

# CONTROL OF HYPERTENSION; EFFICACY AND SAFETY OF LOSARTAN AND ATENOLOL ALONE AND IN COMBINATION

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### Article Citation:

Bhurghri GR, Korejo HB, Qureshi MA, Kumar R, Aamir N. Control of hypertension; Efficacy and safety of losartan and atenolol alone and in combination. Professional Med J Dec 2010;17(3):425-430.

**ABSTRACT... Objective:** To compare the efficacy and tolerability of Losartan and Atenolol in alone and combination in treatment of hypertension. **Study Design:** Comparative study. **Setting:** Medical out patients department of Jinnah Postgraduate Medical Centre Karachi from January 2007 to June 2007. **Methods:** There were 60 patients previously untreated with mild and moderate essential hypertension were registered for study. The selected patients were divided into three groups. Group A was given atenolol, Group B was given Losartan, and Group C was given both drugs. The target blood pressure was 120-140/80-90 mmHg. There were 42 males and 18 females with age range 25-65 years. **Results:** The mean baseline score of groups A, B and C were showed systolic blood pressure  $182 \pm 19$ ,  $174 \pm 20$  and  $168 \pm 12$  respectively. The diastolic blood pressure was  $104.5 \pm 11$ ,  $102.5 \pm 9$  and  $104.5 \pm 10$  respectively. The difference in mean systolic and diastolic blood pressure was not significant statistically as  $P = 0.06$  and  $0.76$  respectively. After 4 months of treatment with atenolol, systolic blood pressure decreased to  $147 \pm 17$ , and diastolic blood pressure fell to  $87 \pm 4$ . Losartan decreased systolic blood pressure  $138 \pm 13$  and diastolic blood pressure  $87 \pm 4$  in 4 months of treatment. The combined therapy decreased systolic blood pressure  $115 \pm 4.6$  and diastolic blood pressure  $75 \pm 4.7$ . The effect of treatments on systolic and diastolic blood pressure was significantly different as ( $p < 0.001$ ) and ( $p = 0.036$ ) respectively. Side effects observed in 2 (10%) patients from group C, 8 (40%) in group A and 4 (20%) in group B. Combination therapy proved more effective in controlling hypertension than mono therapy and also fewer side effects. Patients showed better control on combination therapy as compared to mono therapy. Losartan proved a little better in controlling hypertension than atenolol and was more expensive. **Conclusion:** Patients showed better results with combination therapy for hypertension compared to individual drug.

**Key words:** Hypertension, Angiotensin Converting Enzyme Inhibitor, Calcium Channel Blockers, Angiotensin Receptor Blockers

## INTRODUCTION

Hypertension is defined as sustained high blood pressure more than 140/90 mmHg. Hypertension is dangerous because it can lead to strokes, heart attacks, heart failure, or kidney disease.

The goal of hypertension treatment is to lower blood pressure and protect important organs, like brain, heart, and kidneys from damage. It is one of the most important preventable causes of premature death worldwide<sup>1</sup>.

Hypertension is estimated to cause 4.5% of current global disease burden and is as prevalent in many developing countries, as in the developed world. Blood pressure-induced cardiovascular risk rises continuously

Article received on: 06/03/2010  
Accepted for Publication: 08/05/2010  
Received after proof reading: 02/08/2010

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across the whole blood pressure range<sup>2</sup>.

It is 'the silent killer' as often asymptomatic and one of the most common cardiovascular diseases in America. There are approximately 73 million people suffer from high blood pressure in the United States<sup>3</sup>. Out of them 14.8% population is untreated and 26.2% is inadequately treated, in another 31.4% the condition remains undiagnosed. Pathophysiology of high blood pressure is unknown in 95% of the cases and this is called essential blood pressure where exact cause cannot be pinpointed. The hereditary factor may be one reason for essential hypertension. Diet and lifestyle also play a role in the pathophysiology. Overweight, irregular sleep, excessive salt intake is contributing factors.

The development of arteriosclerosis and atherosclerosis are also affected by hypertension. Hypertension reduces the elasticity of arteries causing other secondary conditions which lead to decrease blood flow and ischemic diseases<sup>3</sup>.

The complications of hypertension principally involve the central nervous system, retina, heart and kidneys<sup>4</sup>.

Hypertensive patients should be encouraged to make life style modifications, such as eating a healthier diet, quitting smoking and getting more exercise<sup>1</sup>. when used properly, drug therapy can control the progression of end-organ damage<sup>2</sup>.

Atenolol was commonly used cardiovascular drug introduced in 1976 as replacement of propranolol in the treatment of hypertension. The drug works by slowing down the heart rate and reducing workload. It is cardio selective beta-blocker and has no partial agonist or membrane stabilizing activity. Its oral bioavailability being of 50-60% and half life of atenolol is about 6 hours allowing once daily dosing<sup>5</sup>.

Losartan is the prototype angiotension receptor blocking (ARB) drug. Their pharmacological effects are similar to those ACE inhibitors in that they produce vasodilatation and block aldosterone secretion thus lowering blood

pressure<sup>6</sup>.

## MATERIAL AND METHODS

This study was conducted in the medical out patients department (OPD) of Jinnah post graduate medical centre Karachi from January 2007 to June 2007.

### Type of study

Comparative study.

### Methodology

There were 60 patients previously untreated with mild and moderate essential hypertension, were registered for study.

The selected patients were divided into three groups.

**Group A:** Atenolol prescribed in 20 registered patients.

**Group B:** Losartan prescribed 20 registered patients.

**Group C:** Atenolol and Losartan prescribed in 20 registered patients.

In this study, the doses of two selected anti-hypertensive drugs were increased to 100mg of both drugs, when blood pressure not controlled. The therapeutically, our target was 120-140/80-90mmHg reached at 4 months for all patients. There were 42 males and 18 females and age range between 25-65 years.

## STATISTICAL ANALYSIS

All variables have been expressed in mean  $\pm$  standard deviation. The observation of the parameters was recorded in a tabulated form and repeated measure analysis of variance was to observe treatments and days effect.

## RESULTS

Total patients included in study were sixty and divided into three groups A, B and C. The baseline score of Atenolol group was systolic blood pressure  $182 \pm 19$ , and diastolic blood pressure was  $104.5 \pm 11$ . The reduction of blood pressure were in month of treatment with atenolol in 20 patients systolic  $176 \pm 18$ , and diastolic  $99 \pm 8$ , in two

months the systolic blood pressure  $168\pm 18$  and diastolic  $95\pm 6$ , in 3 months of treatment systolic blood pressure  $158\pm 18$ , and diastolic  $91\pm 5$ , and in 4 months of treatment systolic blood pressure  $174\pm 20$ , diastolic blood pressure  $103\pm 9$ . The reduction of blood pressure were in one month of treatment with Losartan in 20 patients systolic  $166\pm 19$ , and diastolic  $97\pm 9$ , in two months the systolic blood pressure  $157\pm 18$  and diastolic  $94\pm 7$ , in 3 months of treatment systolic blood pressure  $150\pm 15$ , and diastolic  $90\pm 6$ , and in 4 months of treatment systolic blood pressure  $138\pm 13$ , diastolic blood pressure  $87\pm 4$ . The baseline score of Atenolol and Losartan group was systolic blood pressure  $168\pm 11.9$ , and diastolic blood pressure was  $104.5\pm 10$ . The reduction of blood pressure were in one month of treatment with Losartan and Atenolol in 20 patients systolic blood pressure was  $154\pm 10$ , and diastolic blood pressure was  $97\pm 6$ , in 3 months of treatment systolic blood pressure  $128\pm 4$ , and diastolic  $85\pm 5$ , and in 4 months of treatment systolic blood pressure  $115\pm 4.6$ , diastolic blood pressure  $75\pm 4.7$  table no. I.

The treatment effect is significantly different on systolic blood pressure ( $p < 0.001$ ) and diastolic blood pressure (0.036).

Days significantly decreased the systolic and diastolic blood pressure Fig-1 and 2.

Side effects observed in 2 (10%) patients from group C, 8(40%) in group A and 4 (20%) in group B. This showed

that combination therapy of both Atenolol and Losartan is more effective and having fewer side effects as compared to single drug therapy. More so combination therapy took less duration to control hypertension in majority of patients in table-II.

Table-II. Adverse effects of drugs side effects were observed and reported by patients			
Adverse effects	Atenolol	Losartan	Combination of both drugs
Fatigue	3(15%)	-	-
Orthostatic Hypotension	-	3(15%)	1(5%)
Leg pain	3(15%)	-	-
Weight Loss	-	1(5%)	1(5%)
Impotency	1(5%)	-	-
Cold extremities	1(5%)	-	-
Total Reactions	8(40%)	4(20%)	2(10%)

## DISCUSSION

Total patients included in this study were sixty and divided into three groups. The baseline score of all groups were showed systolic blood pressure  $168\pm 11.9$ , and diastolic blood pressure was  $99.7\pm 11$ . After 4 months of treatment with atenolol systolic blood pressure  $147\pm 17$ , diastolic blood pressure  $87\pm 4$  were decreased. Losartan decreased systolic blood pressure  $138\pm 13$ , diastolic blood pressure  $87\pm 4$  in 4 months of treatment. These results were significant statistically. There were different

Table-I. Changes in mean systolic and diastolic B.P from day-0 to 120 days of treatment with atenolol, Losartan and combined therapy with both drugs in patients with essential hypertension.

Reduction Score	Age	Sex M/F	Atenolol		Losartan		Atenolol+Losartan	
			Sys	Dys	Sys	Dys	Sys	Dys
Day-0	41.5 $\pm$ 6.7	14/6	182 $\pm$ 19	104.5 $\pm$ 11	174 $\pm$ 20	103 $\pm$ 9	168 $\pm$ 11.9	104.5 $\pm$ 10
Day-30			176 $\pm$ 18	99 $\pm$ 8	166 $\pm$ 19	97 $\pm$ 9	154 $\pm$ 10	97 $\pm$ 8
Day-60			168 $\pm$ 18	95 $\pm$ 6	157 $\pm$ 18	94 $\pm$ 7	139 $\pm$ 7	90 $\pm$ 6
Day=90			158 $\pm$ 18	91 $\pm$ 5	150 $\pm$ 15	90 $\pm$ 6	128 $\pm$ 4	85 $\pm$ 5
Day-120			147 $\pm$ 17	87 $\pm$ 4	138 $\pm$ 13	87 $\pm$ 4	115 $\pm$ 4.6	75 $\pm$ 4.7

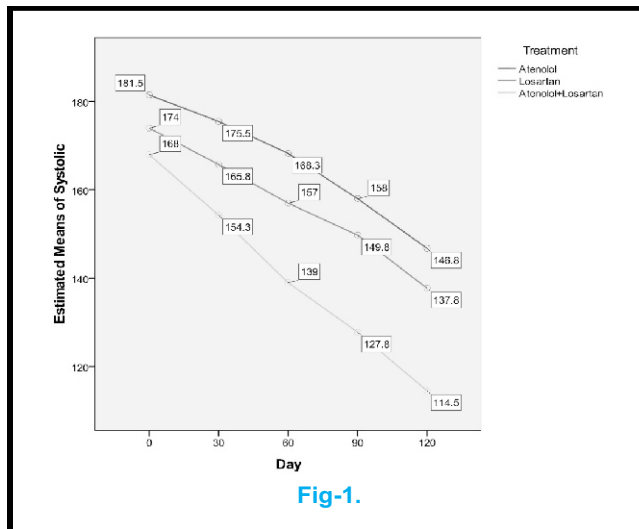


Fig-1.

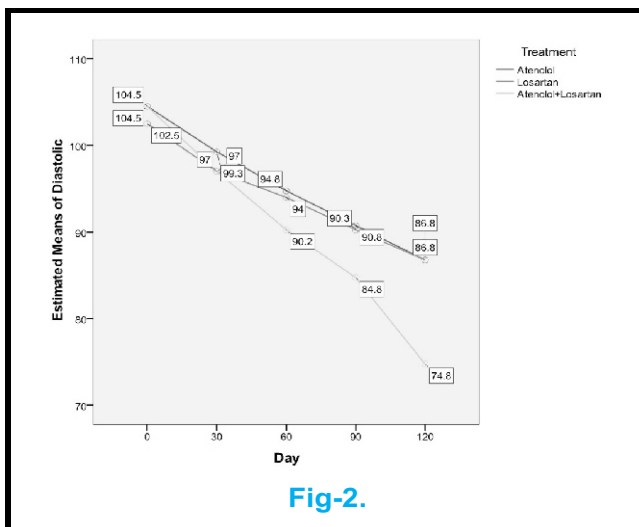


Fig-2.

in efficacy of Losartan and atenolol showed Losartan was more efficacious than atenolol. The combined therapy decreased systolic blood pressure  $115 \pm 4.6$ , diastolic blood pressure  $75 \pm 4.7$ . Side effects observed in 2 (10%) patients from group C, 8 (40%) in group A and 4 (20%) in group B. In our study combination therapy proved very effective in controlling hypertension than mono therapy and also fewer side effects.

Our study matched with the study of Norman 1999, in which Losartan based antihypertensive regimen reduced cardiovascular morbidity and mortality and cardiovascular deaths, stroke, and myocardial infarction. His data suggested Losartan based treatment is more

effective than atenolol-based treatment of patients in hypertension. In our study Losartan was much effective and less side effects that is only four reactions as compared to 8 reactions in atenolol<sup>7</sup>.

This study matched with the study of Keller 2005, in which author compared efficacy and tolerability of Losartan and atenolol in patients with mild to moderate essential hypertension<sup>8</sup>. This is consistent with our study as eight (40%) adverse reactions were noted in patients taking atenolol. Losartan was more efficacious than atenolol in reduction of blood pressure and was well tolerated. In our study group B results were better than group A.

This study matches with study of Lindholm (2002) in which the mean blood pressure fell to 146/79 mm Hg (17/11) in Losartan patients and 148/79 mm Hg (19/11) in atenolol patients. The primary endpoint occurred in 103 patients assigned Losartan (n=586) and 139 assigned atenolol (n=609); relative risk 0.76 (95% CI 0.58-0.98), p=0.031. 38 and 61 patients in the Losartan and atenolol groups, respectively, died from cardiovascular disease; 0.63 (0.42-0.95), p=0.028. Mortality from all causes was 63 and 104 in Losartan and atenolol groups, respectively; 0.61 (0.45-0.84), p=0.002. Losartan was more effective than atenolol in reducing cardiovascular morbidity and mortality as well as mortality from all causes in patients with hypertension, diabetes, and LVH. Losartan seems to have benefits beyond blood pressure reduction<sup>9</sup>. In our study the baseline score of both groups were showed systolic blood pressure  $182 \pm 19$ , and diastolic blood pressure was  $104.5 \pm 11$ . After 4 months of treatment with atenolol systolic blood pressure  $147 \pm 17$ , diastolic blood pressure  $87 \pm 4$  were decreased. Losartan decreased systolic blood pressure  $138 \pm 13$ , diastolic blood pressure  $87 \pm 4$  in 4 months of treatment. There were differences in efficacy of Losartan and atenolol showed Losartan was more efficacious than atenolol. Combined therapy is more efficacious but costly.

Our study consisted with the study of Ferrario 2004. Losartan, however, reduced the risk of stroke by 25% compared with atenolol (p=0.001). For a subgroup of patients with isolated systolic hypertension, Losartan

reduced the risk of stroke by 40%<sup>10</sup>. After 4 months of treatment with atenolol systolic blood pressure  $141 \pm 11.4$ , diastolic blood pressure  $91 \pm 3.8$  were decreased, these results were significant statistically. Losartan decreased systolic blood pressure  $126 \pm 5.0$ , diastolic blood pressure  $85 \pm 4.5$  in 4 months of treatment, these results were significant statistically.

In the study of Farsang, 2000 similar significant reductions in SiSBPs (sitting systolic blood pressure) (mean $\pm$ SD) were obtained with 50 mg Losartan and 50 mg atenolol, from  $173.7 \pm 10.3$  and  $173.5 \pm 10.7$  mmHg at baseline to  $149.0 \pm 15.5$  and  $148.2 \pm 15.3$  mmHg after 16 weeks of Losartan or atenolol treatment, respectively. Sixty-seven percent of the Losartan-treated and 64% of the atenolol-treated patients remained on monotherapy throughout the study. Only 1.5% of the Losartan-treated patients withdrew because of a clinical adverse event (CAE) compared with 7.2% in the atenolol-treatment group. Drug-related CAEs were observed significantly more frequently with atenolol than with Losartan treatment (20.3 versus 10.4%). Losartan 50 mg and 50 mg atenolol produced comparable reductions in SiSBP in patients with ISH but Losartan was better tolerated. This is the first demonstration of the therapeutic value of selective angiotensin II receptor blockade with Losartan in the treatment of ISH (isolated systolic blood pressure)<sup>11</sup>, in our study After 4 months of treatment with atenolol systolic blood pressure  $141 \pm 11.4$ , diastolic blood pressure  $91 \pm 3.8$  were decreased, these results were significant statistically. Losartan decreased systolic blood pressure  $126 \pm 5.0$ , diastolic blood pressure  $85 \pm 4.5$  in 4 months of treatment, these results were significant statistically.

## CONCLUSION

Patients showed significantly better results on combination therapy of Atenolol and Losartan than monotherapy. Losartan was better than Atenolol in reduction of hypertension.

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# CORRECTION

CORRECTION PROF-1450.wpd

The amendment of the Professional Vol:17, No.02 (Prof-1450) titled: Dermatological disorders; psychiatric co-morbidity on page 334 is as under;

## INCORRECT

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**Article Citation:**

Dogar IA, Man MA, Bajwa A, Bhatti A, Naseem S, Kausar S. Dermatological disorders; Psychiatric co-morbidity. Professional Med J Jun 2010;17(2):334-349.

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**Article Citation:**

Dogar IA, Maan MA, Bajwa A, Bhatti A, Naseem S, Kausar S. Dermatological disorders; Psychiatric co-morbidity. Professional Med J Jun 2010;17(2):334-349.