Monitoring effects of atenolol versus olmesartan medoxomil on metabolic parameters

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ABSTRACT

Background: The increase in CVS morbidity and mortality could be significantly reduced by control of SBP and DBP, as well as reduction in Hyperlipidemia.

Methods: The patients of stage-I HTN with either sex according to JNC VII criteria were included and were followed up every 2 weeks from baseline upto 12 weeks. The randomized patients were divided into two groups to receive beta blocker viz. Atenolol 50 mg (group A, N=50) and ARB Olmesartan medoxomil 40 mg (group B, N=50).

Results: The average Total cholesterol measured among Group A subjects was significantly increased by 1.8% by the end of 12th week whereas the average cholesterol measured among Group B subjects at baseline period was reduced by 7.9% after 12 weeks therapy. The average HDL measured among Group A subjects at baseline period significantly reduces by 5.9% by the end of 12th week whereas the HDL levels measured among Group B subjects at baseline period was significantly increased by after 12 weeks therapy. The average Triglyceride (TG) levels measured among Group A subjects at baseline period was significantly increased by 12.4% by the end of 12th week whereas the Triglyceride (TG) levels measured among Group B subjects at baseline period was significantly reduced by 9.5% after 12 weeks therapy. The average LDL levels measured among Group A subjects at baseline period was significantly increased by 1.5% by the end of 12th week whereas the average LDL measured among Group B subjects at baseline period was significantly reduced by 11.2% to after 12 weeks therapy. The average VLDL levels measured among Group A subjects at baseline period was significantly increased by 12.4% by the end of 12th week whereas the average VLDL measured among Group B subjects at baseline period was significantly reduced by 9.5% after 12 weeks therapy.

Conclusions: ARB- Olmesartan medoxomil is a better drug than beta blocker- Atenolol as it leads to greater deduction in lipid profile.

Keywords: Atenolol, CVD, COPD, DBP, HCTZ, HTN, Stage-1 HTN

INTRODUCTION

Throughout the world, including India, the cardiovascular disorders are the most common cause of mortality and morbidity of patients. Among the various cardiovascular disorders, Hyperlipidemia contributes to one of the most common risk factor for cardiovascular disorders, the treatment of which leads to significant reduction in cardiovascular mortality and morbidity. According to JNC VII, term HTN is defined as SBP of 140/90mmhg or more on two occasions measured apart weekly. The prevalence of HTN increases with advancing age, about 50% of people between ages of 60 and 69 years have HTN, and prevalence is increased beyond age of 70 years. It affects approximately one-third of world’s adult population and is predicted to increase with 60% towards...
2025. It is also associated with number of serious conditions and for 13.5% of premature deaths, 54% all strokes and 47% of ischemic heart diseases.

According to Joint National Committee (JNC) 7 report HTN can be classified as:

1. Primary (essential) hypertension - with no obvious underlying medical cause, it results from complex interactions between multiple genetic and environmental factors, accounts for 90-95% of cases.
2. Secondary HTN with identifiable cause revealed by history, physical examination and routine laboratory tests that might be affecting kidneys, arteries, heart or endocrine system.
3. JNC VII.

**Table 1: Various study group with their diagnostic blood pressure.**

| Category       | Systolic mmHg | Diastolic mmHg |
|----------------|---------------|----------------|
| Normal         | ≤120          | And ≤80        |
| Pre-hypertensive| 120-139       | Or 80-89       |
| High BP        |               |                |
| Stage 1        | 140-159       | Or 90-99       |
| Stage 2        | ≥160          | Or ≥100        |

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. However, JNC VIII has been released as new classification for treatment of HTN.

**METHODS**

The present study was conducted to determine the efficacy and safety of drug with respect to more reduction in metabolic parameters. A randomized, prospective, open parallel group study for 12 weeks duration was conducted by Department of Pharmacology in collaboration with Department of general Medicine at outpatient department of Medicine, M.M.I.M.S.R., Mullana. The protocol for study was approved before commencement by Institutional Ethics Committee.

**Inclusion criteria**

- The Patients of either sex with Stage-1 HTN
- Aged between 18-60 years

And they were followed up every 2 weeks from the baseline upto 12 weeks. The Patients were divided randomly into two groups to receive Tab Atenolol 50mg OD orally (Group A, N=50) and Tab Olmesartan medoxomil 20mg OD orally (Group B, N=50). The Patients with stage I HTN as per inclusion and exclusion criteria & documented informed consent were included.

**Exclusion criteria**

- The Patients of secondary HTN
- On other antihypertensive therapy
- Pregnant/lactating.

The Clinical examination of all patients was done by measurement of BP before administration of drug therapy. The response to study treatments was evaluated in terms of effects on metabolic parameters and BP.

**Statistical analysis**

The results were analysed using Student ‘t’ test (paired and unpaired Students ‘t’ test) using computer software - SPSS version 16.0. P-value <0.05 was considered as significant.

**RESULTS**

In demographic baseline parameters no significant changes, viz sex and age in both the groups.

**Table 2: Comparison of total cholesterol levels of subjects in group A and group B.**

|          | Atenolol 50mg (group A) | Olmesartan 20mg (group B) | T- Test (p-value in b/w groups) |
|----------|--------------------------|---------------------------|--------------------------------|
| Mean±SD  | Baseline: 213.7±20.7      | 211.4±20.8                | >0.05                          |
|          | Week 12: 217.5±18.5       | 194.6±12.6                | <0.05                          |
| % Change | 1.8                       | -7.9                      |                                 |

**Table 3: Comparison of High Density Lipoprotein level of subjects group A and group B.**

|          | Atenolol 50mg (group A) | Olmesartan 20mg (group B) | T- Test (p-value in b/w groups) |
|----------|--------------------------|---------------------------|--------------------------------|
| Mean±SD  | Baseline: 39.9±7.8       | 39.6±7.9                  | >0.05                          |
|          | Week 12: 37.6±6.7        | 41.5±7.2                  | <0.05                          |
| % Change | -5.9                     | 4.7                       |                                 |
As shown in Table 2, The average total cholesterol measured among Group A subjects at baseline period was 213.7±20.7mg/dl which significantly increased by 1.8% by the end of 12th week to 217.5±18.5mg/dl whereas the average cholesterol measured among Group B subjects at baseline period was 211.4±20.8mg/dl which significantly reduces by 7.9% to 194.6±12.6mg/dl after 12 weeks therapy.

As shown in Table 3, The average HDL measured among Group A subjects at baseline period was 39.9±7.8mg/dl which significantly reduces by 5.9% by the end of 12th week to 37.6±6.7mg/dl whereas the HDL levels measured among Group B subjects at baseline period was 32.7±2.8mg/dl which significantly increased by 4.7% to 32.8±3.0mg/dl after 12 weeks therapy.

As shown in Table 4, The average TG levels measured among Group A subjects at baseline period was 164.3±15.01mg/dl which significantly increased by 12.4% by the end of 12th week to 184.6±12.9mg/dl whereas the average TG levels measured among Group B subjects at baseline period was 163.7±14.4mg/dl which significantly reduces by 9.5% to 148.0±8.1mg/dl after 12 weeks therapy.

As shown in Table 5, The average LDL levels measured among Group A subjects at baseline period was 140.9±25.4mg/dl which significantly increased by 1.5% by the end of 12thweek to 142.9±23.0mg/dl whereas the average LDL measured among Group B subjects at baseline period was 139.0±21.8mg/dl which significantly reduces by 11.2% to 123.4±15.1mg/dl after 12 weeks therapy.

As shown in Table 6, The average VLDL levels measured among Group A subjects at baseline period was 32.8±3.0mg/dl which significantly increased by 12.4% by the end of 12th week to 36.9±2.5mg/dl whereas the average VLDL measured among Group B subjects at baseline period was 32.7±2.8mg/dl which significantly reduces by 9.5% to 29.5±1.6mg/dl after 12 weeks therapy.

**DISCUSSION**

The average cholesterol measured among Group A significantly increased by 1.8% at 12th week. The average cholesterol in Group B significantly reduced by 7.9% by the 12th week. Thus, present study demonstrates that there is increase of cholesterol after Atenolol therapy while there is decrease of cholesterol after Olmesartan therapy. But in

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another study conducted by Pollare T et al, in patients with primary HTN where they studied the effects of beta blockers viz Atenolol and Metoprolol on lipid metabolism; concluded that beta-selective blockade has no significant (p >0.001) influence on total serum cholesterol levels. While our study demonstrates that Atenolol is significantly increasing cholesterol levels.9 Also Yilmaz MI et al conducted a study to evaluate the effect of antihypertensive agents on plasma adiponectin levels in hypertensive patients with metabolic syndrome as plasma adiponectin levels are well associate with metabolic syndrome. In this study patients were treated for 3 months with Atenolol 10mg/day and Valsartan 80mg/day.10 They showed that Valsartan increase the plasma adiponectin levels significantly higher than other regimens (P <0.05 for both) while Atenolol did not make a significant effect.10 The plasma adiponectin levels were correlated with the total cholesterol (r= -374, P=0.002), high density lipoprotein-cholesterol (r=0.286, P=0.005). But alteration in metabolic parameters with Valsartan, an ARB demonstrates that ARBs viz Olmesartan might have correlation with augmentation of metabolic parameters like serum cholesterol.

The average HDL measured among Group A significantly reduces by 5.9% by the 12th week assessment, this corresponds with the similar comparable results obtained by Pollare T et al, in which they studied the effects of Atenolol and Metoprolol on lipid metabolism on 60 patients with primary HTN and concluded that HDL decreased by about 7%, after administration of Atenolol on 60 patients with primary HTN. The average HDL measured among group B significantly incremented by 4.7% by the 12th week assessment. When authors compared our results with Pollare T et al, study we concluded that although Atenolol has decreased HDL by 5.9%, while Olmesartan has increased HDL by 4.7%, but the decrease of HDL was more observed in Pollare et al study i.e. 7% after administration of Atenolol.9

The average TG levels measured among group A at baseline period significantly increased by 12.4% after the 12th week assessment, the results of our study are similar to results obtained by Leren P in which they reviewed the effects of Atenolol, Metoprolol, Propranolol on lipid metabolism and studied their lipid profile and concluded that Atenolol therapy significantly (p<0.001) increases serum TG levels by 25.8%.11 In group B patients, TG levels significantly reduce by 9.5% after 12 weeks therapy. When authors compared present results with Leren P study, authors concluded that although TG levels were increased by 12.4% with Atenolol, while TG levels were decreased by 9.5% with Olmesartan therapy, but there is greater increase in TG levels by 25.8% after Atenolol in Leren P study.11 Also the results of present study coincides with Galzerano D et al, in which various studies were reviewed to evaluate the antihypertensive efficacy and metabolic effects of Telmisartan, an ARB a congener of this widely prescribed drug category.12 In a study of 533 patients (with HCTZ added as needed to achieve BP control, the effects of Telmisartan on lipid parameters have also been observed in people with and without diabetes and were treated with Telmisartan 40 to 80mg for at least 1 year which led to reduction in triglycerides by 17.4mg/dL and cholesterol by 16.4mg/dL in the population as a whole and were 22.7mg/dL and 23.8mg/dL, respectively, in patients with hypercholesterolemia. Thus, they concluded that Telmisartan is more efficacious, better tolerated than beta-blockers and have beneficial effects on metabolic parameters and these results are comparable with present results in lieu of greater reduction of TG by ARBs.12

In group A patients, LDL significantly increased by after 12 weeks treatment. In Group B patients, LDL significantly reduces by 11.2% after 12 weeks of therapy. The results of our study coincide with the study conducted by Fonseca VA which reviewed the pathophysiology of HTN and dyslipidemia as well as treatment effects from glucose- and lipid-lowering regimens on CVS. Based on a Pub Med literature search from January 1980 to December 2008, the effects of nonvasodilating (Atenolol) on parameters of glucose and lipid metabolism in HTN are studied which showed nonvasodilating beta-blockers are associated with a worsening of glycemic and lipid control.13

**CONCLUSION**

The present study concluded that Olmesartan medoxomil is a better drug for treating stage-1 HTN patients as compared to Atenolol, in general and especially in patients with dyslipidemia in view of greater reduction of total average cholesterol, TGs, LDL, VLDL and increase in HDL.

However, more such multicentric open/blind, studies on larger population with such disorders are required, so that this improved effectiveness in stage 1 HTN could be translated to maintain the target BP.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

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