Prescription Pattern of Antihypertensive Drugs and Its interactions in a Tertiary Care Hospital: A Prospective Clinical Study

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Abstract

The study objective was to analyze the prescription patterns of marketed antihypertensive drugs in MNR hospital, Hyderabad Telangana. The study was carried out during June 2019 to November 2019. The case sheets of patients diagnosed with hypertension were collected and recorded. The demographic data, signs and symptoms were recorded. The therapeutic data was collected from the treatment chart and drug-drug interactions in the treatment were assessed by using Micromedex 2.0 software and rationality assessment was done using medical standard guidelines and statistical analysis were done using student's t test. During the hospital stay of 100 hypertensive cases 50 patients were male and 50 patients were female. It was observed that diuretics of about 30.63% were mostly prescribed to hypertensive patients. The calcium channel blockers is about 26.13%, combination therapy was used more when compared to mono drug therapy to maintain blood pressure. It was found that out of 100 patients 79 prescriptions were rational and 21 were irrational. During this study a total of 252 drug-drug interactions were found. Results revealed that the choice of anti-hypertensive drugs reasonably comply with the national and IGH guidelines. During the management of hypertension, diuretics were the first choice of agents used to treat hypertension. This confirms the best choice and is in compliance with the clinicians as per the standard guidelines.

Keywords: Diuretics; Hypertension, Kidney, Calcium channel blocker, Drug-Drug interactions

Introduction

Blood pressure is measured in millimeters of mercury (mm Hg) and is recorded as two numbers usually written one above the other. The upper number is the systolic blood pressure - the highest pressure in blood vessels and happens when the heart contracts, or beats. The lower number is the diastolic blood pressure - the lowest pressure in blood vessels in between heartbeats when the heart muscle relaxes. Normal adult blood pressure is defined as a systolic blood pressure of 120 mm Hg and a diastolic blood pressure of 80 mm Hg. However, the cardiovascular benefits of normal blood pressure extend to lower systolic (105 mm Hg) and lower diastolic blood pressure levels (60 mm Hg). Hypertension is defined as a systolic blood pressure equal to or above 140 mm Hg and/or diastolic blood pressure equal to or above 90 mm Hg. Normal levels of both systolic and diastolic blood pressure are particularly important for the efficient function of vital organs such as the heart, brain and kidneys and for overall health and wellbeing. Hypertension is an elevated Blood Pressure and perfuse to tissues & organs. Hypertension has been recognized as a

common cardiovascular disease & a major risk factor for congestive heart failure (CHF), ischemic heart disease, chronic renal failure and stroke [Kearney, 2005]. Hypertension is a disease of complex etiology, affecting 972 million people worldwide. Prevalence of HTN in India is reported to vary from 4% to 15% in urban and 2% to 8% in rural population. It is estimated that the worldwide prevalence of hypertension would increase from 26.4% in 2000 to 29.2% in 2025 [Shirley & Nagavi, 2007]. Recent studies in India showed that hypertension is emerging as a major health problem. It is directly responsible for 57% of all deaths due to stroke and 24% of all deaths due to coronary heart disease [Okonta, 2013].

The use of drugs in these patients must be rational; this implies that the appropriate drugs must be prescribed in the right dose, at correct time interval and for a sufficient duration of time [Igbiks, 2011]. The number of hypertensive patients is anticipated (expected) to increase to 1.56 billion according to ISH (2025). The main factors that responsible are lifestyle such as physical abeyant, high sodium diet and fatty food stuff, and consumption of high amount of alcohol, chewing & smoking of tobacco are major reasons for this increased incidence of hypertension, which is growing widely from developed countries to developing countries, such as China, India other countries(Figure-1 &2).

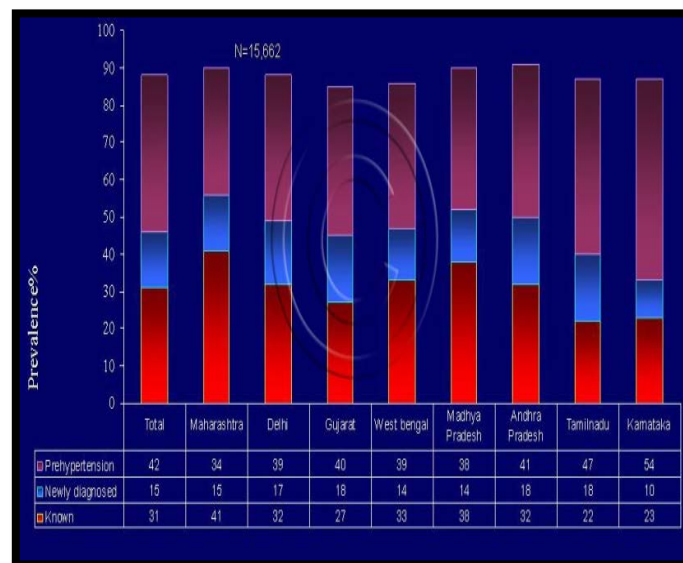Figure 1: Diagram showing the hypertension burden in world wide

Figure 2: Hypertension and Prehypertension and latest detection of hypertension in Indian population

Most patients with hypertension will require two or more drugs to control their hypertension and combination drug formulations may also be useful [Kale, 2013] (Table-1). The study mainly emphasizes on the evaluation pattern, extent, rationality and frequency of use of the antihypertensive drugs in the treatment of essential hypertension [Yuen et.al, 1998]. Non-pharmacological therapy is alone may be required for the management of Stage 1 hypertension. Effective lifestyle modification may reduce blood pressure as single drug therapy. The non-pharmacological treatments discovered a modest decrease in BP, numerous of these treatments is not used and, even though they are not controlled (Rajeev Gupta, 2010. Single drug should be started at first stage treatment for a little increase in BP. Initial treatment should be with a single drug of lower dose according to guidelines. If it is uncontrolled then full dose of the starting drug can be used or the patient and other pharmacological classes of drugs can be used. The blend of two pharmaceuticals with reduced doses is favored as initial treatment when starting blood pressure is in the range of grade II. In case of uncontrolled hypertension people and in the old age
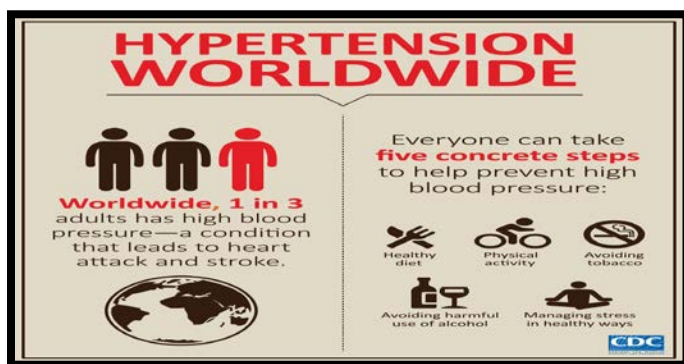
people, the drug therapy started slowly. Antihypertensive with sustained release is preferred (Table-1).

Table 1: The prescriptive pattern of various classes of Oral Anti-Hypertensive Drugs with dosage as per MOHFW.

Class	Drug	Usual dose range, Mg/d	Usual dally frequency
Thiazide diuretics	Hydrochlorothiazide	12.5-50	1
	Indapamide	1.5-2.5	1
Beta blockers (BBS)	Atenolol	25-100	1
	Metoprolol	50-100	1-2
	Propranolol	40-160	2
Angiotensin Ii antagonist (ACE inhibitors)	Ramipril Envas (Enalapril)	2.5-20 2.5-20	1 2
Angiotensin receptor blockers	Losartan	25-100	1-2
Calciumchannel blockers non-dihydropyridines	Nifedipine	30-60	1
CCBs-Dailydropyridines	Nifedipine	30-60	1
	Amlodipine	2.5-10	1
Central α 2 agoinsts and other centrally acting drugs	Clonidine	0.1-0.8	2
	Methyldopa	250-3000	2
Alpha-blockers	Prazosin	2.5-10	1

Table 2: Distribution of the patient pool on the basis of age and sex for hypertensive patients.

Age (Years)	Sex		% of HTN patients
	No. of Males	No .of Females	
20 - 29	2	2	2.67 (4)
30 - 39	8	6	9.33(14)
40 - 49	12	9	14(21)
50 - 59	19	13	21.33(32)
60 -69	14	21	23.33(35)
>70	24	28	34.66(52)
Total	75	75	100

Table 3: Prescriptive pattern of Mono drug regimen for hypertensive patients.

ug regimen	No. of prescriptions	%
Mono drug regimen		
Torasemide	2	4
Hydrochlorthiazide	1	2
Ramipril	4	8
Telmisartan	3	6
Metoprolol	6	12
Propranolol	5	10
Atenolol	2	4
Nebivolol	2	4
Furosemide	10	20
Amlodipine	15	30
Total	50	100

Table 4: Prescriptive pattern of two drug regimen for hypertensive patients.

Drug regimen	No. of prescriptions	%
Two drug regimen		
Telmisartan+Hydrochlorothiazide	11	23.91
Labetolol+Amlodipine	6	13.04
Ramipril+Metoprolol	3	6.521
Torasemide+Spironolactone	3	6.521
Ramipril+Amlodipine	1	2.173
Furosemide+Metoprolol	6	13.043
Telmisartan+Amlodipine	5	10.869
Losartan+Ramipril	3	6.521
Furosemide+Spironolactone	2	4.347
Amlodipine+Atenolol	2	4.347
Amlodipine+Hydrochlorothiazide	1	2.173
Amlodipine+Furosemide	3	6.521
Total	46	99.86

Table 5: Prescriptive pattern of three drug regimen for hypertensive patients

Drug regimen	No. of prescriptions	%
Three drug regimen		
Amlodipine+Furosemide+Ramipril	2	12.5
Furosemide+Losartan+Hydrochlorothiazide	1	6.25
Amlodipine+Metoprolol+Telmisartan	2	12.5
Amlodipine+Hydrochlorothiazide+Olmesartan	1	6.25
Ramipril+Torasemide+Spironolactone	1	6.25
Amlodipine+Furosemide+Spironolactone	2	12.5
Losartan+Hydrochlorothiazide+Metoprolol	2	12.5
Amlodipine+Metoprolol+Hydrochlorothiazide	3	18.75
Furosemide+Spironolactone+Ramipril	1	6.25
Amlodipine+Hydrochlorothiazide+Telmisartan	1	6.25
Total	16	100

Materials and Methods

This is a prospective study conducted in MNR hospital, Hyderabad, Telangana over 6 months on continuous assessment of prescribing patterns of various marketed antihypertensive drugs. The patients included were of Male and Female aged $\geq$ 18 years who have been diagnosed with primary and secondary hypertension in the hospital. The patients attending outpatient department and pregnant women were excluded in the study.

The study was done by reviewing and collecting the case sheets of patients who were diagnosed with Hypertension. Patient demographic details such as name, age, sex were collected before commencement of the study. Common and uncommon signs and symptoms observed in patients, past medical history of patients, family history were noted in the observation book. The habits such as smoking, drinking and other social habits of the patients were also noted. Therapeutic data such as drug name, dose, frequency and duration of therapy were collected from treatment charts. Drug interactions in treatment regimen of patients were assessed using drug data base Micromedex 2.0. Follow up of all patients were done until discharged from the hospital. Rationality assessment of the patient data were analyzed as per the guidelines of IHG-II and JNU 7 standard guidelines. The collected data were reported in the forms of patient profile, drug interaction and intervention.

Table 6: Efficacy of the marketed antihypertensive drugs on hypertensive patients during their tertiary care.

Blood Pressure (Mean ± SEM)	On admission	On discharge	P-value	t-value
Amlodipine				
SBP	128.8 ± 4.417	1010.1 ± 2.37	0.112	2.153
DBP	65.42 ± 3.18	71.16 ± 1.57*	0.013	2.514
Furosemide				
SBP	117.6 ± 5.61	119.3 ± 3.275*	0.0163	2.101
DBP	68.71 ± 3.152	67.57 ± 2.17	0.343	0.782
Amlodipine+Atenolol				
SBP	157.9 ± 8.12	110.3 ± 2.011***	<0.0001	4.125
DBP	91.92 ± 2.747	80.46 ± 2.503**	0.0051	2.939
Furosemide+Amlodipine				
SBP	147.0 ± 20.00	1.30 ± 9.50	0.415	0.689
DBP	60.00 ± 1.000	71.00 ± 4.000	0.28	1.415
Metoprolol+Furosemide				
SBP	1109 ± 10.00	125.0 ± 5.000	0.791	0.5154
DBP	80.00 ± 1.000	80.00 ± 1.000	1	0
Ramipril+Amlodipine				
SBP	112.0 ± 50.0	135.0 ± 5.00	0.618	0.202
DBP	41.00 ± 9.0	80.00 ± 5.00	0.69	0.385

All the values are expressed as mean ± SEM, *P<0.05, **P<0.01 and ***P<0.001 [Unpaired Student t test] as compared to blood pressure on admission.

Statistical Analysis

Statistical data analysis was done using the statistical program Origin Pro 7.5 version software. Continuous data were presented as mean ± SEM, while categorical data was presented as percentages. Differences between means of two groups were compared using student's t test. A P-value less than 0.05 were considered as statistically significant.

Results

During the hospital stay of 150 cases out of 75 male patients the majority were belonging to the age group of 70 and above age groups. The complete distribution of the patient's age wise and gender wise are depicted in Table 1.

The prescriptive pattern of the three drug regime were analyzed and tabulated the data in the Tables 3-5) The

different classes of antihypertensive drugs were prescribed to 150 in-patients during the study. During this period it was observed that mostly diuretics were prescribed for hypertensive patients followed by calcium channel blockers, β blockers, angiotensin receptor blockers, ACE inhibitors. During the study the results revealed that the mono drug regimen were prescribed more 50 (100%) in hypertensive patients followed by two drug regimen 46 (99.8%) and three drug regimen were 16(100%) prescriptions. The authenticity was determined using Medical standards JNC 7 and IGH guidelines. Out of 150 patients 79 (79%) patients were prescribed antihypertensive drugs rationally and remaining 21(21%) patients were prescribed antihypertensive drugs irrationally.

Efficacy Study of Antihypertensive Agents

During the hospital stay various types of antihypertensive drugs were prescribed to patients to reduce SBP (Systolic Blood Pressure) & DBP (Diastolic Blood Pressure). It was observed that Amlodipine significantly reduced DBP (P=0.0121), followed Furosemide reduced SBP significantly (P=0.0185) and a significant reduction was found in SBP (P=0.0023) on discharge when compared with respective BP on admission.

In combination therapy it was observed that significant reduction in SBP (P<0.0001) and DBP (P=0.0036) on discharge when compared with BP on admission respectively and other combinations like Amlodipine + Hydrochlorothiazide [Table 6].

Assessment of DDIs in anti-hypertensive prescriptions

During the study a total of 136 DDI's were found and recorded. Out of these 78 (57.35%) were major, 58 (42.64%) were moderate with little or no drug interactions. Out of 78 major DDI's 23 were of Aspirin+Clopidogrel and 9 DDI's of Albuterol and

Metoprolol and data was recorded as per the standard guidelines.

Discussion

A pattern based prescription study is considered to be one of the most effective methods for evaluating the prescribing attitude of physicians and pharmacists [Dalal,1980]. The increase in economic growth rate, India is not only facing the epidemic coronary artery diseases but also of obesity, diabetes mellitus and hypertension. Prevalence of hypertension is considerably increasing in India [Yusuf and Balogun, 2005]. This may be due to the age, environmental factors and life style. The prevalence of HTN in India is highest in age group nearer to sixties. Whereas in females in urban areas where as in rural areas an age related increase is seen in both the sexes in the age group 60 years to 64 years [Yusuf and Balogun,2005]. This is in context with our study where maximum numbers of patients were found in the same age group.

In our study most prescribed class of antihypertensive drugs majority were of diuretics followed by calcium channel blockers and β blockers. A similar study was conducted in Nigeria and has reported comparable results [Jhai,et.al.,2001]. As we know the diuretics constitute the most prescribed drug class according to JNC VII guidelines diuretics [Pat et.al., 1997]. In our study it was observed that majority of prescriptions containing combination therapy which was lower than recommendations and observations of several other studies demonstrated that the combination therapy was necessary in at least 60-70% of the study population for obtaining normal BP [WHO,1999]. Mono, dual and three combinations were recommended in our tertiary care hospital. Pharmacoeconomic considerations might be the reason which can be attributed to lesser inclination of physicians to go for combination therapy. A study indicated that 60% to 40% of patients received

combination & mono therapy respectively [Chobanian et.al, 2003]. On contrary, mono therapy was preferred for 51% of the patients in a Hong Kong study [Chalmers, 2002].

The study was assessed using JNC-VII and National Guidelines on Hypertension. The guidelines will provide the practitioners a standardized approach for safe and effective use of antihypertensive for prevention of hypertension. The assessment indicated that our hospital physicians were well adhered to both the standard guidelines i.e., JNC 7 and IGH. This was a good sign for controlling hypertension in patients with hypertension.

The study indicated the potential efficacy of mono and combination therapy. It was also observed that combination therapy showed significant raise in mean reduction in SBP and DBP. This again proves that a combination therapy has good control over hypertension. In contrast some of these combination therapies failed to show significant reduction in BP.

As we discussed above more than 50% of prescriptions were combination therapy, thus there was more possibility of DDIs and also various studies have shown that potential drug - drug interactions are frequent when patients receives multiple prescriptions [Bista., 2007]. In present study we found 136 DDIs in 100 prescriptions. These potential DDIs can be reduced in presence of clinical pharmacists which was already proved in a study conducted in Thailand [Janchawee, 2005].

Conclusion

The present study can be concluded that with time, the treatment strategies and prescription pattern need to be changed as per the patient profile. The results showed that the choice of anti-hypertensive drugs reasonably comply with the JNC 7 and IGH guidelines on the management of hypertension, which confirms a fairly good degree of compliance by clinicians with JNC 7 and IGH guidelines.

This study concludes the preferred use of diuretics, calcium channel blockers and β blockers as 1st, 2nd and 3rd choice of drugs for hypertension. It is believe that there is a need for improved patient awareness on medication and much more attention is required to the patients community by the clinicians to address the issues concerning to life style modifications. Further studies are warranted to addresses the issue related to various parameters required to maintain/reduce the levels of hypertension.

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