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CURRENT DIVERSIFICATION IN THE SELECTION OF MOLECULE(s) FOR THE TREATMENT OF HYPERTENSION

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Abstract: The study was carried out on the current diversification of antihypertensive drugs prescribed for the treatment of hypertensive patients irrespective of age and sex in the Government Hospitals of Khulna city, Bangladesh. The study covered only the indoor hypertensive patients. The frequency of hypertension was found maximum with patients above 40 years of age. The study showed that the prevalence of hypertension was more common in females compared to males. Among the therapeutic classes, Calcium channel blockers (CCB) were used most frequently (27%). Diuretics (25%) and Beta-blocker (24%) fell in the 2nd and 3rd position respectively. ACE inhibitors (18%) were also used frequently, but angiotensin-II antagonist, alpha-blocker and centrally acting antihypertensive drugs were used only in limited cases. Both combination therapy (57%) and monotherapy (43%) were used for the management of hypertension. Among the combinations, diuretics and ACE inhibitors combination was prescribed in most cases (20%). There was no combination of two or more molecules under the same therapeutic class. In case of mono-drug therapy metoprolol was used most frequently (25%) which was followed by amlodipine (20%) and nifedipine (18%). When individual drug molecules irrespective of their use either in combination or as single drug were taken into account, it was found that furosemide was most frequently (21%) used. Amlodipine (16%), nifedipine and atenolol (13%) followed furosemide.

Key words: Antihypertensive, hypertension

Introduction

Hypertension is the most common chronic health problem in Western society (Walker and Edwards, 2000). Hypertension is a major risk factor for atherosclerotic-related diseases, which include coronary and cerebrovascular disease. These diseases are the commonest cause of morbidity and mortality in industrialized nations. Hypertension is extremely common, affecting 20-25% of the middle-aged and elderly populations. Complications of hypertension lead to stroke, dementia, myocardial infarction, angina, CABG or angioplasty, peripheral vascular diseases, fundal hemorrhages, proteinurea, renal impairment etc (Ramsay *et al.*, 1999). Clinical consequence of hypertension is related to end organ damage with effect on the heart, brain, peripheral vasculature, kidneys and eyes. Hypertension is also a significant risk factor during pregnancy, causing both maternal and perinatal morbidity and mortality. Conventional management of hypertension leaves patients at an unacceptably high risk of cardiovascular complications and death, particularly from coronary heart disease (CHD) but also from stroke (Collins, 1990; Isles, 1986; Clausen and Jenson, 1992; Thurmer *et al.*, 1994; Merlo, 1996; Andersson, 1998). Effective management of hypertension does significantly reduce the risk of stroke, heart failure, morbidity and mortality.

The prevalence of cardiovascular disorders especially hypertension is increasing alarmingly throughout the world, which varies with age, race, education and many other variables. Like the developed countries, prevalence of hypertension and other associated disorders are increasing in Bangladesh. A number of factors including change in lifestyle, change in nature of food intake, all types of anxiety, tension, environmental pollution etc. are assumed to be involved in contributing to increased incidence of cardiac disorders. For this the market size of cardiovascular drugs in Bangladesh has been increasing from Tk. 424 in million to 1,112

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million in the year 1996 to 2002 respectively (Annon, 2005). These values prove that the prevalence of cardiovascular diseases is also increasing gradually in Bangladesh.

There are many classes of antihypertensive drugs available and under each class there are many individual molecules which have relative indications and contraindications. The rational selection of antihypertensive drug molecule(s) from the current diversification will ensure the effectiveness of the 'hypertension management system'. The present work was designed to study the current diversification in the selection of molecules under antihypertensive therapeutic class in Khulna, Bangladesh. The study also attempted to investigate the rationality of selection of antihypertensive drugs for the management of hypertensives. Whether established guidelines are followed in the selection of antihypertensive drugs was also evaluated.

Materials and Methods

Target area: We targeted Khulna region for our study and selected one teaching hospital, Khulna Medical College Hospital and one generalized hospital, Khulna General Hospital, as our research sites. These two hospitals are the representative health care organizations with respect hypertension management of this region.

Data collection: Data were collected by the method of analytical epidemiological studies which means studies specially designed to investigate cause and percentage of use and abuse of antihypertensive drugs in Khulna region of Bangladesh. Six-months time was spent for collection of required data. Data collection was started in the month of January, 2002 and completed in the month of June, 2002.

Age and sex differentiation: The survey was not carried out according to sex and age differentiation. The data were collected irrespective of age and sex of patients admitted in the above two hospitals during the specified period.

Sample size: The sample sizes were statistically desirable, feasible and satisfactory and were approached randomly according to the standards (Lwanga and Lemeshow, 1991). We decided to take 300 prescriber-patient encounter data (prospective) from the two hospitals on the basis of a prepared format.

The questionnaire of the survey and data collection: Appropriate questionnaires were used to get information about the elements of drugs used for hypertension management which contained the 1. Physicians' profile; 2. Patient's profile; 3. Disease profile/history; 4. Drugs prescribed (current); 5. Drugs prescribed (previous); 6. Prognosis etc.

On the basis of the prepared questionnaires, data were collected from the indoor patients in Coronary Care Unit (CCU), Medicine Ward, Cabin, (both male and female). The required information was collected from the prescriptions as well as consultation with the Physicians, Patients and their relatives, Nurses, Pharmacists.

***Data entry and analysis*:** The data were interpreted by using MS OFFICE 2002 (a latest version) including MS Word and Excel. Data were analyzed by percentile method and is stated below.

$$\% = \frac{n}{N} \times 100$$

Where, n = number of observed sample;
N = number of total sample.

Results and Discussion

The collected data showed that the occurrence of hypertension was found to be highest (32%) with the age ranges between 41-50 years and the second highest (27%) occurred with patients of 60 and above. No hypertensive patient was found below 11 years (Table 1).

Table 1. Showing the percentage of hypertension on the basis of age.

Age (year)	Number of patients	Percentage of total patients
11-20	15	5
21-30	9	3
31-40	36	12
41-50	96	32
51-60	63	21
60+	81	27

It is evident that among the hospitalized hypertensive patients the number of female patients were more than males. On an average the age range of hypertensive females were lower than that of males (Table 2).

Table 2. Percentage of hypertension on the basis of gender.

Gender	Number of patients	Percentage of total patients
Male (20-95 yrs)	135	45
Female (17-83 yrs)	165	55

According to the therapeutic classes of antihypertensive drugs prescribed irrespective of mono- or combination therapy, it was found that these drugs were used both as single or combination therapy. Among the therapeutic classes, calcium channel blocker (CCB) occupies the highest position (27%). Diuretics and Betablockers are in the 2nd and 3rd position. ACE inhibitors are also used frequently. But angiotensin-II antagonist, alpha blocker and centrally acting antihypertensive drugs are used only in limited cases (Table 3).

Table 3. Different therapeutic classes of antihypertensive drugs prescribed irrespective of mono- or combination therapy.

Therapeutic class	Percent of total patients
Calcium channel blocker	27
Diuretics	25
Betablocker	24
ACE Inhibitor	18
Angiotensin II Antagonist	3
Alpha-blocker	2
Centrally acting	1

Table 4. Frequency of use of combination therapy and single drug therapy.

Antihypertensive therapy	Number of patients	Percentage of total patients (%)
Single Drug	129	43
Combination	171	57

Table 5. Different combination of antihypertensive drugs used during the study period.

Combination	Total number of patients	Percent of total patients
Diuretics + ACE Inhibitor	60	20
Diuretics + Betablocker +CCB	39	13
Betablocker + CCB	27	9
Diuretics + CCB	21	7
Diuretics + Betablocker	21	7
Betablocker + ACE Inhibitor	21	7
Diuretics + Betablocker + CCB+ACE Inhibitor	12	4
Diuretics + Betablocker + ACE Inhibitor	12	4
Diuretics + alpha-blocker + CCB	12	4
Diuretics + CCB + Angiotensin II Antagonist	12	4
ACE Inhibitor + Angiotensin II Antagonist	12	4
Diuretic + CCB +ACE Inhibitor + Angiotensin II Antagonist	12	4
Diuretics + CCB + ACE Inhibitor	6	2
Diuretics + alpha-blocker	6	2
CCB + Centrally acting	6	2
Diuretics + ACE Inhibitor + Angiotensin II Receptor Antagonist	6	2
Betablocker + CCB + ACE Inhibitor	0	0
CCB + ACE Inhibitor	0	0

Table 6. Single antihypertensive drugs used during the study period.

Single antihypertensive	Total number of patients	Percent of total patients
Metoprolol (Betablocker)	75	25
Amlodipine (CCB)	60	20
Nifedipine (CCB).	54	18
Atenolol (Betablocker)	27	9
Enalapril (ACE inhibitor)	21	7
Propranolol (Betablocker)	15	5
Furosemide (Diuretics)	6	2
Mannitol (Diuretics)	6	2
Spironolactone (Diuretics)	6	2
Thiazide + Amiloride (Diuretics)	6	2
Captopril (ACE inhibitor)	6	2
Methyldopa (Centrally acting)	6	2

In case of combination therapy, it was found that 57% hypertensives were given combined therapy, whereas 43% were treated with single drug i.e. monotherapy (Table 4). Among the combinations, diuretics and ACE inhibitor were used (20%) in most cases. Combination of diuretics, betablocker and CCB occupied the first position. Combination of more than three drugs were used for management of hypertension with 41% patients. The following two combinations (Betablocker + CCB + ACE Inhibitor and CCB + ACE Inhibitor) were not used at all (Table 5).

From the interpreted data, it was seen that 43% hypertensives were treated with single antihypertensive drug. Among the monotherapy metoprolol is most frequently (25%) used as antihypertensive as monotherapy. Amlodipine (20%) followed metoprolol whereas nifedipine followed amlodipine (Table 6).

When individual drug molecules irrespective of their use either in combination or as single drug were taken into account, it was found that furosemide was most frequently (21%) used. Amlodipine (16%), nifedipine and atenolol (13%) followed by furosemide (Table 6). On the other hand propranolol, prazosin, mannitol and methyldopa were used only in limited cases. In our study methyldopa was only used in hypertensives with pregnancy.

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