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Original research article

A Prospective Evaluation of Adverse Drug Reactions in Geriatric Medication Inpatients at a Tertiary Treatment Facility

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Abstract

Aim: to evaluate the pattern of adverse drug reaction in geriatric inpatients of medicine in a tertiary care center.

Methods: This prospective observational study was carried out in the Department of Pharmacology, A.N.M. Medical College and Hospital, Gaya, Bihar, India for 15 months. Patients more than 60 years of age of both sex, patients those who give consent to participate in the study. A causality analysis was done as per the WHOUMC and Naranjo probability score, preventability of an ADR was assessed by modified schumock thornton scale, severity was evaluated by modified Hartwig and siegel scale, which gives an overview of the severity of ADR whether it is mild, moderate or severe in nature.

Results: Total of 50 patients had the ADRs in the 7 medicine units in the study period of 12 months. Majority of the patients showed the ADRs were in the agegroup of 60-65 years n=20 (40%) while least 5 (10%) in 80-85 years age group. Out of total 50 ADRs, Male were 27(54%) and femaleswere 23 (46%). Most of the ADRs were of type A 25 (50%) followed by type C - 20 (40%). In majority of the instances, it was antimicrobial agents 16 (32%) in which metronidazole was the most common 6 (12%), next was amoxicillin and clavulanic acid combination 5 (10%) followed by antimicrobial agents,NSAIDs 11(22%) were common- in which aspirin 5 (10%) was common. Next was ACE inhibitors were alsoinvolved 5 (10%), anti-diabetic 4 (8%) anddiuretics 3(6%). Another class of drugs that showed adverse drug reaction were anticoagulants 3 (6%) bronchodilators 2 (4%), hypolipidemic drugs 2 (4%) and calcium channel blockers 1 (2%). According to WHO, only 02 (4%)ADRs were certain while 38(76%) were possible. According to Naranjo's only 3 (6%) ADRs were possible while 47 (94%) were probable. The analysis of the severity of ADRs was done according to modified Hartwig Seigle's scale, majority of ADRs 23(46%) were mild, 16 (32%) moderate in nature and 11 (22%)ADRs were severe in nature.

Conclusions: Age is not an independent risk factor of ADRs and suitable monitoring and regular medication review can reduce the incidence of ADRs in geriatric people.

Keywords: Adverse drug reaction, Causality assessment WHO-UMC scale, Geriatric patients

Introduction

World Health Organization (WHO) defines an adverse drug reaction (ADR) as "one which is noxious and unintended, and which occurs in doses normally used in human for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological functions.[1] According to the Centre for Health Policy Research, more than 50 percent of the approved drugs in the United States were associated with some type of adverse effect not detected prior to approval.[2] At least one ADR has been reported to occur in 10 to 20% of hospitalized

patients.[3] Pharmacovigilance or ADR monitoring, launched by WHO in the 1960s in the wake of 'thalidomide' disaster, is currently an integrated global effort of more than 70 countries worldwide. After the "thalidomide tragedy" many countries have established drug monitoring systems for early detection and prevention of possible drug-related morbidity and mortality. The use of traditional and complementary drugs (e.g. herbal remedies) may also pose specific toxicological problems, when used alone or in combination with other drugs.[2]
In the United States, it has been reported that ADRs due to prescription and over the counter drugs during the period 1966 to 1996, affected 6.7% of patients with 3.2% death.[4] While similar figures are not available for India, it is logical to surmise that the figures in relative and absolute numbers would be much higher in view of high levels of unmonitored and indiscriminate drug use widely prevalent in the country.

Most of the advanced countries have set up an adverse drug reaction reporting system at the national level. ADR reporting programs on an institutional basis can provide valuable information about potential problems in drug usage in that institution. Furthermore, reviewing pooled data from diverse geographic, social and medical population enhances the ability to identify rare events and to generate new signals and thus in setting up a sound pharmacovigilance system in the country. Therefore, setting up of ADR monitoring centers at a more regional or hospital level and integrating them with a sound network can reveal unusual or rare ADRs prevalent in Indian population.

ADR monitoring and reporting activity is in its infancy stage in India. Lack of well structured and effective ADR reporting and monitoring programme is a major problem in India in monitoring the drug safety in Indian populations. The clinicians who prescribe and followup on treatment outcomes are best suited to detect adverse reactions in their patients based on information gathered from the patients and their own clinical observations. However, due to the lack of interest and clinical acumen, aptitude and time, many untoward adverse incidents pass unnoticed. Moreover, many physicians are unaware that clinically important ADRs should be reported to the ADR reporting and monitoring centers. As a result, ADRs are often not detected or documented. This could be achieved through establishing or setting up more number of hospital-based or local ADR reporting and monitoring programs that can assist healthcare professionals. It may become a heavy burden on prescribers to ensure that they keep abreast of the evidence regarding ADR to improve the quality of patient care. Therefore, there is a greater and urgent need to create and enhance physicians′ awareness about detection, management, prevention and reporting of ADR. The benefits of pharmacists, pharmacy staffing and clinical pharmacy services to reduce ADRs are documented elsewhere.[5] Studies from various literatures revealed that review and monitoring of prescribed medicines by pharmacists may help to improve the clinical condition of the patients and may reduce the cost of treatment.[6]

Material and Methods

This prospective observational study was carried out in the Department of Pharmacology, A.N.M. Medical College and Hospital, Gaya, Bihar, India for 15 months after taking the approval of the protocol review committee and institutional ethics committee.
The study includes admitted indoor Geriatric patients who develop ADR in ward and geriatric patients who already admitted in the hospital due to ADRs.

Inclusive criteria

Patients more than 60 years of age of both sex, patients those who give consent to participate in the study.

Exclusive criteria

Patients less than 60 years of age, those who refuses to giveconsent to participate in the study, patients treated in intensive care unit and out-patient department, those who does not be followed up after discharge.

In all ADR related patient's necessary data was obtained and recorded on a pre- designed case record form (CRF).

Methodology

General details e.g., name, age, sex, past and presenthistory, general and systemic examination, laboratory investigation, diagnosis and treatment. Suspected medications, treatment given, and the outcome were documented. A causality analysis was done as per the WHOUMC and Naranjo probability score, preventability of an ADR was assessed by modified schumock thornton scale, severity was evaluated by modified Hartwig and siegel scale, which gives an overview of the severity of ADR whether it is mild, moderate or severe in nature. Thedata collected in the manner described above was analyzedunder various heads to ascertain the characteristics of the ADR.[7-9]

Results

For the study purposes the patient's data were divided intotwo groups; group A: Patients that were admitted for other ailments (other than an ADR) but developed the ADRs during hospitalization and; Group B: Those patients that were admitted primarily due to the ADRs that developed outside the hospital.

A total number of 3500 geriatric patients were admitted during the 12 months study period. Out of them, 30patients developed the ADRs during hospitalization (groupA) and 20 patients were admitted primarily for the treatment of ADRs that developed outside the hospital (group B). Total of 50 patients had the ADRs in the 7 medicine units in the study period of 12 months.

Majority of the patients showed the ADRs were in the agegroup of 60-65 years n=20 (40%) while least 5 (10%) in 80-85 years age group (table 1)

Out of total 50 ADRs, Male were 27(54%) and femaleswere 23 (46%).

Table 1: Demographic profile of the patients

Gender	**Number**	**Percentage**
Male	27	54
Female	23	46
Age in years		
60-65	20	40
65-70	8	16
70-75	10	20
75-80	7	14
80-85	5	10

ADRs were subdivided as type A (Augmented), type B (Bizarre), type C, type D, type E and type F. Most of the ADRs were of type A 25 (50%) like metronidazole induced chills, Augmentin induced diarrhoea. These ADRs were dose related and the pharmacological reactions that usually subside withstoppage of drug/reduction in dose. Followed by type C - 20

(40%) which were dose related and time related / chronic use like Furosemide induced dilutional hyponatremia, enalapril induced angioedema.

Table 2: Subdivision of ADRs

Types	Number of patients	Percentage
Type A	25	50
Type B	3	6
Type C	20	40
Type D	1	2
Type E	1	2

Table 3: Administered

administered	Number of patients	Percentage
Oral	35	70
Intravenous route	15	30

Suspected medication was usually administered by oral 35 (70%) or intravenous route 15 (30%). A study of association between the time of drug intake and the onset of ADR showed that most 40 (80%) were developed within a days of drug intake like chills, nausea. Only 10 (20%) ADRs were reported to have developed after one week of drug administration like hepatotoxicity, upper GI bleeding, weight gain etc. Most of the ADRs 17 (34%), were resolved within a day after starting treatment like stomach pain due to aspirin, chills due to metronidazole etc. Maximum reactions 42 (84%) were resolvecompletely within week. Some reactions took more than 7 days of period to resolve 3 (6%) for example serious reaction such as SJS syndrome (1) due to acetaminophen, fixed drug eruption (1) due to paracetamol In majority of the instances, it was antimicrobial agents 16(32%) in which metronidazole was the most common 6 (12%), next was amoxicillin and clavulanic acid combination 5 (10%) followed by antimicrobial agents,NSAIDs 11(22%) were common- in which aspirin 5 (10%) was common. Next was ACE inhibitors were alsoinvolved 5 (10%), anti-diabetic 4 (8%) and diuretics 3(6%). Another class of drugs that showed adverse drug reaction were anticoagulants 3 (6%) bronchodilators 2 (4%), hypolipidemic drugs 2 (4%) and calcium channel blockers 1 (2%) (Table 3).

Table 4: Distribution of ADRS amongst variousclasses of drugs

	Number of patients	Percentage
Antibiotic	16	32
NSAIDs	11	22
ACE inhibitors	5	10
anti-diabetic	4	8
diuretics	3	6
anticoagulants	3	6
bronchodilators	2	4
hypolipidemic drugs	2	4
calcium channel blockers	1	2
Haematinics	1	2
Antiviral	1	2
Opioid	1	2

The causality assessment of the ADRs was carried out frompatient's data using both the WHO-UMC criteria and Naranjo's scale. According to WHO, only 02 (4%)ADRs were certain while

38(76%) were possible. According to Naranjo's only 3 (6%) ADRs were possible while 47 (94%) were probable. The analysis of the severity of ADRs was done according to modified Hartwig Seigle's scale, majority of ADRs 23(46%) were mild, 16 (32%) moderate in nature and 11 (22%)ADRs were severe in nature.

Discussion

ADRs are a cause of significant morbidity and mortality inpatients of all areas of healthcare today. It is important to monitor and report adverse drug reaction in order to promote safe and rational use of medicines. Unfortunately,drugs can act as a double edged sword. A total safe drug isyet to be discovered. Therefore, continuous monitoring of ADRs should always be on when the drug is allowed for a general use and during its total life span. This activity of pharmacovigilance can be undertaken in various ways andeach of these methods has their own strengths and weaknesses. In view of this it was decided to conduct the present study at a large care teaching hospital with objectives of estimation of incidence of ADRs, their types,causative factors and number of other characteristics features.

We have observed that out of total population, Male were 27(54%) and femaleswere 23 (46%) were affected by the ADRs, whilein Mahesh Kumar et al study reported 73.19% males and 26.80% females had ADRs. In international study Gurwitzet al reported 41.3% Males and 58.7% females were affected by the ADRs.[10,11] We have seen that predominantly the ADRs observed in group A and B were type A 25 (50%). These ADRs were dose related and the pharmacological reactions that usually subside with stoppage of drug/reduction in dose. Second most type were Type C (dose related and time related/chronic use) 20 (40%). These are comparable by other study Mandavi et al in which most of the ADRs wereof type A 46% and 2nd most common were type C which is similar to over study.[12] In another study Shah et al mostcommon type of ADRs were type C 45.62% where 2nd most common were type A 36.84%.[13]

Time-to-onset is one of the most fundamental criteria whenassessing the likelihood of a causal relationship between asuspected ADR and a drug. In our study most 40 (80%) were developed within a days of drug intake like chills, nausea. Only 10 (20%) ADRs were reported to have developed after one week of drug administration like hepatotoxicity, upper GI bleeding, weight gain etc. It is possible that hospitalized patients are usually admitted for acute condition and thesepatients any new symptoms or laboratory abnormalities arequickly observed, documented and treated. On the other hand, patients developing the ADRs outside the hospital are usually on chronic medication and hence they either developed the ADRs after a substantial lag period or they report them quite late.

We have seen that a large number of ADRs 90% resolvedquickly and within a week of their appearance, while 8%took a much longer time to resolve. Several reasons can beattributed to this. Most of the non-serious ADRs were in group A and these group patients were already in hospital and therefore their ADRs were quickly spotted and treatedwhich may not the case with patients in group B who maynot have reported their problem quickly.

ADRs are coded using the WHO adverse reactionterminology. In present study Gastrointestinal system is themost commonly affected which is similar to other studies like Shah et al (43.8%), Kamejaliya et al (30%), Harugeriet al (29%), Gray et al (32%), Granziano et al (29.9%).[14,15]

Antimicrobial drugs are among the most frequently prescribed drugs in the hospital and to a great extent the large amount of their use may be considered injudicious. They are, therefore, quite likely to be the most common offending agents. In Shah et al study, antimicrobials (32%) as the most common drug group involved in ADRs. In Mahesh Kumar et al study most

commonly prescribed drugs were antibiotics like Ofloxacin, Ceftriaxone, Metronidazole Ampicillin followed by NSAIDS Diclofenac Sodium, Aspirin. In Mandavi et al instead of antimicrobial agents the cardiovascular drugs were most common offending agents, followed by haematinics, antiplatelet agents and heparin.

The WHO causality system is basically a combined assessment, taking into account the clinical pharmacological aspects of the case history and the qualityof documentation of observation. In our findings According to WHO, only 02 (4%) ADRs were certain while 38(76%) were possible, those are comparable with another study Kamejaliya et al possible 68.2% next is probable 31.7%.[16] Those results were similar to our findings. We have, however, experienced that the WHO- UMC method is simple and less time consuming.
The Naranjo probability scale is another widely used scalefor causality assessment.
In this study according to Naranjo's only 3 (6%) ADRs were possible while 47 (94%) were probable.

These questionnaires and many more aspects of ADR profile (alternate causes, placebo effects, past history, blood concentration of drug etc.) and taken based on the response to each question. The total score is then used to decide the category.
The analysis of the severity of ADRs was done according to modified Hartwig Seigle's scale, majority of ADRs 23(46%) were mild, 16 (32%) moderate in nature and 11 (22%)ADRs were severe in nature. Inother studies like Kamejaliya et al and Mandavi et al, majorcomponent of ADRs was similarly mild in nature in our study.

Schumock and Thornton scale is an acceptable method for classification preventability of adverse drug reaction .It is divided into definitely preventable, probably preventable and not preventable. Comparison between different study like Kamejaliya et al and Mandavi et al in-Preventability Assessment scale is similar to my study.[12,16] This helps to prevent the undesirable drug effects and undertake the rightsteps in right direction. In our study, however had a few short-coming also.

Conclusion

Age is not an independent risk factor of ADRs and suitable monitoring and regular medication review can reduce the incidence of ADRs in geriatric people.

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