



DRUG UTILIZATION PATTERN OF ANTIHYPERTENSIVE DRUGS AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: Drug utilization studies conducted at regular intervals help to guide the physician in prescribing drugs rationally.

Methods: A prospective, observational study was conducted in the outpatient of department of general medicine of NC Medical college & Hospital a tertiary care teaching hospital. Data was collected from patients who have been diagnosed with hypertension as per JNC-8 guidelines and patients receiving or prescribed with antihypertensive medications were included. Frequency and proportions of utilization of antihypertensive medications in were figured.

Results: A total of 200 prescriptions were analysed during the eight-month study period. The age of the patients with range 18-80 years. 53.5 % (107) of patients were male and 46.5 % (93) of patients were female. The most common medication prescribed for hypertension in the study was CCBs 19.5 %, significantly higher than dual therapy, triple therapy and poly therapy. The CCBs prescribed pattern was followed by BBs, ACEIs and CCBs. The most frequently prescribed anti-hypertensive fixed dose combination therapy was CCBs+ARB, CCBs + BBs followed by CCB+Diuretic. Among 200 patients' only 43 patients were reported ADR. Maximum no of ADRs were reported from patients receiving ACE inhibitor.

Conclusion: This type of studies gives the base line idea of prescription pattern and ADRs of antihypertensive drugs. These helps to design policy for rational use of drugs and motivation of physician for rational use of drugs.

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INTRODUCTION

Drug utilization review (DUR) is a systemic ongoing process of collection of explanatory and evaluating methods for the quantification, understanding and analysis of the processes of prescribing, dispensing, and consumption of medications and for the testing of interventions to speed up the quality of these processes.^[1] DUR helps in investigating the prescribing pattern followed by feedback to physicians setting up of the guidelines, building up the novel approach toward evidence based decision making process.^[2] Current study was conducted to determine the demographic profile of the patients. To evaluate the different classes of antihypertensive medications with respect to diagnosis and to carry out the drug utilization review in hypertension with its different combinations.

Hypertension is an extremely common condition and quantitatively the most important risk factor for cardiovascular disease and mortality. Cardiovascular risk factors other than

hypertension occur more frequently in hypertensive subjects and contribute to the elevated cardiovascular risk. It is reported to be the fourth contributor to premature death in developed countries and the seventh in developing countries. In India, this condition is an important public health problem and leads annually to 1.1 million deaths.^[3] It is estimated to account for 10.8 % of all deaths. Globally it is responsible for 9.4 million deaths.^[4] Hypertension occurs in 25-30 % of middle aged individuals in urban and 15-20 % in rural areas of the country.^[5]

The guidelines for the treatment of hypertension are put forward by the Joint National Committee (JNC) on detection, evaluation, and treatment of blood pressure. The Indian guidelines, endorsed by the cardiology Society of India, the hypertension Society of India, and the Indian College of Physicians, closely follow the JNC Guidelines (JNC8).^[6] These guidelines are updated from time to time, based on evidence emanating from basic and clinical research, and

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guide physicians to select the most appropriate antihypertensive agent in a patient. Pharmacoepidemiological studies such as drug utilization and prescription pattern studies are an important research tool by which the impact that such guidelines have on the selection of therapeutic agents can be assessed and analysed. It has been observed that evidence-based clinical research is not adequately incorporated into clinical practice, which can in turn result in suboptimal patient health-care practices. [7] The objective of this study is to observe the pattern of utilization of antihypertensives in a tertiary care teaching hospital and relate the findings to current standard treatment guidelines.

MATERIALS AND METHODS

This is a prospective cross-sectional drug utilization study, conducted between January 2019 to August 2019 at outpatient department of General Medicine, NC Medical college & Hospital, Israna, Panipat. After Institute Ethical Committee approval, prescriptions of 200 patients of either sex and age >18 years who have been diagnosed with hypertension as per JNC-8 guidelines and patients receiving or prescribed with antihypertensive medications were included. Patients in emergency, life threatening medical or surgical conditions, pregnant and lactating women and patients with incomplete data were excluded. The patient's sociodemographic profile, receiving or current prescribing patterns of antihypertensive medications were recorded in a predesigned data collection record form. Those receiving or with prescription of a one active principle medication was considered as monotherapy and those receiving or prescription of a more than one active principle medications were defined as a polytherapy. Informed written consent was obtained from the patients before their participation in the study and all the data collected was kept confidential.

The main aim of study was evaluating the different classes of antihypertensive medications with respect to diagnosis and to carry out the drug utilization review in hypertension with its different combinations. Patient's demographics, type of antihypertensive drug prescribed, lab reports, detailed medical history, concomitant medications for co morbid diseases were recorded. Frequency of drug prescription among different age groups, frequency of administration of individual drugs, frequency of prescribing combination drugs, frequency of prescribing fixed drug combinations, number of prescriptions per drug, number of drugs prescribed per total number of prescription, percentage of patients in the treatment of hypertension with comorbidities, percentage of economic difference, percentage of expenditure cost, and average drug acquisition cost (ADAC) were calculated.

Data was analyzed using the software, Statistical Package for Social Sciences (SPSS for windows. Version 24 software. Percentage describes categorical data mean±standard deviation (SD) describes continuous data Subjects were recruited in the study after obtaining approval from Institutional Ethics Committee (IEC). Confidentiality and anonymity of the patient's information was and will be maintained during and after the study. Informed consents were taken from the subjects. All drug related adverse events were evaluated according to the "WHO causality Assessment Scale" was used to describes causality of adverse drug event into adverse drug reaction.

RESULTS

Age distribution of patient: In table 1, the highest age group patients were between 41-60 years accountable 53.5 % and least age group patients were between 18-40 years 10.5 %.

Table 1 Distribution of age group

Age group in years	No. of patients (n=200)	Percent
18-40	21	10.5
41-60	107	53.5
61-80	72	36

Gender distribution of patient: In table 2, the gender ratio of the patients' male: female was found to be 1.2:1. Out of the 200 patients, 53.5 % (107) of patients were male and 46.5 % (93) of patients were female. Test of proportion showed that the male patients were slightly more than the female patients.

Table 2 Distribution of gender

Gender	No. of patients	Percent
Male	107	53.5
Female	93	46.5

Duration of hypertension: In table 3 shows that 103 (51.5%) patients were between < 3 years, 73 (36.5%) patients were between 4-6 years and 24 (12%) were having history of >7 years.

Table 3 Duration of hypertension

Duration in years	No. of patients	Percent
< 3 years	103	51.5
4-6 years	73	36.5
> 7 years	24	12

Systolic blood pressure distribution in patients: In table 4 depicts most of the patients 91 (45.5 %) were significantly higher systolic blood pressure ranging between 160-179 mmHg (Stage 2 HTN) and least patients were emergency hypertensive were 5.5 %.

Table 4 Distribution of Systolic blood pressure

Systolic blood pressure (mmHg)	No. of patients	Percent
120-139 (Pre HTN)	31	15.5
140-159 (Stage 1 HTN)	67	33.5
160-179 (Stage 2 HTN)	91	45.5
>180 (HTN emergency)	11	5.5

Diastolic blood pressure distribution of patients: In table 5, test of proportion showed most of the patients 93 (46.5 %) were significantly higher diastolic blood pressure ranging between 100-119 mmHg and least patients were emergency hypertensive were 6 %.

Table 5 Distribution of Diastolic blood pressure

Diastolic blood pressure (mmHg)	No. of patients	Percent
80-89 (Pre HTN)	32	16
90-99 (Stage 1 HTN)	63	31.5
100-119 (Stage 2 HTN)	93	46.5
>120 (HTN emergency)	12	6

Drug therapy distribution among patients

In table 6 shows most of the patients 93 (46%) were on Mono therapy significantly higher than dual therapy, triple therapy and poly therapy, 64 (32 %), 27(13.5%), 16 (8 %) respectively.

Table 6 Distribution of drug therapy

Drug Therapy	No. of patients	Percent
Monotherapy	93	46.5
Dual therapy	64	32
Triple therapy	27	13.5
Poly therapy	16	8

Utilization pattern of different antihypertensive drugs

Calcium channel blocker was the frequently used class of drug for monotherapy (19.5 %). In dual drug therapies were CCB+ARB accounting for 18.5 %, and 5.8% of patients were on triple drug therapy with CCB+ARB+Diuretic.

Table 7 Utilization pattern of different antihypertensive drugs

Treatment	No. of patients use antihypertensive drug	Percent
Monotherapy		
Calcium channel blocker	39	19.5
ARB	19	9.5
ACE Inhibitor	13	6.5
Beta Blocker	21	10.5
Alpha Blocker	3	1.5
Diuretics	5	2.5
Dual therapy		
CCB+ARB	37	18.5
CCB+Beta Blocker	31	15.5
CCB+ Diuretic	11	5.5
ARB+ Diuretic	9	4.5
Triple therapy		
CCB+ARB+Diuretic	7	5.8
CCB+B Blocker+Diuretic	5	4.1

Adverse drug reactions reported: In the present study, causality assessment between the drug and suspected reaction was determined by using WHO-UMC Scale, Naranjo Scale and Hartwig and Siegel scale. According to Naranjo Criteria, the ADRs are analysed on the basis of a questionnaire comprising 10 questions in which each question is given a score of +2, +1, 0 or -1 depending on the analysis. When total if the score is >9 – labelled as definite ADR, if 5-8 – probable ADR, if 1-4 –possible ADR, if 0 – doubtful ADR.

Table 8 WHO causality assessment of ADRs

Type of reaction	No. of patients reported ADR (43)	Percent
Certain	7	16.2
Probable/likely	29	67.4
Possible	6	13.9
Unlikely	1	2.3
Conditional/unclassified	-	-
Unassessable/unclassifiable	-	-

Among 200 patients only 43 patients experienced ADRs. Causality assessment of ADRs was done using WHO-UMC scale which categorizes ADRs as “certain”, “probable”, “possible” and “unlikely”. Table 8 shows that type of reactions and their percentage are as certain (16.2 %), Probable/ Likely (67.4%), Possible (13.9 %) and Unlikely (2.3 %).

Table 9 Severity of reported ADRs by modified Hartwig and Siegel scale

Type of reaction	No. of patients reported ADR (43)	Percent
Lethal	-	-
Severe	3	6.9
Moderate	9	20.9
Mild	31	72.0

In table 9, it was found that from all ADRs, reported (72 %) were mild, (20.9 %) moderate and only (6.9 %) was classified as severe.

Table 10 Common ADR Reported

Class of drugs	Adverse events experienced	No of patients (43)	%
CCB	Pedal edema, giddiness, headache, abdominal pain, bradycardia	11	25.5
ARB	Anxiety, Nausea and Vomiting, Headache, Abdominal pain, Restlessness, Itching and inflammatory swelling	9	20.9
ACE Inhibitor	Dry cough, dizziness, headache, drowsiness, diarrhea, hypotension, weakness, cough, rash, metallic or salty taste.	13	30.2
Beta Blocker	Constipation, nausea and vomiting, headache, hypoglycemia, postural hypotension	5	11.6
Diuretics	Hypotension, muscle cramps, headache vertigo, pain in legs, dysuria	2	4.6
Other	Skin reaction	3	6.9

Total 43 patients were reported ADR. 30.2% patients were on ACE inhibitors. 25.5 % patients receiving Calcium channel blocker reported side effect.

DISCUSSION

The WHO defines drug utilization studies as “the marketing, distribution, prescription and the use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.” Prescription pattern surveys are an important methodological instrument of drug utilization studies, which help provide an in-depth insight into the disease profile of patients and prescribing behavior of clinicians. Hypertension is a serious public health problem worldwide. [8] It is the leading cause of death in the world and is the most common cause for outpatient visits to physicians. [9]

Our study shows a higher incidence of hypertension in elderly male patients aged between 41 and 60 years (53.5 %). The hypothetical cause of higher number of male patients is elevated levels of androgen such as testosterone as they play a role in elevation of blood pressure. [10,11] A similar study was also conducted by Amira et al., 2006 which is supporting our study. [12]

The present study observed that single-drug therapy (19.5 %) with CCBs was more commonly employed than multiple-drug therapy. These results support the work of Sindhu et al. which showed blood pressure could be adequately controlled with the help of single-drug therapy. [13] This might be attributed to patient’s compliance, good response, and less incidence of adverse effects. In a study by Anand et al, CCBs were found to be the most frequently used group of drugs which is parallel to findings of our study. [14] In our study, BBs were prescribed most frequently next to CCBs the findings of which are similar to the study performed in a tertiary care hospital of India by Rachana et al. [15]

In this present study, it was observed that there was a significant change in antihypertensive prescribing pattern with a considerable increase in the frequency of intake of CCBs, ARBs, ACEIs and BBs. These observations line with other study. (7) CCBs and ARBs constitute the most frequently prescribed antihypertensive drug class. Increased prescription of ARBs and CCBs probably suggest that clinicians are more aware of the long term cardiovascular and renovascular benefits. The prescriptions were also in accordance with the evidence and the guidelines, as these medications will reduce the chance of occurrence of diabetic nephropathy, retinopathy

and other related complications in diabetes patients. When calcium channel blockers were concerned the most commonly prescribed drugs were the dihydropyridine type of calcium channel blockers (ie., Amlodipine, Felodipine), whereas the prescription of non-dihydropyridine type of calcium channel blockers was very less.

Observations on combination therapy reflect that the most commonly prescribed drugs in combination were diuretics (i.e., Thiazide and potassium sparing diuretic groups). The joint national committee on prevention, detection, evaluation and treatment of High blood pressure (JNC-8) report notes that volume overload due to inadequate diuretic therapy is one of the commonest reason for resistance observed in HTN treatments.⁽⁹⁾ So, there is a paradigm shift towards increased prescribing of combination therapy. The present observational study depicts that the patients with co-morbidity were prescribed one or two antihypertensive along with other medications to treat their associated diseases such as diabetes mellitus, IHD, CVA and Bronchial asthma. In a study by Mohd AH et al, the most commonly prescribed antihypertensive among elderly patients was Amlodipine.^[16] This is also in consonance with the recommendations of the JNC on Prevention, Detection, Evaluation, and Treatment of high blood pressure guidelines which state that low dose of different classes of antihypertensive drugs is more beneficial than a high dose of one.^[17]

According to WHO-UMC Scale maximum number of ADRs in probable class followed by possible, unlikely and certain class. Moreover, as per the modified Hartwig and Siegel's scale maximum number of ADRs was mild category and lowest in severe type of reaction was observed in this study. No ADRs were found in lethal type of reaction. These findings were consistent with the literature reported by Ganachari et al, and Singh et al, Total 37 patients were reported ADR.^[18] 30.2 % patients were on ACE inhibitors. 25.5 % patients receiving Calcium channel blocker reported side effect.

Finally, the strength of this study lies firstly in the unparalleled period of consideration (8 months). Earlier studies have been characterized by a relatively short period of consideration (usually not exceeding 3 months) with a tangible majority of them having comparatively smaller sample sizes.^[19-22] It is noteworthy also that there is no prior study of this kind in a secondary healthcare setting. Furthermore, the result of this study represents a much more recent (and arguably more reliable) assessment of the subject matter and, as such, is hoped to not only merit publication but also attract attention as a renewed, data-driven basis for further research in the management and control of hypertension, ultimately.

CONCLUSION

In conclusion, our study analysed the drug utilization of antihypertensive medication and found that the prescribing pattern was totally consistent with the JNC 8 (the Eighth Report of the JNC on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) guidelines for the treatment of hypertension. Monotherapy was consistently more recommended in the early stages of hypertension to achieve target goal of blood pressure, and CCBs were the drugs of choice for hypertensive patients.

The knowledge and prescription of drug was concluding to be the base line idea of ADRs of antihypertensive drugs in hypertensive patients visiting OPD of tertiary teaching care

hospital in India. In this study, we can say that all of the prescriptions found were rational; furthermore, more changes are needed to be done in prescription of antihypertensive drugs are needed in drug prescribing practices in hypertensive patients. Patients are needed to provide information and proper counselling regarding the ADRs of drugs; this would refine the quality of life.^[23- 26]

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