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Study of Pharmacovigilance among Hypertensive Patients in Karachi, Pakistan

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The study of reporting of adverse drug reactions (ADRs) is called Pharmacovigilance. Adverse events are 4th leading cause of death which is more prevalent than accidents, aids, pulmonary issues and automobile death. Therefore, ADR monitoring is obligatory as newer drugs are being discovered and launched in the market. Naranjo's scale is the adverse drug reaction probability scale is described as, "the probability that the adverse event is related to drug therapy is expressed as definite, probable, possible or doubtful" Hypertension is defined as a persistent increase in blood pressure (BP) ≥140/90 mm Hg. This study was aimed to assess the prevalence of potential ADRs due to antihypertensive medicines and to evaluate knowledge and perception of subjects about pharmacovigilance. A pre-validated self-administered questionnaire was administered among 124 patients of hypertension through convenient sampling in Karachi, Pakistan. Majority of patients (39.3%) never reported the adverse effects to any health care professional and only 17.9% always reported the unwanted effects they have experienced. The practice of observing and reporting the unwanted effects of hypertensive medications among patients was found unsatisfactory and needs to be addressed by Drug Regulatory Authority of Pakistan (DRAP). Also, the health care professionals should actively participate in the awareness of Pharmacovigilance system of the country and should aware the patients about possible undesired effects.

Keywords: Pharmacovigilance, Hypertension, Adverse Drug Reactions, Regulatory Authority, Healthcare Professional,

INTRODUCTION

Pharmacovigilance is the monitoring of harmful drug reactions (Dinesh Badyal and R.S bhatya, 2006). Pharmakon is a Greek word which means "drug", and vigilance is a Latin word means "to alert" from these words the term pharmacovigilance is derived (WHO Technical Report, 2015) .Pharmacovigilance is defined as "the science and activities relating to the detection, assessment, understanding and prevention of adverse events or any other drug-related problem" (WHO, the importance of Pharmacovigilance, 2002). The perception of pharmacovigilance was established by WHO in 2004 as "Science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions (ADR) or any other medicine related problems"(Helper and

Strand, 1990).

Guidelines are setup for medications as calculation of possible adverse effects in minimum time is done through pharmacovigilance that is a part of Post Marketing Phase (Phase IV trials). Both pre and post approval stages involves Pharmacovigilance studies. Along with beneficial effects, medicines also possess Adverse Drug Reactions (ADRs) that maybe avoidable or may arise chances of morbidity (World Health Organization Collaborating Centre for International Drug Monitoring, 2015). Adverse events are 4th leading cause of death which is more prevalent than accidents, aids, pulmonary issues and automobile death (Katzung and Trevor, 2015).

WHO defines an adverse drug reaction (ADR) as "any noxious, unintended & undesired effect to a drug that is administered in standard doses by the proper route for the purpose of prophylaxis, diagnosis or treatment" (World Health Organization International drug monitoring, 1972). ADRs are classified into mild, moderate and severe by Hart Wig and Seigel (Naranjo et al. 1981). There are various factors that can contribute to ADRs such as medicines or patient's sensitivity. Therefore, ADRs are considered among top ten causes of death in various countries (World Health Organization Collaborating Centre for International Drug Monitoring, 2015).

In order to carry out appropriate drug therapy, it is the duty of a health care provider to look out for patient safety. Observation of adverse effects is important as new drugs are being developed and introduced to be used in market. By removing the causative agent from regimen or by reducing the dose, adverse effects can be diminished. Management, detection, documentation and reporting of adverse events must be encouraged by the health care professionals. Naranjo's scale is the adverse drug reaction probability scale is described as, "the probability that the adverse event is related to drug therapy is expressed as definite, probable, possible or doubtful" (WHO policy perspective of medicines, 2004). Other important aspects of pharmacovigilance comprise of reasonable drug use, to reduce risk of adverse drug reactions and low-cost of therapy. Awareness sessions on pharmacovigilance should be conducted to spread knowledge in community (Hartwig et al. 1992; Volume et al. 2001).

A persistent rise in blood pressure (BP) ≥140/90 mm Hg is defined as hypertension in patients at risk cardiovascular diseases that might require medical care. However this risk of cardiovascular diseases decline in individuals with blood pressure < 120 systolic blood pressure and <80 mm Hg diastolic blood pressure (Chobanian et al. 2003). Combination therapy of 2 or 3 anti-hypertensive agents are required to attain normal blood pressure levels which can increase the risks of ADR (World Health Organization Collaborating Centre for International Drug Monitoring, 2015).

AIMS AND OBJECTIVES

This study was conducted to assess the knowledge of individuals about the concept of pharmacovigilance and to assess the reporting of ADRs faced by hypertensive patients. Also, this study aim to assess patient's views on whether reporting of ADR can make a difference in the healthcare system.

MATERIALS AND METHODS

Development and Validation of Questionnaire

A self-administered questionnaire was designed to assess patient perception on the reporting of Adverse Drug Reactions. Initially the questionnaire comprised of 15 questions but after expert peer-review and validation, it was consisted of 9 questions. The Cronbach's Alpha was 0.84 that showed strong internal consistency. The final version of the questionnaire was consisted of demographics of the patients, duration of illness, information about adverse drug reaction faced by the subjects, frequency of reporting of ADR, knowledge of subjects regarding ADRs reporting, reasons for not reporting the experienced ADRs and perception of subjects about pharmacovigilance.

Sample size

The sample size was calculated to be 889 using online calculator open Epi at confidence level 95%. Out of 1000 selected subjects, 954 subjects gave their consent to participate in the study. The complete response was collected from 924 patients while 30 questionnaires were not completely filled.

Subjects

Hypertensive patients from Out-Patient Departments (OPD) of one Public and one Private Sector Tertiary Care Hospitals in Karachi, Pakistan were selected by convenient sampling method after having taken their informed consent. All subjects were adult.

Informed Consent

The selected patients were informed about the significance of the study and were requested for their consent to participate in this study.

Data Collection

The study was conducted from November 2020 to February 2021. The Questionnaire was administered to the selected subjects who visited the OPDs at the selected Tertiary Care Hospitals. The data was collected using pre-validated questionnaire.

Study Design

This was a descriptive cross-sectional study, conducted on hypertensive out-patients visited in OPDs of Public and Private tertiary care hospitals. This study was performed to evaluate the reporting practices of adverse drug reactions of the medications that the subjects were taking to treat their hypertension. This study was also aimed to assess the prevalence of potential ADRs due to antihypertensive medicines and to evaluate knowledge and perception of subjects about pharmacovigilance.

RESULTS

Out of total 924 subjects, there were 46.4% male and 53.6% female. Majority of the respondents (85.71%) were in between the age group of 40-60 years (Table 1). It was found that 50.0% subjects were suffering from hypertension for more than 10 years (Table 2). Table 3 shows that 35.7% of the selected patients had faced unwanted effects often due to the medications that they were taking, while 46.4% had never encountered any ADRs. Majority of patients (39.3%) never reported the encountered ADRs to any of health care professional while only 17.9% responded that they always report the unwanted effects they experienced. However, 35.7% responded that they report the unwanted effects to their physicians/consultants, 7.1% report to nurses and similarly 7.1% reported to pharmacist, while the remaining 50% reported the unwanted effects to none of the healthcare professional. 57.1% of the selected patients strongly agreed that the undesired effects must be reported. Upon the assessment of the reason of not reporting adverse effects it was calculated that 75.0 % patients were not aware of the reporting of unwanted effects (Table 4).

The respondents 96.4% were also suggestive that the reporting must be done for such undesired effects.

Table 1: Age range of Participants

Age Range	%
21-30 years	3.57
31-40 years	10.71
41 years-above	85.71

Table 2: Duration of Illness of Participants

Duration (Years)	%
1-3 years	25.00
4-6 years	14.29
7-9 years	10.71
More than 10 years	50.00

Table 3: Reasons for Not Reporting the Experienced ADRs

RESPONSE	%
Do not know about reporting ADR	75.00
Do not know how to submit ADR reporting form	17.86
Do not know how to fill the ADR reporting form	7.14

Table 4: Evaluation of ADRs Monitoring and Reporting Practices

Adverse Effects Experienced Due to Hypertensive Medications		Frequency of Reporting Unwanted Effects		Reporting of Unwanted Effects to Healthcare Professional		Patient Views on Reporting of Unwanted Effects	
Response	***%***	***Response***	***%***	***Response***	***%***	***Response***	***%***
Always	0	Always	17.9	Doctor	35.7	Strongly agree	57.1
Often	35.7	Often	17.9			Agree	39.3
Sometimes	17.9	Sometimes	14.3	Nurse	7.1	Neither agree nor disagree	3.6
Rarely	0	Rarely	10.7	Pharmacist	7.1	Disagree	0
Never	46.4	Never	39.3	none	50.0	Strongly Disagree	0

DISCUSSION

The aim of anti-hypertensive medications is to reduce the blood pressure in the direction of the normal limits (Khurshid et al. 2012). Specific concerns must be supplied for exceptional lifestyles issues, as hypertension commonly gives an asymptomatic medical image (Arshad et al. 2012). The use of multidrug therapy is excessive amongst hypertensive patients, comparable findings were made in different researches (John et al. 2013). Multi drug therapy appears to be extra rationale technique to diminish cardiovascular hazard element in high blood pressure (Mancia and Grassi et al. 1998).

There is an increase possibility of adverse drug reactions with increase in variety of medications. Therefore, adverse events are more common in patients' receiving combination therapy. Other researchers also found related outcomes (Chobanian et al. 2003). The increase in variety of prescription drug notably raises the quantity of unfavorable drug reaction due to drug-drug interaction (Katzung and Trevor, 2015).

Risk elements for ADRs had shown that sufferers on a multiple therapy regimen were suspected to increase ADRs in comparison to sufferers on monotherapy (Sato et al. 2013). Pharmacovigilance actions and strategies should be reinforced to protect public from dangerous effects of drug treatments (Kale et al. 2011).

CONCLUSION

It was concluded that the practice for observing and reporting the ADRs of hypertensive medications among patients in Karachi were not rationale. Pharmacovigilance has an essential role in minimizing the problems related to ADR but this element was not properly found among the subjects. The patients had experienced some ADRs but they didn't report due to lack of awareness to report the ADRs. The positive impact found was that the subjects after this study were strongly agreed that the ADRs should be reported. The health care professionals should actively participate in the awareness of Pharmacovigilance system of the country and should aware the patients about possible undesired effects.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

For example NS, MTB and AJ designed and performleed the experiments and also wrote the manuscript. AH, ML and AS and UB performed collection of questionnaire and data analysis. SAK AH and TM designed experiments and reviewed the manuscript. All authors read and approved the final version.

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