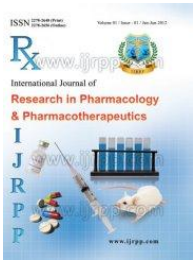
International Journal of Research in Pharmacology & Pharmacotherapeutics



ISSN Print: 2278-2648 ***IJRPP |Vol.6 | Issue 4 | Oct - Dec - 2017***
ISSN Online: 2278-2656 ***Journal Home page: www.ijrpp.com***

Research article ***Open Access***

An observative study of comparison of efficacy and tolerability between atenolol and combination of amolodopine with atenolol in the maintence therapy of hypertension in a tertiary care hospital

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ABSTRACT

Background

Hypertension is one of the most common non-communicable disease. There are a number factors, presently prevalent in our daily life that are increasing the prevalence of hypertension in nearly all age groups, but more as age increases. Beta receptor antagonists are one of the groups of drugs used in all grades of hypertension. Ca^{2+} channel blockers are the other class of antihypertensive agents, used in different situations of hypertension. But many times, single drug therapy is not sufficient to maintain normal blood pressure. And combination therapy has its own problems like increase side effects, cost etc. Hence, present study is undertaken to determine the difference between efficacy and tolerability of atenolol and combination of amolodopine and atenolol.

Objectives

To compare the efficacy and tolerability of atenolol and combination of amolodopine and atenolol in maintaining normal blood pressure.

Materials and methods

A total of hundred patients were taken for the study. Fifty patients are given atenolol and other fifty are given combination of amolodopine and atenolol, once a day, daily for one month. Blood pressure of all the patients is recorded daily in laying position for one month. Data collected was analyzed statistically using descriptive statistics. Any adverse effects, symptoms of hypertension and patient compliance is also noted in the follow up visits.

Results

Blood pressure levels were maintained at normal limits, more in combination therapy compared to atenolol alone therapy. Blood pressure variations were also less with combination therapy. Side effects were somewhat more in the combination therapy. Patient compliance was good.

Interpretation and conclusion

Combination of amolodipine and atenolol seems to be more effective in the treatment of hypertension in comparison to atenolol alone.

Keywords: Atenolol, Amolodopine, Hypertension

INTRODUCTION

Hypertension is one of the most common non-communicable disease. There are a number factors, presently prevalent in our daily life that are increasing the prevalence of hypertension in nearly all age groups, but more as age increases. Beta receptor antagonists are one of the groups of drugs used in all grades of hypertension. Ca^{2+} channel blockers are the other class of antihypertensive agents, used in different situations of hypertension. But many times, single drug therapy is not sufficient to maintain normal blood pressure. And combination therapy has its own problems like increase side effects, cost etc. Hence, present study is undertaken to determine the difference between efficacy and tolerability of atenolol and combination of amolodopine and atenolol.

REVIEW OF LITERATURE

Hypertension, increase in blood pressure, is one of the most common clinical condition seen in day-to-day life. Hypertension is responsible for 6% of deaths worldwide. Long term constant increase in blood pressure increases the risk of coronary artery disease, congestive heart failure, ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease. Blood pressure variability, other than normally occurring in physiological conditions, is associated with premature death and cardiovascular events. So the blood pressure is maintained within normal limits by using different groups of antihypertensive drugs, singly or in combination to prevent the complications of hyperyension. [3, 22, 18].

Pathophysiology of increased blood pressure Arterial blood pressure is decided by two important factors, cardiac output and peripheral resistance. While cardiac output is determined by heart rate and stroke volume (stroke volume is related to myocardial contractility and size of the vascular compartment), Peripheral resistance is determined by any functional or anatomical changes in small blood vessels. [3].

Following are some of the important determinants, that has significant role in the regulation of blood pressure. They are:

Intravascular Volume

Increase in intravascular volume is associated with increase blood pressure. Vascular volume increases when the sodium intake exceeds the capacity of the kidney to excrete it. Increase intravascular volume leads to increase cardiac output. [3]

Autonomic Nervous System

Autonomic nervous system maintains blood pressure by changes in blood volume, by changes in blood vessels reactions and by chemoreceptor signals. Release and amount of secretion of three endogenous catecholamines are norepinephrine, epinephrine, and dopamine along with hormonal factors regulates the arterial pressure. [3]

Renin-Angiotensin-Aldosterone

Angiotensin II, generated from renin-angiotensin-aldosterone system has vasoconstrictor property that increases blood pressure. Aldosterone causes sodium retention that increases intravascular volume. Renin-angiotensin-aldosterone system regulates arterial pressure by this way. [3]

Vascular Mechanisms

Even a small decrease in the lumen size of the blood vessels greatly increases the peripheral resistance. Many factors that affects the blood vessel wall, particularly of small arteries and arterioles reduces lumen diameter and this causes increase in blood pressure. [3]

Classification of Hypertension

Blood pressure is recorded for two or more times on more than two outpatient visits, before been classified under various levels of blood pressure.

2017 updated Blood pressure classification		
Classification	**Systolic, mmHg**	**Diastolic, mmHg**
Normal BP	<120	*and* <80
Elevated BP	120–129	<80
Stage 1 Hypertension	130–139	*or* 80–89
Stage 2 Hypertension	≥ *140*	≥ *90*

Source: Whelton, P.K, et al. J Am Coll Cardiol. 10.1016/j.jacc.2017.11.006 [5]

Treatment of Hypertension

They are mainly two ways of treatment of hypertension, Nonpharmacological therapy and Pharmacological therapy.

1. Nonpharmacological therapy is the lifestyle modifications like aerobic exercise, weight loss (in overweight individuals), restricting sodium intake, decreasing stress and avoiding smoking and alcohol. Nonpharmacological therapy is applied to all the patients of hypertension, in all stages, with or without pharmacological therapy. Many of the elevated hypertensive patients and in some of the stage 1 hypertensive patients, nonpharmacological therapy is sufficient. [4]
2. Pharmacological therapy includes use of various antihypertensive drugs, as monotherapy or in combination to maintain the normal blood pressure. There are different groups of antihypertensive drugs of different mechanisms of action like: Diuretics, ACE Inhibitors, Angiotensin receptors blockers, Calcium channel blockers, β Adrenergic blockers, α Adrenergic blockers, α+β Adrenergic blockers, Central sympatholytics, Vasodilators etc. Different types of drugs are tired in different stages of hypertension in different age related or comorbid conditions. [20]

MATERIALS AND METHODS

A total of hundred patients were taken for the study. Fifty patients are given atenolol and other fifty are given combination of amolodopine and atenolol, once a day, daily for one month. Blood pressure of all the patients is recorded daily in laying position for one month. Data collected was analyzed statistically using descriptive statistics. Any adverse effects, symptoms of hypertension and patient compliance is also noted in the follow up visits.

RESULTS

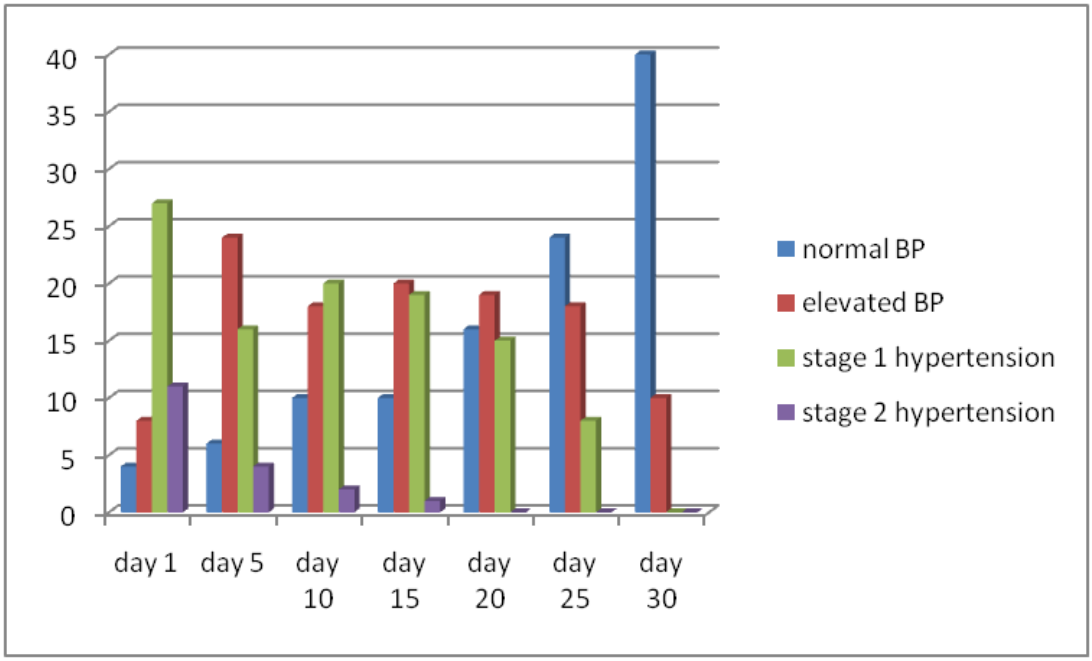
Table 1 shows age of the patients

Age group	Total number of patients	Number of patients with atenolol treatment	Number of patients with combination therapy
0-18	0	0	0
19-60	70	32	38
>60	30	18	12
Total	100	50	50

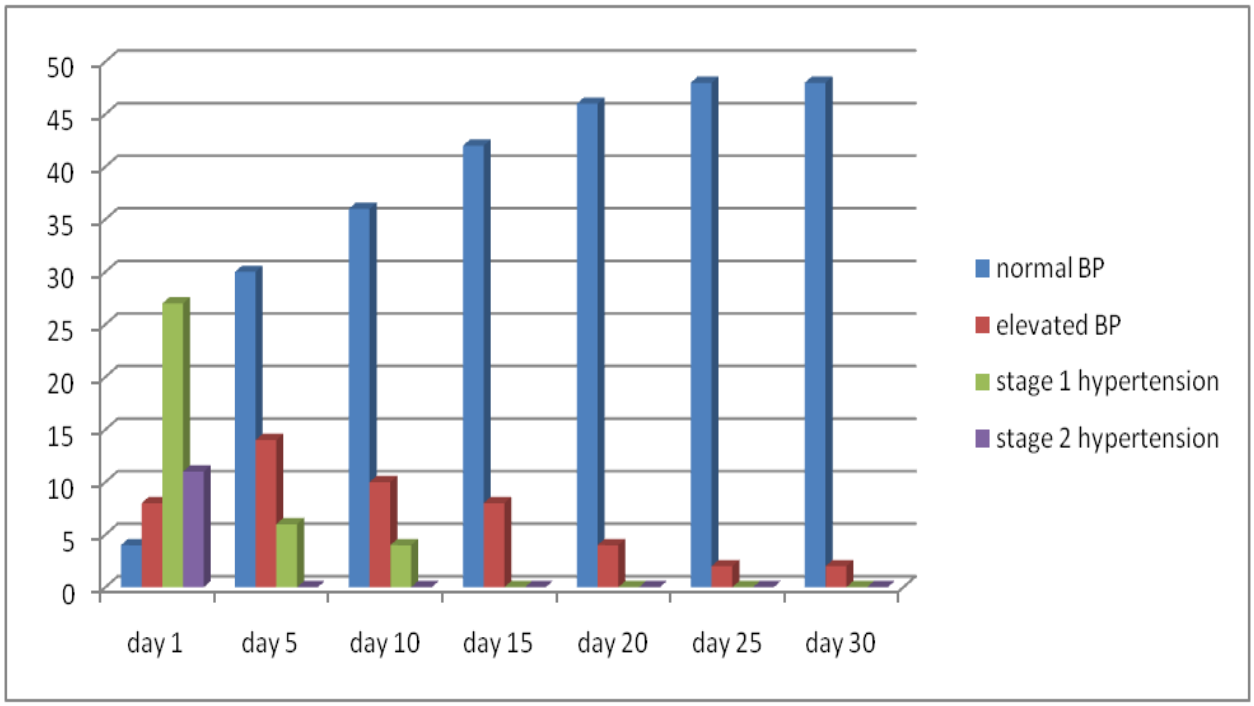
Table 2 shows blood pressure of the patients on different days of the study.

	Atenolol treatment				Combination therapy			
Visits	Normal BP	Elevated BP	Stage 1 Hypertension	Stage 2 Hypertension	Normal BP	Elevated BP	Stage 1 Hypertension	Stage 2 Hypertension
Day 1	4	8	27	11	4	7	30	9
Day 5	6	24	16	4	30	14	6	0
Day 10	10	18	20	2	36	10	4	0
Day 15	10	20	19	1	42	8	0	0
Day 20	16	19	15	0	46	4	0	0
Day 25	24	18	8	0	48	2	0	0
Day 30	40	10	0	0	48	2	0	0

Graded as per 2017 Hypertension classification. [5]



Graph 1 shows Comparison of blood pressure of patients on atenolol treatment at selected intervals
Note: number of patients on y axis and day on x axis.



Graph 2 Shows Comparison of blood pressure of patients on combination therapy at selected intervals
Note: number of patients on y axis and day on x axis.

DISCUSSION

This is an observational study in which the efficacy and tolerability of atenolol and that of combination of Amolodopine and Atenolol in the treatment of hypertension is compared. Subjects are either are given atenolol 50mg tablet once daily or a combination of amolodopine 5mg and atenolol 50mg tablet single dose daily. According to McGill JB et al, once daily betablockers have good patients

compliance in mild to moderate hypertension. According to Barrett J, et al, increasing the dose of amolodopine dose from 5mg to 10mg notably decreases blood pressure in older patients. [7, 25, 12]

Table 1 shows the age distribution of the patients. Most of the patients are in the age group of 19 to 60 years (70%). 30% of the patients are above 60 years.

The objective parameters i.e recording of blood pressure is done daily for one month, patient is first asked to relax for 10 minutes and blood pressure is recorded in laying position. Patients are also asked about daily intake of medicine, any adverse effects or any symptoms of hypertension.

Table 2 shows blood pressure of all patients noted at different days of the study. Baseline blood pressure readings of all patients is taken on day 1. On day 5, 11 patients had stage 2 hypertension in atenolol treatment group of patients and 9 patients in combination therapy group. At day 10, 20 patients on atenolol treatment and only 4 patients on combination therapy had stage 1 hypertension. At day 20, 19 patients on atenolol treatment and 4 patients on combination therapy had elevated blood pressure. At the end of the study i.e on the day 30, 40 patients shown normal blood pressure in atenolol group as compared to 48 patients in combination therapy group. There was a gradual decrease in the blood pressure levels as the study progressed in all patients, but more faster decline in blood pressure is seen in combination therapy group of patients than in atenolol alone treatment. At the end of the study, most of the patients were maintaining normal blood pressure level with their respective treatments.

Bar graph 1 and 2 shows the comparison of blood pressure recordings of all patients on atenolol therapy and combination therapy respectively at different days of the study. In both the graphs, there is decline in blood pressure levels as the study progress, more in combination therapy.

Adrenergic Receptor Antagonist

β blockers are one of the main group of drugs used in hypertension. β blockers acts by antagonism of adrenergic receptors that causes reduction in myocardial contractility, heart rate, and cardiac output leading to fall in blood pressure. β blockers decreases the production of circulating Angiotensin II by acting on adrenergic receptors of the juxtaglomerular complex of kidney. β blockers are mild antihypertensive drugs and their effects last for 24 hour with single dose. According to Aursnes I, et al, atenolol caused decrease in heart rate is associated with increased cardiovascular events and stroke in hypertensive patients. Atenolol is associated with glucose intolerance particularly in diabetics, that's why it is not use as first line drug in hypertensive patients. According to Ibrahim MM, et al, Even better other β blockers are also available like metropolol than atenolol. Low-dose thiazides diuretics are preferred first-line drugs, next is calcium channel blockers and next to calcium channel blockers are β blockers. According to Morgan TO, et al, atenolol is not preferred as reference drug, sounds logical as compared to this study. [20, 19, 31, 17, 30, 36, 6, 35, 23, 37, 11, 9, 21, 28, 24]

Calcium channel blockers (CCBs)

Calcium channel blockers causes fall in blood pressure by inhibition of calcium influx in vascular smooth muscles leading to vasodilatation. The difference in different calcium channel blockers in the selectivity for arterial, venous or heart muscles cells, results in the variations in their actions that decides the choice of a particular calcium channel blocker in different hypertensive conditions. Nifedipine has less cardiac muscles effects in relation to verapamil and diltiazem. They have equal ability to prevent stroke in hypertensive patients as compare to ACE Inhibitors. According to Barrett J, et al, amolodopine has shown good response in the treatment of hypertension with diabetes or renal dysfunction patients. [1, 2, 37, 8, 10, 27, 33]

BPV, blood pressure variations occurring in minutes, hours or days throughout in the patients, significantly effects the cardiovascular outcomes. Usually it is less with amolodipine treatment as seen in different studies, In this study, blood pressure variations is more with atenolol therapy group of patients as compared to combination therapy. [32, 16, 23]

Combination of amolodopine and atenolol is commonly used for the control of blood pressure, not controlled by single drug therapy. Presently, maximum number of hypertensive patients are in the need of combination therapy to maintain normal blood pressure. Combining different groups of drugs has higher efficacy in reduction of blood pressure as compared to increasing the dose of single drug. According to Wald DS, et al, combination of amolodopine and atenolol have superior effect on

reduction in blood pressure, blood pressure variations and end organ damage than single drug therapy. UV-spectrophotometric is used to calculate the dose of individual drug in different combinations in different studies. According to Boutouyrie P, et al, Combination of amolodopine and valsartan has greater central systolic blood pressure reduction compared to combination of amolodopine and atenolol. That means we got other better combinations of drugs than combination of amolodipine and atenolol. And certainly, combination of amolodipine and atenolol causes more reduction of blood pressure than atenolol alone. [29, 26, 34, 13, 14, 15]

CONCLUSION

Blood pressure levels were maintained at normal limits, more in combination therapy compared to atenolol alone therapy. Blood pressure variations were also less with combination therapy. Side effects were somewhat more in the combination therapy. Patient compliance was good.

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