



## Comparative Study of Adverse Effect of Amlodipine with Lisinopril and Amlodipine with Losartan in Control of Blood Pressure

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### ABSTRACT

*This was a comparative study, spanning over a period of two years on 100 selected hypertensive patients who satisfied certain inclusion and exclusion criteria. The study was carried out in Indira Gandhi institute of cardiology, Patna, Bihar to compare the adverse effect of combination antihypertensive agents i.e. Amlodipine (5mg) with Lisinopril (10mg) and Amlodipine (5mg) with Losartan (50mg). All the patients were followed up regularly at an interval of one month for clinical history, and compliance, and relevant physical examination and biochemical parameters. After treatment for two years it was observed that Amlodipine with Losartan combination is better than Amlodipine with Lisinopril combination because the former group reported lesser adverse effects like cough, ankle edema and better control of blood pressure*

**Keywords:** Hypertension, Amlodipine, Losartan, Lisinopril.

### Introduction

Hypertension, which affects over one billion adults worldwide is a major risk factor for cardiovascular and renal diseases.

BP above 139mm Hg systolic or above 89mm Hg diastolic on several occasions qualifies as hypertension, at all ages.

Hypertension if untreated, leads to a variety of disabling cardiac, cerebrovascular and renal complications with shortened life expectancy, regardless of its etiology.

In the largest outcome study, ALLHAT, Amlodipine had the same primary outcome (fatal and nonfatal coronary heart disease) as did the diuretics and ACE inhibitor groups but with increased heart failure and decreased new diabetes<sup>1</sup>. Perhaps unexpectedly, Amlodipine slowed renal deterioration better than other agents. In Amlodipine treated cases of hypertension peripheral edema is most troublesome occurring in about 10% of patients at 10 mg daily.

In women there is more edema (15%) than in men (6%). Next insignificances are dizziness (3% to

4%) and flushing (2% to 3%) compared with verapamil, Amlodipine gave an excellent quality of life compared with other agents in the TOMH study.

The very long half life of Amlodipine, good tolerability, excellent trial data and virtual absence of drug interaction makes it an effective once a day antihypertensive and antianginal agent ACE inhibitors have not only become the cornerstone of the treatment of heart failure but increasingly also play a major role in hypertension therapy and in cardiovascular protection<sup>2</sup>.

Because ACE inhibitors exert most of their major effects by inhibiting the formation of angiotensin – II, it follows that direct antagonism of the receptors for angiotensin-II (ARB) should duplicate many or most of the effects of ACE inhibition. They should largely avoid the bradykinin related side effects of ACE inhibitors such as cough and angioedema so that they virtually free of subjective side effects. Hence these new ARBs of which the prototype is Losartan are being used more and more both in hypertension in heart failure.

As with all the ARBs a dose increase is usually less effective than the addition of a low dose diuretic in achieving greater blood pressure control<sup>3</sup>. In diabetic nephropathy in the RENAAL study, Losartan in a higher dose (50-100 mg daily) reduced end stage renal disease and proteinuria<sup>4</sup>.

## Material and Method

### Study Design

The study was designed as a comparative study of adverse effect of Amlodipine in combination with Lisinopril and Amlodipine in combination with Losartan on control of blood pressure (BP <140/90 mm Hg) was taken as therapeutic goal.

### Place and Time

The study was conducted in Indira Gandhi Institute of Cardiology, Patna. This study was carried out from June 2005 to June 2007.

### Approval

This study has been approved by Institutional ethics, PMCH, Patna

## Subject

The subject included were healthy volunteers with elevated blood pressure (140/90 – 179/109 mm of Hg). Both genders were included in the study. These volunteers met the inclusion criteria of elevated B.P. and were willing to participate in the study. Written informed consent was obtained from participants, Total number of participants was 100.

### Inclusion criteria

1. Age 40 – 70 years
2. No history of cardiovascular events.
3. Blood pressure in the range of 140/90 – 179/109 mm Hg.

### Exclusion Criteria

1. Cigarette smokers.
2. Family history of premature coronary heart disease.
3. Diabetes mellitus.
4. Pregnancy.
5. Hypercholesterolemia and recent or ongoing therapy with lipid lowering drugs like clofibrates or statins.
6. Any major illness in the last three months like any kidney, liver disease, tuberculosis etc. Clinical evaluation.

All subjects were subjected to following clinical protocol.

1. A detailed history including
  - i. Name and Address.
  - ii. Age (Years)
  - iii. Sex
  - iv. Smoking History
  - v. Family history – particularly for congenital heart disease.
2. A thorough scrutiny of available medical records.
3. A biochemical work up including fasting blood glucose (FBG), lipid profile.

### Treatment method

There are two groups of patients each consists of 50 patients (1) Group A (2) Group B  
Group A – Patients were treated by Amlodipine (5 mg) with Lisinopril (10 mg) combination once daily.

Group B – Patients were treated by Amlodipine (5 mg) with Losartan (50 mg) combination once daily.

### Patient management

Follow up visits are taken once a month.

1. The clinical history compliance, weigh and blood pressure were reviewed.
2. Biochemical lipid profiles were obtained.
3. The results obtained were tabulated and analyzed.

### Result

The observation of the data, which were obtained from the study for the analysis of adverse effect of Amlodipine combination with Lisinopril and Amlodipine combination with Losartan on B.P. control in Group A and Group B are as follows.

In our study, out of 100 cases of Hypertension was divided into two groups (Group A and Group B) as in Table 1\In this study group (Group A) the total number of cases of hypertension was 50. All group A patients were treated by Amlodipine 5mg and Lisinopril 10mg combination once a day.

In this study group (Group B) the total number of cases of hypertension was 50. All Group B patients were treated by Amlodipine 5mg and Losartan 50mg combination once a day.

Group A patients were examined for any adverse effects induced by combination of Amlodipine plus Lisinopril and Group B patients was examined for any adverse effects induced by combination of Amlodipine plus Losartan.

Adverse effects were seen in patients who were treated by Amlodipine plus Lisinopril

combination with placebo controlled, parallel group study. (Table 2 and Chart 1)

No of Amlodipine + Lisinopril treated patients = 50

No of Placebo treated patients = 50

Tablet of Placebo is just like tablet of AML + Lis

Tablet of Placebo is composed of glucose only.

In this study an incidence of adverse effects like headache and dizziness produced in Group A patient which was treated by Amlodipine + Lisinopril combination was similar to the Placebo but adverse effects like ankle edema and cough produced in group A patient was significantly more common than placebo. Ankle edema was found in 6% patients and cough in 10% patients.

Adverse effects were seen in patients who were treated by Amlodipine + Losartan combination with Placebo controlled parallel group study. (Table 3 and Chart 2)

Number of Amlodipine + Losartan treated patients = 50

Number of Placebo treated patients = 50

Tablet of Placebo is just like the tablet of Amlodipine + Losartan

Tablet of Placebo is composed of glucose only.

In this study an incidence of adverse effect like headache produced in Group B patients which were treated by Amlodipine + Losartan combination were similar to the placebo but dizziness were found in 4% patients and cough in 2% patients but ankle edema were found in 6% patients.

**Table 1:** Total no of hypertensive cases are 100, divided into 2 equal groups. i.e. Group A & Group B.

Age groups (in years)	No of cases in Group A	No of cases in Group B	Total no of cases
40-45	3	3	6
46-50	7	7	14
51-55	10	10	20
56-60	14	14	28
61-65	11	11	22
66-70	5	5	10
Total	50	50	100

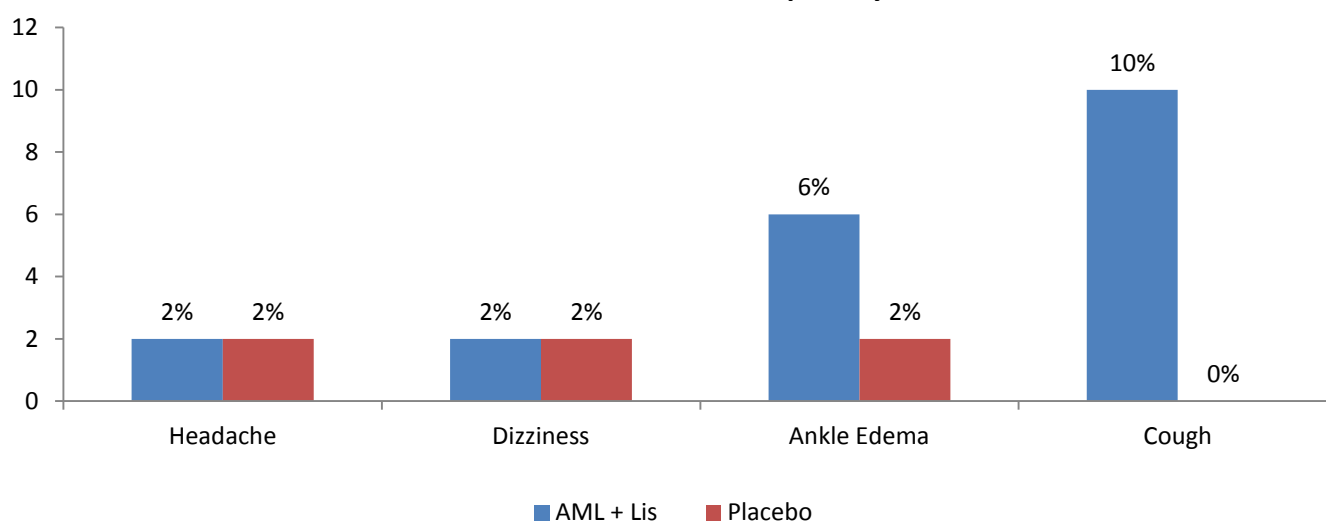
**Table 2:** In Group A Patient no of cases which shows different adverse effects.

	Headache		Dizziness		Ankle edema		Cough	
	AML + Lisinopril	Placebo	AML + Lisinopril	Placebo	AML + Lisinopril	Placebo	AML + Lisinopril	Placebo
No of cases which shows adverse effects	1	1	1	1	3	1	5	0

**Table 3:** In Group B Patient no of cases which shows different adverse effects

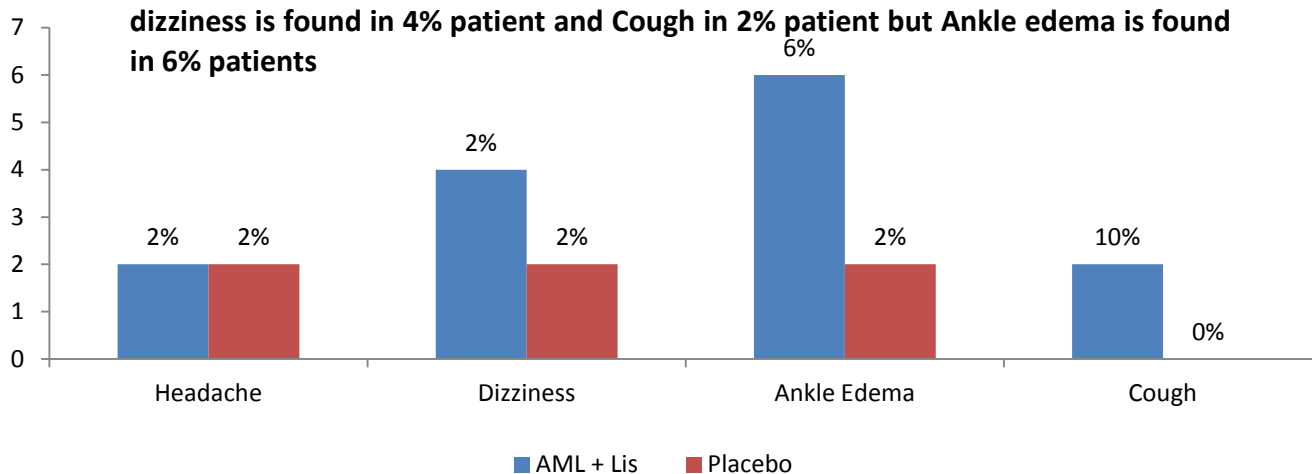
	Headache		Dizziness		Ankle edema		Cough	
	AML + Losartan	Placebo	AML + Losartan	Placebo	AML + Losartan	Placebo	AML + Losartan	Placebo
No of cases which shows adverse effects	1	1	2	1	3	1	1	0

**Adverse Reaction Seen in Patients which are treated by AML (5mg) + Lis (10mg) combination with Placebo control, Parallel Group Study**



**Side Effects**

**The incidence of Adverse Events like headache Produced in Group-B Patients which is treated by AML (5mg) + Los (50mg) Combination is similar to be Placebo but dizziness is found in 4% patient and Cough in 2% patient but Ankle edema is found in 6% patients**



**Side Effects**

### Discussion

The present study was undertaken to detect the adverse effects of Amlodipine with Lisinopril and Amlodipine with Losartan in controlling blood pressure in hypertensive patients, blood pressure in a population is distributed continuously as a bell shaped curve, a concept that was first formulated by Sir George Peckering. Patient distribution in our report is similar to that of Sir George Peckering.

Each study group contains equal number of hypertensive patients in every age group. These two groups are called Group A and Group B each containing 50 patients. Group A patients were treated by Amlodipine (5mg) + Lisinopril (10mg) combination once a day.

Group B patients were treated by Amlodipine (5mg) + Losartan (50mg) combination once a day. These combinations of drugs were chosen in this study because these combination attacks both the rennin angiotensin system and the increased peripheral vascular resistance. These may be specific renal benefits because all these drugs (i.e. Amlodipine, Lisinopril and Losartan) delay the diabetic and non diabetic nephropathy. Both types of agents are free of metabolic and central nervous system side effect.

ACE inhibitors plus CCBS are now increasingly used in the therapy of hypertension. In addition to B.P. lowering the overall evidence is that these agents also confer vascular protection.

ACE inhibitors combine well with diuretics and CCBS and have relatively infrequent side effects, Angiotensin receptor blockers (like Losartan) have an excellent record in comparative studies showing better cardiovascular outcome benefits, virtually without the major side effects of ACE inhibitor and provide symptoms free control of hypertension.

In this study shows that Group A patients which were treated by Amlodipine + Lisinopril had developed headache 2%, Dizziness 2%, ankle edema 6%, cough 10% Where as adverse effects produced in Group B patients were headache 2%, Dizziness 4%, ankle edema 6%, cough 2%

This report is consistent with the report of book "Drug for the heart" edition 6<sup>th</sup>, chapter 3, page no 74, which says that the side effects of Amlodipine are peripheral edema is most troublesome occurring in about 10% of patients at 10mg daily. In women there is more edema (15%) than in men (6%). Next insignificance is dizziness (3% to 4%) and flushing (2% to 3%).

The book "The drug for heart" edition 6<sup>th</sup>, chapter 5, page no 116 says that in some centers the incidence of cough is thought to be as high as 10% to 15% where as other reports a much lower incidence such as 5.5% in HOPE<sup>5</sup>.

### Conclusion

The adverse effects produced by Amlodipine + Lisinopril combination are headache – 2%, dizziness – 2%, ankle edema – 6%, cough – 10%.

The adverse effects produced by Amlodipine + Losartan combination are headache – 2%, dizziness – 4%, ankle edema – 6%, cough – 2%.

So the Amlodipine + Losartan combination is better than the Amlodipine + Lisinopril combination because Amlodipine + Losartan combination control blood pressure in more numbers of patients and having less adverse effects.

### References

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