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Original Research Article

Pattern of adverse drug reaction in geriatric inpatients of medicine in a tertiary care center: a prospective observational study

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ABSTRACT

Background: Adverse drug reactions (ADRs) represent a major public health problem in older age. In order to better evaluate this problem, this study was designed to assess the prevalence and spectrum of ADRs in terms of frequency, type, severity and preventability in geriatric patients in medicine ward of Guru-Gobind Sing hospital, Jamnagar during 12 months study period.
Methods: All ADR related patient's necessary data was obtained and recorded on a pre- designed case record form (CRF). The data record includes general details e.g., name, age, sex, past and present history, general and systemic examination, laboratory investigation, diagnosis and treatment. Details regarding suspected medications, treatment given, and the outcome were documented with prior permission of institutional ethics committee.
Results: Demographic analysis of prospective study revealed that out of 84 patients, 45 male and 39 were female. The patients had developed ADR within the age ranges of 31 (65-69) followed by 23 (75-79). The majority of ADR was vomiting and diarrhea 15 followed by chills 08 and cough 04. It is evident that antimicrobials 31 agents were mainly suspected followed by NSAIDs 18. According to WHO-UMC scale, the possible cases had a higher incidence 63, followed by probable 19 and certain 2. After estimating the severity by Hartwigs scale 79.8% were mild to moderate while 20.23% 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

Adverse Drug Reaction (ADR), as defined by WHO is "A response to a drug that is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis or treatment of disease, or for modification of physiological function."[1]

The pre-marketing clinical trials do not have the statistical power to detect rare ADR nor do they have significant follow-up to identify delayed ADRs. Pharmacovigilance plays an important role in establishing the safety profile of marketed drugs.[2] Pharmacovigilance helps in early detection of ADRs and identification of risk factors. Older age is not a predictor for adverse drug reactions but simply a marker for co-morbidity, altered pharmacokinetics-pharmacodynamics and polypharmacy- that are the constantly correlated with ADR.[3] In older patients, the collection of disorders necessitates the use of numerous drugs. Indian studies have expressed that polypharmacy is common and correlated with raised potential for ADRs, inappropriate prescription and drug interactions.[4] Since elder people are not habitually involved in clinical trials, publications of ADRs in older people among launching a

new drug in the market are limited. Underreporting of ADRs can be improved by imparting knowledge regarding pharmacovigilance to healthcare professionals. Multimorbidity is the principal cause of polypharmacy, which in turn the prime risk factor for adverse drug reactions and events. ADRs monitoring is an ongoing and continuing process used by health care professionals to enhance effective patient care and to improve quality of life.[5]

Why is ADR monitoring needed? The therapeutic trials are conducted in controlled conditions; in limited number of patients, so that the exact safety profile of the drug in the real life situations is not known.[6] Children, pregnant women, and elderly are not included in clinical trials for ethical reasons. Therefore, the safety of the drug in these cases remains unknown. Another important drawback of clinical trials is that they can only report adverse reactions that appear within the finite duration of trial. Delayed reactions would be missed.

The polypharmacy and multimorbidity experienced by the patients put them at increased risk for ADRs and makes detection more difficult. Awareness of ADRs, increased reporting of ADRs, and increased opportunities to review drug selection and prescribing practices affecting patient outcome.[7]

The present study was carried out to conduct an intensive monitoring of ADRs in indoor geriatric patients and is aimed to find occurrence of ADRs in them over a period of 12 months. It was thought that this hospital data based monitoring of ADRs can shed light on their pattern of occurrence. Such a study is expected to enable us in obtaining information on the incidence and pattern of ADRs in them. The present evaluation was also considered to provide opportunities for interventions especially for the preventable ADRs which will help in promoting safer drug use.

METHODS

This is a prospective, observational single center study at G.G. hospital, tertiary care hospital, Jamnagar over a period of 12 months from June 2017 to May 2018. 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 65 years of age of both sex, patients those who give consent to participate in the study.

Exclusive criteria

Patients less than 65 years of age, those who refuses to give consent 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).

The data record includes the following

General details e.g., name, age, sex, past and present history, 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. The data collected in the manner described above was analyzed under various heads to ascertain the characteristics of the ADR.[8-10]

Prior permission from institutional ethical committee and from the heads of the Medicine department was taken.

RESULTS

For the study purposes the patient's data were divided into two 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 6048 geriatric patients were admitted during the 12 months study period. Out of them, 46 patients developed the ADRs during hospitalization (group A) and 38 patients were admitted primarily for the treatment of ADRs that developed outside the hospital (group B). Total of 84 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 age group of 65-69 years n=31 (36.9%) while least 9 (10.7%) in 80-84 years age group (Figure 1).

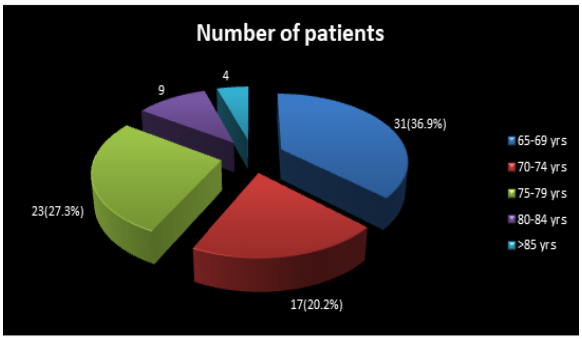

Figure 1: Distribution of ADRs according to age groups.

Out of total 84 ADRs, Male were 45 (53.57%) and females were 39 (46.42%). 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 46 (54.76%) like metronidazole induced chills, augmentin induced diarrhoea. These ADRs were dose related and the pharmacological reactions that usually subside with stoppage of drug/reduction in dose. Followed by type C - 38 (45.23%) which were dose related and time related / chronic use like Furosemide induced dilutional hyponatremia, enalapril induced angioedema.

Suspected medication was usually administered by oral 58 (69.04%) or intravenous route 26 (30.95%). A study of association between the time of drug intake and the onset of ADR showed that most 68 (80.9%) were developed within a days of drug intake like chills, nausea. Only 14 (16.4%) ADRs were reported to have developed after one week of drug administration like hepatotoxicity, upper GI bleeding, weight gain etc. Most of the ADRs 30 (35.7%), were resolved within a day after starting treatment like stomach pain due to aspirin, chills due to metronidazole etc. Maximum reactions 48 (57.14%) were resolve completely within week. Some reactions took more than 7 days of period to resolve 06 (7.14%) for example serious reaction such as SJS syndrome (1) due to acetaminophen, fixed drug erruption (1) due to paracetamol.

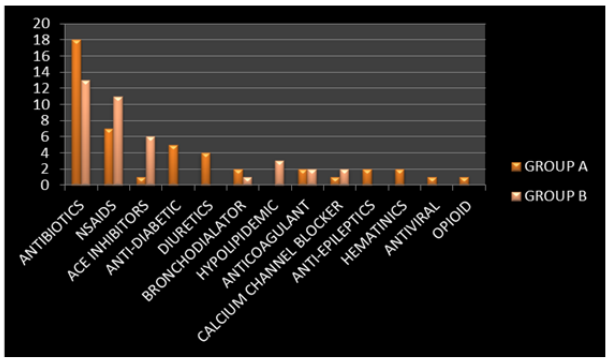

Figure 2: Distribution of ADRS amongst various classes of drugs.

In majority of the instances, it was antimicrobial agents 31 (36.90%) in which metronidazole was the most common 09 (10.71%), next was amoxicillin and clavulanic acid combination 08 (9.52%) followed by antimicrobial agents, NSAIDs 18 (21.42%) were common- in which aspirin 07 (8.33%) was common. Next was ACE inhibitors were also involved 07 (8.33%), anti-diabetic 05 (5.95%) and diuretics 4 (4.76%). Another class of drugs that showed adverse drug reaction were anticoagulants 04 (4.76%) bronchodilators 03 (3.57%), hypolipidemic drugs 03 (3.57%) and calcium channel blockers 03 (3.57%) (Figure 2).

The causality assessment of the ADRs was carried out from patient's data using both the WHO-UMC criteria and Naranjo's scale. According to WHO, only 02 (3.57%) ADRs were certain while 63 (75%) were possible. According to Naranjo's only 05 (5.95%) ADRs were possible while 79 (94.04%) were probable. The analysis of the severity of ADRs was done according to modified Hartwig Seigle's scale, majority of ADRs 39 (46.42%) were mild, 28 (33.3%) moderate in nature and 17 (20.23%) ADRs were severe in nature. Systems affected by the ADRs are shown in Figure 3.

Gastro Intestinal Tract	Vomiting	15(17.85%)
	Diarrhoea	15(17.85%)
	Nausea	11(13.09%)
Group A=22;Group B=19	Abdominal Pain	05(5.95%)
	Constipation	04(4.76%)
	Gastritis	05(5.95%)
	Hepato Toxicity	02(2.38%)
	Stomach Pain	04(4.76%)
Miscellaneous	Chills	08(9.52%)
Group A=8;Group B=1	Weight Gain	01(1.16%)
Central Nervous Sestem	Giddiness	02(2.38%)
Group A=2;Group B=5	Dysguesia	03(3.57%)
	Headache	02(2.38%)
Renal System	Dilutional Hyponatremia	03(3.57%)
Group A=4;Group B=0	Darkness Of Urine	01(1.16%)
Blood	Thrombocytopenia	02(2.38%)
Group A=4;Group B=3	Upper Gi Bleed	04(4.76%)
	Gum Bleeding	01(1.16%)
Cardiovasuclar System	Pedal Edema	02(2.38%)
Group A=2;Group B=3	Angioedema	03(3.57%)
Respiratory System		
Group A=0;Group B=4	Dry Cough	04(4.76%)
Skin & Subcutaneous System	Red Blisterning Skin Lesion	01(1.16%)
Group A=2;Group B=3	Steven-Johnson Syndrome	01(1.16%)
	Fixed Drug Reuptions	02(2.38%)
	Peripheral Edema	01(1.16%)
Endocrinal System	Hypoglycemia	02(2.38%)
Group A=2;Group B=0		

Figure 3: Distribution of drugs causing adverse drug reactions according to ATC classification.

DISCUSSION

ADRs are a cause of significant morbidity and mortality in patients 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 is yet 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 and each 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, 53.57% male and 46.42% female were affected by the ADRs, while in Maheshkumar et al study reported 73.19% males and 26.80% females had ADRs. In international study Gurwitz et al reported 41.3% Males and 58.7% females were affected by the ADRs.[16,17]

Table 1: Comparison of causality assessment by Naranjo Scale.

Study	Naranjo scale	Percentage
Present study	Probable	94
Pauldurai et al[16]	Probable	70.1
Mandavi et al[18]	Probable	88.6

We have seen that predominantly the ADRs observed in group A and B were type A 46 (54.76%). 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) 38 (45.23%). These are comparable by other study Mandavi et al in which most of the ADRs were of type A 46% and 2nd most common were type C which is similar to over study.[18] In another study Shah et al most common type of ADRs were type C 45.62% where 2nd most common were type A 36.84%.[19]

Table 2: Comparison between different studies in severity of ADRs.

Severity of ADRs	Present study	Kamejaliya et al[22]	Pauldurai et al[16]	Shah et al[19]	Mandavi et al[18]
Mild	46.42%	55.1%	20.6%	12.28%	82%
Moderate	33.3%	44.9%	76.28%	68.4%	16%
Severe	20.23%	0.0%	3.09%	19.3%	1.6%

Time-to-onset is one of the most fundamental criteria when assessing the likelihood of a causal relationship between a suspected ADR and a drug. In our study 12 (14.3%) developed within a day of drug intake and only 14 (16.4%) of the ADRs were reported to be developed after one week of drug administration. It is possible that hospitalized patients are usually admitted for acute condition and these patients any new symptoms or laboratory abnormalities are quickly 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 92.8% resolved quickly and within a week of their appearance, while 7.2% took a much longer time to resolve. Several reasons can be attributed 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 treated which may not the case with patients in group B who may not have reported their problem quickly.

ADRs are coded using the WHO adverse reaction terminology. In present study Gastrointestinal system is the most commonly affected which is similar to other studies like Shah et al (43.8%), Kamejaliya et al (30%), Harugeri et al (29%), Gray et al (32%), Granziano et al (29.9%).[20,21]

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 (32.4%) as the most common drug group involved in ADRs. In Maheshkumar 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 quality of documentation of observation. In our findings maximum ADR were possible 63 (75%) next is probable 19 (22.6%) but only 02 (3.57%) were certain those are comparable with another study Kamejaliya et al possible 68.2% next is probable 31.7%.[22] 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 scale for causality assessment. 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. A comparison of our study with a number of Indian studies that have used the Naranjo scale for the establishment of causality is shown in Table 1. The analysis of the severity of ADRs was done according to modified Hartwig seigle's scale. In other studies like Kamejaliya et al and Mandavi et al, major component of ADRs was similarly mild in nature as observed by us in (Table 2).

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.[18,22] This helps to prevent the undesirable drug effects and undertake the right steps in right direction. In our study, however had a few short-coming also.

CONCLUSION

Elders are the most neglected in various aspects and are more vulnerable. Variation in pharmacodynamics and pharmacokinetics parameters accounts for difference in ADR manifestation and severity. Normally the geriatric database is limited at the time of approval. Therefore, post marketing surveillance is particularly important. The

pharmacovigilance activity can help in providing continuous information on safety of the drug used. The awareness of spontaneous reporting of ADRs among health care professionals and general population should be given due consideration for preventing morbidity and mortality among Geriatric population. Providing good geriatric care is pivotal to preventing ADRs.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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