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DRUG UTILIZATION STUDY OF ANTIHYPERTENSIVE TREATMENT BEING PRESCRIBED IN PATIENTS COMING TO MEDICINE OPD OF A TERTIARY CARE HOSPITAL IN NORTHERN INDIA

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ABSTRACT: Introduction: Hypertension, is a global public health issue. It is a significant contributor to rising morbidity and mortality because of its associations with cardiovascular, renal and cerebrovascular complications. Given the prevalence and impact of the disease on health care a drug utilization study becomes essential to determine the current drug utilization pattern. **Materials and Methods:** 127 patients of hypertension coming to the OPD of medicine of King George's Medical University were enrolled in the study after screening and giving consent. The data from the prescription of the drugs were recorded in pre-specified case record forms and analyzed for drug utilization parameters. **Results:** The average number of drugs encountered per prescription was 4. Whereas prescriptions with the generic name were 38% and drugs from an essential drug list were found to be 74%. The most commonly prescribed antihypertensive group was calcium channel blocker (25.1%) in monotherapy followed by angiotensin receptor blocker (21.2%). In combination therapy, the most commonly prescribed combination was found to be calcium channel blocker + angiotensin receptor blocker (17.3%). The drugs were prescribed in doses either equal to or less than the WHO DDD prescribed except telmisartan which was prescribed in a higher dose. A major finding was decreased in the angiotensin-converting enzyme inhibitor prescription and rise in angiotensin receptor blocker. **Conclusion:** Results of our study showed a lower rate of polypharmacy reporting and adherence to a national essential list of medications. The drugs being prescribed also fell well within the WHO recommended Daily Defined Dose (DDD).

INTRODUCTION: Hypertension is a global public health issue. It is a significant contributor to rising morbidity and mortality because of its associations with cardiovascular, renal and cerebrovascular complications.

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As per the DHLS 4 report, the prevalence of hypertension in India is estimated to be around 25% [1]. In terms of attributable burden of disease high blood pressure (BP) is ranked as the third most important risk factor in South Asia [2]. Rational prescription and burden of hypertension thus become mandatory to be estimated to know the current patterns.

Drug utilization research is defined by WHO as the promoting, distributing, prescribing and consumption of drugs in a population emphasizing the resulting clinical and socioeconomic

consequences [3]. The drug utilization study aims at evaluating the quality of medical prescriptions and patterns of use of specific drugs. A drug utilization study is, therefore, a study planned to describe-quantitatively and qualitatively-the population of users of a given drug or class of drugs and/or the conditions of use which include indications, compliance and adherence. A drug utilization study helps in identifying the pattern of drug used in population and if the therapy being followed is complying with rational drug prescription patterns [4].

In the context of an individual patient the rational use of drug prescription which is documented according to the standards must assure the use of a drug at a correct dose, with correct information and at costs which can be availed easily by the population without any economic burden. Drug auditing studies can also be benefited from such drug utilization studies.

A drug utilization research of various treatment alternatives being prescribed to the patients coming to the medicine OPD. The study aims at evaluating the drug utilization of antihypertensives and antidiabetic medications which will help paint a clearer picture of the overall qualitative and quantitative use pattern of drugs.

METHODS: The study was conducted at the Department of Pharmacology and Therapeutics in collaboration with the Department of Medicine, King George's Medical University, Lucknow. The study was started after ethical clearance from the institutional ethics committee (IEC) of King George's Medical University, Lucknow (Ref code: 93rd ECM II B- Thesis/P24). All patients with proven hypertension and put on antihypertensive medications were recruited from the Department of Medicine of King George's Medical University. The total duration of the study was 10 months *i.e.* November 2018 to August 2019.

Inclusion Criteria:

- Patients of hypertension (diagnosed according to JNC8 criteria; systolic blood pressure >140 mmHg, diastolic pressure > 90 mmHg).
- Patients of either sex of age 18 to 60 years.
- Patients having no associated comorbidities.

Exclusion Criteria:

- Patients unwilling to participate and did not give consent to the study.
- Patients are unable to give an interview.
- Pregnancy/breastfeeding.
- Patients with incomplete medical records.
- Patients with chronic liver disease such as cirrhosis, chronic hepatitis, cigarette, drug addiction, alcohol, acute viral hepatitis.
- Terminally ill or comatose patients.
- Patients with concurrent major psychiatric illness and/or concurrent major medical illnesses.
- Patients already on treatment from some other institution for other indications.
- Patients taking alternate medicines along with the prescribed one'.

The diagnosis of hypertension was confirmed prior to enrolment. Patients were allotted a unique patient identification number for ease of follow up. On the first visit, a case record form (CRF) designed as per the study protocol was filled according to the prescription of the patient (which includes patient demographic details, treatment charts, and investigation reports of patients of medicine). Charting of blood pressure was also done on the first visit. The patient medication chart was recorded every follow-up visit and at 3 months for keeping a record of prescriptions and improvement in terms of clinical parameters. If any serious interaction was observed, health care professional for necessary modifications was informed.

Statistical Analysis: Data was entered in the MS Excel spreadsheet and analyzed. Categorical variables were presented in number and percentage (%) and chi-square test (χ^2) was applied to establish statistical significance. Drug utilization indicators in the study used were:

Drug Utilization Indicators: On the basis of WHO core prescribing indicators. Data were expressed according to a number of encounters and percentage frequency.

Defined Daily Dose (DDD): World Health Organization (WHO) has defined the unit of drug utilization research as a measure of defined daily dose (DDD) which uses anatomical therapeutic chemical [ATC] classification. Thus, drug utilization was expressed as the average dose prescribed per day and DDD/1000 patients /day.

DDD/1000 patients/day was calculated by applying the following formula:

Total amount of drug consumed during the study period × 1000 / WHO recommended DDD of a drug x duration of treatment × sample size

RESULTS: Out of 127 patients diagnosed with hypertension, 56 patients had concomitantly been diagnosed with diabetes mellitus type 2. Number of males in the study was 69 (60.06%) and females were 50 (39.3%). The most common age group affected was 51 - 60 years.

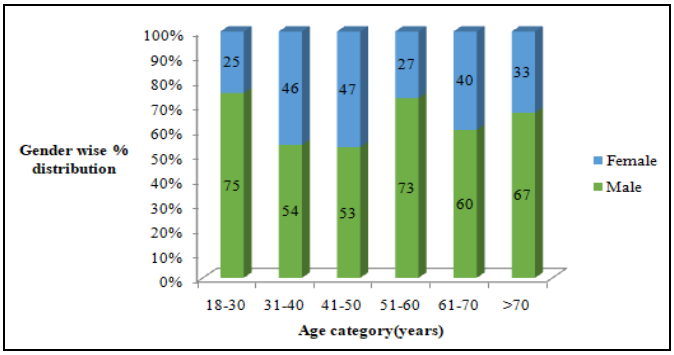

FIG. 1: DEMOGRAPHIC CHARACTERISTICS OF THE PATIENTS

Out of a total 127 (58.79%) hypertensive, 56 (25.92%) had both hypertension and diabetes. Concomitant medical diseases were present in 67 patients (31.01%). These included COPD, hyper-lipidaemia, chronic alcoholic liver disease, thyroid abnormalities and insomnia.

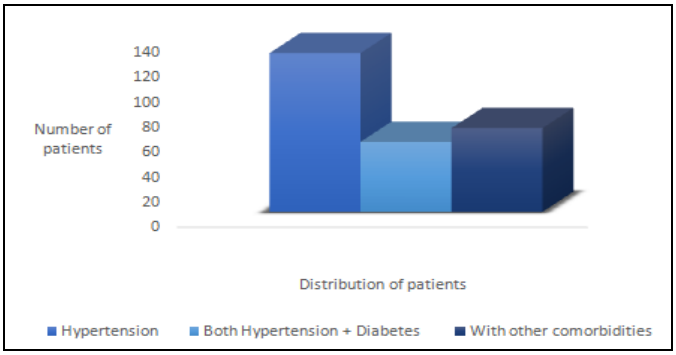

FIG. 2: DISEASE CHARACTERISTICS OF THE PATIENTS

Drug Use Indicators: In this study, the WHO drug utilization indicators were analyzed. The average number of drugs encountered per prescription was 4. Whereas prescriptions with the generic name were 38% and drugs from an essential drug list were found to be 74%. During the study, indicators of patient care such as mean consulting time were found to be 5.6 min and the availability of key drugs in the hospital was scarce.

TABLE 1: DRUG USE INDICATORS OF ANTIHYPERTENSIVE MEDICATIONS

Indicators	Number and Percentage
Core Indicators	
Average no. of drugs per prescription	4
Average no. of antihypertensive per prescription	1.34
Prescription by generic name	38%
Drugs in the essential drug list	74%
Facility Indicators	
Availability of essential drug list	Yes
Availability of key drugs	80%
Patient Care Indicators	
Average consulting time	5.6 min

Pattern of Drug Therapy of Antihypertensive Medications: Out of a total of 127 patients with hypertension prescriptions, monotherapy was found in 59.1% prescriptions whereas 40.9% of the patients were prescribed either dual therapy or more than 2 drugs.

The utilization pattern of different antihypertensive drugs according to the type of therapy *i.e.*, monotherapy, dual therapy, and triple therapy is shown in the table below.

TABLE 2: PATTERN OF DRUG THERAPY

Drug therapy	n (%)
Monotherapy	75 (59.1)
Dual therapy	46 (36.2)
Triple therapy	6 (4.7)

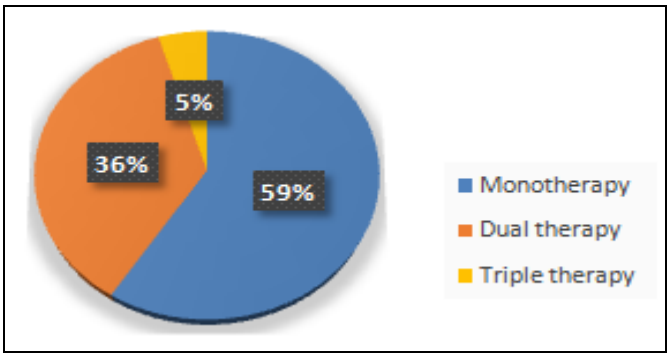

FIG. 3: DISTRIBUTION AS PER NUMBER OF ANTIHYPERTENSIVE DRUGS PER PRESCRIPTION

Types of Antihypertensive Medications Prescribed According to their Classes: Most commonly prescribed antihypertensive group was calcium channel blocker (25.1%) in monotherapy followed by angiotensin receptor blocker (21.2%) and beta-blockers (16%).

TABLE 3: TYPES OF ANTIHYPERTENSIVE MEDICATIONS PRESCRIBED ACCORDING TO THEIR CLASSES

Classes of Therapy	n (%)
Mono Therapy	
CCBs	32 (25.1)
ARB	27 (21.2)
β blockers	16 (12.5)
Dual Therapy	
CCB + Diuretics	18 (14.1)
CCB + ARB	22 (17.3)
ARB + Diuretics	13 (10.2)
Triple Therapy	
CCB + ARB + Diuretics	6 (4.7)

In combination therapy, the most commonly prescribed combination was found to be calcium channel blocker + angiotensin receptor blocker (17.3%) followed by calcium channel blocker + diuretics (14.1%). Other combinations prescribed were angiotensin receptor blockers + diuretics (10.2%) and calcium channel blocker + angiotensin receptor blockers + diuretic combination (4.7%).

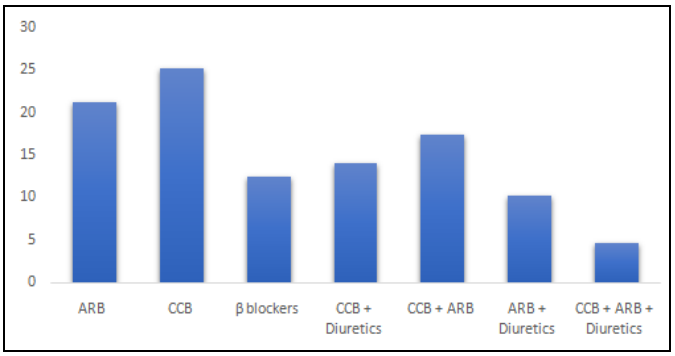

FIG. 4: TYPES OF ANTIHYPERTENSIVE MEDICATIONS PRESCRIBED ACCORDING TO THEIR CLASSES

Antihypertensive according to the frequency of prescription encountered, their ATC classification code and most commonly prescribed drug in mono-therapy and combination therapy are mentioned in the table below. Amlodipine 25.1% was most commonly prescribed in monotherapy and amlodipine + telmisartan combination therapy 13.3% was the most commonly prescribed drug in combination therapy.

TABLE 4: COMMONLY USED ANTIHYPERTENSIVE MEDICATIONS

Drug Therapy	n (%)	ATC classification	Most commonly used drug
Monotherapy			
Telmisartan 40 mg	21 (16.5)	C09CA07	Amlodipine 5mg (25.1% of the patients)
Amlodipine 5 mg	32 (25.1)	C08CA01	
Cilnidipine 5 mg	6 (4.7)	-	
Nebivolol 2.5 mg	12 (9.4)	C07AB12	
Bisoprolol 2.5 mg	1 ((0.7)	C07AB07	
Metoprolol 50 mg	3 (2.3)	C07AB02	
Dual Therapy			
Amlodipine 5mg + Losartan 50 mg	5 (3.9)	C09DB06	Amlodipine 5mg + Telmisartan 40mg (13.3% of the patients)
Amlodipine 5mg + Telmisartan 40 mg	17 (13.3)	C09DB04	
Azilsartan 40mg + Chlorthalidone 12.5 mg	5 (3.9)	C09DA09	
Chlorthalidone 6.25mg + Telmisartan 80 mg	8 (6.2)	C09DA07	
Clinidipine 10mg + Chlorthalidone 12.5 mg	13 (10.2)	-	
Hydrochlorthiazide 2.5mg + Olmesartan 40 mg	5 (3.9)	C09DA08	
Triple Therapy			
Telmisartan 40mg + Chlorthalidone 12.5mg + Clinidipine 10mg	6 (4.7)		Telmisartan 40mg + Chlorthalidone 12.5mg + Clinidipine 10mg (4.7% of the patients)

Utilization of various antihypertensive medications on the basis of their average daily dose prescribed and DDD/1000 patients/day has been presented in the table below. According to our study all drugs were prescribed in doses either equal to or less than the WHO DDD prescribed except telmisartan which was prescribed in a higher dose.

While comparing the average daily dose of oral antidiabetics with WHO/ATC defined daily dose it was found that all antidiabetic drugs were less than their DDD.

Teneligliptin could not be compared as the DDD, and the WHO ATC code is not available.

TABLE 5: DEFINED DAILY DOSE OF ANTIHYPERTENSIVE MEDICATIONS

Drug Therapy	Number of encounters	ATC classification	Average dose per day	WHO DDD (mg)	DDD/1000 patients/day
Angiotensin receptor blockers (ARBs)					
Telmisartan	52	C09CA07	46.15 mg	40 mg	4.723
Olmesartan	5	C09CA08	40 mg	20 mg	0.437
Calcium channel blockers (CCBs)					
Amlodipine	54	C08CA01	5 mg	5 mg	4.724
Clinidipine	19	-		-	-
Beta blockers (BBs)					
Nebivolol	12	C07AB12	2.5 mg	5 mg	0.472
Bisoprolol	1	C07AB07	2.5 mg	10 mg	0.022
Metoprolol	3	C07AB02	100 mg	150 mg	0.715
Diuretics					
Chlorthalidone	27	C03BA04	9.7 mg	25 mg	1.067
Hydrochlorthiazide	5	C03AA03	12.5 mg	25 mg	0.219

DISCUSSION:

Assessment of Drug Utilization of Anti-hypertensive Based on Drug Use Indicators: Drug utilization as per pre-defined indicators of world health organization (WHO) in our studies showed an average number of drugs per prescription in hypertensive patients to be 4 and average number of antihypertensive to be 1.34. The percentage of drugs prescribed by their generic name was 38% and drugs prescribed from the national essential drug list (NELM 2015) was 87% which is in accordance with WHO norms which require 80 - 100% of the drugs to be from the EDL [5].

WHO drug utilization indicators were assessed after analyzing the drug prescriptions of the screened patients. The average number of drugs prescribed per prescription in our study was 4. As per WHO the average number of drugs prescribed should be 2-3 [6]. This finding was also supported by a study by Raikar, Shrinivas R. *et al.* [7] Average number of antihypertensive drugs per prescription in our study was 1.34 which were in favor of findings of other studies. According to Rimoy *et al.*, [8] average number of antihypertensives was 1.6 whereas Ramada S. *et al.*, [9] reported a similar number of average 1.4 antihypertensive drugs. The reason for a higher number of average drugs per prescription can be explained by the fact that most of the patients had associated comorbidity with hypertension.

Assessment of Drug Utilization Based on Pattern and Class of Antihypertensives: In our study, the pattern of drug utilization based on the class of antihypertensives being employed indicated most commonly prescribed drug as monotherapy to be calcium channel blocker which was 25.1%, followed by angiotensin receptor blockers (ARBs) which were 21.2% and beta-blockers which were prescribed in 12.55% of the patient. According to a study done by Vummareddy *et al.*, [10] utilization of antihypertensive drugs was maximum for CCBs which was 49.81% followed by beta-blockers which was 12.7%. A similar finding was found in a study by Behanan *et al.*, [11] where maximum prescriptions encountered were CCBs accounting for 33%, followed by ACE Inhibitors and ARBs which were 22% and 9%. In accordance with similar finds were results of a study done by Gu *et al.*, [12] the use of angiotensin receptor blockers has increased by 100%. Ramadas *et al.*, 72 mentioned calcium channel blocker as the most commonly prescribed class of drugs both as monotherapy and overall with 36.4% and 42.8%.

According to Behanan *et al.*, [11] monotherapy was prescribed in 72% of the patients followed by dual therapy 22% and triple therapy 6%. Studies conducted by Sharma *et al.*, [13], Tandon *et al.*, [14] and Konwar *et al.*, [15] also showed a preference for single therapy over combination therapy. This reason for inclination towards prescribing monotherapy was to achieve target goal blood pressure before stepping up for dual combination therapy which is in accordance with the JNC VIII guidelines. The results of our study are in favour of the findings of most of the studies performed in India to define the prescription pattern and drug utilization with context to the most commonly used class of antihypertensive utilized as a calcium channel blocker.

Though, the second most commonly used class of drugs was found to be ARB which was, in contrast, to find of above-mentioned study. Caceres *et al.*, [16] and Xu *et al.*, [17] which show a consistent increase of ARBs and CCBs. were utilized.

According to the finding of our results combination of CCBs + ARBs in 17.3% patients were most commonly employed followed by CCBs + Diuretics and ARBs + diuretic FDCs which were prescribed to 14.1% and 10.2%. Vummareddy *et al.*, [10], the most commonly prescribed class was CCB + beta-blocker 29.11% followed by CCBs + ARBs combination which was prescribed in 21.51% of the patients. Whereas results from Gupta R *et al.*, [1] indicated ARBs + Diuretics to be most commonly prescribed (67%) class followed by ACE inhibitors + diuretics (17.4%).

The prescription pattern in our study clearly shows an inclination towards angiotensin receptor blocker (ARBs) in comparison to angiotensin-converting enzyme inhibitor (ACEIs). This shift might be to avoid inadvertent side effects associated with ACEI. The increase in trends of the similar prescribing pattern has been seen in earlier studies. A high proportion (40.9%) of patients being prescribed combination antihypertensives was observed to achieve adequate control even as first-line option in certain patients. This can be explained by previous studies Wald *et al.*, [18] and Burnier M. [19] which mention a significant improvement in blood pressure management of 2- 5 times as compared to mono-therapy.

CONCLUSION: Results of our study showed a lower rate of polypharmacy reporting and adherence to national essential list of medications. The drugs being prescribed also fell well within the WHO recommended Daily Defined Dose (DDD). The study might provide a framework for larger sample studies conducted across multiple sites. The data can generate drug utilization data which can be used for hospital formularies and achieve more sustainable, accessible health care delivery.

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CONFLICTS OF INTEREST: None declared

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