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Original Research Article

A study of adverse drug reactions among elderly patients in a tertiary care hospital

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ABSTRACT

Background: Adverse drug reactions are major setback in the advancement of current therapeutic modalities and safe treatment becomes a challenge in elderly patients. Multifarious health issues in elderly patients require assorted groups of drugs leading to prominent ADRs (Adeverse drug reactions). This study was designed to analyse the most affront drug group causing ADRs among elderly patients and the most frequent signs and symptoms of ADR in tertiary care hospital.
Methods: All elderly inpatients aged 60 years and above were included in the study. Clinical pharmacist monitored and reported ADRs which were analysed by pharmacologist and physicians. The drugs causing ADRs were identified and different signs and symptoms of ADR were evaluated.
Results: A total of 810 (7.26%) ADRs were reported from 11157 inpatients. Out of 810 ADRs reported 320 (39.5%) ADRs were among elderly patients. ADR analyses showed a sight male predominance among elderly patients. Antibacterial agents were the most offended drug group contributing for 18.76% of ADR's. Gastointestinal tract was the most frequently affected system with maximum number of ADRs 102 (31.88%).
Conclusions: ADRs are major threat to hospitalized elderly patients. The risk of ADRs can be reduced by dosing the drug according to the age of the patient and by close monitoring of patients.

Keywords: Adverse drug reaction, Antibacterial agents, Elderly patients, Gastrointestinal

INTRODUCTION

The medical prescription for patients over 60 years accounts for one-half of total prescriptions, yet adequate studies have not been put forth to explain the effects of medication in older adults.[1] The WHO has described adverse drug reactions (ADRs) as an effect that is "noxious and unintended, which occurs at dose used in man for prophylaxis, diagnosis or therapy".[2] The ARDs in elderly adults are four times more common than younger adults. One in six hospital admissions of elderly patients is due to ADRs.[3] There are controversial arguments that elderly age is not a predictor for ADR, but various contributing factors along with co-morbidity, altered renal function, altered pharmacokinetics, polypharmacy practice, altered pharmacodynamic changes and doctor shopping can result in ADR. The physiological changes in older age group alter the pharmacokinetics of many drugs and increase the risk of ADR caused due to (i) one half decrease in hepatic and renal blood flow (ii) decrease in first pass clearance and (iii) decrease in lean body weight to body fat ratio.[4,5] There is a steady drop in the proportion of total serum protein binding to various drugs in elderly people, mainly due to dietary changes, malnutrition, altered appetite and lifestyle changes, thereby raising the toxicity by increasing the fraction of unbound drugs.

The current study was aimed at analysing the incidence of ADRs among elderly patients in tertiary care hospital and to evaluate the commonly prescribed group of drugs causing ADR.

METHODS

The present study was conducted in DM Wayanad Institute of Medical Science, Wayanad, Kerala for a period of six months.

Inclusion criteria

Inpatients of both sexes aged 60 years and above who had developed ADRs formed the subject for the study.

Exclusion criteria

- Patients who developed ADRs during transfusion of blood or blood products
- Patients treated on outpatient department (OPD)
- Patients with drug abuse
- Patients with intentional or accidental poisoning

All the required patient's details including age, gender, weight, duration of hospitalization, patient's allergic status was collected along with drug therapy details and recorded in patient data form. The data regarding the onset of drug reaction, drug dosing, frequency and route of drug administration were also noted. The patient medication history was analysed for drug interaction related ADR.

"Suspected adverse drug reaction form" was downloaded and made available at the wards and Intensive care units (ICU). WHO definition of ADR was adopted. Clinical discussions and brief demonstration about ADR reporting was given to sensitize medical staffs and clinical pharmacist. Different approaches were adopted to identify ADR (1) Clinical pharmacist and medical pharmacologist were posted in all wards and ICU for monitoring ADR (2) Pharmacist and nurses were asked to report the ADRs (3) Any reaction noted was discussed with the concerned physicians and if established, the ADR form was filled.

The drugs causing ADR were grouped into 14 categories and analysed for the more offended drug in elderly patients. The signs and symptoms of ADR were classified into 14 groups of disorders and the frequently affected system was scrutinized.

RESULTS

A total of 11157 patients were admitted during the six months study period. The total number of ADRs reported were 810 (7.26%), out of which 320 (39.50%) ADRs were observed among elderly patients contributing to 2.86% of overall ADRs. Among 320 ADRs reported among elderly 177 (55.31%) were males and 143 (44.69%) were females with a male: female ratio of 1.24:1 showing a slight male predominance (Figure 1).

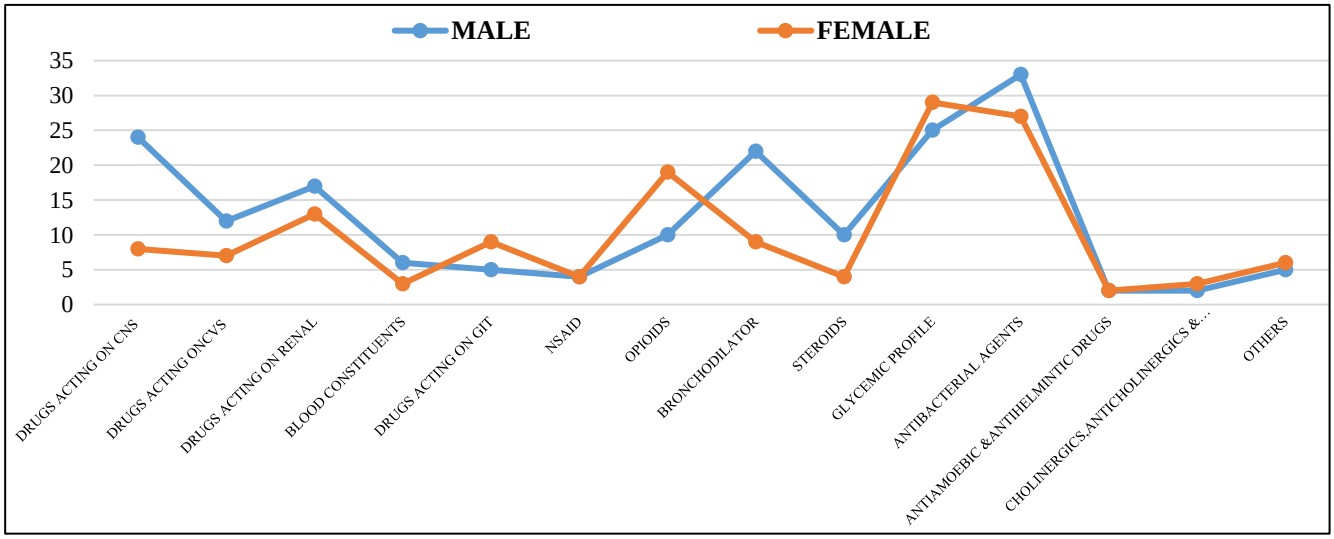

Figure 1: Sex Distribution of Adverse drug reactions.

The age of patients ranged from 60 years to 93 years with a mean age of (70.11±7.56). Clustering of ADRs were seen between 60 to 80 years of age group with maximum number 118 (36.88%) were recorded in the age group 60-65 years, followed by age groups 66-70 years 68 (21.25%), 71-75 years 60 (18.75%) and 76-80 years 46 (14.38%). Events were infrequently seen in age groups 81-85 (5.63%) and 86-90 (2.5%). Age group of 91-95 years showed least number of ADRs (0.63%) (Figure 2).

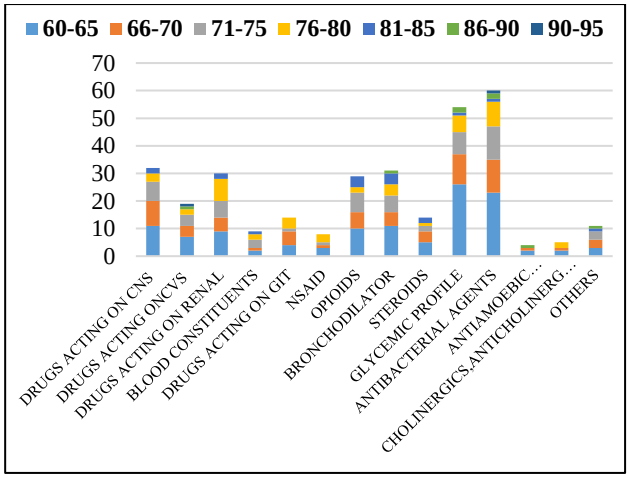

Figure 2: Age distribution of adverse drug reactions.

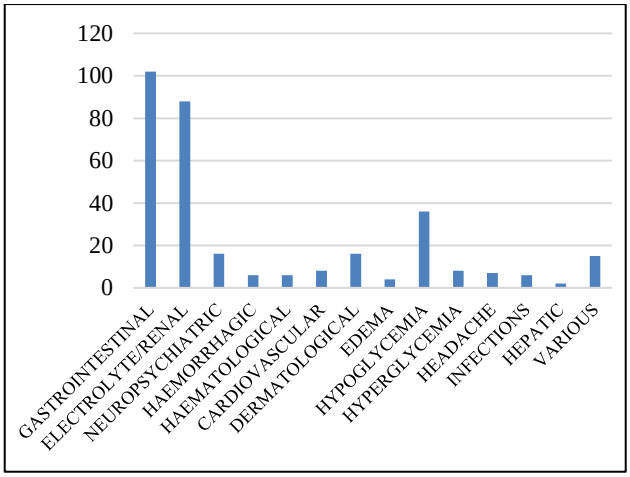

Figure 3: Frequency of adverse drug reactions.

In the present study ADRs were associated with a wide spectrum of drug reactions. The drug categories most frequently associated with ADR were antibacterial agents (18.75%) followed by drugs altering Glycemic profile (16.88%) and drugs acting on central nervous system (10%). Antiameobic and Antihelminthic drugs (1.25%) were relatively infrequent in causing ADRs (Table 1).

Table 1: Drug category responsible for ADR.

Drug category	Total	Percentage
Antibacterial agents	60	18.75%
Glycemic profile	54	16.88%
Drugs acting on CNS	32	10.00%
Bronchodilator	31	9.69%
Drugs acting on renal	30	9.38%
Opioids	29	9.06%
Drugs acting on CVS	19	5.94%
Drugs acting on GIT	14	4.38%
Steroids	14	4.38%
Blood Constituents	9	2.81%
NSAID	8	2.50%
Cholinergics, anticholinergics and alfa blockers	5	1.56%
Antiamoebic and antihelmintic drugs	4	1.25%
Others	11	3.44%

CNS = Central nervous system, CVS = Cardiovascular system, GIT = Gastrointestinal system, NSAID = Non steroidal antiinflammatory agents

In the current study about 49 different signs and symptoms of ADR were identified and grouped into fourteen categories. In order of frequency, the signs and symptoms related to Gastrointestinal tract (GIT) accounted for maximum number 102 (31.88%) of ADRs. Signs and symptoms related to electrolyte and renal category attributed to 88 (27.5%) ADR's. The rare signs and symptoms were grouped under the category "various" contributing to a total number of 15 (4.69%) ADRs (Figure 3).

DISCUSSION

Though there are tremendous advancement in medicine, India still remains in an infant state in monitoring and reporting ADR's. The literatures clearly state the lack of adequate Indian studies to identify ADRs, study done by Parthasarathi et al reported that about one third of hospitalized elderly experienced more than 400 ADR's.[6]

In the present study among elderly patients admitted in tertiary care hospital, recorded ADR's were found to be 2.6% which is in discordance with the studies done by Mandavi et al, and Schneider et al, which showed increased rate of ADR.[7,8]

Although ADR's were observed in both genders a slight predominance of 10.62% was observed in the male population, this finding was congruent with the study done by Shalini Chawla et al.[9]

In our study an increased occurrence of ADRs were observed among 60-65 years (36.88%) and it decreased as age progressed towards 90-95 years (0.63%). Which may be explicated due to lack of physical ability of patient to reach the hospital without dependent, uncooperative family members, low socioeconomic status, self-medications, more belief in Ayurveda, homeopathy and use of other home remedies.[10]

The 320 ADR's were associated with 95 different drugs. They were grouped into 15 drug groups. The most affront group of drugs were antibacterial agents contributing to 18.75% of total ADR.

Piperacillin, Tazobactam combination produced 19 signs and symptoms of ADR contributing to 5.94%. Other antibacterial agents like Azithromycin, Ceftriaxone, Cefotaxime, Ciprofloxacin, Augmentin and Isoniazid produced 7 (2.19%), 6 (1.88%), 6 (1.88%), 5 (1.56%), 3 (0.94%) and 3 (0.94%) of ADRs respectively (Table 2).

Table 2: Category of adverse drug reactions detected and drugs implicated.

Type of ADR'S	Signs and symptoms of ADR'S	Frequency of ADR no. (%)	Drugs Implicated
Gastro intestinal	Abdominal-Discomfort, Constipation, Diarrhea, Nausea, Vomitting Abdominal pain	102 (31.88%)	Piperacillin Tazobactam, Tramadol, Clindamycin, Azithromycin Ceftriaxone, Moxifloxacin, Levofloxacin, Donepezil, Metronidazole Resperidone, Ceftriaxone, Sulbactam, Isoniazid, Augmentin, Metrogyl, Ivermectin, Albendazole, Cefotaxime, Potasiumchloride, Diclofenac, Gabapentin, Rabeprazole, Pantaprazole, Linezolid, Ceftriaxone, Amoxicillin Clavulonic Acid, Aspirin, Ciprofloxacin.
Electrolyte/ renal	Acute kidney injury Hyperkalemia, Hypokalemia, Hyponatremia, Lactic acidosis, Nephrotoxicity	88 (27.50%)	Torsemide, Salbutamol, Piperacillin Tazobactam, Furosemide, Human Actrapid, Metformin, Thiazide, Telmesartan, Cefaperazone, Potasium Chloride Hydrochlorthiazide, Furosemide+Spironolactone, Salbutamol, Gentamycin, Furosemide, Losartan, Azithromycin, Ramipril, Carbamazepine, Levosalbutamol, Insulin, Salbutamol+Ipratropium, Torasemide, Amilodipin, Salbutamol+Hydrocortisone, Meropenam
Hypo glycemia	Hypoglycemia	36 (11.25%)	Glimipride, Metformn, Human Actrapid, Mixtard Human, Insulin, Metformin+Glimipride, Glibenclamide.
Neuro psychiatric	Drowsiness, Hallucin-ation, Insomnia, Mania, Neurotoxicity Sedation, Tremor	16 (5%)	Levochlorperastine, Phenytoin, Cetirizine, Pregabalin, Resperidone, Quetiapin, Lorazepam, Colistimethate, Olanzapine, Trihexyphenidyl, Carbidopa+Levodopa, Tramadol
Dermato logical	Itching Rashes	16 (5%)	Ceftriaxone, Thiocolchioside, Hydrocortisone, Ciprofloxacin, Ofloxacin, Salbutamol, Cefataxim, Piperacillin+Tazobactam, Paracetamol, Levosalbutamol
Cardio vascular	Bradycardia, Hypotension, Orthostatic-Hypotension, Palpitation	8 (2.50%)	Enalapril, Ivabradine, Atenolol, Metformin, Tamsulosin, Bisoprolol, Losartan, Carvedilol
Hyper glycemia	Hyperglycemia	8 (2.50%)	Dexamethasone, Betamethasone, Carvedilol
Headache	Headache	7 (2.19%)	Ciprofloxacin, Azithromycin, Pantaprazole, Zolpidem, Glyceryl Trinitrate, Tramadol
Haemo rrhagic	Bleeding Hematuria	6 (1.88%)	Naltokinse, Heparin, Enoxaparin, Heparin
Haema tological	Anemia increase PTINR Thrombocytopenia	6 (1.88%)	Clonazepam, Phenytoin, Nicoumarol, Isoniazid, Pyranzinamide, Heparin
EDEMA	Edema of tongue facial puffiness pedal Edema	4 (1.25%)	Amilodipine, Hydrocortisone, Salbutamol, Amilodipine
Infections	Candidiasis, Recurrent UTI	6 (1.88%)	Carbidopa Levodopa, Budesonide, Piperacillin+Tazobactam
Hepatic	Elevated liver function test	2 (0.63%)	Bicalutamide, Isoniazid
Various	Blurring of vision cough, dehydration, dry mouth, fatigue, fever, giddiness, metallic taste, oral ulcer, redness of eye	15 (4.69%)	Moxifloxacin, Clonazepam, Losartan, Cholecalciferol Meropenam, Pregabalin, Metformin, Tramadol, Paracetamol Resodium, Piperacillin+Tazobactam, Diclofenac, Prazosin

Drugs that alter glycemic profile produced 54 ADR's (16.88%) and the foremost in the group was Insulin with 31 (9.69%) of hypoglycemic ADR's then in occurrence were Metformin 7 (2.19%), Human Actrapid 6 (1.88%),

Glibenclamide 3 (0.94%) and other hypoglycemic agents showed less than three ADR's. Opioids have been categorized as a separate group to show that it caused 9.06% of total ADR against all other CNS drugs which constituted only for 10% of ADR. Similarly, the studies done by David W Bater et al, showed that morphine compounds accounted to 9% of all ADR.[11] The use of opioids, sedative, hypnotics, antipsychotic in elderly people should be restricted to lower the risk of falls.[12] As age progress the first pass clearance of various drugs decreases, thus common prescriptions like opioids, sedatives, hypnotics requires a low dosing schedule to avoid recurrent ADRs. Drugs acting on renal system and cardiovascular system, were the next most affronted groups of drugs. Due to use of multiple drugs like antihypertensives, hyperlipidaemic agents, anti-anginal agents for discrete patients; cardio vascular drugs are consistently given as one of the most implicated drug group.[13-17]

The most common type of ADR was GIT type with symptoms of constipation accounting to 52 (16.25%), vomiting 23 (7.18%) and diarrhoea 17 (5.31%). The most common drugs causing GIT type ADRs were tramadol and piperacillin,Tazobactam combination. The next common ADR was Renal/Electrolyte type amounting to 88 (27.50%) ADRs, the most frequent symptom identified in this type was hypokalemia 66 (20.63%) caused majorly by salbutamol and furosemide. Hypoglycemia 36 (11.25%) caused by anti-diabetic agents like Insulin and sulfonylureas are next in listicle similar to studies done by Rupawala et al, which reports diabetic, anticoagulants and drug with narrow therapeutic index accounts for most ADRs.[18]

The study results clearly unveiled that ageing process of the patients combined with various attributing factors has worsened the scenario. The recurrent use of offending drug in elderly patients can lead to increased prevalence of ADR. The new Beer's criteria has identified about 48 drugs to be avoided in elderly patients and 20 inappropriate drugs for patients with comorbid conditions.[19] In this study we noted that the most affected system due to ADR were Gastrointestinal and renal system, hence treatment to elderly patient should be periodically altered in accord to their renal function.[20] The central drug standard control organization(CDSCO) has initiated nationwide Pharmacovigilance program from 2010 and about 90 ADR monitoring centres in all four zonal categories have been established. Yet ADR reporting in India is still in preliminary level. A study by Amrita P et al showed that inspite of good ADR monitoring knowledge and awareness among physicians, the rate of reporting ADR was very low.[21] Various computer detection program searching for ADR can be combined with spontaneous reporting by computerized information system and trained person for evaluation of ADR.[22,23] This has been the most effective, economical method for quick identification of ADR and can be used as the future strategy for ADR reporting.[24] Thus bringing awareness to clinicians about ADR preventing criteria's (Beer's, STOP.), altering dosage schedule in accord to renal parameter and by incorporating various clinical tools (STOPP, START..) into electronic prescribing system we can have better sensitivity and clinical acceptance.[25]

CONCLUSION

The increased incidence of ADR among elderly adults clearly indicate that close monitoring is required. Thus awareness of risk factor and various preventive criteria's can significantly reduce the harmful consequences of drugs in elderly age groups.

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