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Original Research Article

Assessment of the Effect of Different Anti-Hypertensive Medications on Hemodynamic and Renal Parameters in Hypertensive Patients: A Comparative Study

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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 in collaboration with Department of Medicine, Darbhanga Medical College, Darbhanga, Bihar, India. Total 160 patients with hypertension were included in the study. These patients were assigned to one of the 4 groups randomly. There were 40 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: 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. 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 was seen by Atenolol followed by amlodipine, enalapril & thiazide. The effects of drugs on mean heart rate before & after were studied. Mean change in blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease was seen by Atenolol followed by enalapril, amlodipine & thiazides.

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

Introduction

Hypertension (HTN) – also known as high blood pressure (BP) – is a significant medical illness in which the arterial BP remains consistently high, with a systolic BP (SBP) of 140 mmHg or higher or a diastolic BP (DBP) of 90 mmHg or higher. [1] The World Health Organization has identified HTN as one of the most important risk factors for morbidity and mortality worldwide, with roughly 9 million people dying each year. [2] Even though other risk factors play a role, poor diets, such as excessive salt consumption, a diet high in saturated fat and trans-fats, low intake of fruits and vegetables, physical inactivity, tobacco/alcohol use, and being overweight/obese, appear to be the most common contributing factor to HTN. Non-modifiable risk factors include a family history of HTN, elderly age, and comorbidities such as diabetes or kidney disease. [3] According to recent analysis and observational research, people in Western countries have a higher prevalence of HTN and higher BP levels than those in other parts of the world, and this disparity is narrowing as non-Westerners adapt to Western culture and lifestyle. [4]

HTN continues to be the greatest cause of premature mortality, affecting roughly 1.13 billion people

globally and accounting for nearly 45% of deaths due to heart disease, 51% of deaths due to stroke, and 85%-95% of patients with chronic kidney disease (CKD). [5] The overall prevalence of HTN in India was 29.8% from 1950 to 2014, according to data, and a meta-analysis of prior Indian prevalence studies showed a considerable increase in the incidence of HTN from the 1960s to the mid-1990s.[6] HTN prevalence studies in urban and rural populations from the mid-1990s to the present show a growing trend, with a bigger increase in urban (33.8%) than rural (27.6%) populations. [6]

Blood pressure is the force exerted by the blood against any unit area of the vessel wall. The systolic arterial pressure is the Maximum pressure in the arteries during systolic phase and diastolic pressure depends upon cardiac output and peripheral vascular resistance. It has long been recognized that mortality and morbidity increase as both systolic and diastolic blood pressure rise. This may lead to changes in heart rate. [7] Hypertensive cardiovascular diseases are a major public health challenge, representing 10% of the global burden of disease. The annual number of deaths caused by cardiovascular disease is expected to rise by more than 33% over the coming two or three decades. Hypertension is among the most important modifiable risk-factors for cardiovascular diseases. Antihypertensive drugs are available which can prevent, or postpone myocardial infarction and stroke. Several clinical trials and systematic reviews have addressed this issue, but have failed to convincingly show that one or more drug-classes are superior to the others. [8]

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 in collaboration with Department of Medicine, Darbhanga Medical College, Darbhanga, Bihar, India for 12 months. Total 160 patients with hypertension were included in the study. These patients were assigned to one of the 4 groups randomly. There were 40 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 was recorded manually while doing selection for study. If blood pressure recorded is equal to or more than ≥ 140/90, then only patient was included in the study. After that, these 160 patients was divided in 4 groups I, II, III, IV. Each cohort contained 40 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 was recorded. Same procedure was repeated after 4 months from selection of patients for study. Data was 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.

Inclusion Criteria

1) All newly diagnosed hypertensive patients were included in study.

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

Exclusion Criteria

1) All patients having emergency condition like myocardial infarction, stroke was not included in study.
2) All pregnant patients were excluded from study.
3) Patients with nephropathy were excluded from the study.
4) Patients who were not ready to give consent were excluded from study.

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 ± 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)		P-value
	Before (Mean + SD)	After (Mean +SD)	
Group I Amlodipine	158.42+ 4.86	112.68+7.43	<0.05
Group II Atenolol	170.65+22.48	114.26 +8.52	<0.05
Group III Enalapril	202.52+3.62	126.64 +8.62	<0.05
Group IV Thiazide	192.42+22.28	129.71 +12.28	<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)		P-value
	Before (Mean + SD)	After (Mean +SD)	
Group I Amlodipine	112.58+14.26	88.64+7.43	<0.05
Group II Atenolol	110.70+22.48	82.42 +8.52	<0.05
Group III Enalapril	106.44 +24.66	90.68 +8.62	<0.05
Group IV Thiazide	105.45 +22.28	88.60 +12.28	<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, thiazides and enalapril.

Table 4: Comparison of effect of drugs on heart rate

Groups	Mean heart rate		P-value
	Before (Mean + SD)	After (Mean +SD)	
Group I Amlodipine	84.06 +14.28	74.66+7.40	<0.05
Group II Atenolol	72.42+24.46	69.92+8.52	<0.05
Group III Enalapril	84.96 +22.68	82.18 +8.72	<0.05
Group IV Thiazide	82.68 + 24.26	76.04 +12.28	<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 amlodipine followed by thiazides & Atenolol.

Discussion

Hypertension is a risk factor for cardiovascular disease – uncontrolled hypertension increases the relative risk from two to four times for coronary disease, stroke, heart failure, peripheral arterial disease, renal insufficiency, atrial fibrillation and dementia/cognitive impairment. Undoubtedly, poorly controlled hypertensive patients have an increased risk for cardiovascular complications. [9] Its prevalence continues to increase with age. Consequently, in subjects over 70 years, the prevalence of hypertension reaches 60–70%. [10] Before 1995, almost all randomized trial evidence on hypertension management related to diuretic agents and to a lesser extent bblockers. [11] 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 β-blocker with a diuretic.

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. 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, thiazide and enalapril. In the study by Psaty BM et al [12] 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. 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.

A Cochrane review revealed the inferiority of first-line β-blockers in prevention of death compared with CCBs and stroke compared with CCBs or renin-angiotensin system inhibitors for hypertension. [13] In another meta-analysis of 147 randomized trials by Law et al [14] β-blockers were associated with an 18% higher risk for stroke compared with other antihypertensive drugs. In a meta-analysis of 123 studies that included 613 815 people, β-blockers, mostly atenolol, were inferior to other antihypertensive drugs in reducing major cardiovascular events, stroke, and renal failure. [15] 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. [16] 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. [12] The risk of developing these complications is continuous, starting at a blood pressure (BP) level as low as 115/75 mm Hg. [17]

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. [18] 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. [19]

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. [20,21] 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. [22,23]

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. 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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