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Study on Essential Hypertensive Drugs and their Compliance

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ABSTRACT

Hypertension (HTN) affects approximately 1 billion people worldwide. The prevalence of HTN increase with age and even further unless broad and effective preventive measures are implemented. Age, obesity, lifestyle, smoking and alcohol use play significant role in prevalence of essential HTN. The use of antihypertensive drugs was observed in overall population. Out of total 156 patients, the distribution of Antihypertensive Agents (AHA) were- Calcium Channel Blockers (CCB) (65%), Beta Blockers (BB) (52%), Angiotensin converting enzyme inhibitors (ACEI) (19%), Diuretics (28%) and Angiotensin Receptor Blockers (ARB) (9%). Among individual drugs, 102 patients were on Amlodipine, 39 on Hydrochlorothiazide, 82 on Atenolol, 14 on Losartan, and 30 subjects were on Enalapril. With respect to overall utilization, Calcium Channel Blockers (Amlodipine) were observed to be the most frequently prescribed AHAs, Beta Blockers (Atenolol) ranked second followed by Angiotensin converting enzyme inhibitors (Enalapril), Angiotensin Receptor Blockers (Losartan) and Diuretics (Hydrochlorothiazide). Within each class of AHA used the most frequently used were Calcium Channel Blockers, (Amlodipine- 97.14% and Nifedipine- 2.86%) followed by Beta Blockers (Atenolol) 97.6% and Metoprolol 2.4%, Angiotensin convertin enzyme inhibitors (Enalapril 96.77% and Lisinopril 3.23%), Diuretics (Hydrochlorothiazide 88.63% and Loop Diuretics 11.35%), Angiotensin Receptor Blockers (Losartan). Both in monotherapy and combination therapy, the most preferred AHA remains Amlodipine. In combination therapy, the most extensively used combination was Amlodipine with Atenolol. Calcium Channel Blockers were appropriately prescribed in significant number of patients above 50 years. Angiotensin Receptor Blockers account for a very small proportion of drug use profile, which may be due to the high cost and lower availability of these drugs.

Key words: Hypertension, Essential hypertension, Compliance, Antihypertensive agent.

Introduction

Hypertension (HTN) is the term used to denote elevated blood pressure. It is defined as the condition in which the blood pressure remains consistent to Systolic Blood Pressure (SBP) >140mm Hg and Diastolic Blood Pressure (DBP) > 90mm Hg.¹ HTN can lead to heart disease, kidney disease, ocular disease or blindness and stroke. HTN is one of the major public health problems in Bangladesh.

High blood pressure is called "the silent killer" because it usually has no symptoms. Some people may not find out they have it until they have trouble with their heart, brain, or kidneys². Arterial

HTN, which is one of the main causes of coronary vascular disease, is responsible for nearly 20% of all deaths worldwide (nearly 10 million). These are the principal cause of death in all developed countries accounting for 50% of all deaths and are also emerging as a prominent public health problem in developing countries, ranking third with nearly 16% of all deaths.³ There is a lack of representative data on the prevalence of hypertension in the Bangladeshi population. One meta-analysis conducted by Zaman and Rouf in 1999 on the prevalence of hypertension in the Bangladeshi adult population included studies from 1976 to 1994, and estimated the prevalence to be 11.3%.²

High blood pressure is a risk factor for death from cardiovascular causes such as heart attacks, heart failure, and stroke, but also from kidney failure and blood vessel disease^{4,5,6,7,8} with proper treatment however, this risk can be reduced. In randomized controlled studies of drug treatment of HTN, one-third reduced stroke mortality, whereas one-fourth reduced mortality from coronary artery disease.⁹

Arterial HTN (AH) is the most common cardiovascular disease and is a major public health problem in the world. It produces a marked effect on patients, relatives and society, either because of HTN per se or through its complications (stroke, heart attack, ischaemic heart disease, renal dysfunction and heart failure), which can produce premature death or permanent disability. The risk of developing a cardiovascular complication is higher when the individual combines HTN with other risk factors such as hypercholesterolemia/ dyslipidemia or smoking.³

It is known that more than 95% of hypertensive patients in the community are of essential (idiopathic/unknown) aetiology and only a small percentage has an identifiable cause (secondary HTN). Epidemiological evidence also shows that there are several factors which play an important role in the development, evolution and prognosis of arterial HTN, some of them non-modifiable, such as age, sex, heredity, and others modifiable, such as body weight, salt intake, alcohol intake, use of hormonal contraceptives and drugs retaining sodium, sedentary life and psychosocial factors.³

Researches have shown that it is highly advisable to reduce and maintain the blood pressure to normal due to the various complications that arise due to high blood pressure. For this purpose numbers of antihypertensive agents (AHA) are used. Different guidelines for the management of arterial HTN suggests various protocols to be

followed while using antihypertensive agents (AHA) for the treatment of different stages of essential HTN.

Besides using drug therapy for controlling HTN, lifestyle modification (also termed as non-pharmacological therapy) can help to control BP in many people with HTN. These changes are useful by themselves or when implemented in conjunction with drug therapy. They can enhance the efficacy of AHAs and decrease cardiovascular risks and reduce the number of required drugs and their dosage. Major lifestyle modifications shown to lower BP include weight reduction in those individuals who are overweight or obese.^{10,11}

Apart from all the above factors, patient's compliance to the therapy is the key factor. Compliance involves not only taking the prescribed medications but also adherence to follow-up appointments and maintaining the recommended lifestyle modifications. Furthermore, the patient should be an active participant in the plan of care. Patients' knowledge of HTN and its complications is an important factor in achieving better compliance, and hence control.¹²

The objective of this study was to assess drug use pattern and compliance of antihypertensive agents in essential HTN, to assess the drug use pattern in terms of class and action of antihypertensive drugs, to evaluate the compliance of the antihypertensive agents used in terms of reduction in the blood pressure to goal BP and to evaluate the risk factors related to HTN and their effect on therapy.

Materials and Methods

The study carried out in the Department of Cardiology, TMSS Medical College & RCH, Bogra is a tertiary level hospital. This is a quantitative, prospective study involving review

of available documents and interviewing the patient during regular physician visits. The patients were followed up for their blood pressure change after 2 weeks of the interview. The patients with controlled blood pressure during the interview were not followed up. The total of 156 patients included in this study. The patients were selected randomly during the regular physician visits in out patient departments of TMSS Medical College & RCH. Data collection was done by developing a structured questionnaire for interview with the out patients and from the patient history records available at the hospital. Study Variables are age, sex, occupation, smoking/alcohol use status, hereditary links, Blood pressure status, Total No. of drug prescribed, No of classes of drugs prescribed, Compliance to the drugs used.

The collected data were coded as per variables and entered in SPSS data sheet and analyzed using the SPSS statistical software (SPSS for Windows, version 20.0). Pearson's chi- square tests were used to determine the relationship between the use drugs and patient demographics. Chi square analysis was also performed to evaluate the association between the variables. $P < 0.05$ was considered statistically significant.

Results

Table-1: Overall use of Anti-hypertensive agents

Anti-hypertensive agents	Frequency	Percentage (%)
ARB	14	9.0
ACEI	31	19.2
BB	85	54.5
CCB	105	67.3
Diuretics	44	28.2

Table-2: Drug use in Monotherapy (n=156)

AHAS used in monotherapy	Frequency	Percentage (%)
Diuretic	7	4.5
Calcium channel blockers	71	45.5
Beta-blockers	40	25.6
Ace-inhibitors	26	16.7
Ace-receptor blockers	12	7.7
Total	156	100.0

Table-3: Proportion of individual drugs used

Class of AHA	Individual drugs	Percentage (%)
CCB	Amaldepine	97.14
	Nefedipine	2.86
Diuretics	Hydrochlorthiazide	88.63
	Fruzemide+Spironolactone	11.36
BB	Atenolol	97.6
	Metoprolol	2.4
ARB	Losartan	100.0
ACEI	Enalapril	96.77
	Lisinopril	3.23

Table-4: Therapy received vs. control

BP status	Monotherapy No. (%)	Combination therapy No. (%)	Total No. (%)
Controlled	51(40.8%)	74(59.2%)	125(100.0%)
Uncontrolled	15(48.4%)	16(51.6%)	31(100.0%)

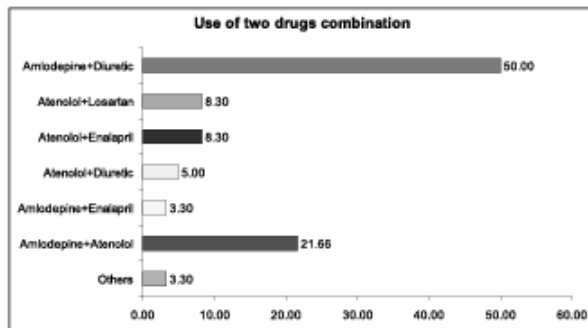


Fig. 1: Two drugs combination

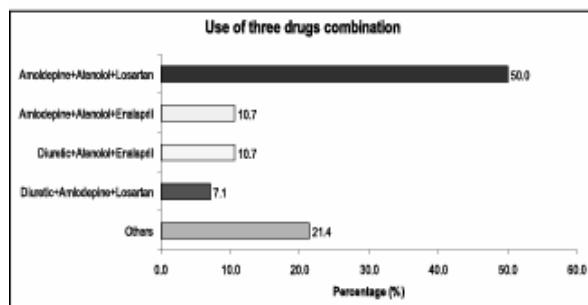


Fig. 2: Triple drug combination

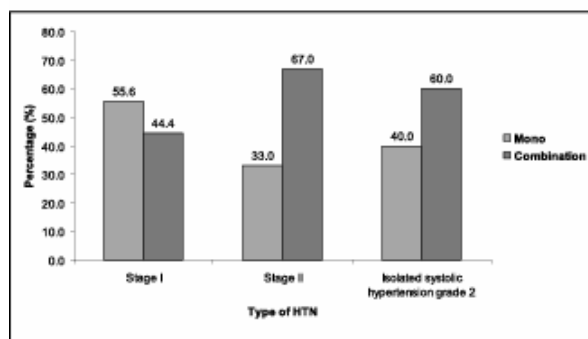


Fig. 3: Types of HTN vs therapy.

Table-5: Type of HTN vs. Therapy

Type of HTN	Therapy	
	Mono No. (%)	Combination No. (%)
Stage 1	35(55.60%)	28(44.40%)
Stage 2	29(33.0%)	59(67.0%)
Isolated systolic hypertension	2(40.0%)	3(60.0%)

Discussion

A total of 156 patients were included from the Department of Cardiology, TMSS Medical College & RCH from January 2010 to March 2010.

Among which 75 female and 81 male aged over 18 years were under medication for the treatment of essential HTN. The ratio of male to female was 1.32:1

Among the total sample, 40.4 % of 156 patients were diagnosed having stage 1 HTN, 56.4 % having stage 2 HTN and only about 3.2 % having isolated systolic HTN.

More than half of the total subjects included in this study had stage 2 HTN. It has been reported that increase in blood pressure occurs progressively through out the age and that about two third of the elderly can be defined as hypertensive with stage two HTN.

In this study more than 50% of the subjects fall under the age group >50 years .due to this greater proportion of above 50's patients the incidence of stage 2 HTN may have become greater. It was found that about 3% of the patients were of age group in the range of 20-29, 13% were between 30-39, 31% between 40-49, 29% between 50-59 and 24% of the patients were above 60 years of age. The result that the incidence of HTN is greater in patients above 50 years of age is supported by the longitudinal data collected over a 30-year period has shown that the prevalence of HTN increases with age.¹³

This study also showed that the proportion of stage2 HTN is high in the age group between 40-60 years. Stage 2 HTN is not observed in the age group between 20-30.the prevalence of isolated systolic HTN is highest in the elderly i.e. age >60. It was observed in a study that the incidence of HTN increases with age. In that too the incidence of stage 2 HTN is particularly high in above 40s group which supports the findings of European Working Party on High Blood Pressure In The Elderly Trial which suggests that the blood pressure increases progressively with age.¹⁴

But this association is not statistically significant at $p=0.057$, $p>0.05$. The study showed that 52% of the subjects were not engaged in any job whereas 31 % have jobs of sedentary nature and only 17 % have jobs, which include physical activity. This results shows that the incidence of HTN is less common in patients who have jobs

that involve physical activity that those that led sedentary lifestyle. The highest percentage of the patients was without jobs. They were either housewives or retired and stay home. This could be because international guidelines suggest that regular physical activity is also one of the factors responsible for BP lowering in hypertensive patients so the result meets the hypothesis that HTN is related to the life style relating to occupation.^{15,16,17}

Weight, height and blood pressure were recorded during the visit. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. BMI of 27.8 kg/m² for men and 27.3 kg/m² for women was considered obese.

It was observed that out of 156 subjects included in the study, 54% were overweight, and 8% were obese. 37% forms the group with normal BMI and very small percentages were under weight. The highest percentage of the hypertensive group falls under the category of overweight. BMI greater than 24.9-kg/sq m is a contributing factor the essential HTN and obese/overweight people are more prone to have elevated blood pressure. The result confirms to the previous findings that HTN is associated with BMI or weight.

As for the use of alcohol, 5.1% are using alcohol although they are aware that they have HTN, 59.6% have not used alcohol ever, 5% of the subjects used to take alcohol but have left now, and 10.3% used to take alcohol but have reduced their amount and frequency after the diagnosis. Though smoking is one of the risk factors for HTN, 98 patients have never taken up smoking ever. This group mostly consists of housewives. About 29% use to smoke but have left after the diagnosis. 5% have not quit smoking though they know they have HTN whereas 3.2% have reduced their no of sticks per day. The percentage of the smokers who have left forms 29%. Smoking contributes to elevated blood pressure due to higher level of thromboxane which is a

vasoconstrictor though no specific data is available about its being the cause of HTN. Since smoking directly affects the lungs there is maximum chance of it to affect the circulatory system. International guidelines suggest cessation of smoking as one of the major step in improving the lifestyle for the reduction of the blood pressure.¹⁸

In overall observation i.e. in both monotherapy and combination therapy the highest use antihypertensive drug is CCBs 67% followed by beta blockers 54%, diuretics 28%, ace inhibitors 19.8% and ace receptor blockers 9%. British HTN society guideline (BHSg) recommends use of either [ACEI or BB] or [CCB or Diuretic].¹⁸

The result obtained indicated the high use of CCBs. This may be because the subjects were chosen such that they had no complications and CCB is preferred in case of the treatment of hypertension with no complications. This may also be because of the easy availability, physicians prescribing trend or may even be affected by heavy promotion of the drugs by the manufacturer. It was also observed that physicians follow the British guideline and the pattern meets the guidelines suggested by BHSg.

It was observed that out of 105 subjects, who were on CCBs, 102 were prescribed amlodipine and only 3 were prescribed Nefedipine. Similarly, out of 41 subjects on diuretics 39 were prescribed Hydrochlorthiazide and 5 were prescribed Frusemide, out of 84 subjects on beta blocker 82 were prescribed atenolol and only two were prescribed Metoprolol, out of 14 subjects who were prescribed ARB, all were prescribed losartan, and out of 31 subjects on ACEI, 30 were prescribed enalapril and only one was prescribed Lisinopril. Atenolol, amlodipine and enalapril were found to be the most extensively used AHAs. This could be due to the easy availability and physician trend in the hospital. Also that most of the combination regimens include atenolol or amlodipine. This use also meets the

recommendation made by the BHS¹⁸.

In 66 patients receiving monotherapy, the most prescribed AHA is CCBs 45.45%, then 25.8% were prescribed beta-blockers, and 16.7% were on ace inhibitors. Only 4.5% and 3% were on ace receptor blockers and diuretics respectively.

This indicated the high use of CCBs when monotherapy for essential HTN is concerned, followed by BB and ACEI. Since a major proportion of the sample comprises of the above 50 years age group, the use of CCB has been extensively done because drug of choice for the patient above 55 years of age is CCB or Diuretic. Diuretics are not as much used, as it should be because of the reason including heavy promotion of other medications and the perception that diuretics produce adverse metabolic effects and do not reduce coronary heart disease events.¹⁹ As far as a specific drug for monotherapy is concerned; recommendations have been very flexible. Researches have also shown that there is a very minor gain in switching the drugs between ACEI or BB and CCB or Diuretic.¹⁸

The study showed that out of the total subjects included in the study, 42.3% were on single drug therapy, 38.5% were on two-drug therapy, 17.9 % were on triple drug therapy and only 1.3 % was on four drugs. The use of single and two-drug therapy is higher in proportion (80.8%). HTN guidelines suggests the use of single drug initially and to add up according to the patients response to the drug. The use of triple drug therapy is mainly low in proportion and is only used in cases when the double drug fails to achieve the goal BP. The use of 4 drugs for the treatment of HTN seems irrelevant and also doesn't meet the recommendations of the guidelines. But in some cases due to the physiological requirements and in emergency cases, the physicians add four-drug combination.

Out of 60 subjects, in which two drug combination were used, 50% of the subjects got

the combination of amlodipine and atenolol followed by amlodipine and diuretic (21.66%) and amlodipine and enalapril (8.3%) and atenolol and diuretic (8.3%) and the least used were atenolol and enalapril (5%) and atenolol with losartan (3.3%).

Two drugs therapy are used only when single drug combination fails to achieve target BP. The choice of drugs in combination therapy was seen to include conventional drugs and there was little impact of the newer drugs on prescribing. This may mainly be due to the unavailability of the newer molecules.¹⁸ The highest prescribed combination of three drugs is amlodipine atenolol and enalapril - (CCB+BB+ACEI) 50% of all the subjects in which three drug combination were used followed by the combination of amlodipine+atenololo+losartan (10.7%).

Use if three drug combinations were initiated in stage 2 hypertension only when the two-drug combination fails to lower the BP to goal BP. In most of the cases ACEI was added after the combination of atenolol and amlodipine was insufficient.

Out of 81 male patients, 65 have blood pressure controlled at goal blood pressure of SBP<140mm Hg and DBP<90 mm Hg and 16 have BP greater than goal BP. Similarly out of 75 female patients, 60 have their BP controlled to goal BP and 15 have BP greater than goal BP. There is no association between the controls in BP to goal BP with the sex of the patient ($p=0.561$, $p>0.05$). The overall compliance of the patients does not appear to be affected by age or sex.²⁰

Out of 125 patients who have controlled HTN 74(59.2%) patients were on combination therapy and 51(40.8%) were on mono therapy whereas out of 31 patients with uncontrolled HTN 15(48.4%) were on monotherapy and 16(51.6%) were on combination therapy.

The results showed the higher proportion of the subjects with the controlled blood pressure were

on combination therapy. But this result could be affected by the result obtained previously that combination therapy is mostly prescribed in stage 2 HTN. The control is related to the type of HTN of the subjects and the prescribed therapy. The blood pressure was effectively controlled by combination therapy rather than by monotherapy while keeping the diagnosis controlled.

The result shows that in the patients with stage 1 HTN, 55.6% were prescribed monotherapy and 44.4 % were prescribed combination therapy. Similarly inpatients with stage 2 hypertension 67% were treated with combination therapy and 33% were treated with monotherapy and in patients with isolated systolic HTN 40% were treated with monotherapy and 60% were treated with combination therapy.

In large proportion of stage 2 HTN (67%), combination therapy is used than in stage one HTN, which is only 44.4%. BHSG also recommends the use of combination therapy in stage 2 HTN. The use of monotherapy is not adequate for the control of stage 2 HTN. The use of combination therapy in isolated systolic HTN is relevant because systolic HTN is difficult to control and combination therapy is appropriate.

The use of combination therapy is initiated in stage 1 HTN only when the monotherapy fails to achieve goal BP. The over all use of combination and monotherapy in different stages of HTN meets the recommendation of BHSG.¹⁸ There is a significant association between the type of therapy used and the type of hypertension ($p=0.012$, $p<0.05$).

Conclusion

The evidences observed in this perspective study showed that CCBs, BBs and ACEIs were the most used classes of AHAs in both monotherapy and combination therapy. Among these different classes also specific drugs like Amlodipine, Atenolol, and Enalapril occupy a large proportion

of the prescription. Multiple drugs were often used to control the stage II HTN and the combination of amlodipine (CCB) and atenolol (BB) was extensively used. The study also revealed that the effectiveness of the therapy is independent of the use of the class of the drug. The hospitals were more inclined to prescribing for the treatment of essential HTN. The major classes of antihypertensive agents- diuretics, blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor antagonists are suitable for the initiation and maintenance of therapy. Apart from the use of drugs for the control of BP, patients should be highly motivated to apply life style modifications, which should continue even if the patient is taking anti hypertensive agent.

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