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Research Article

PHARMACOVIGILANCE STUDY IN GERIATRIC POPULATION

KIRAN NAGARAJU[1]*, MANASA S[1], MANJUNATH R[2]

[1]Department of Pharmacy Practice, Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, Karnataka, India. [2]Department of General Medicine, KIMS Hospital and Research Centre, Bengaluru, Karnataka, India. Email: kirantoxicology@gmail.com

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ABSTRACT

Objective: Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines. Main goal of pharmacovigilance in geriatric is to improve the safe and rational use of medicines and thereby improving patient care, health of the society. Pharmacovigilance is particularly concerned with the adverse drug reactions (ADR's). Hence, a closer pharmacovigilance studies are much needed in the older age group due to polypharmacy, which can cause ADR's leading to hospital readmission and the direct and indirect treatment cost to treat the ADR's. The objective of this study was to assess the prescribing practice and ADR's in geriatric patients with two or more comorbid condition during the stay in the hospital and to follow-up on 15th, 30th, 45th, 60th, 75th and 90th day after discharge.

Methods: The study was conducted in Medicine Department, Kempegowda Institute of Medical Science Hospital and Research Centre, Bengaluru. It is a non-randomized observational prospective study conducted for a period of 6 months, to assess the prescribing pattern and incidence of ADR in the geriatric population. We made an attempt to assess the incidence of ADRs after discharge from the hospital by doing follow-ups.

Results: Among the 50 patients included during the study, 29 (58%) patients were between the age group of 60 and 65 years, out of which 20 were female, and 9 were found to be male patients. Out of 50 patients, 40 (37.7%) patients suffered from hypertension, 30 (28.3%) patients had diabetes mellitus. The most commonly used antihypertensive drug was found that 20 (33.8%) patients were on calcium channel blockers which were used majorly, in anti-diabetic drugs, insulin was used in 19 (44.1%) patients, followed by 10 (23.2%) patients who were prescribed oral hypoglycemic like metformin. Number of drugs prescribed per prescription was found that 68% of patients were prescribed with 6-10 drugs. Among the study population, we found the incidence of three mild ADRs during follow-up. During analyzing of prescription, we found totally 122 drug interactions, out of which 83 (68%) were moderate, 30 (25%) were mild and 9 (7%) were found to be severe drug interactions.

Conclusion: We observed that monitoring of drugs for ADRs in the geriatric population is mandatory due to their polypharmacy. Follow-up studies after discharge for monitoring of ADR will be one step ahead to improve the quality of life. This can reduce the hospital readmission, which can in turn reduce to the economic burden of the patients.

Keywords: Pharmacovigilance, Adverse drug reactions, Geriatric, Polypharmacy.

INTRODUCTION

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines. Main goal of pharmacovigilance in geriatric is to improve the safe and rational use of medicines and thereby improving patient care, health of the society [1]. Pharmacovigilance is particularly concerned with the adverse drug reactions (ADR's), According to World Health Organization's (WHO) definition an ADR is a response to a drug that is noxious and unintended, and occurs at doses normally used in human for the prophylaxis, diagnosis and treatment of diseases, or for modification of physiological function [2]. It was estimated that ADR's were the fourth to sixth largest cause of death in United States [1,3,4]. ADR's are associated with increased mortality, fatal ADR's account for 3% of all deaths in the general population rising to 5% in hospitalized patients [5].

The detection of ADR has become increasingly significant because of the introduction of large number of potent toxic chemicals as drugs in the last two or three decades [3]. ADR's occur more frequently in older people, where most developed world countries have accepted the chronological age of 65 years as a definition of elderly or older person [2], at the moment, there is no. United Nations standard numerical criterion, but as agreed cutoff is 60+ years to refer the older population [2,3,6]. Health problems are supposed to be the major concern of the geriatric population, and it is estimated that one out of two elderly in India suffers from at least one chronic disease, which requires lifelong medication [7]. People aged 65 and over make up approximately 13% of the total population and consume about 40% of all type of medications [8].

Indian elderly represent 12.8% of the entire global elderly population [9]. In the year 2000, there were an estimated 600 million people aged 60 years and above in the world. By 2025, this would double to about 1.2 billion people and by 2050 there will be 2 billion with 80% of them living in developing countries [10]. In India, the elderly population is fast growing from 5.6% in 1961 and it is projected to rise to 12.4% of the population by the year 2026. A share of 22% of definitely preventable ADRs observed in the study is an indicator on the degree of preventability of drugs use related problems among Indian elderly [7]. In India, life expectancy has steadily gone up from 32 years at the time of independence to over 63 years in 2001. In 2011 life expectancy has reached 66.8 years [2,6].

In geriatrics, ADR's occur due to multiple comorbidities, as increase in age there will be several incidence of one or more chronic conditions, like hypertension, diabetes, asthma, thyroid disease, arthritis, depression etc., where comorbidity will lead to use of polypharmacy [11]. Polypharmacy is defined as concurrent use of multiple medications by a patient. Polypharmacy had a major influence on the occurrence of ADR's with a total of 64.28% with patients using four or more medications [12]. A review of several studies indicated that patients aged >65 years use on an average 2-6 prescribed medications and 1-3.4 nonprescribed medication which can lead to drug interactions [4].

A study by Joshi *et al*. showed an ADR rate of 7% in patients taking 6-10 drugs increasing to 40% in those taking 16-20 drugs. Polypharmacy is a common occurrence of ADR's in elderly patients due to a variety of reasons like increasing number of chronic health conditions, patients being treated by multiple prescribing physicians, availability of nonprescription drugs, inadequate patient knowledge of medications and medical conditions [10].

Polypharmacy also increases the incidence of drug interactions, noncompliance which in turn leads to increase in hospital admissions and thus health expenditure [10]. Where minimizing or controlling polypharmacy requires periodic evaluation of patient's drug regimen, the evaluation may reveal the need to change the prescribed drug therapy. Noncompliance in elderly due to age factor, living alone, less educated, with more diagnoses and low economic conditions which also contribute to the occurrence of ADR's [13].

ADR also occurs due to decreased hepatic metabolism, progressive deterioration of renal function [14], altered pharmacokinetics and pharmacodynamics [14-17] slower homeostatic responses, inappropriate prescription where like wrong dosing, incorrect frequency of administration, prescribing ineffective medication duplicate therapy About one fourth of the ADR's are due to inappropriate medication use [7]. Several studies have demonstrated that the frequency of unnecessary or non-recommended medications use is higher in patients taking many medications than in those taking few medications [18].

Factors connected with very old age such as frailty, falls, abnormal sensitivity to medications and polypathology, all directly impact on ADR occurrence [19]. ADR's are often difficult to detect in the older population because of their atypical or nonspecific nature like lethargy, confusion, light headedness, or falls [7]. Hence the clinicians must look for the side effects of the drugs to identify the ADR's, since most ADR's in the elderly are predictable and, therefore, preventable by using the knowledge of pharmacological principle and how ageing affects kinetics process [4]. Although many of risk factors for ADR's are often irreversible, example like renal impairment, burden of co-morbidity and liver disease [5].

Recent studies have shown that ADR related hospital admissions are increasing and account for approximately 5-12% of all hospital admissions in older patients with a high hospital mortality rate of 8-10%, and ADR related hospital admissions appear to be preventable in two fifth of cases [20]. An average rate of ADR related hospital admission is 16.6% in the elderly compared to 4.1% in younger patients, where 88% is preventable [11,15]. ADR's are a leading cause of hospitalization in older patients, with recent studies showing that 11.5-14% of older patients had an ADR that was causal or contributory to admission [5].

In India, management of ADR is estimated to cost 921.53-9215.32 INR [3,8]. Hence preventing an ADR's by identifying the individuals at high risk is central to improving patient care, health outcomes and reduce health expenditure [2]. There is a clearly a need to reduce readmission rates to hospital, whether they are due to drugs or not. Unnecessary hospital admission caused by ADR's is an unnecessary loss of health as well as loss of quality of life. Preventing these hospitalizations will keep seven times more elderly people out of the hospital than nonelderly ones [5,21]. Therefore, ADR related hospital admissions are a significant and expensive public health problem in older age group.

Measures have to be taken to ensure frequent patient follow-ups. Reassessing the need of drugs in the present dose regimen has to be given priority during routine follow-ups, any drug related problem has to be assessed [7,19]. New or improved routes for following up with patients after they are discharged are clearly needed, based on the recent finding that 22% of patients admitted to general medicine services either die, are readmitted, or visit an emergency room within 30 days of discharge [22].

ADR's monitoring and reporting activity is in its infancy in India. ADR reporting rate in India is just 1% as compared to the world rate of 5% [23]. The important reason is lack of awareness and lack of interest of health care professionals in ADR reporting and documentation. Hence an awareness about reporting ADR's should be improved. Many studies have shown that active involvement of pharmacists is critical for success of the pharmacovigilance system, in addition to their responsibilities regarding drug dispensing and compliance [23]. Pharmacists can have an important role in reporting ADR, by monitoring the patients for both therapeutic and toxic effects of the drug, along with medication adherence, which can be done by regular follow-up of the patients, assess their conditions and if any problems, resolve it as soon as possible and improve the quality of care and health of the society.

A scope of closer pharmacovigilance studies is much needed in the older age group due to polypharmacy, which can cause ADR's leading to hospital readmission and the direct and indirect treatment cost to treat the ADR's. Hence, we have taken up this study to assess the incidence of ADR's after discharge from the hospital by doing a follow-ups.

METHODS

It is a non-randomized observational prospective study carried out in Medicine Department, Kempegowda Institute of Medical Science (KIMS) Hospital and Research Centre, Bangalore. It is a 1200 - bedded tertiary care teaching, super specialist hospital, providing specialized health care services to all strata of people in and around Bengaluru. Study was conducted for a period of 6 months in the year 2013-2014. The study protocol was presented in the Ethical Committee and for the same, approval was taken to conduct the study. In this study all the inpatients ≥60 years of either sex with two or more comorbidity and on polypharmacy in medicine department, KIMS Hospital. Patients who give informed consent were included. Patients who use of alternative system of medicines like Ayurveda, Homeopathy, Unani etc., patients who had the reported ADR in the past, patients suffering from hepatic and renal dysfunction, patients with complications like carcinoma, HIV and any other immunocompromised status, patients having language barriers communicating with the investigator were excluded.

The information was collected from patients care record forms and patients and care giver verbal information over telephonic interview during follow-up period. Inform consent was taken from patients who met the inclusion criteria, with the address and phone number and documented in a well-designed data collection form. In the well-designed data collection form required information was extracted from inpatient's case records which included all the details of patient like, patient demographic like name, age, sex, weight, personal history, medication history, presenting complain, past medical history, laboratory investigation, present medications given in hospital and the discharge medications prescribed. Follow-up of all the recruited patient after discharge from hospital for every 15 days (i.e. 15^{th}, 30^{th}, 45^{th},60^{th}, 75^{th} and 90^{th}) for a period of 3 months telephonically was carried out. During every follow-up patient were asked about their present health condition, medication taking behavior, assess the prescribing pattern, and monitor the occurrence of any ADR's, during their treatment. If any occurrence of ADR during the follow-up phase, the patient was called for the work up on the incidence of the ADR in the medicine department at KIMS hospital. Reported ADR will be documented in the well-designed customized yellow card, which includes all relevant data such as name of the patient, age, sex, date of occurrence of events, medication history, duration of reaction, description of the reaction and any other information needed for compiling the results in accordance with the WHO guidelines. The obtained data was analyzed by using simple percentage method to conclude the study results.

RESULTS

Table 1: Demographic details

Age in years	Number of patients	Male	Female
60-65	29	9	20
66-70	9	3	6
71-75	4	0	4
76-80	3	1	2
>81	5	2	3
Total	50	15	35

Table 2: Social habits

Habits	Number of patients
Smoker	8
Alcoholic	4
Tobacco chewing	1
None	40

Table 3: Chronic conditions

Diseases	Number of patients suffering from diseases	Female	Male
Hypertension	40	29	11
Type II diabetes mellitus	30	23	7
COPD	9	1	8
Asthma	7	6	1
Thyroid	7	7	0
Others	13	11	2
Total	106	77	29

COPD: Chronic obstructive pulmonary disease

Table 4: Prescribing pattern of anti-diabetic drugs

Drugs	Number of patients	Female	Male
Insulin	19	15	4
Metformin	10	8	2
Glimepride+metformin	10	7	3
Glipizide+metformin	2	1	1
Glimepride	1	1	0
Vildagliptin+metformin	1	1	0
Total	43	33	10

Table 5: Prescribing pattern of antihypertensive drugs

Antihypertensive drugs	Number of patients	Female	Male
Calcium channel blockers	20	13	7
Beta blockers	9	6	3
Angiotensin II antagonist+diuretics	9	9	0
Angiotensin II antagonist	7	4	3
Diuretics	7	5	2
Angiotensin converting enzyme inhibitor	3	1	2
Calcium channel blockers+Beta blocker	2	2	0
Alpha+beta adrenergic blockers	1	0	1
Alpha blocker	1	1	0
Total	59	41	18

Table 6: Number of drugs prescribed per prescription

Number of drugs	Number of patients
1-5	11
6-10	34
10-15	4
15-20	1

DISCUSSION

A prospective observational study was taken up to study the prescribing pattern and ADR in geriatric population by doing follow-ups for 3 months. A total of 50 patients who satisfied the inclusion criteria were included in the study. Among the recruited patients, 29 (58%) patients were in between the age groups of 60 and 65 years, followed by 9 (18%) patients between 66 and 70 years majorly. In our study, we found that, 35 (70%) patients were female upper handed the male with 15 (30%) patients. This was correlated with a similar study conducted by Veena *et al*. in Bengaluru. They had done a prescription analysis of various drugs in 106 elderly patients. They took the data from the case records, which determined most of the patients in between the age group of 65 and 70 years with 79.24%. Overall in the study group, male patients were dominated with 55.66% [35]. Another study by Fadare *et al.* in Nigeria showed that out of 220 patients, their mean age was found to be 72.8±7.2 years and female patients represented 58.2% of the overall study population along with 42.8% represented by males [32].

Considering the age and gender distribution of the study population it was found that 29 (58%) patients were between the age group of 60 and 65 years, out of which 20 (68.9%) patients were female and 9 (31.1%) patients were found to be male. 9 (18%) patients were between the age group of 66-70 years, of which 6 (66.6%) patients were female and 3 (33.3%) of them were found to be male. when correlated with a study by Lohani *et al*. in Nepal, showed that majority of which 63 (43 males, 20 females) patients were aged between 65 and 74 years, followed by 25 (15 males, 10 females) patients who were between 75 and 84 years and remaining 12 (5 males and 7 females) patients were found to be 85 years and over [36].

Considering the social habits of the study population 40 (75%) patients had none of the habits, 8 (15%) patients had the habit of smoking followed by 4 (8%) patients who were alcoholic and 1 (2%) patient was found to have the habit of tobacco chewing.

Among the study population the most commonly found chronic conditions were hypertension in 40 (37.7%) patients, followed by

Table 7: ADR's

Suspected drug	ADR
Montelukast	Headache
Metformin	Chronic diarrhoea
Telmisartan	Cough

ADR: Adverse drug reactions

Table 8: Drug interactions

Drug interactions	Number of interactions
Mild	30
Moderate	83
Severe	9
Total	122

Table 9: Follow-up details

Number of days	Patient feeling good	Patient feeling better	Patient feeling bad
15th day	5	33	4
30th day	18	22	2
45th day	33	9	0
60th day	39	2	1
75th day	39	3	0
90th day	39	3	0
Total	173	72	7

Type II diabetes mellitus in 30 (28.3%) patients which were the two majorly found chronic diseases in our study. Other chronic diseases were chronic obstructive pulmonary disease in 9 (8.4%) patients, asthma in 7 (6.6%) patients and also thyroid diseases in 7 (6.6%) patients. We also considered other diseases like osteoarthritis, dyslipidemia, gastroesophageal reflux disease and peptic ulcers which were found in 13 (12.2%) patients. When correlated with a study by Mahesh *et al*. in Tamil Nadu, they found that cardiovascular system (39.13%), followed by endocrine system (25%) were most common reasons for hospital admissions [37]. In other similar study by Lohani *et al*. in Nepal, found that most common diagnoses were respiratory disease in (39%) and cardiovascular disease in (31%) of the patients [36].

While considering the prescribing pattern of anti-diabetic drugs, 19 (44.1%) patients used insulin which was the most commonly used injectable, 10 (23.2%) patients used oral hypoglycemic drugs like metformin and 10 (23.2%) patients used the fixed combination of glimepride and metformin. In a study by Taskeen *et al*. in Hyderabad, they found metformin was the most prescribed anti-diabetic [33].

In the prescribing pattern of antihypertensive class of drugs, 20 (33.8%) patients were prescribed with calcium channel blockers like amlodipine which was the most commonly used drug, 9 (15.2%) patients were prescribed with beta blockers like metoprolol, atenolol and 9 (15.2%) patients used angiotensin II antagonists with diuretic combination like telmisartan with hydrochlorothiazide, losartan with hydrochlorothiazide. Which is correlated with other study by Arshad *et al*. in Warangal, a study on antihypertensive used in geriatric, found that most common drug classes involved in the prescribing was calcium channel blockers 37% followed by angiotensin II receptor antagonists 21% [16].

In the total prescription analysed among the number of drugs prescribed per prescription, we found that 34 (68%) patients were using between 6 and 10 drugs, 11 (22%) patients were using between 1 and 5 drugs, 4 (8%) patients used 10-15 drugs and 1 (2%) patient used about 15-20 drugs. When correlated with a study by Mahesh *et al*. in Tamil Nadu, 6-8 drugs were prescribed for 56.52%, 9-12 drugs were prescribed for 23.91%, followed by >12 drugs in 8.69% [37]. Another study by Fadare *et al*. in Nigeria, found 65 (29.5%) patients had five or more drugs prescribed and 114 (51.8%) patients had 3-4 drugs prescribedin their prescription [32].

Out of 50 prescription analysed in our study, a total of drug-drug interactions we found out of which, 83 (68%) were moderate drug interaction, 30 (24.5%) were mild interactions and 9 (7.3%) were severe drug interactions. In a similar study by Taskeen *et al*. in Hyderabad found 16 (10.6%) prescriptions with drug-drug interactions [33]. Also a study by Sapkota *et al*. in Nepal, he found that 114 potential drug-drug interactions had occurred in the prescription analysed for the study [38]. During our follow-up study period, we found three mild ADR's like headache due to montelukast, chronic diarrhoea due to metformin and cough due to telmisartan. We also found one readmission to hospital within 15 days of discharge of the patient from the hospital. During the follow-up phase 8 (16%) patients were dropped out of the study due to different reasons like not responding to the phone calls, not willing to answer the questions asked by the investigator, transferred to different place after discharge from hospital, hence we were unable to contact the patients or caregiver.

While considering the six follow-ups of the study carried out for the duration of 3 months we found that 33 patients were feeling better then in hospital by 15th day, 22 patients were feeling better by 30th day, followed by which 33 patients were in good condition through 45th day and 39 patients were good by the end of 60th, 75th and 90th day of the follow-up and we also found that four patients had complained of bad health condition within 15th day of discharge from hospital and two patients complained of bad health by 30th day of the follow-up.

CONCLUSION

We observed that monitoring of drugs for ADR's in geriatric population is mandatory due to their polypharmacy. Follow-up studies after discharge is much more needed to assess the appropriateness of prescribing practice in geriatrics by the general practitioners. Also, to improve the reporting of ADR's that has occurred, due to delayed reactions in the patients after discharge from hospital, which will be one step ahead to improve the quality of life. This can reduce the hospital readmission which can in turn reduce to economic burden of the patients.

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