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Pharmacological control via assessment of various combination therapy on hypertensive Patients

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Abstract
Aim and objective: To identify, describe and assess the pharmacological management of hypertensive patients visit at the Pacific Medical College and Hospital, Udaipur (Rajasthan).
Introduction: Hypertension (HPT) is a major public health issue because of its high prevalence and serious complications. Appropriate and timely management using pharmacological and non-pharmacological therapy is essential to minimize complications and death resulting from hypertension.
Materials and Methods: A cross sectional retrospective study involving 90 patients was employed in this study. Data was collected through the administration of semi structured questionnaires from 1st July to 31st October, 2019. Case notes of the patients were also reviewed to obtain additional information and also to confirm and validate the clients' responses.
The classes of Antihypertensive Agents (AHA) commonly used in this study are calcium channel blockers (CCB), diuretics (DIU), angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), and beta blockers (BB). Centrally acting agents (CAA) and vasodilators (VAS) are used sparingly.
Result and discussion: Clients' pharmacological management was frequently initiated with of the patients on monotherapy, 76.4% (34/47) were on CCB, 9.8% (6/47) were on DIU, 6.0% (5/47) were on BB, with ACEI, ARB and CAA contributing 4.8%. Dual- and three-drug therapies are also used in initiating management. Among the CCB, Nifedipine was the most prescribed both in the initially (70.4%) and after study AHA (56.3%). Atenolol was the most prescribed among the BB with 82.3% baseline prescriptions. In the after study prescription there was an increase to 98.2%. In case of DIU prescription, Furosemide accounted for 4.9% and Bendrofluazide 92.1% in the baseline AHA prescriptions. Aspirin 44 (46.8%) was the most prescribed non-AHA.
The target or goal blood pressure (BP) for hypertension patients from World Health Organization/International Society of Hypertension (WHO/ISH) and European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines is <130/85 mmHg.
Conclusion: AHA in use at the Pacific Medical College and Hospital and prescription pattern are in accordance with that of the national guidelines.

Keywords: Pharmacological control, hypertensive Patients

Introduction
Hypertension (HPT) is a major issue in public health because of its high prevalence and serious complications. High blood pressure (BP) is a major public health problem in India and its prevalence is rapidly increasing among both urban and rural populations (Gupta and Gupta, 2010; Gupta *et al.*, 1996) [1, 2]. In fact, hypertension is the most prevalent chronic disease in India. The prevalence of hypertension ranges from 20-40% in urban adults and 12-17% among rural adults. The number of people with hypertension is projected to increase from 118 million in 2000 to 214 million in 2025, with nearly equal numbers of men and women (Reddy, 2009) [3].
This study, therefore, is to assess the pharmacological management of HPT patients in the pacific medical college and hospital to help in making proposals that will streamline management protocols in the hospital to conform to national and international standards. Since there is no previous study of the management of HPT in the hospital, this research can serve as baseline for future assessments. The resulting deficiencies and shortcomings identified would be included in recommendations that will go a long way to improve the care and management of HPT patients in the hospital. This will eventually improve the quality of

life of HPT patients and prevent and/ or reduce complications, morbidities and mortalities. The findings will also form an important part in the formulation of regional and national drug policies on any HPT control programme.
Information on pharmacological management of HPT in Udaipur is scanty. Therefore, this study will throw more light on the pharmacological management of HPT and the pattern of AHA usage in the Department of Medicine, Pacific Medical college and Hospital and serve as baseline for future studies.

Materials and methods

Study setting

Pacific Medical College & Hospital is a unit of Tirupati Balaji Educational Trust. It is spread over an area of 32.14 acres, beautifully landscaped and, surrounded by lush green hills of Bhillo Ka Bedla Pratap pura, National Highway 27, Udaipur (Raj), a 'B' class city.
This Hospital is a 900 bedded, multispecialty, tertiary level health care center with state of the art equipment, infrastructure & a team of highly experienced, qualified, skilled & motivated technical manpower. The hospital has well established departments both in diagnostic & therapeutic fields as well as in supporting logistics services.

Study design

Study type

This study was a cross-sectional study undertaken at the Department of Pharmacology of the Pacific medical college and Hospital, Udaipur (Rajasthan). A retrospective search was carried out on the patient's notes to assess the pharmacological management of HPT patients.

Sampling and questionnaire administration

Sampling

A ease sampling procedure was employed for data collection. Semi structured questionnaires were used arbitrarily on appointment days to patients who consented to take part in the project. 370 patients were intended to be randomly sampled for the study, however for some unforeseen limitations, 90 patients were sampled randomly for the study. A pilot study using 7 patients was done at the department.

Inclusion Criteria

- hypertensive patients ≥ 18years but ≤ 75 years;
- Visiting the hospital (in department) in the last 24 months
- Currently or had previously been treated with at least one antihypertensive medication.

Exclusion Criteria

- Patients with pre-hypertension which do not require drug therapy
- HPT patients with DM and hypertensive's with other severe co-morbidities such as heart failure or renal disease
- Patients attending the clinic on the day of data collection who are very sick and may need hospital admission; defaultants, and patients who refused to take part in the study.

Questionnaire Administration

Consent was obtained from all the patients.
The objectives of the survey and survey procedures were explained to them. In addition, prospective patients were made aware that participation is entirely voluntary and that they have the right to refuse to participate or to withdraw from the survey at anytime and that their decision will not in any way affect the care that they receive in the hospital.
Administration of questionnaires was used to collected the data through the from 1st July to 31st October, 2019. Case notes of the patients were also reviewed to obtain additional information and also to confirm and validate the patients' responses.

Study variables

In the collection of data obtained involve, classes of antihypertensive agents used, initiation of time management, duration, BP (measured in millimeters of mercury, mmHg), age, weight (kilograms, kg) and height (meters, m). The weight and height were used to calculate the body mass index (BMI, kg/m2) of patients.

Statistical analysis

Data were incorporated to determine mean ± SD using descriptive statistics and categorical data expressed as proportions. Unpaired *t*-test and Chi-square test were used to compare means and compare proportions respectively. In all comparisons, a p-value <0.05 was considered to be statistically significant. GraphPad prism® version 5.01 were used to analyze the data significantly.

Ethical consideration

Patients were subjected to semi- structured questionnaire and each respondent was interviewed separately in a room after consent and permission. Informed consent was also taken from the research participants.

Result and discussion

Hypertension continues to be an important public health concern because of its associated morbidity, mortality and economic impact on the society. It is a significant risk factor for cardiovascular, cerebrovascular and renal complications. It has been estimated that by 2025, 1.56 billion individuals will have hypertension.
The mean age of the study population was 56.4 ± 10.0 years. There were no statistical differences between the mean ages for males (55.0 ±11.1 years) and females (54.1 ± 10.7 years) p = 0.032. Though, 32.10% of the study population was within the age brackets of 49 – 58 years, followed by the age groups of 41 – 48, 60 – 69, 30 – 39, 70 – 75 and ≥18 - 30 years. Almost same weight was observed between males (74.5 ± 11.5 kg) and females (72.1 ± 14.0 kg) (p = 0.025). In case of BMI, females having a significantly higher BMI (28.4 ± 6.0 kg/m2) than males (26.2 ± 4.8 kg/m2) (p= 0.643). It was also found on the basis of BMI, 38.2% of the females being obese compared to 12.2% of the males and the variation in fraction was statistically significant i.e. p = 0.001. It was found that 75.0% of the patient's marital status were married, 9.0% were single, 7.0% divorced and 5.0% widowed (Table 1). Similar patterns of parameters were taken by several authors (Bramlage *et al.*, 2007; Hijazi and Alourfi, 2020; Olowofela and Isah, 2017) [4, 5, 6].
Aronson *et al.* (2007) [8] analyzed total of 100 prescriptions during the six-month study period. 72% of the patients were in the age group of 65-67 years and this was found to be higher in men 69%. During the study period 80% of the

patients were Pre-Hypertensive systolic (80-89 mmHg) and Diastolic (120-139 mmHg) followed by Stage-I Hypertension and Stage-II Hypertension.

Out of a total of 90 study participants, 1 (1.0%) had no record of baseline antihypertensive therapy leaving a total of 89 for further analysis. Out of the remaining 89, 47 (58.6%) were on a baseline antihypertensive monotherapy, 26 (35.4%) were on a baseline antihypertensive dual therapy and 16 (6.1%) were on a baseline antihypertensive three-drug combination. Of the patients on monotherapy, 76.4% (34/47) were on CCB, 9.8% (6/47) were on DIU, 6.0% (5/47) were on BB, with ACEI, ARB and CAA contributing 4.8% (2/47) respectively (Figure 1).

For study participants on dual therapy, 35.0% were on a combination of CCB+ BB, 33.2% each on ACEI + CCB and CCB + CAA respectively, 28.7% on DIU + CCB, 21.4% on CCB + ARB and 16.6% each were on CAA + BB and DIU + BB respectively (Figure 2(A). For this study participants on three-drug combination therapy of antihypertensives, 2 each were on a combination therapy of DIU + ACEI + CCB and DIU + CCB + CAA respectively and 1 each on a combination therapy of ACEI + CCB + CAA and ACEI + CCB + BB respectively (figure 2(B).

The choice of antihypertensive drug should be determined by the drug's capacity to lower pressure, to protect the diabetic patient's kidney from ongoing injury and cardiovascular complications. Antihypertensive and lipid-lowering teatment to prevent heart attack trial (ALLHAT) compared metabolic, cardiovascular, and renal outcomes in individuals assigned to initial hypertension treatment with a thiazide-like diuretic (chlorthalidone), a calcium channel blocker (CCB; amlodipine), or an ACE inhibitor (lisinopril) in nondiabetic individuals with or without metabolic syndrome. It showed despite a less favorable metabolic profile, thiazide-like diuretic initial therapy for hypertension offers similar, and in some instances possibly superior, CVD outcomes in older hypertensive adults with metabolic syndrome, as compared with treatment with CCBs and ACE inhibitors strategies based on renin-angiotensin system inhibitors were not clearly superior to conventional (i.e., diuretic-based) strategies (Tatti *et al.*, 1998) [9]. Furthermore, ACEIs showed to reduced incidence of coronary heart disease compared to diuretics (ALLAHAT) and reducing cardiovascular event compare to CCB (Schrier *et al.*, 2007; Holman *et al.*, 1998) [10, 11], but heart failure and stroke were lower in diuretics.

A comparison of administered baseline antihypertensives prescribed as monotherapies in male and female study participants showed that CCB were more likely to be prescribed as a monotherapy in females compared to males (p = 0.004). However, males were more likely to receive DIUs as monotherapy compared to females (p = 0.011). A comparison of the other classes of antihypertensives being administered as mono-therapeutic agents among males and females showed no statistical significance ($p > 0.07$).

For antihypertensives administered as dual therapy among the study participants, with the exception of dual therapy of ACEI + CCB which were more likely to be prescribed in males compared to females (p = 0.011), all the other dual antihypertensive class combinations among males and females showed no statistical significance difference ($p > 0.05$). Patients with >55 years were more likely to receive diuretics compared to patients with ≤55 years. (OR: 1.17, 95% CI 1.03–1.35).

Table no 2 depicted that among the CCB, Nifedipine was the most prescribed both in the initially (70.4%) and after study AHA (56.3%). Prescription of Amlodipine increased by 28.4% initially to 42.6% in the after study prescription.

Atenolol was the most prescribed among the BB with 82.3% baseline prescriptions. In the after study prescription there was an increase to 98.2%. Initial Propranolol prescription was 17.8% but negligibly used in the after study prescriptions.

Among the ACEI, Lisinopril was the most prescribed with a initial prescription of 100% to 69.4% in the after study prescription of AHA.

In case of ARB, Losartan was the only drug that was prescribed in the baseline AHA prescriptions. Losartan accounted for 82.4% and Candesartan 25.6% in the after study prescription of AHA.

Methyldopa is the only CAA in use at the hospital. Its prescription remaned maintained in baseline as well as after study prescription of AHA. In case of DIU prescription, Furosemide accounted for 4.9% and Bendrofluazide 92.1% in the baseline AHA prescriptions. In the after study DIU prescriptions, Furosemide accounted for 7.1%, Bendrofluazide 81.8% and Hydrochlorothiazide 8.1%. VAS was not prescribed as a baseline AHA; however in the after study prescriptions, hydralazine was the only VAS in use, accounting for 100% prescriptions. (Table 2)

Thus the present study confirms that prescribing trends are rational and are as per recommended guidelines existing during that period. The study also provides the baseline data for similar studies in future, as patterns in prescribing antihypertensive drugs keep changing. According to these diuretics, CCBs, ACEIs, and ARBs are considered as the first line antihypertensive drugs without any preference. As per these guidelines, BBs are not considered as the first line antihypertensive drug because in one study the use of BBs resulted in the higher rate of the cardiovascular deaths compared to use of ARBs. ABs are also not recommended for first line therapy as they worsen cerebrovascular, heart failure and combined cardiovascular outcomes in comparison to diuretic therapy.

Table 1: General characteristics of the studied population stratified by gender

Variables	Male (N = 40)	Female (N = 50)	All Clients	*p values*
Age (years)	55.0 ±11.1	54.1 ± 10.7	53.5 ± 11.0	0.032
Age Groups				
≥18 – 30	1(2.3)	0(0.0)	1(1.0)	0.207
30 – 39	1(4.5)	7(14.3)	8(10.0)	0.007
40 – 49	10(25.0)	15(30.4)	25(28.0)	0.034
50 – 59	16(38.6)	12(23.2)	28(30.0)	0.085
60 – 69	11(25.0)	12(25.0)	23(25.0)	0.980
70 – 75	1(4.5)	4(7.1)	5(6.0)	0.247
Weight (kg)	74.5 ± 11.5	72.1 ± 14.0	73.4 ± 12.8	0.025

Height (m)	1.8 ± 0.1	1.5 ± 0.1	1.76 ± 0.1	< 0.0001
BMI (kg m-2)	26.2 ± 4.8	28.4 ± 6.0	27.8 ± 26.8	0.643
***BMI Class* Underweight**	0(0.0)	1(1.1)	1(1.0)	0.173
Normal	22(50.0)	16(33.9)	38(41.0)	0.005
Overweight	16(38.8)	14(26.8)	30(32.0)	0.117
Obese	2(12.2)	19(38.2)	21(26.0)	0.001
Marital Status				
Single	5(13.6)	5(8.9)	10(9.0)	0.325
Married	32(75.0)	38(71.4)	70(75.0)	0.410
Divorced	2(9.1)	4(8.9)	6(7.0)	0.768
Widowed	1(2.3)	3(10.7)	4(5.0)	0.001

Table 2: Class and specific antihypertensive agents

Class of Antihypertensive Agents (AHA)	Specific AHA (initially)	Specific AHA (after study)
Calcium channel blockers (CCB)		
Amlodipine	28.4%	42.6%
Nifedipine	70.4%	56.3%
Furosemide		
Beta blockers (BB)		
Atenolol	82.3%	98.2%
Propranolol	17.8%)	0.1%
Angiotensin converting enzyme inhibitors (ACEI)		
Lisinopril	100%	69.4%
Angiotensin II receptor blockers (ARB)		
Losartan	100%	82.4%
Candesartan	0 (0%)	25. 6%
Centrally-Acting Agents (CAA)		
Methyldopa	100%)	100%
Diuretics (DIU)		
Furosemide	4.9%	7.1%
Hydrochlorothiazide	0.1%	8.1%
Bendrofluazide	92.1%)	81.8%
Vasodilators (VAS)		

Hydrallazine 0% 100%

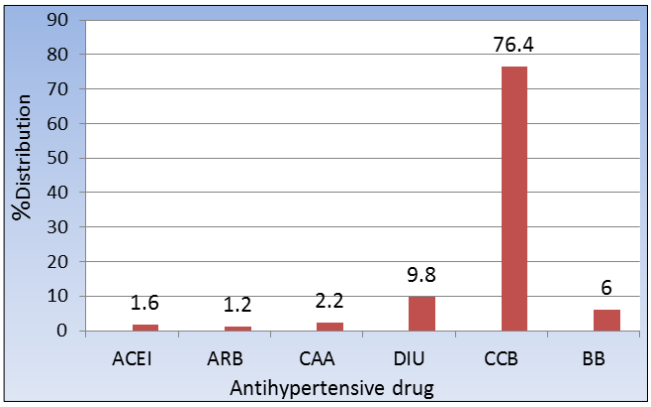
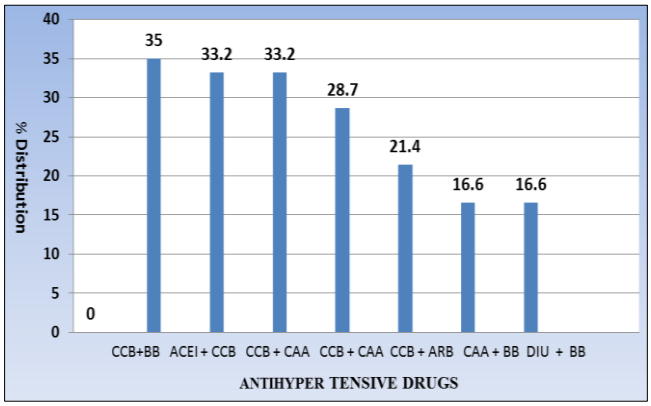
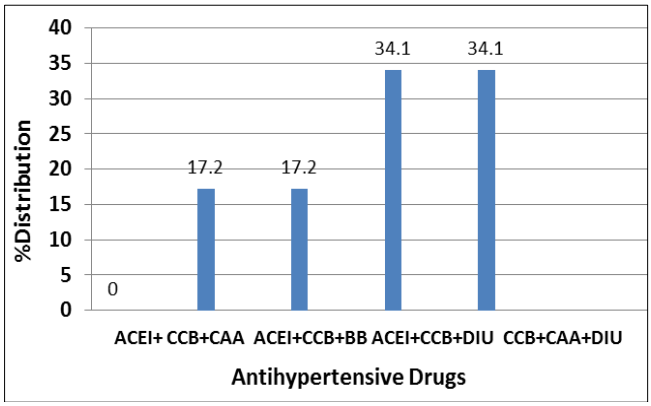


Fig 1: Baseline pattern of prescription of antihypertensives as mono therapeutic agents



(a)



(b)

Fig 2: (A) Baseline patterns of prescription of antihypertensives as 2-drug (A) and three-drug combinations (B)

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