



## Effect of telmisartan on blood pressure and lipid profile in hypertensive patients with dyslipidemia

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### Abstract

Cardiovascular diseases are of major concern globally and lead to increased risk in mortality and morbidity. Hypertension is a common cardiovascular disease and coexists with conditions like dyslipidemia and ischemic heart disease. The aim of this study is to assess the effect of Telmisartan on blood pressure and to evaluate the lipid lowering property of Telmisartan. This was a prospective open labeled unicentric study. Thirty patients of both sexes above 30 yrs of age with newly diagnosed hypertension with dyslipidemia were selected and treated with Telmisartan 40 mgs daily orally for 12 weeks. Prior to and after the treatment blood pressure and lipid profile were evaluated. The results were tabulated & analyzed with paired "t" test. There was a significant decrease in systolic blood pressure and diastolic blood pressure after 12 weeks of treatment with Telmisartan. Similarly there was a significant decrease in TG, TC and a significant increase in HDL. In conclusion Telmisartan administration regulated blood pressure to within normal limits & there is a protection against cardio vascular risks by its action on lipid profile.

Key-Words: Telmisartan, Hypertension, Lipid profile, PPAR

### Introduction

Cardiovascular diseases are the leading cause of morbidity and mortality globally. The current burden of cardio vascular diseases in developing countries reflects what is termed as epidemiological transition. The important feature of this epidemiological transition is a shift from cardiovascular conditions predominantly related to blood pressure such as hemorrhagic stroke, towards atherothrombotic vascular diseases where other risk factors including blood lipids and tobacco use play a greater role (Chow, 2010).

Hypertension is the most common cardiovascular disease. The prevalence of hypertension is about 50% between the ages 60-69 years and it is further increased beyond 70 yrs (Brian, 2011). It remains the readily identifiable risk factor for myocardial infarction, stroke, heart failure, atrial fibrillation, aortic dissection and peripheral vascular disease (Ronald and Norman, 2008). Hypertension is also frequently associated with metabolic abnormalities such as insulin resistance and lipid profile derangement. Serum lipids and lipoprotein levels have been proven to be among the most potent risk factors for atherosclerosis and ischemic heart disease.

Telmisartan, an angiotensin receptor blocker (ARB) that is highly selective for AT1 receptor has been found to be a PPAR $\alpha$  agonist and a selective PPAR $\gamma$  modulator (Luis and Julian, 2008). This unique action of Telmisartan on PPAR leads to favorable effects on lipid and carbohydrate metabolism which is independent of its BP lowering effect. This provides additional benefit in the treatment of dyslipidemia. Hence in this present study an attempt has been made to evaluate the effect of the anti hypertensive drug Telmisartan on lipid profile in addition to its blood pressure lowering potential.

### Material and Methods

This was a prospective open labeled unicentric study conducted in the outpatient Department of Medicine in collaboration with the Department of Biochemistry and Institute of Pharmacology, Madurai Medical College, Madurai. Thirty newly diagnosed hypertensive patients with dyslipidemia of both sex above 30 years were selected and treated with Telmisartan 40 mg once daily orally for 12 weeks. Prior to and after the treatment with Telmisartan blood pressure and lipid profile were evaluated. The results were tabulated & analyzed applying paired "t" test.

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**Duration:** 12 weeks

**Selection of cases:** 30 patients who fulfilled the inclusion criteria. After obtaining ethical approval from the Institutional Ethical Committee and obtaining the informed consent from the patients in vernacular language the study was conducted.

**Inclusion criteria:**

Newly detected JNC-7 Stage 1 hypertension (Aram et al, 2004).

Dyslipidemia: Total cholesterol (TC): 200-240mg% ( or ) High density lipoprotein (HDL) < 40mg% in male.< 50 mg% in female (or)

Low density lipoprotein (LDL) 100-160 mg% (or) Triglyceride 150-200 mg%

Male & Female above 30 years

Women of child bearing age group were advised to follow adequate method of contraception to minimize the risk of pregnancy.

**Exclusion criteria:**

1. Hypersensitivity to Telmisartan.
2. Pregnant and breast feeding women.
3. Patients with the following diseases:
  - A. Renal artery stenosis.
  - B. Severe congestive cardiac failure.
  - C. Aortic valve stenosis.
  - D. Secondary hypertension.
  - E. Malignant hypertension.
  - F. Unstable angina.
  - G. Post myocardial infarction.
4. Liver & renal impairment.
5. Any psychiatric illness.
6. Patients taking the drugs like Digoxin, Lithium & Potassium sparing diuretics.

After the patient selection they were administered with Tab. Telmisartan 40 mg daily for 12 weeks. Blood pressure and lipid profile were evaluated before and after drug treatment. The results were tabulated & analyzed using paired "t" test.

**Results and Discussion**

In this study, there were 16 male and 14 female patients aged between 30 to 80 years. Data were collected before and 12weeks after treatment with Telmisartan & is shown as Mean  $\pm$ SD (see Table 1). Data analysis was performed using SPSS statistical software package (version 13.0 SPSS Inc., Chicago, USA). Statistical analysis was performed using the students paired t test. A P- value of <0.05 was considered as significant.

The present study comprised of patients who were in stage 1 hypertension and with dyslipidemia. At the end of treatment with Telmisartan 40 mg for 12 weeks, there was a significant control of trough systolic blood

pressure and diastolic blood pressure. This may be attributed to the long terminal half life of Telmisartan (Amy and Cheryle, 2003). The advantages of the longer action of Telmisartan may extend to the prevention of cardio vascular events which follow a similar circadian pattern, with an increase in their incidence being associated with early morning blood pressure surge (White, 2003).

In patients achieving a blood pressure of 144/82mmHg, risks of heart failure, stroke were significantly decreased (Giuseppe, 2004). In the present study after treatment with Telmisartan, the mean $\pm$ SD of systolic/diastolic BP was (118.6 $\pm$ 11.24 /73.87 $\pm$ 5.89) (see Fig. 1 & 2).

The plasma lipid profile of hypertensive patients is especially important, given the high incidence of atherosclerosis. In the present study after treatment with Telmisartan there was a significant decrease in plasma total cholesterol (p<0.01) and triglyceride level (p<0.001) (see Fig.3, 4). There was also a significant increase in HDL level (p<0.001) (see Fig 5). The decrease in LDL was not significant (see Fig.6). Studies show that among Angiotensin Receptor Blockers, Telmisartan favorably affects lipid profile. This may possibly be explained by the high lipophilicity of Telmisartan compared to other ARBs and its PPAR modulating effect. Structural differences among the ARBs may also contribute to the possible differences in metabolic profile.

PPARs are ligand activated transcription factors belonging to the superfamily of nuclear receptors. PPAR $\gamma$  is abundantly expressed in adipose tissue and is a major regulator of insulin and glucose metabolism. In contrast, PPAR $\alpha$  is highly expressed in tissues displaying a high metabolic rate of fatty acids, such as the liver and skeletal muscle. PPAR $\alpha$  modulates intracellular lipid metabolism by transcriptional regulation of genes involved in fatty acid uptake, mitochondrial fatty acid oxidation and triglycerides catabolism. PPAR $\alpha$  is the molecular target of fibrates such as Gemfibrozil, etc.

Telmisartan acts as a partial PPAR $\alpha$  agonist and induces PPAR $\alpha$  expression. Thus there is induction of hepatic ACSL1 (acyl coA synthetase long chain) and CPT1A (carnitine palmitoyl transferase). This causes significant decrease of triglyceride level. PPAR $\alpha$  in skeletal muscle is not affected by Telmisartan. Hence the myopathy associated with fibrates is not seen with Telmisartan. Thus PPAR $\alpha$  activation by Telmisartan is liver specific because of its specific pharmacokinetic profile (Markus et al., 2008).

Telmisartan has also been approved for the primary prevention of stroke and prevention of MI. It decreases



the cerebral infarct area in dose dependent manner without affecting cerebral blood flow. Thus it could be a potential target for the treatment of post – ischemic injury by partially inhibiting the inflammatory reaction after cerebral ischemia via a PPAR – gamma dependent mechanism.

It is widely believed that the currently available ARBs are metabolically neutral and have little or no impact on carbohydrate and lipid metabolism when administered in conventional doses used to treat hypertension. However, the current findings suggest that Telmisartan might be an exception in this regard and provide insight into new strategies for developing molecules that could improve many if not all of the biochemical and blood pressure disturbances that compose the metabolic syndrome (Kurtz, 2004).

The multimodal mechanism of action of Telmisartan, including AT1 receptor blockade, PPAR $\gamma$  modulation and hepatic PPAR $\alpha$  activation, characterizes this compound as a therapeutic option for the treatment of patients suffering from multiple cardio metabolic disorders such as hypertension, glucose intolerance, and dyslipidemia.

Thus the study suggests that Telmisartan after administration for 3 months conferred significant advantages in terms of BP control and plasma lipid levels in patients with hypertension.

#### Strength of the study

- a. Rigid inclusion criteria,
- b. Close monitoring and supervision by specialists, and
- c. Regular follow up of the patients.

#### Limitations

- a. Post study follows up not done
- b. Small sample size
- c. Not all stages of hypertensive patients were included
- d. Short study duration

#### Conclusion

The antihypertensive treatment with Telmisartan may result in an amelioration of cardiovascular risk factors, not only through arterial pressure regulation but also through the reduction of lipid markers.

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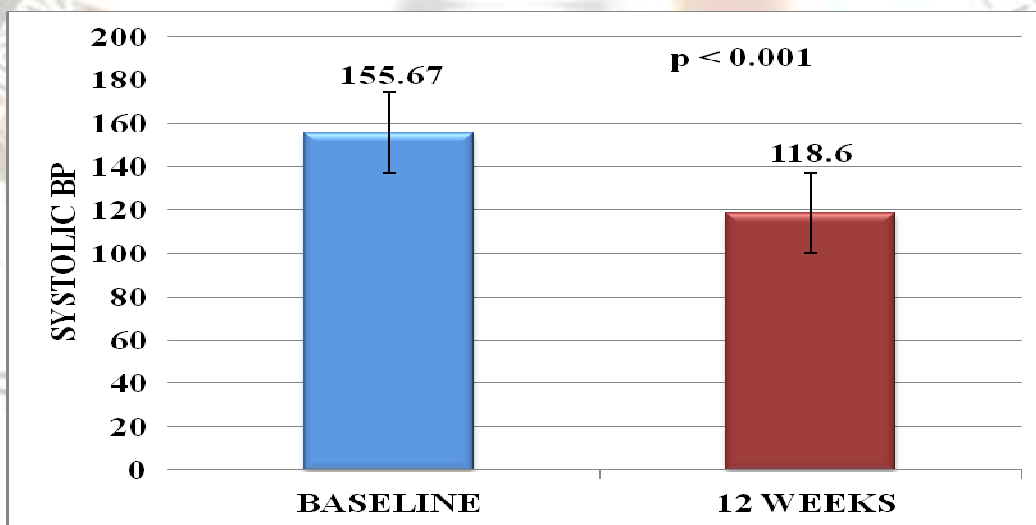
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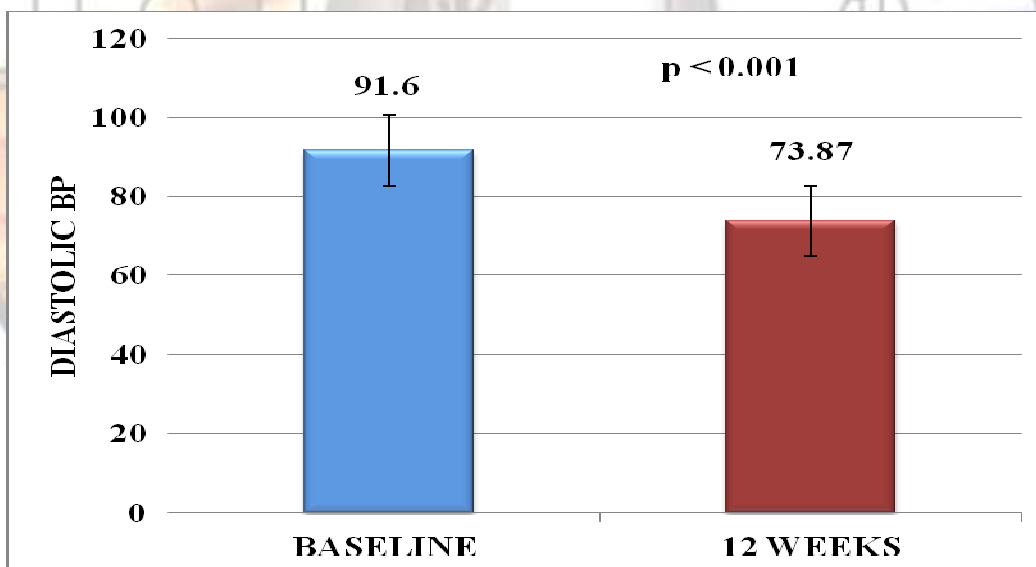
**Table 1: Blood pressure and lipid profile**

Parameter	Before drug Mean ± SD	After drug Mean ± SD	P Value
SYSTOLIC BP	155.67 ± 4.46	118.6 ± 11.24	< 0.001*
DIASTOLIC BP	91.6 ± 11.43	73.87 ± 5.89	< 0.001*
TOTAL CHOLESTEROL	195.1 ± 26.08	179.57 ± 27.44	< 0.01*
TRIGLYCERIDES	189.71 ± 71.03	151.45 ± 73	< 0.001*
HDL	44.44 ± 8.53	48.43 ± 8.55	< 0.001*
LDL	109.14 ± 21.99	103.4 ± 23.89	> 0.05

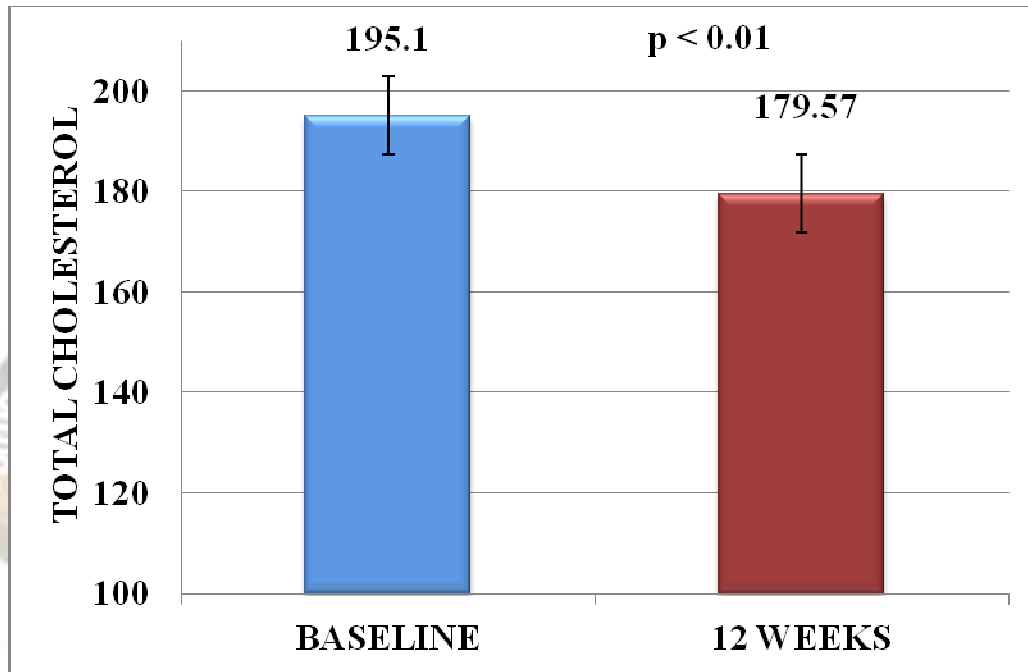
\*P< 0.05 is Significant



**Fig. 1: Systolic BP**



**Fig. 2: Diastolic BP**



. 3: Total cholesterol

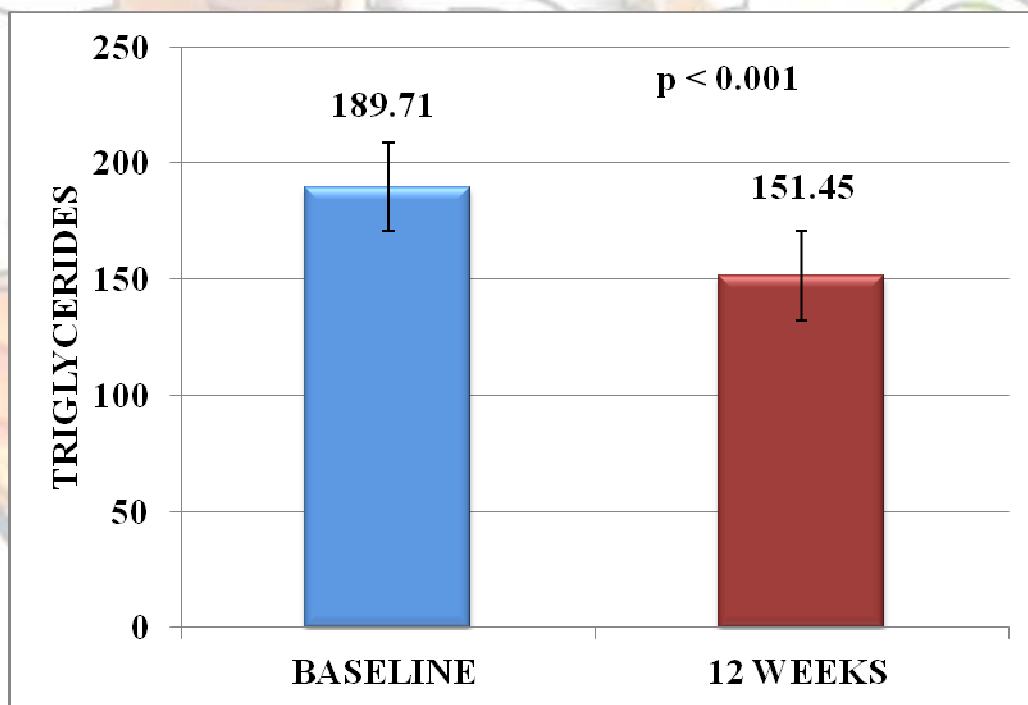


Fig. 4: Triglycerides

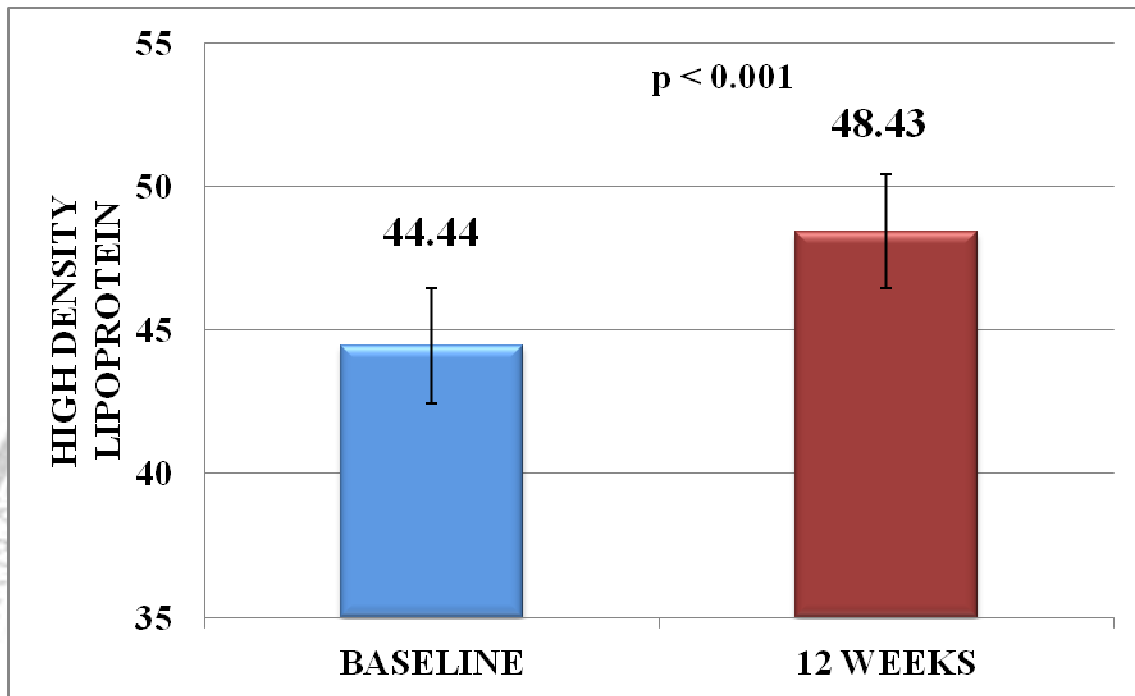


Fig. 5: High Density Lipoprotein

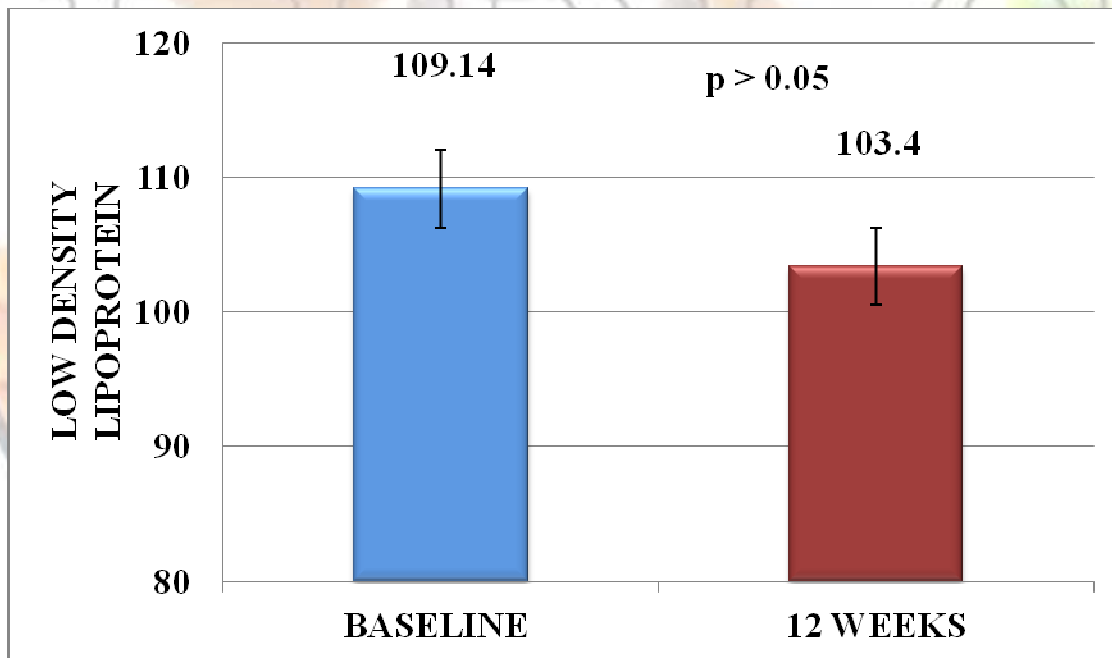


Fig. 6: Low Density Lipoprotein