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A Pharmacovigilance Study In Geriatric Patients In A Tertiary Care Hospital

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ABSTRACT

Objective: The present study was conducted to find out the occurrence of ADRs and assessed their causality and severity of in ambulatory geriatric population.

Methods: This was a prospective, cross sectional, observational study, performed in the geriatric outpatient department of Gauhati Medical College and Hospital (GMCH) between the period of August 2013 – February 2014. Suspected ADRs were evaluated for causality by using Naranjo's probability scale and severity by modified Hartwig's criteria.

Results: A total of 1000 patients were screened, 69 patients were reported with ADRs, resulting incidence rate of 10% among the geriatric population. Most of the ADRs were mild (76.8%) and none of the patient experienced serious adverse reactions. Approximately, half of the ADRs (53.63%) were categorized as probable. The most common ADRs were found to be pedal edema (31.8%). Other ADRs experienced by the patients are gastritis, arrhythmia, diarrhoea, skin rashes, raised liver enzymes etc. Majority of ADRs (49.2%) were managed by changing the suspected drug.

Conclusions: In this study, 6.9 % of geriatric population were found to have ADRs. Therefore, close monitoring of this group of patients are essential. The results of this study will be helpful for the formulation of strategies for pharmacovigilance services in geriatric population.

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INTRODUCTION

An adverse drug reaction (ADR) has been defined as "any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of a disease, or for the modification of physiological functions [1]." No matter how efficacious the drugs are, it always associated with the risk of ADRs. Drastic changes have been done on modern therapy despites ADRs remain a common drawback with all the medications.

ADRs can be mild to severe, often it can lead disability and even death [2]. In some countries, ADRs rank among the top ten leading causes of death [3]. Adverse drug reaction (ADRs) increase morbidity, mortality, which in turn increase the health care cost [4,5,6]. Immediate identification, evaluation and monitoring of ADRs are paramount important to minimize harm to patients and thus improves public health.

An adverse drug reaction (ADR) as defined by world health organization is "a noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of a disease, or for the modification of physiological function"[1]. Approximately 2.9-5.6% of patients are hospitalized due to ADRs [7]. Two different systematic review reported that median hospital admission rate due to ADR-related cause were 10% and 11%, respectively, among ≥65 years [8,9].

Pharmacovigilance is the scientific term that describes the assessment, recognition and prevention of ADRs [10]. The main purpose of pharmacovigilance is to protect the patients from the untoward medical occurrence.

Geriatric population are often suffers with multiple disorders as a result number of prescription and non prescription drug usage among these populations also increase. Which will increase the likelihood of drug-drug interaction, medication error, inappropriate prescription and adverse drug reaction. A pharmacovigilance study in India reported the incidence of ADRs is 10% among ambulatory geriatric patients [6]. Aged more than 80 years, patients taking multiple drugs, prolonged treatment duration and patients suffering with multiple diseases are identified as a risk factor for ADRs among the elderly [6].

As the age increase physiological changes such as metabolizing capacity of liver, fat storage, glomerular filtration rate also decrease, which ultimately affects the pharmacokinetics and

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pharmacodynamics of many drugs. Simultenously, cognitive impairment and depression also found to be high among the geriatric age group which will lead to poor compliance of drug. Wrong medication administration procedure and modification of dosing regimen have also been identified to be associated with the development of ADRs [11]. As a results geriatric population are of high risk of development of ADRs and moreover, many of these ADRs are preventable. With the view of the above, we therefore, planned to assess the ADRs in geriartric population. This study will be helpful for the clinicians for improving the therapeutic management plan for geriatric patients.

METHODOLOGY

Study design and setting:

This was a prospective, cross sectional, observational study, carried out in the Geriatric department of Gauhati Medical College and Hospital (GMCH), It is the largest and undoubtedly the most advanced tertiary care Govt. hospital of the entire northeast, catering to millions of people in this region.This study was conducted for a period of 7 months that is from August 2013- February2014. Institutional Ethics Committee of Gauhati Medical College and Hospital (GMCH) approved the study and permission from the respective department head was obtained prior to the study initiation. Patients of both sexes, aged ≥ 60 years were included in the study. Prescriptions having incomplete patient details, patients with past history of cardiac disorders, hepatic and renal impairment, psychiatric disorders, drug addicts and patients who were not agree to sign the inform consent form were excluded from the study.

All patients attending the geriatric department for various indications were screened for ADRs and only those patients showing ADRs and fulfilling the inclusion criteria were included in the study. Their details were recorded in the case report forms. For validation all ADRs were discussed and confirmed with the practicing physicians.

Data collection

Data related to demographic characteristics of the patients, diagnosis, prescribed medications, route of administration, frequency, doses, types of ADRs, ADRs description, final outcome(recovered/not yet recovered/fatal/unknown) was collected. Causality and severity of ADRs were assessed by Naranjo's scale and Hartwig scale respectively.

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Causality Assessment Forms:

All the suspected ADRs were assessed for causality by using "Naranjo's causality assessment scale" [12]. It contains a number of questionnaires, a score has been provided to each question (ranging from -1 to +2). This scale classifies the ADRs as "highly probable", "probable", "possible" and "unlikely" according to score calculated for a particular drug-ADR combination. "Total scores range from -4 to +13, the ADRs are considered definite if the score is 9 or higher, probable if 5 to 8, possible if 1 to 4, and doubtful if 0 or less".

Severity Assessment Forms:

This form contains severity assessment scale proposed by Hartwig et.al [13]. This scale contains "different levels of severity from level 1 through level 7", to describe the degree of the severity of patient reported to have ADR. "Levels 1 and 2 indicated mild, 3 and 4 considered as moderate and level 5 and above as severe ADRs".

Statistical analysis

Data was analyzed by using Microsoft Excel (MS Office 2010) were used. Descriptive statistics such as frequencies and percentages were used to interpret the data.

RESULTS

A total of 1000 patients were screened during the study period, 574 (57.4%) were male and 426 (42.6%) were female. ADRs were detected in 69 (6.9%) patients, out of which 41(4.1%) were male and 28 (2.8%) were female. The incidence of ADR was found to be more in the age group of 60-70 years. The distribution of ADRs based on the age group are presented in Table number 1.

Age group(years)	No.(%) of patients
60-70	56(81.1)
71-80	13(18.8)
81-90	0

Table 1: Distribution of ADRs based on the age group

The most commonly occurring ADRs were pedal edema (31.8%), gastritis (17.5%), arrhythmia (10.1%), diarrhoea (14.5%), skin rashes (10.1%), hepatitis (5.7%), and others (nephrotoxicity,

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dizziness, cough, nausea, vomiting). The occurrence of different types of ADRs are listed in Table 2.

Type of ADRs	No. (%) of ADRs
Pedal edema	22(31.8)
Gastritis	11(15.9)
Arrhythmia	7(10.1)
Diarrhoea	10(14.5)
Skin rashes	7(10.1)
Elevated liver enzymes	4(5.7)
Thrombocytopenia	2(2.9)
Others	6(8.7)

Table 2: Occurrence of different type of ADRs

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Amlodipine, a calcium channel blocker was found to be commonest drug causing ADRs (31.8%) followed by amoxicillin (8.7%), insulin (8.7%), metaprolol & ofloxacin (7.2%), erythromycin, rifampicin, diclofenac (5.8%) and others (erythropoietin, ramipril, aspirin, paracetamol, amphetamine (11.6%). Number and percentage of individual drugs causing ADRs are listed in Table 3.

Name of drug	**No.(%) of ADRs**
Amlodipine	22(31.8)
Amoxycillin	6(8.7)
Insulin	6(8.7)
Metaprolol	5(7.2)
Ofloxacin	5(7.2)
Erythromycin	4(5.8)
Rifampicin	4(5.8)
Diclofenac	4(5.8)
Propranolol	3(4.3)
Methotrexate	2(2.9)
Others	8(11.6)

Table 3: List of drugs caused ADRs

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Different measures were taken to manage the ADRs. Most of the ADRs were managed by changing the suspected drug (49.2%), followed by other drugs added without changing the suspected drug (14.4%). The details of measures taken for the management of ADRs are presented in table 4.

Measures Taken	No.(%) of patients
Drug changed	34(49.28)
Other drug added	10(14.49)
Drug withdrawn	8(11.6)
Dose reduced & other drug added	7(10.14)
No change	5 (7.24)
Dose reduced	5(7.24)

TABLE 4: Management of ADRs

According to Naranjo's probability scale, majority of ADRs 37 (53.63%) were detected as probable and followed by possible (39.1%). Most of the ADRs (76.8%) were found to be mild and none of the patient develops serious or severe adverse reaction. Causality and severity assessment of ADRs are presented in Table 5.

Outcome	No.(%) of ADRs
Causality	
Probable	37(53.62)
Possible	27(39.1)
Definite	5 (7.2)
Doubtful	0
Severity	
Mild	53(76.8)
Moderate	16(23.1)
Severe	0

Table 5: Classification of ADRs on the basis of causality and severity

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DISCUSSION

The incidence of ADRs in our study were found to be 6.9%, which is lower in comparison to a study conducted in ambulatory elderly patients by Mandavi et.al [6]. A study conducted by Schneider et al. where the incidence rate was found to be 21% [14]. The most commonly occurring ADRs in our study was pedal edema. A similar observation was also reported by Mandavi et.al [6]. The causative drugs for this ADR was amlodipine. This drug generally used for the treatment of hypertension and acts by blocking calcium channel. Peripheral edema is one of the most commonly occurring ADRs of amlodipine often leading to nonadherence to treatment [15]. The main cause for amlodipine induced peripheral edema is increased capillary hydrostatic pressure by arteriolar dilation [15]. This is the major limiting factor for this drug. Drug withdrawal and lowering the dose is a common intervention taken by the physician to mange this ADRs. The second most commonly occurring ADRs in our study was gastritis. It was commonly found with the antibiotics (amoxycillin, erythromycin) and nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs are the drugs prescribed for the treatment of pain and fever. It acts by inhibiting cyclooxagenase enzymes, thereby inhibits the prostaglandin synthesis. Inhibition of prostaglandin is a main contributing factor for the development of gastritis [16]. Withdrawal of NSAIDs is preferably the first choice for the management of this ADRs however, many times it is not feasible. Hence, an antacid is prescribed concomitantly. Similar to our results as reported by other study gastritis, arrhythmia, headache, skin rashes, elevated liver enzymes were also found to be the ocuurence of different ADRs among ambulatory geriatric patients [6].

In this study, majority of ADRs (63.6%) found to have a probable relationship with the drugs, concordant to our results Suh et.al also reported the maximum number of ADRs were probable [17]. Only 5 ADRs in our study had a definite relationship with the drug. Similar to our results, a study has reported 11 ADRs had a definite causal relationship with the suspected drugs [6]. Most of the ADRs reported in our study were found to be mild (76.8%) and no intervention were required.
The major limitation of this study is most of the ADRs are reported from outpatients department and collected from a single center.

In conclusions, the results of our study showed that a majority of the ADRs are associated with cardiovascular drugs and antibiotics. Therefore, careful monitoring of these drugs in geriatric population are essential to prevent the harmful consequences.

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