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A study on drug prescription pattern of antihypertensives in hypertensive patients with related comorbidities

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Abstract

Background: Hypertension (HTN) or high blood pressure is a chronic medical condition in which the blood pressure in the arteries is elevated. Hypertension is a cardiovascular disease that is not sufficiently prevented and controlled at both hospital and community levels. This has resulted in significant morbidity and mortality. Hypertension related complications manifest as target-organ damage which include cardiovascular disease and are the primary causes of the death in hypertensive patients. Organ systems adversely affected by the hypertension include heart, brain, kidneys, peripheral arterial disease and eyes.

Objectives: The objectives of this work is to study the drug prescription pattern in patients with hypertension and with related comorbidities (DM,STROKE,CKD,CVD) and to study the outcome of therapy in terms of reduction in blood pressure and also to educate the patients about disease and lifestyle adaptations.

Materials and Methods: It was a Prospective observational study done over a period of six months (November 2017 to April 2018) in Rajah Muthiah Medical College Hospital, Chidambaram, and Tamil Nadu. The study was approved from Institutional Human Ethics Committee. A 66 samples were collected from the clinically suspected patients diagnosed with hypertension along with comorbidities. The patient's blood pressure data, prescription data and other disease conditions of the patient are collected from patient case sheets and recorded into data collection form. Patient prescription and disease conditions were studied to collect the drug usage pattern.

Results: The results were obtained from 66 patients with hypertension along with co-morbidities, who were enrolled into the study after fulfilment of the selection criteria described above on obtaining consent from the same. Among the 66 patients, majority were male (59%) as compared to female patients (41%). Overall, 3 patients belong to the age group of 30-39 years, accounting for 4.5% of total. A total of 17 patients belonged to the age group of 40-49 years, accounting for 25.7% in total. A total of 28 patients belonged to the age group of 50-59 years, accounting for 42.4%. A total of 16 patients belonged to the age group of 60-69 years accounting for 24.2%. The remaining 2 patients belonged to the age group of 70-79 years accounting for the 3% of the total patients included in the study.

Conclusion: The benefit of blood pressure reduction with Antihypertensive drug treatment has become increasingly evident. Our study shows that Mono therapy was the most common approach in hypertension therapy. Enalapril was the most common drug used in both Mono therapy as well as other combinational therapies of hypertension and its co-morbidities. Cardio vascular disease is the highest prevalent co-morbid condition associated with hypertension accounting for 27.2%.The patients were counsel led about use of medication and life style modifications. As a result of patient counselling, there is a gradual increase in patient health condition in the majority of patients towards better control of disease and Quality of life.

Keywords: Hypertension, comorbidities, diabetes mellitus, stroke, CVD and CKD

Introduction

Hypertension is an important cause of a variety of cardiovascular and cerebrovascular disease and risk factors. It is still by far the leading cause of death from cardiovascular disease. Hypertension or high blood pressure, sometimes called arterial hypertension, is a chronic medical condition in which blood pressure in the arteries is elevated. Blood pressure is summarized by two measurements, systolic and diastolic, which depend on whether the heart muscle is contracting or relaxing between the beats. This equals the maximum and minimum pressure, respectively. Normal blood pressure at rest is within the range of 100-140mmHg systolic and 60-90mmHg diastolic.

High blood pressure is said to be present if it is often at or above 140/90mmHg. It is recommended that every hypertensive patient who also has other risk factors for coronary heart disease be given prompt and optimum antihypertensive treatment to minimize their overall risk for heart disease.

The study of prescription pattern is in fact, a part of medical audit involving monitoring and evaluation of various prescriptions of medical practitioners to ensure the rationality in medical care. This study therefore envisages the evaluation of pattern, extent, rationality and frequency of use of antihypertensive drugs in the treatment. The ultimate aim of antihypertensive drug therapy is to minimize or control the morbidity and mortality associated with persistent hypertension. The purpose of treating is to prevent complications and to improve patient survival.

Hypertension is a cardiovascular disease that is not sufficiently prevented and controlled at both hospital and community levels. This has resulted in significant morbidity and mortality. It is reported that blood pressure is under control in less than 20% of population with hypertension in many countries.

Over the past decade, antihypertensive prescribing patterns in elderly individuals with diabetes have changed in directions consistent with the evolving evidence base in Ontario, Canada. Also, there is evidence that physician management of hypertension in elderly Canadians became more aggressive between 1994 and 2002. This has resulted in satisfactory control of hypertension and reduction in hypertension-related morbidity and mortality.

Evaluating the drug prescriptions pattern of anti hypertensives in the hospital could help in making proposals that will streamline the treatment protocols in the hospitals to conform the national and international standards. Since there is no record of the past performance of the hospital in the management of hypertension, this research can serve as baseline for future assessments. The resulting gaps and updates identified could form a block of recommendations that will improve the care and management of hypertensive subjects in the hospital. Although elevated blood pressure cannot be linked to a known cause, there are certain risk factors.

Materials and Methods

This is a prospective observational study conducted in Department of Medicine, Rajah Muthiah Medical College Hospital, Annamalai University, Chidambaram, Tamil Nadu which is a 1400 bedded multi- speciality tertiary care university teaching hospital located in rural south India. Study duration was 6 months, from November 2017 to April 2018. The study was approved by Institutional Human Ethics Committee (IHEC). All the patients provided written informed consent prior to the interview.

Data was collected from the total of 66 patients, who visited the department of Medicine with Hypertension during the study period. The subjects taken for study are aged between more than 30 and less than 80 years old of both genders and diagnosed with hypertension; a systolic blood pressure reading ≥ 140 mm Hg and a diastolic blood pressure reading ≥ 90 mm Hg on at least two abnormal BP readings on different occasions and treated with anti-hypertensive medications.

The patient demographics, Blood Pressure data, disease conditions and treatment given were collected from patient case sheets and recorded into data collection forms. Patient prescriptions were studied to collect the anti-hypertensive drugs prescribed for the management of hypertension. For the drugs given in brand names, generic name is found and all the active ingredients are separated and recorded. The treatment provided for the hypertensive patients were compared to Joint National Committee 8 guidelines.

Patients receiving single antihypertensive medication were defined as receiving mono therapy; those who were receiving two antihypertensive medications were defined as receiving dual therapy; those receiving three antihypertensive medications are on triple therapy. Other drugs used along with the antihypertensives are also recorded. The 2017 AHA/ACC hypertension guidelines were used to classify the hypertension stages among the patients. The information extracted was entered in Microsoft Excel sheet and were analyzed as percentage and average.

Results

By applying inclusion and exclusion criteria, a total of 66 samples were enrolled in the study. The subjects are divided into 5 age trends and male and female is recorded separately. The study shows the comorbidity that shows maximum percentage is cardiovascular disease.

Table 1: Demographic Characteristics of Study Population

Gender	Number of Patients (N)	Percentage of Patients (%)
Male	39	59%
Female	27	41%
Total	66	100%

Table 2: Distribution of Study Population

Age (in Years)	Male	Female	Total (%)
30-39	2	1	3(4.5%)
40-49	10	7	17(25.7%)
50-59	15	13	28(42.4%)
60-69	11	5	16(24.2%)
70-79	1	1	2(3%)
Total	39	27	66(100%)

Table 3: Comorbidities of the Patients

Comorbidity	Number		Total	Percentage
	Male	Female		
Hypertension	9	7	16	24.2%
HTN+ Diabetes	6	8	14	21.2%
HTN+ Stroke	9	3	12	18.1%
HTN+ CKD	5	1	6	9.1%
HTN+ CVD	10	8	18	27.2%
Total	39	27	66	100%

Table 4: Classification of Hypertension

Classification	Blood Pressure			
	SBP(mmHg)	N	DBP(mmHg)	N
Normal	<120	4	<80	4
Pre-hypertension	120-139	6	80-89	4
Stage 1 Hypertension	140-159	18	90-99	21
Stage 2 Hypertension	≥160	38	≥100	37

Table 5: Drug Prescription Pattern of Anti-Hypertensives

Drugs	N	%
Diuretics	13	14.4%
β-Blockers	18	19.1%
CCB's	25	27.8%
ACEI's	36	38.7%
TOTAL	92	100%
Diuretics	13	14.4%
β-Blockers	18	19.1%

Table 6: Most Common Mono - Therapy (n=31)

Drugs	HTN		HTN+DM		HTN+Stroke		HTN+CKD		HTN+CVD	
	N	%	N	%	N	%	N	%	N	%
Enalapril	4	44.5%	4	40%	1	33.3%	2	50%	1	20%
Atenolol	1	11.1	2	20%	0	0	0	0	1	20%
Amlodipine	1	11.1	1	10%	0	0	1	25%	2	40%
Furosemide	1	11.1	1	10%	1	33.3%	1	25%	1	20%
Propranolol	1	11.1	1	10%	0	0	0	0	0	0
Nifedipine	1	11.1	0	0	0	0	0	0	0	0
HCT	0	0	1	10%	1	33.3	0	0	0	0
Total	9	100%	10	100%	6	100%	4	100%	5	100%

Table 7: Most Common Dual Therapy

Drugs	HTN		HTN+DM		HTN+stroke		HTN+CKD		HTN+CVD	
	N	%	N	%	N	%	N	%	N	%
Enalapril+ Atenolol	2	41.6	2	50	1	14.3	0	0	1	10
Enalapril+ Amlodipine	1	25	1	25	0	0	1	50	1	10
Enalapril+ Furosemide	1	16.6	1	25	2	28.6	1	50	6	60
Atenolol+ Amlodipine	1	8.4	0	0	3	42.8	0	0	2	20
Enalapril+ Metoprolol	1	8.4	0	0	1	14.3	0	0	0	0
Total	6	100%	4	100%	7	100%	2	100%	10	100%

Table 8: Most Common Triple Therapy

Drugs	HTN		HTN+DM		HTN+stroke		HTN+CVD	
	N	%	N	%	N	%	N	%
Enalapril + Atenolol + Amlodipine	0	0	1	100%	0	0	1	50%
Enalapril + Atenolol + Furosemide	1	100%	0	0	1	50%	1	50%
Enalapril + Amlodipine + Furosemide	0	0	0	0	1	50%	0	0
Total	1	100%	1	100%	2	100%	2	100%

Table 9: Other Drugs Prescribed in patients with Hypertension (N=16)

Drug	Dosage form	Dose	Frequency	No. of patients (n=16)
Paracetamol	Tablet	500mg	BD	10
Pantoprazole	Tablet	40mg	OD	7
Atorvastatin	Tablet	10mg	OD	9
Clopidogrel	Tablet	75mg	BD	5

Ciprofloxacin	Tablet	200mg	BD	11
Ranitidine	Tablet	150mg	BD	9
Metoclopramide	Tablet	10mg	TID	3
Fourtus-B	Tablet	300mg	OD	4
Rabeprazole	Capsule	20mg	OD	6
Pantoprazole	Injection	40mg	OD	8

Table 10: Other Drugs Prescribed in patients with HTN+DM

Drug	Dosage form	Dose	Frequency	No. of patients (14)
Metformin	Tablet	500mg	BD	11
Gemer	Tablet	2mg	BD	3
Syndopa	Tablet	225mg	6 times (1/2 a tab)	4
Ofloxacin	Tablet	2mg	BD	3
Ranitidine	Tablet	150mg	BD	10
Cefotaxime	Injection	1gm	BD	9
H. Actrapid	Injection	8u-8u-6u	TID	3
Paracetamol	Tablet	500mg	SOS	7
Pantoprazole	Injection	40mg	OD	5
Vitamin supplements	Tablet		OD	8

Table11: Other Drugs Prescribed in Patients with HTN+SROKE

Drugs	Dosage form	Dose	Frequency	Number of patients (12)
Atorvastatin	Tablet	20mg	OD	11
Clopidogrel	Tablet	75mg	OD	9
Aspirin	Tablet	150mg	OD	8
Pantoprazole	Injection	40mg	OD	10
Warfarin	Tablet	5mg	OD	5
Phenytoin	Tablet	5mg/kg	OD	7
LMWH	Injection(SC)	40mg	BD	4
Neurobion forte	Tablet		OD	11
Ranitidine	Tablet	150mg	BD	12

Table 12: Other Drugs Prescribed in Patients with HTN+CKD

Drugs	Dosage form	Dose	Frequency	Number of patients (06)
Torsemide	Tablet	5mg	OD	1
Ofloxacin	Tablet	400mg	BD	3
Neurobion forte	Tablet		OD	5
Paracetamol	Tablet	500mg	TDS	4
Mebendazole	Tablet	100mg	TDS	2
FST	Tablet	250mg	BD	4
Ranitidine	Tablet	150mg	BD	4
Albendazole	Tablet	400mg	STAT	1
Doxophylline	Tablet	400mg	BD(1/2 tab)	2
ciprofloxacin	injection	200mg	BD	4

Table13: Other Drugs Prescribed in Patients with HTN+CVD

Drugs	Dosage form	Dose	frequency	No. of patients (18)
Enoxaparin sodium	Injection (SC)	40mg	BD	7
Clopidogrel	Tablet	75mg	OD	15
GTN	Tablet	2.5mg	BD	8
Fibator	Tablet	10mg	OD	10
Diazepam	Tablet	5mg	BD	3
Neurobion forte	Tablet		OD	10
Ranitidine	Injection	50mg	BD	7
Pantoprazole	Tablet	40mg	OD	5
Aspirin	Tablet	150mg	OD	13
Digoxin	Tablet	0.25mg	OD	4
Ranitidine	Tablet	150mg	BD	13

Table 14: Prescribing indicator

S. No	Prescribing indicator	Frequency
1	Total number of prescription analyzed	66
2	Total number of drugs used in this study	406
3	The average number of drugs per prescription	6.15
4	Average number of drugs per encounter	6.15

5	Total no of antihypertensive drugs prescribed	92
6	The Percentage of antihypertensive drugs prescribed	22.66%

Patient Counselling

In this study, 66 patients were counsel led about medication use and life style modifications. As a result of patient counselling, there is a gradual increase in patient health condition in the majority of patients towards antihypertensive medications.

Counselling content

- Patient was advised to take medication regularly, and explained about the drugs, their uses and side effects, precautions to be taken.
- Dietary sodium restrictions (2-3 gm. per day; no added salt in cooking and no table salt)
- Regular exercise and yoga will reduce blood pressure.
- Explained about the consequences of the uncontrolled hypertension and the need for long term control with medications.
- Diuretics should be taken in the morning and if two doses are required second dose should be given before 4 pm, most preferred timings are (8AM and 2PM)
- Patient is educated about the compliance of medication
- Reduce weight
- Quit smoking and alcohol
- Restrict fat intake in order to control serum lipids
- Discontinue drugs with negative inotropic actions
- Fluid restriction depends on the output and other conditions
- Patient should be advised to contact the physician if an adverse reaction persists.
- Emphasize need for regular follow up and regular monitoring of blood pressure.

Discussion

The study describes the drug prescription pattern of antihypertensives in a cohort of 66 hypertensive patients in medicine ward. The aim of the study is to establish he most prescribed antihypertensive medication and to describe the pattern of antihypertensive drug usage among patients with compelling indications and to provide information on the clinical and demographics characteristics of patients that are associated with hypertension.

Patients Demographic Characteristics

Overall 66 patients were completed the study. Among these 39 (59%) were male and 27 (41%) were female. Prevalence depends upon several ethnic, genetic, environment and psychological factors. In India prevalence of hypertension (BP \geq 140/90 mm of Hg) is reported to be in urban & 10-15% in the rural adults and it further increases with age. In elderly Indian population, a prevalence rate of 51.8% is reported. In our study the prevalence of hypertension is found to be 18% more in males than in females. Higher prevalence of hypertension was reported in patients among the age group of 50-59 i.e., (42.4%). Among 66 patients cardiovascular disease (CVD) was the most common associated comorbidity which accounts for 27.2%.

Drug prescription pattern

Hypertension

Enalapril is the most commonly prescribed ACE Inhibitor i.e., 4 out of 9 (44.5%) of monotherapy. Followed by β - blocker

(Atenolol, propranolol), CCB (Amlodipine, nifedipine), Diuretics (Furosemide, HCT), each of (11.1%) respectively where the other monotherapy drugs more commonly used in this study.

ACE + β - blockers (Enalapril + Atenolol) was the most common dual therapy prescribed in 2 out of 6 (33.3%) prescriptions. Diuretics(Furosemide), CCB (Amlodipine) and β - blockers (metoprolol)3 out of 6 prescriptions (16.6%) each respectively are the other combinations prescribed with ACE Inhibitors (Enalapril). Atenolol + Amlodipine (16.6%) were prescribed. ACE+ β - blockers+ Diuretics (Enalapril+ Atenolol+ Furosemide) is the mostly prescribed triple combination therapy in patients with hypertension which accounts for 100% out of 1 prescription.

Hypertension with Diabetes Mellitus

Enalapril is the most commonly prescribed ACE inhibitors i.e. 4 out of 10 (40%) prescriptions of mono therapy followed by β - blockers(Atenolol) 2 out of 10 prescriptions (20%) and CCB (Amlodipine), Diuretics(furosemide, HCT), β blockers (propranolol) are the most common prescribed antihypertensives prescribed 1 out of 10 prescriptions (10%) each respectively.

ACE + β blockers (Enalapril + Atenolol) was the most common dual therapy prescribed in 2 out of 4(50%) Prescriptions. Amlodipine and furosemide along with enalapril was prescribed 1 out of 4 prescriptions (25%) each was most commonly used. ACE + β blockers + CCB (enalapril+ atenolol+ amlodipine) is the only prescribed triple combination therapy used in patients with diabetes mellitus with hypertension.

Hypertension with stroke

Furosemide, enalapril and HCT are the most commonly prescribed monotherapy in stroke 1 out of 3 prescriptions each (33.3%).

In dual combinations β blockers + CCB (atenolol+ amlodipine) is the most prescribed combination 3 out of 7 (42.8%) prescription. other combinations are ACE+ Diuretics (enalapril+ furosemide) accounting for 2 out of 7 prescriptions (28.6%). ACE+ β blockers (enalapril+ atenolol) and enalapril+ metoprolol are other combinations 1 out 7 each respectively (14.3%).In triple combination ACE+ β blockers+ Diuretics (enalapril+ atenolol+ furosemide) and enalapril+ amlodipine+ furosemide are the most used triple combinations accounting 1 out of 2 prescriptions each (50%).

Hypertension with CKD

ACE (Enalapril) is the most commonly prescribed monotherapy 2 out of 4 prescriptions (50%) and CCB (Amlodipine) and diuretics (furosemide) are the other commonly prescribed monotherapy i.e.,1 out of 4 prescriptions accounting for (25%) each.

Most common dual combination in CKD are ACE+ Diuretic (Enalapril + Furosemide) and ACE+ CCB (Enalapril+ Amlodipine) are most common dual therapy used in 1 out of 2 prescriptions (50%) each.

Hypertension with CVD

Amlodipine was the most commonly prescribed monotherapy

i. e 2 out of 5 prescriptions (40%) followed by diuretics (Furosemide), ACE (Enalapril), β -blockers (Atenolol) are the other drugs used in monotherapy 1 out of 5 prescriptions (20%) each.

In cardiovascular disease ACE+ Diuretic (Enalapril+ Furosemide) was the most prescribed dual combination i.e, 6 out of 10 prescriptions (60%). Followed by β -blocker +CCB (Atenolol+ Amlodipine) is the other drug prescribed commonly 2 out of 10 prescriptions (20%), ACE+ β -blockers (Enalapril+ Atenolol), ACE+CCB (Enalapril+ Amlodipine) are the other combinations used 1 out of 10 prescriptions (10%) each.

ACE+ β -blockers+ Diuretics (Enalapril+ Atenolol+ Furosemide) and enalapril+ atenolol+ amlodipine accounts for 1 out of 2 prescriptions (50%) was the commonly prescribed triple combination.

Conclusion

Hypertension (HTN) is a chronic medical condition in which the blood pressure in the arteries is elevated. The benefit of blood pressure reduction with Antihypertensive drug treatment has become increasingly evident.

Our study shows that Monotherapy was the most common approach in hypertension therapy. Enalapril was the most common drug used in both Monotherapy as well as other combinational therapies of hypertension and its co-morbidities.

(Enalapril+ Furosemide) is the most commonly used dual combination in hypertension and its co-morbidities. Enalapril + atenolol + furosemide is the most commonly used triple combination.

In our study, cardio vascular disease is the highest prevalent co-morbid condition associated with hypertension accounting for 27.2%, Hypertension alone found in (24.2%) of the subjects followed by Diabetes & Stroke with (21.2%) and (18.1%) and chronic kidney disease (9.1%) is the least associated co-morbid condition associated with hypertension.

This study provided a baseline data regarding the prescription pattern in hypertensive patients. There is a scope for improvement, particularly the underutilization of diuretics and calcium channel blocker in the present study is a concern.

The patients were counsel led about use of medication and life style modifications. As a result of patient counselling, there is a gradual increase in patient health condition in the majority of patients towards better control of disease and Quality of life.

References

1. Go AS, Mozaffarian D, Roger VL, American Heart Association Statistics Committee and Stroke Statistics Subcommittee, *et al.* Heart disease and stroke statistics – 2014 update: A report from the American Heart Association. *Circulation.* 2013; 129:28-292.
2. World Health Organization (WHO). A global brief on hypertension. Available at: http://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en/. Accessed on: 02 Jan 2015.
3. James PA, Oparil S, Carter BL. Eighth Joint National Committee (JNC 8) Members, *et al.* evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8), Supplemental Content. *JAMA.* 2014; 311:507-20.
4. Lim SS, Vos T, Flaxman AD *et al.* A comparative risk

assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012; 380:2224-60.

5. Causes of Death [online database]. Geneva, World Health Organization (http://www.who.int/healthinfo/global_burden_disease/cod_2008_sources_methods.pdf), 2008.
6. Gupta R, Gupta VP. Hypertension epidemiology in India: lessons from Jaipur Heart Watch. *Current science.* 2009; 97(3):349–55.
7. Sandozi T, Emani VK. Survey of prescription pattern of anti-hypertensive drugs in hypertensives and hypertension associated diabetics. *Int J Pharm Bio Sci.* Rimoy GH, Justin-Temu M, Nilay C. Prescribing Patterns and Cost of Antihypertensive Drugs in Private Hospitals in Dar es Salaam, Tanzania. *East Cent Afr J Pharm Sci.* 2010; 1(4):23-6.
8. Kotchen TA. The Search for Strategies to Control Hypertension. *Circulation.* 2010; 122:1141-3.
9. Jackson JH, Sobolski J, Krienke R, Wong KS, Frech-Tamas F, Nightengale B. *et al.* Blood pressure control and pharmacotherapy patterns in the United States before and after the release of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) Guidelines. *J Am Board Fam Med.* 2008; 21:512-21.
10. Ibrahim NA, Sulieman AA. Relation of atenolol with development of myocardial infarction in hypertensive patients. *Relation.* 2019 May;4(3).
11. Jeschke E, Thomas O, Horst CV, Matthias K, Angelina B, Claudia MW, *et al.* Evaluation of prescribing patterns in a German network of CAM physicians for the treatment of patients with hypertension: A prospective observational study. *BMC FamPract.* 2009; 10:78.
12. Caceres MC, Moyano P, Farinas H, Cobaleda J, Pijierro A, Darado P, *et al.* Trends in Antihypertensive Drug Use in Spanish Primary Health Care 1990–2012. *AdvPharma coepidemiol Drug Saf.* 2015; 3:172.
13. Xu H, He Y, Xu L, Yan X, Dai H. Trends and patterns of five antihypertensive drug classes between 2007 and 2012 in China using hospital prescription data. *Int J Clin Pharmacol Ther.* Liu PH, Wang JD. Antihypertensive medication prescription patterns and time trends for newly-diagnosed uncomplicated hypertension patients in Taiwan. *BMC Health Serv Res.* 2015; 53:430-7.
14. Ohta Y, Tsuchihashi T, Fujii K, Matsumura K, Ohya Y, Uezono K, *et al.* Improvement of blood pressure control in a hypertension clinic: A 10-year follow-up study. *J Hum Hypertens.* 2004; 18:273-8.