

Randomised Double Blind Comparative Study of Efficacy and Tolerability of Telmisartan versus Enalapril in Patients of Stage 1 Essential Hypertension

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Abstract: 1.Compare the efficacy and tolerability of telmisartan versus enalapril in patients of stage-1 essential hypertension, according to JNC 7 classification. 2.Compare safety with each drug in study group.

Materials and Methods: The present study protocol was approved by IEC. The randomized study of 12 weeks from January to March 2013 conducted on 60 newly diagnosed stage 1 hypertensive patients in between 20-65years of age. After taking written explained informed consent the patients are allocated into 2 groups. Group A (n = 30) were given Telmisartan 40mg Once Daily morning dose and Group B (n = 30) were given. Enalapril 10mg Once Daily morning dose. Complete blood picture, serum creatinine, blood urea, SGOT, SGPT urine analysis, ECG of all patients recorded at 0 and 12 weeks of study. Blood pressure was recorded at 0th, 4th, 8th, 12th weeks of study in sitting, standing and supine positions, mean of three taken for comparison.

Results: Fall in systolic blood pressure(SBP) and diastolic blood pressure(DBP) was observed in both groups after completion of study. But Mean systolic blood pressure after completion of the study in group A and group B are 126.66 ± 2.59 and 126.46 ± 2.60 respectively, with no significant difference ($p > 0.05$). Mean diastolic blood pressure after completion of the study in group A and group B are 79.2 ± 1.12 and 79.33 ± 0.95 respectively, with no significant difference ($p > 0.05$). Dry cough was seen in 30% of group B patients, which is significant.

Conclusion: In the 2 groups the 2 drugs are found to be equally effective in the reduction of SBP and DBP .In group B patients dry cough was significant side effect noticed.

I. Introduction

Hypertension is one of the most common worldwide diseases afflicting humans and in the general population. It is the most common cardiovascular disease. Its prevalence increases with advancing age. Elevated arterial pressure causes pathological changes in the vasculature and hypertrophy of the left ventricle.¹

Due to the associated morbidity and mortality and cost to society, preventing and treating hypertension is an important public health challenge. Fortunately, recent advances and trials in hypertension research are leading to an increased understanding of the pathophysiology of hypertension and the major risk factor for stroke, myocardial infarction, vascular disease, and chronic kidney disease.

Despite extensive research over the past several decades, the etiology of most cases of adult hypertension is still unknown, and control of blood pressure is suboptimal promise for novel pharmacologic and interventional treatments for this widespread disease.²

Hypertension is nothing but sustained elevation of blood pressure $\geq 140/90$ mm of Hg. Depending upon etiology of hypertension it is classified as primary or essential and secondary hypertension. Among these two primary or idiopathic contributes up to 95%, remaining is secondary hypertension.³

Trends in hypertension epidemiology in India:

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.

Hypertension is the most prevalent chronic disease in India with prevalence increasing rapidly both in urban and rural population. The prevalence of hypertension ranges from 20 – 40 % in urban adults and 12-17% among rural adults. The number of people with hypertension is projected to increase from 118 million in 2000 to 214 million in 2025.

In india, 23.10% men and 22.60% women over 25 years old suffer from hypertension. It is released in may 2012 by WHO global health statistic 2012. Recent(2012) studies show that for every known person with hypertension in india, there may possibly be 2 persons with undiagnosed hypertension or prehypertension. With over 139 million patients india accounts for, 15% of worlds uncontrolled hypertension patients⁴.

II. Patients And Methods

This was a double-blind, parallel group, randomized study carried out over a period of 12 weeks. The present study was carried out on patients with stage 1 hypertension (JNC7) attending the medicine department of GOVERNMENT GENERAL HOSPITAL, RANGARAYA MEDICAL COLLEGE, KAKINADA. The protocol regarding the present study was submitted to the Institutional Ethics Committee and the permission was taken before starting the study. The patients are newly diagnosed hypertensives of both sexes in between 20-65 years of age group. The study was conducted from January 2013 to March 2013. Written informed consent was taken before enrolment in English and in Telugu.

Patients with diabetes mellitus, secondary hypertensives, sensitivity to drugs, prior medication with anti hypertensives, clinically significant renal or hepatic impairment are excluded from the study. Patients with any cardiac or endocrinal complications, pregnant and lactating women are also excluded from the study.

III. Methodology

A total of 60 patients were enrolled in the study as per the selection criteria. They were randomly allocated to two groups with 30 patients each.

Group A – n=30 who received Telmisartan 40mg Once Daily morning dose.

Group B – n=30 who received Enalapril 10mg Once Daily morning dose.

Complete blood picture, serum creatinine, blood urea, SGOT, SGPT urine analysis, ECG of all patients recorded at 0 and 12 weeks of study. Blood pressure (Both Systolic and Diastolic) was recorded at 0th, 4th, 8th, 12th weeks of study in sitting, standing and supine positions, mean of three taken for comparison.

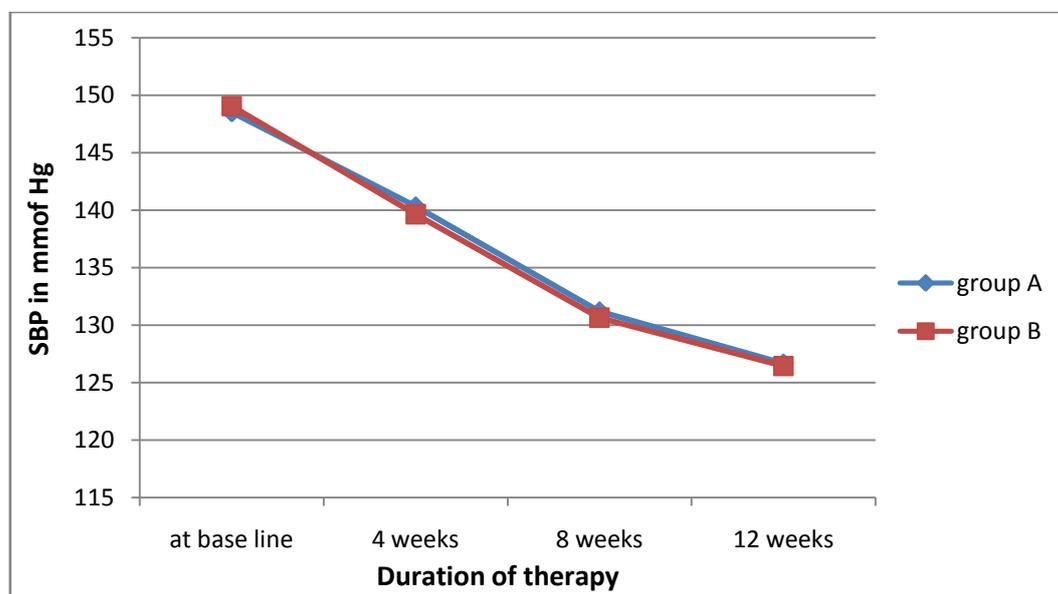
Equipment

Standard Mercury sphygmomanometer

IV. Results

Reduction In Systolic Blood Pressure (Supine)

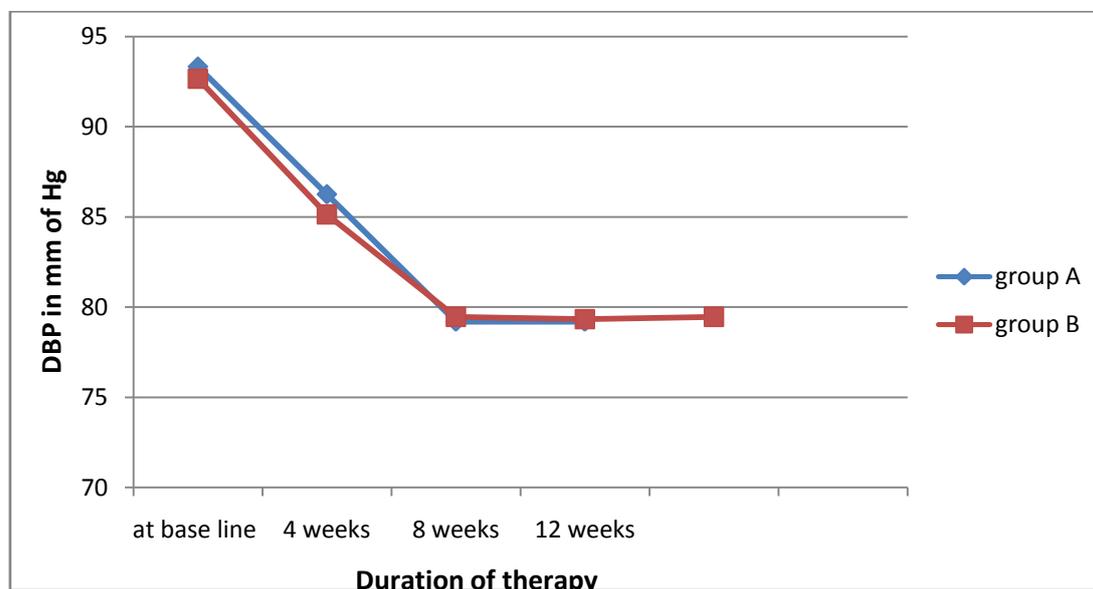
Duration of therapy	Group A (Mean±SD)	Group B (Mean±SD)	P value
At base line	148.53±5.75	149.06±6.09	-
4 weeks	140.33±4.07	139.66±3.15	-
8 weeks	131.20±2.99	130.66±1.91	-
12 weeks	126.66±2.59	126.46±2.60	>0.05



In the present study the mean systolic blood pressure after 4 weeks of the study in group A and group B are 140.33±4.07 mmHg and 139.66±3.15 respectively, with no significant difference (p>0.05). Mean systolic blood pressure after completion of the study in group A and group B are 126.66±2.59 and 126.46±2.60 respectively, with no significant difference (p>0.05).

Reduction In Diastolic Blood Pressure (Supine)

Duration of therapy	Group A (Mean±SD)	Group B (Mean±SD)	P value
At base line	93.33±2.69	92.66±2.84	-
4 weeks	86.26±1.55	85.13±2.76	-
8 weeks	79.2±1.78	79.46±1.16	-
12 weeks	79.2±1.12	79.33±0.95	>0.05



In the present study the mean systolic blood pressure after 4 weeks of the study in group A and group B are 86.26±1.55 and 85.13±2.76 respectively, with no significant difference (p>0.05). Mean systolic blood pressure after completion of the study in group A and group B are 79.2±1.12 and 79.33±0.95 respectively, with no significant difference (p>0.05)

Occurrence Of Side Effects (Safety Parameters)

SIDE EFFECT	GROUP A	GROUP B	SIGNIFICANCE
HEAD ACHE	4	3	N.S
DIZZINESS	2	1	N.S
FATIGUE	1	1	N.S
NAUSEA	3	2	N.S
DRY COUGH ⁶	0	9	S
HYPOTENSION ⁷	0	0	N.S

Table 6

- In the total study head ache is seen in 13% (4) patients in group A and 10% (3) patients in group B.
- Dizziness is seen in 7% (2) patients in group A and 3% (1) patient in group B.
- Fatigue is seen in 3% (1) patient in group A and 3% (1) patient in group B.
- Nausea is seen in 10% (3) patients in group A and 7% (2) patients in group B.
- Dry cough is seen in 30% (9) patients in group B only.
- Hypotension is not seen in either group.

V. Discussion

Hypertension is one of the leading causes of the global burden of disease. Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease. It often is associated with additional cardiovascular disease risk factors, and the risk of cardiovascular disease increases with the total burden of risk factors. Although antihypertensive therapy clearly reduces the risks of cardiovascular and renal disease, large segments of the hypertensive population are either untreated or inadequately treated.

The present study is a double blind randomized study comparing telmisartan (40mg) and Enalapril (10mg) in male patients with stage 1 essential hypertension. The principal aim was to study efficacy and tolerability of both the drugs and compare them.

In the present study, the number of patients in the age group 36-40 years and 41-45 years are the highest consisting of 20% and 30% patients in group A. And in the age group 56-60 years are 26% patients in group B. Remaining patients are randomly distributed with zero patients between age group 20 – 30 years.

The present study constituted of 40% male patients and 60% female patients with stage 1 essential hypertension. The mean reduction of systolic blood pressure with telmisartan is 21.87 ± 3.16 mmHg with no significant difference ($p > 0.05$) compared to enalapril group mean reduction in systolic blood pressure of 22.6 ± 3.49 mm Hg. This shows that there was no significant difference in the mean reduction of systolic blood pressure between the two groups.

The mean reduction in diastolic blood pressure after completion of the study in telmisartan group is 14.13 ± 1.57 mm Hg with no significant difference ($p > 0.05$) compared to enalapril group mean reduction in diastolic blood pressure of 13.33 ± 1.89 mm Hg. This shows that there was no significant difference in diastolic blood pressure reduction between the two groups.

In the study compared with Group A (telmisartan), Group B (enalapril) was associated with a higher incidence of cough 0% versus 30% found to be significant.

In a similar study to that of this study^[42] there are significantly greater proportion of patients who achieved low values of diastolic BP with telmisartan than with enalapril (59% versus 50%; $P < 0.05$). This variation in results may be due to large number of patients in the study and the procedure of measuring Blood pressure (Ambulatory Blood Pressure Monitoring)

In a randomized, double-blind, double-dummy, parallel group study.^[43] Telmisartan 40 mg produced a significantly greater reduction from baseline diastolic BP compared with enalapril 10 mg (11.7 versus 8.7 mmHg, respectively; $P = 0.02$). This may due difference in the race (Taiwanese).

In another comparative multicentre trial^[44] between telmisartan 80 mg and enalapril 20 mg, the mean reduction in systolic and diastolic BP were significantly higher with telmisartan as compared with enalapril (systolic BP, $P = 0.013$; diastolic BP, $P = 0.002$).this variation of reduction in blood pressure compared to our study is due to the higher doses of the study drugs.

The present study showed that both telmisartan and Enalapril are effective drugs in reducing both systolic and diastolic blood pressure throughout study period when measured at the 4th, 8th and 12th week. When efficacy of telmisartan is compared with enalapril it showed that there was no statistical difference in systolic blood pressure (SBP) and diastolic blood pressure (DBP) reduction between telmisartan and enalapril¹⁴.

In the present study when tolerability is compared between telmisartan and enalapril the overall frequency of adverse effects was similar, but in enalapril group ,the incidence of dry cough was higher as compared to that in telmisartan group (30% and 0% respectively, $p < 0.05$).

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