

## **A Comparative Assessment of the Effect of Amlodipine, Atenolol, Enalapril and Thiazide on Hemodynamic Parameters and Renal Function Tests in Hypertensive Patients**

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Conflict of interest: Nil

### **Abstract**

**Aim:** The aim of the present study was to study effect of amlodipine, atenolol, enalapril and chlorothiazide on arterial blood pressure, heart rate and renal function tests.

**Methods:** The study was carried out in the Department of Pharmacology, Sri Krishna Medical College, Muzaffarpur, Bihar, India for 1 year. Total 100 patients with hypertension were included in the study. These patients were assigned to one of the 4 groups randomly. 4 There were 25 patients in each group. Patient prescribed with tablet amlodipine 5mg or 10 mg was be considered as Group I, likewise, prescription of tablet atenolol 25 mg or 50 mg was be considered as group II, prescription of tablet enalapril 2.5 mg or 5 mg was considered as group III and prescription of tablet thiazide diuretics 12.5 mg or 25 mg was be considered as group IV.

**Results:** Mean change in systolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Enalapril followed by thiazides, Atenolol & Amlodipine. Mean change in diastolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Atenolol followed by amlodipine, enalapril & thiazide. Mean change in systolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Atenolol followed by enalapril, amlodipine & thiazides. Mean change in blood urea was analyzed by chi square test. It was statistically significant. Highest decrease in blood urea level was seen by Thiazides followed by enalapril, amlodipine & atenolol.

**Conclusion:** Antihypertensives have effect on blood pressure, heart rate, renal functions. Patient's renal function, heart rate should always be considered while prescribing antihypertensive drugs.

**Keywords:** Antihypertensive Drugs, Cardiovascular Disease, Renal Functions, Hypertension, Therapeutic Goals.

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### **Introduction**

Optimal first-line treatment and subsequent sequencing of antihypertensive drugs has been controversial for decades. This is reflected in different recommendations

made in recent guidelines world-wide.[1–4] Before 1995, almost all randomized trial evidence on hypertension management related to diuretic agents and to a lesser

extent  $\beta$ -blockers.[5] However, newer drug classes were increasingly being used and have consequently been evaluated in major trials. Enthusiasm for any potential advantages of the newer agents (at least on surrogate end points) has been tempered in some situations by concerns over their increased cost. Despite the reality that the majority of hypertensive patients need at least two agents to reach currently recommended targets, until recently no trial data were available to compare the benefits of newer combinations of drugs with the standard most commonly used regimen of a  $\beta$ -blocker with a diuretic.

Globally, hypertension affects more than 1 billion people and is projected to reach 1.56 billion by 2025. It is the leading cause of death and the second leading cause of lost disability adjusted life-years worldwide.[6] Randomized controlled clinical trials have shown that control of hypertension reduces the risk of stroke, coronary artery disease, congestive heart failure, end-stage renal disease, peripheral vascular disease, and mortality.[2,7] The risk of developing these complications is continuous, starting at a blood pressure (BP) level as low as 115/75 mm Hg.[8]

Despite the effectiveness of modern antihypertensive drugs, approximately 70% of hypertensive patients fail to achieve the therapeutic goal of blood pressure <140/90 mmHg with monotherapy; and even less patients will reach the new therapeutic goals <130/80 mmHg recommended in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults [9], using only one antihypertensive drug. In fact, long-term prospective studies have shown that hypertensive patients were not effectively treated with monotherapy and needed an average of three drugs for adequate control.[10,11]

Looking only at the cost of medication, newer treatments (such as amlodipine and

perindopril) are typically more expensive than their older comparators (such as atenolol and thiazides) but in ASCOT they induced better preventive effects on all major cardiovascular outcomes. To make a rational decision when allocating resources in healthcare, it is necessary to take potential savings due to decreased morbidity and mortality into consideration. If the net costs still indicate that the newer strategy adds costs, a formal estimation of the cost effectiveness of the treatment is necessary.

When hypertensive patients do not achieve adequate control of their blood pressure, the options to try and achieve required treatment goals are to increase the dose of monotherapy (which increases the risk of side effects) or to use drug combinations with minimum side effects. In order to avoid complications, it is important to start treatment as soon as possible, achieve the goals in the shortest time possible and ensure treatment adherence.[10,12]

Hypertension treatment as a disease is an important public health challenge. Achieving recommended goal appears to be difficult. The variation of Antihypertensive drugs and also extensive clinical studies has led medical practitioners to different ideas for administration of these drugs. The ideal goal is that drug must be efficacious, free from side-effects, enable us to prevent all the complications of hypertension, easy to use and affordable. The aim of the present study was to study effect of amlodipine, atenolol, enalapril and chlorothiazide on arterial blood pressure, heart rate and renal function tests.

## Materials And Methods

The study was carried out in the Department of Pharmacology, Sri Krishna Medical College, Muzaffarpur, Bihar, India for 1 year

## Inclusion criteria

- All newly diagnosed hypertensive patients will be included in study.

- At the time of screening their blood pressure should be equal to or more than 140/90 mmHg.

#### Exclusion criteria

- All patients having emergency condition like myocardial infarction, stroke etc., shall not be included in study.
- All pregnant patients shall be excluded from study.
- Patients with nephropathy were excluded from the study.
- Patients who will not be ready to give consent shall be excluded from study.

#### Methodology

Total 100 patients with hypertension were included in the study. These patients were assigned to one of the 4 groups randomly. 4 There were 25 patients in each group. Patient prescribed with tablet amlodipine 5mg or 10 mg was be considered as Group I, likewise, prescription of tablet atenolol 25 mg or 50 mg was be considered as group II, prescription of tablet enalapril 2.5 mg or

5 mg was considered as group III and prescription of tablet thiazide diuretics 12.5 mg or 25 mg was be considered as group IV. (Table 1)

Newly diagnosed hypertensive patient was selected from medicine outpatient department randomly. Their blood pressure and heart rate will be recorded manually while doing selection for study. If blood pressure recorded is equal to or more than  $\geq$  140/90, then only patient will be included in the study. After that, these 100 patients were divided in 4 groups I, II, III, IV. Each cohort contained 25 patients having prescribed data of tab amlodipine, atenolol, enalapril and chlorothiazide respectively. After 1 month all patients was recalled for follow up. Their blood pressure and heart rate were recorded. Same procedure will again repeat after 4 months from selection of patients for study. Data will be collected for analysis. Renal function test was done before and after the study. Analysis of data was done by calculating mean, standard deviation and p value.

**Table 1: Treatment Groups**

Study medication	Group I	Group II	Group III	Group IV
Medicine	Amlodipine	Atenolol	Enalapril	Thiazide
Dose	5 mg or 10 mg	25 mg or 50 mg	2.5 mg or 5 mg	12.5 mg or 25 mg
Dosage	Once a day	Once a day	Once a day	Once a day

#### Statistical Analysis

Intension to treat analysis (ITT) for safety data and per protocol analysis for efficacy data was performed. Mean SBP, DBP and mean BP were calculated as mean  $\pm$  standard deviation (SD) and compared between the groups/baseline values using t-

test. Fischer's exact test was applied to observe if there was significant difference between responder rates and to observe if there were significant difference between proportions of subjects having peripheral edema not attributable to any concomitant drug.

#### Results

**Table 2: Comparison of effect of drugs on systolic blood pressure**

Groups	Mean systolic blood pressure (mmHg)		Mean change in blood pressure (mmHg)	P-value
	Before (Mean + SD)	After (Mean +SD)		
Group I Amlodipine	160.40+ 4.89	111.65+7.38	48.75	<0.05
Group II Atenolol	175.70+23.43	116.25 +9.54	59.45	<0.05
Group III Enalapril	208.56+3.65	130.67 +08.56	77.89	<0.05
Group IV Thiazide	190.40+23.28	128.70 +12.29	61.7	<0.05

The effects of drugs on systolic blood pressure (mmHg) before & after were studied. Mean change in systolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Enalapril followed by thiazides, Atenolol & Amlodipine.

**Table 3: Mean change in diastolic blood pressure before & after**

Groups	Mean diastolic blood pressure (mmHg)		Mean change in blood pressure (mmHg)	P-value
	Before (Mean + SD)	After (Mean +SD)		
Group I Amlodipine	125.50+15.30	86.65+7.38	38.85	<0.05
Group II Atenolol	120.90+23.43	80.40 +9.54	40.5	<0.05
Group III Enalapril	128.47 +23.65	94.65 +08.56	33.82	<0.05
Group IV Thiazide	115.45 +23.28	85.60 +12.29	29.85	<0.05

The effects of drugs on diastolic blood pressure (mmHg) before & after were studied. Mean change in diastolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Atenolol followed by amlodipine, enalapril & thiazide.

**Table 4: Comparison of effect of drugs on heart rate**

Groups	Mean heart rate		Mean change in blood pressure (mmHg)	P-value
	Before (Mean + SD)	After (Mean +SD)		
Group I Amlodipine	85.05 +14.29	75.65+7.38	9.40	<0.05
Group II Atenolol	73.40+23.43	68.90+09.54	4.50	<0.05
Group III Enalapril	85.94 +23.65	81.19 +08.56	4.75	<0.05
Group IV Thiazide	84.65 + 23.28	75.05 +12.29	9.60	<0.05

The effects of drugs on mean heart rate before & after were studied. Mean change in systolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Atenolol followed by enalapril, amlodipine & thiazides.

**Table 5: Mean change in blood urea level before & after**

Groups	Mean change in blood urea level		Mean change in blood pressure (mmHg)	P-value
	Before (Mean + SD)	After (Mean +SD)		
Group I Amlodipine	21.75 + 4.29	13.60 + 5.45	8.15	<0.05
Group II Atenolol	20.05 + 3.43	13.25 + 3.61	6.80	<0.05
Group III Enalapril	18.90 + 3.65	09.30 + 6.68	9.60	<0.05
Group IV Thiazide	20.39 + 3.28	10.09 + 2.41	10.30	<0.05

The effects of drugs on mean change in blood urea level before & after were studied. Mean change in blood urea was analyzed by chi square test. It was statistically significant. Highest decrease in blood urea level was seen by Thiazides followed by enalapril, amlodipine & atenolol.

## Discussion

Antihypertensive management should be individualized according to the

characteristics of each patient, so it is difficult to generalize. However, two meta-analyses have recently found advantages for combinations that include a RASI with a calcium antagonist. The goal of hypertension treatment is to reduce BP to <140/90 mm Hg; however, in patients with hypertension and diabetes or renal disease, the BP goal is even lower, targeted at ≤130/80 mm Hg.[2] Nonpharmacologic interventions should be instituted in all patients with hypertension. When used

early, lifestyle modifications can decrease other disease risks and may avoid the need for drug therapy. Maintaining a healthy lifestyle, however, is not sufficient or is difficult to comply with, and most patients will require pharmacologic interventions to control their BP.

A study by Brookhart et al. reported that beta blockers like propranolol has prominent effect on heart rate. Our study corresponds with the study. In another study by Majumdar et al., focusing on patients admitted to hospital with community acquired pneumonia, statin users were more likely to be former smokers and have up-to-date immunizations for pneumococcus and influenza. Furthermore, Dormuth et al. reported that for action on mean arterial pressure atenolol had significant effect. Our study corresponded to the study. Although the studies differ in terms of design, outcome measure and definition of adherence, they all suggest a healthy adherer or healthy user effect.[7]

The limitation is that our interpretation of sub-meta-analysis findings were based on our clinical judgement that assumed prescription of BBs could occur in patients with worse cardiovascular comorbidity. For instance, patients taking certain antihypertensives like BBs may not necessarily have a worse cardiovascular condition. Similarly, even though ACEIs are good choice of antihypertensives in patients without any comorbidity, they are also preferred drugs in those who had myocardial infarction or systolic dysfunction.[13] On the other hand, the strength of this meta-analysis is that we excluded studies that compared hypertensive patients who were taking RAAS inhibitors to those that were not taking any form of antihypertensive (e.g., on dietary management). This helped us to have comparable groups.[14]

Beta-blockers (atenolol) were superior to all drug-classes for all primary outcomes, and although the difference in many cases

was non-significant and the quality of the evidence was mixed, this may be seen as evidence against opting for these drugs as the first choice. Beta-blockers and alpha-blockers were the only drug-classes that were not significantly superior to any drug, for any outcome, which could suggest not recommending these as first line medication.[15,16]

## Conclusion

Hypertension is a global epidemic, yet many guidelines and pharmacologic options are available to prevent the morbidity and mortality associated with this disease. Although lifestyle modifications are frequently neglected, they should be started early and continued indefinitely. Some patients will require more than 1 antihypertensive agent to control their BP. Antihypertensives have effect on blood pressure, heart rate, renal functions. Patient's renal function, heart rate should always be considered while prescribing antihypertensive drugs. Effective communication between physicians, other healthcare professionals, and patients is paramount in the successful treatment of hypertension.

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