reduction in heart rate was 11 beats per minute after Metoprolol treatment. In group B (Telmisartan) mean baseline heart rate was observed to be 86.8 ± 2.0 per min which at the end of treatment period reduced to 78.8 ± 1.6 per min. (Table 2) i.e. an average reduction of 7.8 beats per min. Yuhei Shiga et al. [14] conducted a study which showed insignificant heart rate reductions from 73 beats per min. to 71 beats per min. This difference could be attributed to the dietary and lifestyle modifications which many of the patients in our study acclaimed to have adopted or due to difference in the lifestyle of urban and rural.

The present study concluded that Telmisartan is a better choice for treating Grade I hypertensive patients as compared to Metoprolol, in view of greater reduction in BP (both Systolic & Diastolic), less reduction of heart rate as compared to Metoprolol indicating its use in organ failure conditions. Here, it is pertinent to suggest that more clinical and biochemical studies need to be done on a larger population to confirm these results, so that this improved effectiveness in hypertensive patients could be translated into an advantage in achieving and maintaining the target Blood Pressure levels.

Despite our best efforts we had a number of limitations in our study, First, the study included only a limited number of patients from a single centre and secondly, the patients were not blinded. Blinding would have provided a more valid assessment of efficacy of both the drugs. Therefore, it would be prudent if a large randomized, multi-centric trial is conducted, further to look into the biochemical and clinical outcome of the patients who were treated either with Metoprolol or Telmisartan.

Acknowlegement- This work was supported by Dr. Shafiqa Aslam and Dr Ashish Puri. I convey my heartfelt thanks for their constructive and invaluable suggestions.

References

1. Stafylas PC, Sarafidis PA. Carvedilol in hypertension treatment. Vasc Health Risk Manag. 2008 February;4(1):23–30.
2. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC report. JAMA 2003; 289(19):2560-72.
3. Lawes CM, Hoorn V S, Rodgers A. Global burden of blood-pressure-related disease, 2001. Lancet 2008 May 3;371(9623):1513-28.

4. Bundgaard M, Jarbol DE, Paulsen MS, Jacobsen JL, Pedersen ML. Prevalence of the use of antihypertensive medications in Greenland: a study of quality of care amongst patients treated with antihypertensive drugs. Int J Circumpolar Health 2012;71:10.3402
5. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004 February;18(2):73-78.
6. Chrysant SG, Chrysant GS, Dimas B. Current and Future Status of Beta-blockers in the Treatment of Hypertension. Clinical Cardiology 2008 June;31(6):249-252.
7. Friedrich MG, Dahlöf B, Sechtem U, Unger T, Knecht M. Telmisartan Effectiveness on Left ventricular Mass Reduction (TELMAR) as assessed by magnetic resonance imaging in patients with mild-to-moderate hypertension – a prospective, randomised, double-blind comparison of telmisartan with metoprolol over a period of six months – rationale and study design. Journal of the Renin-Angiotensin- Aldosterone System 2003 December;4(4):234-243.
8. Anand MP. Essential hypertension. In: Shah SN, Anand MP, Acharya VN, Bichile SK, Karnad DR, Kamath SA, Munjal YT, editors. API text book of Medicine 7 th ed. Mumbai: The Association of Physicians of India; 2003.p.452-61.
9. Dahlof B, Hosie J. Antihypertensive efficacy and tolerability of a fixed combination of metoprolol and felodipine in comparison with the individual substances in monotherapy. The Swedish/United Kingdom Study Group. Journal of Cardiovascular Pharmacology 1990;16(6):910-916.
10. Zachariah PK, Bonnet G, Chrysant SG, De Backer G, Goldstein R, Herrera J et al. Evaluation of antihypertensive efficacy of lisinopril compared to metoprolol in moderate to severe hypertension. Journal of Cardiovascular Pharmacology 1987;9(3):S53-8.
11. Freytag F, Schelling A, Meinicke T, Deichsel G. Comparison of 26-week efficacy and tolerability of telmisartan and atenolol, in combination with hydrochlorothiazide as required, in the treatment of mild to moderate hypertension: a randomized, multicenter study. Clin Ther 2001 Jan;23(1):108-23.
12. Pramod B. Akat, Tushar R. Bapat, Mangala B. Murthy, Vitthal B. Karande, Shreyas R. Burute. Comparison of the efficacy and tolerability of telmisartan and enalapril in patients of mild to moderate essential hypertension. Indian J Pharmacol 2010 June; 42(3): 153–156.
13. Pollare T, Lithell H, Selinus I, Berne C. Sensitivity to insulin during treatment with atenolol and metoprolol: a randomised, double blind study of effects on carbohydrate and lipoprotein metabolism in hypertensive patients. British Medical Journal 1989 Apr 29;298(6681):1152-7.
14. Yuhei Shiga, Shin-ichiro Miura, Ryoko Mitsutake, Kenji Norimatsu, Itsuki Nagata, Tadaaki Arimura et al. Efficacy and safety of a single-pill fixed-dose combination of high-dose telmisartan/hydrochlorothiazide in patients with uncontrolled hypertension. Journal of Renin-Angiotensin-Aldosterone System 2012-13: 394-400.

Cite this article as: Agarwal A, Chhabra MK, Walia R, Gupta PD. Comparative evaluation of Metoprolol and Telmisartan in hypertensive patients. Int J Med and Dent Sci 2014; 3(2):403-410.

Source of Support: Nil

Conflict of Interest: No