

A PHARMACOVIGILANCE ANALYSIS OF ANTIHYPERTENSIVE DRUGS IN ESSENTIAL HYPERTENSION PATIENTS IN TERTIARY CARE HOSPITAL

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Abstract

INTRODUCTION

Hypertension is the most common cardiovascular disease and most important public health problem. Elevated arterial pressure causes hypertrophy of the left ventricle and pathological changes in the vasculature. Pharmacovigilance analysis study provided an insight into the drug use pattern and rational use of a drugs (prescribe well documented drug at an optimal dose, together with the correct information, at an affordable price). The outcomes of this contribute to our knowledge about drugs effectiveness and safety.

MATERIALS AND METHODS:

A pharmacovigilance analysis study was an observation, prospective. The pharmacovigilance analysis of ADRs of antihypertensive drugs observed study was conducted at tertiary care hospital in medical sciences teaching hospital. After pharmacovigilance analysis design and planning data collection was done for 4 months of period. After observation study and data collection analysis was done. Total duration of the pharmacovigilance ADRs Data analysis study was 2 years of duration.

RESULT

Total of 380 prescriptions were collected as per inclusion and exclusion criterion and ADRs were also collected and 89 ADRs were collected and analysed. In my research study, it was

detected that CCBs were the most common used anti-hypertensive drugs incidence to ADRs i.e., 31 (34.83%) and other anti-hypertensive drugs with incidence to ADRs were ACEIs (n=24, 26.96%), ARBs (n=16, 17.98%), β -blockers (n=5, 5.62%) and diuretics (n=13, 14.61%). In my research study, it was found that CNS (n=39, 43.82%) were the most common. Other affected system was CVS (n=21, 23.60%), Musculo-skeletal system (n=11, 12.36%), GI system (n=9, 10.11%), respiratory system (n=5, 5.61%) and skin (n=4, 4.50%).

CONCLUSION

In pharmacovigilance research study, calcium channel blocker (CCBs) was noted the most frequently associated drugs both as monotherapy and in combined therapy have been used, in present study were found most ADRs followed by ACEI, ARB and Diuretics.

Keywords: PHARMACOVIGILANCE, ANTIHYPERTENSIVE DRUGS, ESSENTIAL HYPERTENSION.

INTRODUCTION

Hypertension is the most common cardiovascular disease and most important public health problem. Elevated arterial pressure causes hypertrophy of the left ventricle and pathological changes in the vasculature. Hypertension is the principal cause of stroke; a major risk factor for CAD and its attendant complications. Hypertension is common non communicable lifestyle disease today in India and around the world mostly in developing and underdeveloped countries. MI and sudden cardiac death; and a major contributor to heart failure, renal insufficiency and dissecting aneurysm of the aorta. [1]

The prevalence of hypertension increases with age; about 50% of people between the ages of 60 – 70 years old have hypertension. In 90% patients, the cause is idiopathic. Around 81.5% of those with hypertension are aware they have it, 74.9% are being treated. According to physicians' experts, hypertension is likely to end up being an epidemic in the near future and 1/3 of the population suffer from hypertension by the year 2023.[2]The W H O in 2013 has estimated that high BP is a major public health issue and causes one in every eight deaths, hypertension has often described as the silent killer. [3]

Although symptoms are usually absent, persistently elevated blood pressure causes long-term damage to numerous organs and can result in overt cardiovascular disease, chronic kidney damage and stroke, and is a frequent cause of premature death. Intensive control of blood pressure, and the importance of pharmacological intervention, in all high-risk individuals with hypertension.[4]

Hypertension is one of the commonest cardiovascular disorders affecting 20% of populations in globally. Nearly 63% of total deaths in India are due to noncommunicable disease, of which 27% are attributed to cardiovascular disease which affects 45% people in the age of 40-70 age group.[5] Moreover, it remains poorly controlled due to low awareness about hypertension, lack of appropriate care through primary care and poor follow-up.[6] In

2021, the WHO released a new guideline for on the pharmacological treatment of hypertension in adults. Globally, an estimated 26% of the world's population (972 million people) has hypertension, and the prevalence is expected to increase to 33% by 2030.[7]

Pharmacovigilance analysis study provided an insight into the drug use pattern and rational use of a drugs (prescribe well documented drug at an optimal dose, together with the correct information, at an affordable price). The outcomes of this contribute to our knowledge about drugs effectiveness and safety.[8] Also provides information about price effectiveness of the drugs. The study can be used to evaluate the extent to which drugs are overused or underused. It can also help in comparison of the trend in drug use with standard guidelines.[9] The information on pattern of pharmacovigilance analysis of drug utilization can be useful for designing a drug policy and reviewing the health care budget. A pharmacovigilance analysis study can be used to evaluate the pattern of use a particular class of drugs according to age group patients, gender group patients, morbidity at various levels of health care systems which may contribute to make improvements in the drug policy of a health care systems. The triplet issue of rationality and minimization of ADRs demands a careful contemplation during any drug analysis study in a developing country, India.[10]

AIM AND OBJECTIVE

- ✓ To study the pharmacovigilance analysis of drugs in essential hypertension patients
- ✓ To find out the incidence of Drug safety and adverse drug reaction of antihypertensive drugs
- ✓ To find out how to provide safe margin efficacy and low adverse reaction of the prescribed antihypertension drugs in essential hypertension patients- attending in outdoor of medicine department in tertiary care hospital.

MATERIALS AND METHODS:

A pharmacovigilance analysis study was an observation, prospective. The pharmacovigilance analysis of ADRs of antihypertensive drugs observed study was conducted at tertiary care hospital in medical sciences teaching hospital. After pharmacovigilance analysis design and planning data collection was done for 4 months of period. After observation study and data collection analysis was done. Total duration of the pharmacovigilance ADRs Data analysis study was 2 years of duration.

The pharmacovigilance analysis data was collected from attending OPD of tertiary care hospital in cardiology medical sciences teaching hospital, who gave the information consent to participate in the research study, for the treatment of essential hypertension patients was taken for the pharmacovigilance analysis research study for period of November2019 to October 2021.

INCLUSION CRITERIA:

- Consent of the patient

- Age of the patient:18 – 70years.
- Sex – Both male and female
- Family history of hypertension

EXCLUSION CRITERIA:

- Hypertension due to pregnancy (PIH)
- Secondary hypertension

STATISTICAL ANALYSIS:

Statistical analysis was done on SPSS software with latest version

PROCEDURE:

The study was carried out in cardiology medical science teaching tertiary care hospital, after getting approval from the Institutional human ethics committee. Patients visiting the cardiology department of the tertiary care hospital was included in this study after satisfying the inclusion and explained in detail about the study and informed written consent was obtained from each patient before recruiting them into the study. Details of prescribed anti-hypertensive drugs like formulation, whether drug is prescribed using brand name or generic name, dose, route of administration, drugs taken before or after food, frequency, duration of the treatment, any adverse drug reaction, cost of drugs prescribed, any other co-morbid conditions and any other associated medications taken concurrently were recorded in the case record from.

RESULT

Total of 380 prescriptions were collected as per inclusion and exclusion criterion and ADRs were also collected and 89 ADRs were collected and analysed.

Table 1: DISTRIBUTION OF AGE GROUP AND SEX OF THE STUDY POPULATION

AGE PROUP (YEARS)	GANDER		NUMBER OF PATIENTS	PERCENTAGE (%)	X ² P Value
	MALE	FEMALE			
18 – 30	05	00	05	1.31%	X ² =19.927 P <0.05
31 – 40	25	15	40	10.52%	
41 – 50	40	20	60	15.78%	
51 – 60	120	85	205	53.94%	
61 - 70	60	10	70	18.45%	
TOTAL	230	130	380	100%	

During my present research, among the 380 patients. The most vulnerable age group with hypertension under medication was 51 to 60 years, 205 patients (53.94%) belonged to this age group of 51 – 60 years followed by 61 to 70 years populations, 70 patients (18.45%).

There were 60 patients (15.78%) in age group of 41 to 50 years populations followed by 31 to 40 years populations (40 or 10.52%) and 5 patients (1.31%) belongs to 18 to 30 years populations. The mean age of the research populations was 48+57.7, there is highly significant association between essential hypertension and age ($P<0.05$) as found in the present study as shown in TABLE:1

Table 2: GROUP OF ANTI-HYPERTENSIVE DRUGS WITH INCIDENCE OF ADRs AMONG THE RESEARCH POPULATION (n=89):

CLASS OF DRUGS INCIDENCE TO ADRs	NUMBER OF PATIENTS	PERCENTAGE (%)
CALCIUM CHANNEL BLOCKER	31	34.83
ACEI	24	26.96
ARB	16	17.98
β -BLOCKERS	5	5.62
DIURETICS	13	14.61
TOTAL	89	100

In my research study, it was detected that CCBs were the most common used anti-hypertensive drugs incidence to ADRs i.e., 31 (34.83%) and other anti-hypertensive drugs with incidence to ADRs were ACEIs (n=24, 26.96%), ARBs (n=16, 17.98%), β -blockers (n=5, 5.62%) and diuretics (n=13, 14.61%). These observations are presented on the below table 2:

Table 3: ANTI-HYPERTENSIVE DRUGS AFFECTING VARIOUS SYSTEM (ADVERSE DRUG REACTIONS):

VARIOUS SYSTEM AFFECTED WITH ANTI-HYPERTENSIVE DRUG	NUMBER OF PATIENTS	PERCENTAGE (%)
CNS	39	43.82
CVS	21	23.60
MUSCULO-SKELETAL SYSTEM	11	12.36
GI SYSTEM	9	10.11
RESPIRATORY SYSTEM	5	5.61
SKIN	4	4.50
TOTAL	89	100

In my research study, it was found that CNS (n=39, 43.82%) were the most common. Other affected system was CVS (n=21, 23.60%), Musculo-skeletal system (n=11, 12.36%), GI system (n=9, 10.11%), respiratory system (n=5, 5.61%) and skin (n=4, 4.50%). These affected systems are shown in below table 3.

Table 4: ADRs OF CENTRAL NERVOUS SYSTEM DUE TO ANTIHYPERTENSIVE DRUGS

ADRs	Amlodipine	Enalapril	CTD	Losartan	Metoprolol	Nifedipine	Ramipril	Total
Insomnia	02	00	03	02	01	01	00	09
Headache	03	00	02	00	00	00	00	05
Dizziness	09	04	04	04	00	02	02	25
Total	14	04	09	06	01	03	02	39

Table 5: ADRs OF CARDIOVASCULAR DUE TO ANTIHYPERTENSIVE DRUGS

ADRs	Amlodipine	Atenolol	CTD	Losartan	Metoprolol	Ramipril	telmisartan	Total
Postural Hypertension	03	01	02	00	01	02	01	10
Pedal Oedema	07	00	00	00	00	00	00	07
Perspiration	00	00	00	01	00	01	00	02
Flushing	01	00	00	00	00	00	00	01
Chest Pain	01	00	00	00	00	00	00	01
Total	12	01	02	01	01	03	01	21

Table 6: CLASSIFICATION OF RESULT OF NARANJO ALGORITHM SCALE AND ADRs ACCORDING TO WHO CAUSALITY ASSESSMENT SCALE AMID THE RESEARCH POPULATION

TYPE OF ADRs ACCORDING TO WHO CAUSALITY ASSESSMENT	NUMBER OF ADRs (%)
PROBABLE	48 (53.93%)
POSSIBLE	25 (28.08%)
UNCLASSIFIABLE	12 (13.48%)

UNLIKELY	04 (4.50%)
TOTAL	89 (100%)

Classification of result ADRs according to W H O causality assessment scale most of the ADRs were **PROBABLE** 48 (53.93%), followed by **POSSIBLE** 25 (28.08%), **UNCLASSIFIABLE** 12 (13.49%) and **UNLIKELY** 04 (4.50%) as represented in TABLE 6.

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 behaviour of clinicians.

In pharmacovigilance research study 65.78%% patients were male and 34.22% patients were female and it was found that essential hypertension was more prevalent in male than females. However, some studies have reported a relatively higher incidence of hypertension in females than in males. The mean age of males (46 ± 20) was more than that of females (26 ± 19.3). The hypothetical cause of higher number of male patients is due to the elevated levels of androgen (such as testosterone) as they play a significant role in elevation of blood pressure¹¹. This study was analogous to the studies conducted by Reckelhoff et al¹².

Among the different ADRs reported from different systems due to antihypertensive medications, most of the ADRs were of central nervous system followed by cardiovascular system, and gastrointestinal and respiratory system.

In the present study amlodipine was the most commonly used drug as monotherapy in 70.52 % of patients. CCBs have very less or no metabolic effects which is beneficial for diabetic hypertensive patients and also it is cheap. These could be the reasons for it to be the most commonly prescribed drug. DUS of antihypertensive drugs by Sachdeva et al¹³ also showed amlodipine as the most frequently prescribed drug. The antihypertensive effect of CCBs is independent of sodium intake or concurrent use of NSAIDS which is not the case with ACE inhibitors. In patients having hypertension with coexisting nephropathy, CCBs remarkably reduce the blood pressure. CCBs are the most preferred drugs in case of hypertensive patients with coexisting diabetes mellitus. They also have additional natriuretic effect and thus it rules out the need for adding a diuretic¹⁴.

One of the important reflections this study was, CCBs were the common group of antihypertensive drugs associated with ADRs (34.83%) which was similar to the study by Basak et al¹⁵. In CCBs, amlodipine was found to be the commonest drug associated with ADRs. The most common individual ADR was Dizziness which was seen in 64.10% of the patients which was similar to the study done by Alomar et al¹⁶. This could be due to arteriolar vasodilatation caused by CCBs. In our study Postural hypertension is also one of the common ADR seen with the use of CCBs. It occurs due to diuretic drugs.

This study showed that according to WHO causality assessment scale 53.93% of the ADRs were probable which means that these reactions are caused by the use of antihypertensive drugs and not due to any disease or by the use of other drugs and clinical improvement is seen when the drug is de-challenged. Possible ADRs were seen in 28.08% of the patients which could be due to presence of a disease or simultaneous use of other drugs.

The causality assessment by Naranjo scale showed that 28.08% ADRs were possible. Naranjo scale helps to determine whether ADR is due to the drug or due to other factors. A study done by Rende et al¹⁶ showed a probable association in 92% and a possible association in 8%.

In this study it was reflected that elderly individuals were at high risk of developing ADRs and most of the ADRs were preventable. Prescribing doctors should have sound knowledge regarding the basic pharmacology and how age affects pharmacokinetics of the drugs which will help to prevent various ADRs.

CONCLUSION

In pharmacovigilance research study, calcium channel blocker (CCBs) was noted the most frequently associated drugs both as monotherapy and in combined therapy have been used, in present study were found most ADRs followed by ACEI, ARB and Diuretics. There is a need of awareness amongst the physicians that they can follow the different latest guidelines of international and national bodies while giving the treatment to essential hypertension patients. The healthcare doctors provide the importance of reporting and monitoring of ADRs especially in elderly populations with hypertension who might suffer significant deleterious effects associated with the drugs.

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