

Assessment of Comparative Efficacy of Amlodipine Alone and in Combination With Enalapril for Treatment of Moderate/ Severe Hypertension

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ABSTRACT

Background: Patients with mild/moderate hypertension are easily managed by prescribing a single drug but in case of severe hypertensive cases combination of drugs are necessary for controlling blood pressure. Hence, we planned this study for the assessment of comparative efficacy of amlodipine alone and in combination with enalapril for treatment of moderate/severe hypertension.

Materials and Methods: The study was conducted in the department of general medicine of Career Institute of Medical Sciences & Hospital Ghaila, Lucknow, Uttar Pradesh (India) after obtaining ethical approval from the ethical committee. For the study, 80 patients reporting to the outpatient department were selected. The patients were randomly grouped into 2 groups, Group A and Group B. Group A was prescribed Amlodipine alone whereas Group B was prescribed combination of Amlodipine+enalapril.

Results: The mean age of the subjects in group A was 57.3 + 10.8 years and in group B was 59.5 + 8.2 years with age ranging from 21-80 years. After the 98 days, we observed non-significant difference for systolic and diastolic blood pressures between both the groups.

Conclusion: Both the prescriptions, amlodipine alone and combination of amlodipine+ enalapril are effective in lowering the blood pressure of hypertensive patients efficiently.

Keywords: Amlodipine, Blood pressure, Enalapril, Hypertension.

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INTRODUCTION

Calcium antagonists were introduced in 1970s and since that moment they have a significant role in the management of hypertension and ischaemic heart disease.¹ The mechanism of action of calcium antagonists is by restraining the transmembrane influx of calcium ions which leads to vasodilatation of blood vessels because vascular smooth muscles depend upon calcium ions for maintenance of tone.^{2,3} In recent times, a new calcium antagonist is developed having structure similar to nifedipine. It has special action on vascular smooth muscle cells contrasted against myocardium.^{4,5} As compared to its previous counterparts, amlodipine has been proved to have high bioavailability (60-65%), moderate absorption rate (6-12 h to accomplish crest plasma concentration) and a long disposal half-life (35-50 h). Subsequently, daily single dose can achieve controlled blood pressure for 24 h.⁶ Patients with mild/moderate hypertension are easily managed by prescribing single drugs but in case of severe hypertensive cases combination of drugs are necessary for controlling blood pressure.⁷ Henceforth, we planned this study for the assessment of comparative efficacy of amlodipine alone and

in combination with enalapril for treatment of moderate/ severe hypertension.

MATERIALS AND METHODS

The study was conducted in the department of general medicine of Career Institute of Medical Sciences & Hospital Ghaila, Lucknow, Uttar Pradesh (India) after obtaining ethical approval from the ethical committee. An informed consent form was signed by the patients before beginning the study. For the study, 80 patients reporting to the outpatient department were selected.

Inclusion Criteria

- History of stage I and II hypertension
- Age between 21 to 80 years

Exclusion criteria

- Pregnancy
- History of other systemic diseases (renal diseases, liver diseases, etc.)
- History of long term corticosteroids therapy
- Unstable myocardial ischemic syndrome in last six months

The patients were randomly grouped into 2 groups, Group A and Group B. Group A was prescribed Amlodipine alone whereas Group B was prescribed combination of Amlodipine + enalapril. Drugs were prescribed for a time period of 98 days. Doses of drugs prescribed depended upon Dap of patients. If DAP increased more than 85mmHg, prescription doses were increased.

For group A, dose of Amlodipine prescribed was 2.5mg, 5 mg or 10mg in a single dose daily. For group B, doses prescribed were, amlodipine 2.5 mg + enalapril 10 mg, amlodipine 5mg + enalapril 10mg and amlodipine 5mg + enalapril 20mg.

Various demographic variables like age, sex, habit of alcohol consumption, smoking etc were also recorded. The patient's blood pressure was measured on the first visit. Patients were recalled 4 times at 14th, 42nd, 70th and 98th day by the clinician and blood Pressure was measured 3 times in the supine and orthostatic positions at every visit. The lowest value of DAP was considered for the records.

The statistical analysis of the data was done using SPSS version 11 for windows. For the assessment of significance of data, Chi square test and Student's t-test were used. P-value less than 0.05 were predefined to be statistically significant.

Table 1: Demographic data of the patients

Variables	Group A (n=40)	Group B (n=40)	P value
Age	57.3 ± 10.8	59.5 ± 8.2	0.22
Male sex	25 (62.5%)	29 (72.5%)	0.09
Alcohol consumption	3 (7.5%)	5 (12.5%)	0.80
Smoking	7 (17.5%)	9 (22.5%)	0.12
Obesity, (BMI > 30)	2 (5%)	3 (7.5%)	0.55
Diabetes	5 (12.5%)	4 (10%)	0.01
Physical activity	21 (52.5%)	19 (47.5%)	0.43

Table 2: mean Systolic and Diastolic Blood Pressure comparison between Group A and Group B

Days	Mean Systolic Arterial Pressure (mmHg)		Mean Diastolic Arterial Pressure (mmHg)	
	Group A	Group B	Group A	Group B
0	152	147	94	94
14	133	135	78	85
42	130	128	75	83
70	131	132	74	79
98	128	125	72	78

Figure 1: Comparative analysis of mean systolic arterial blood pressure between Group A and Group B

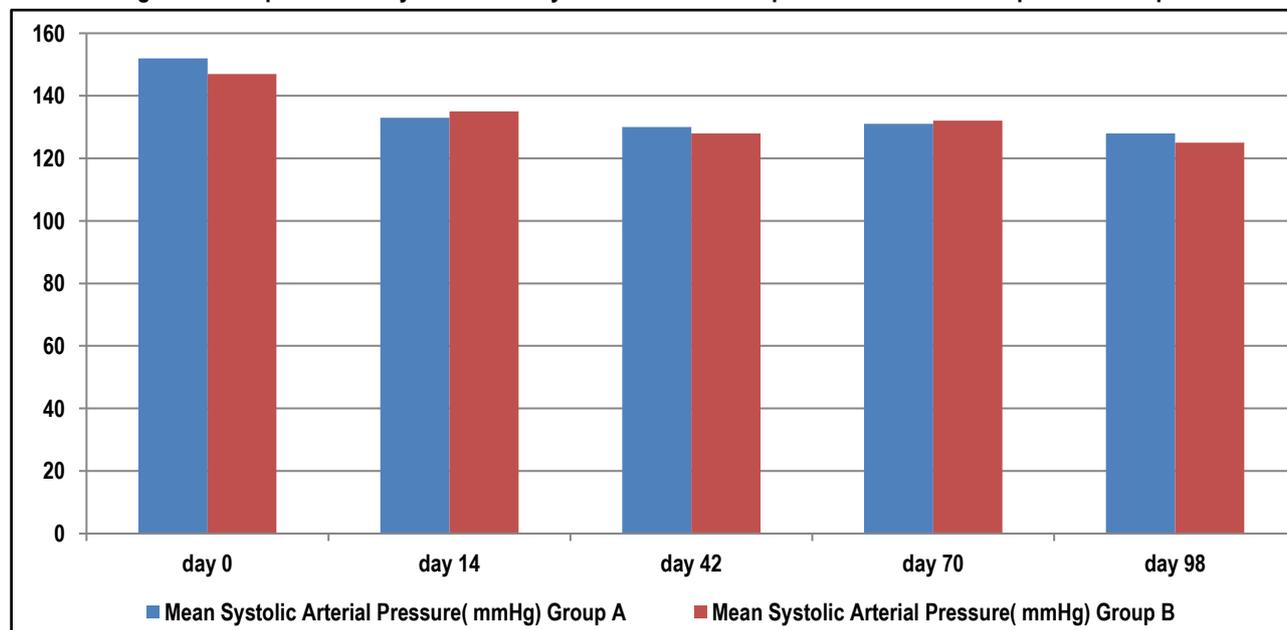
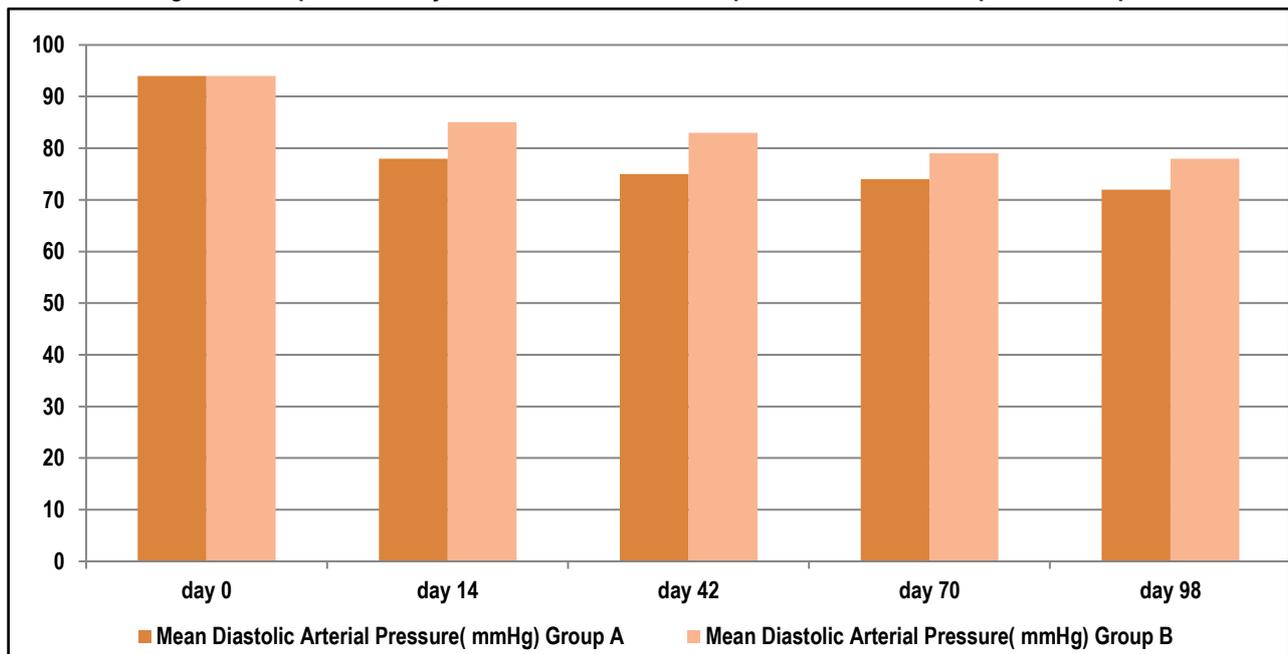


Figure 2: Comparative analysis of mean diastolic blood pressure between Group A and Group B



RESULTS

In the present study, 80 patients were included and randomly grouped into two groups, Group A and Group B, 40 patients in each group. The mean age of the subjects in group A was 57.3 ± 10.8 years and in group B was 59.5 ± 8.2 years with age ranging from 21-80 years. The number of male patients in Group A was 25 (62.5%) and in Group B were 29 (72.5%). Habit of alcohol consumption was present in 3 patients (7.5%) in Group A and 5 patients (12.5%) in Group B. Habit of smoking was present in 7 patients (17.5%) in Group A and 9 patients (22.5%) in Group B. 2 patients (5%) in Group A were obese as compared to 3 patients (7.5%) in Group B. Physical activity was present in 21 patients (52.5%) in Group A and 19 patients (47.5%) in Group B. All the above results were statistically insignificant with $p > 0.05$. 5 patients (12.5%) in Group A and 4 patients (10%) in Group B were diabetic and this result was statistically significant with $p < 0.05$. [Table 1] Table 2 shows comparative analysis of mean systolic arterial pressure and mean diastolic arterial pressure between Group A and Group B. After the 98 days, we observed non-significant difference for systolic and diastolic blood pressures between both the groups. [Table 2, figure 1 & figure 2]

DISCUSSION

The risk of mortality and morbidity in cardiovascular patients with hypertension is very high. It is known that the risk of cardiovascular diseases in hypertensive patients is reduced with the effective treatment of SAH. The decrease in the cardiovascular morbidity and mortality observed in the last 50 years can be mostly attributed to a broader availability and use of anti-hypertensive drugs.⁵⁻⁸ In the present study, we comparatively assessed the efficacy of amlodipine alone and in combination with enalapril for treatment of moderate/ severe hypertension. We observed that there is no statistically significant difference between systolic and diastolic blood pressures at 98 days of the treatment between both the groups. Also, there was no statistically significant difference between the demographic variables of the patients between both

the groups. G Fowler et al evaluated safety and efficacy of amlodipine vs enalapril as monotherapy in patients with moderate/severe hypertension (supine DBP 105-125 mm Hg, SBP 140-220 mm Hg). After 2 weeks placebo treatment 31 patients were randomised by the technique of minimisation in an observer-blind study to receive once daily treatment with either amlodipine (15 patients) 5-10 mg, or enalapril (16 patients) 5-20 mg for 8 weeks. The study design concluded with 2 weeks placebo treatment. In addition to clinic measurements, home blood pressure monitoring (Copal UA-251) was performed during the study. Clinic supine systolic blood pressure was reduced from 177 to 152 mm Hg (amlodipine) and 183 to 169 mm Hg (enalapril) after 8 weeks treatment. Clinic supine diastolic blood pressure was reduced from 110 to 93 mm Hg (amlodipine) and 109-102 mm Hg (enalapril) after 8 weeks treatment. Home blood pressure recordings confirmed these reductions in blood pressure. Although the reduction in blood pressure was greater for the amlodipine treated group, the differences between treatments were not statistically significant.⁸ Cocco G et al undertook a study to evaluate the contribution of the calcium antagonist amlodipine and of the angiotensin-converting-enzyme inhibitor enalapril to blood pressure regulation by studying their effect on neurohormonal activation. Fifty hypertensive patients with RD were studied. After a placebo run-in period of 4 to 6 weeks, patients were randomly assigned to receive either amlodipine (10 mg once daily) or enalapril (20 mg once daily) for 6 months. Both drugs significantly lowered blood pressure. Enalapril did not result in activation of the sympathetic system (as determined by measurement of the plasma norepinephrine level). On the other hand, the hypotensive effect of amlodipine occurred with an increase in heart rate and in the levels of plasma norepinephrine and angiotensin II. It was concluded that it is unclear whether amlodipine may reduce cardiac dysfunction in patients with RD.⁹ Kraicz H et al compared the effects of atenolol (50 mg), amlodipine (5 mg), enalapril (20 mg), hydrochlorothiazide (25 mg), and losartan (50 mg) given in once-daily oral doses on office and ambulatory blood pressures (BPs) in patients with hypertension

and obstructive sleep apnea (OSA). Each of 40 randomized patients was treated in sequence with two of the five agents (balanced incomplete block design). Treatment periods lasted 6 wk and were separated by a 3-wk washout period. Changes in BP from baseline with the study substances were compared through analysis of variance. Office diastolic BP, our primary outcome variable, was most effectively lowered by atenolol, with all four post hoc differences between atenolol and the remaining substances being statistically significant. Reductions in office systolic and daytime ambulatory BP was not significantly different among the five compounds. However, atenolol reduced mean nighttime ambulatory diastolic and systolic BP more effectively than did amlodipine, enalapril, or losartan (but not hydrochlorothiazide). Severity of sleep-disordered breathing and well-being during the day were not significantly influenced by any of the study compounds.¹⁰

CONCLUSION

From the results of the present study, we conclude that both the prescriptions, amlodipine alone and combination of amlodipine+enalapril are effective in lowering the blood pressure of hypertensive patients efficiently but the difference was non-significant.

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