National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Pattern of adverse drug reactions among geriatric population of Anand district, Gujarat, India

Zalak P Dalwadi, Bharat M Gajjar, Nazima Y Mirza

Department of Pharmacology, Pramukhswami Medical College, Karamsad, Gujarat, India

Correspondence to: Zalak P Dalwadi, E-mail: zalakdalwadi92@gmail.com

Received: April 03, 2020; **Accepted:** May 01, 2020

ABSTRACT

Background: The elderly population is increasing rapidly worldwide. Physiological and pharmacological variations in the elderly population make them prone to high drug-drug interactions and adverse drug reactions (ADRs). ADRs in geriatric people are common cause for increased hospital admission as well as morbidity and mortality. **Aim and Objective:** The aim of the study was to observe the type and pattern of ADRs among the geriatric population. **Materials and Methods:** A cross-sectional study was conducted on the geriatric population of Anand district. A total of 500 patients were enrolled. Participant of either gender who has completed 65 years of age and who were on medication was included in the study. The participants were interviewed at their homes after taking informed consent. Information regarding demography, disease, and drugs was taken and entered into the case record form. Reported ADRs experienced by patients were confirmed by their treating physicians. **Results:** Of 500 participants, 55.2% were male and 44.8% were female. Among them, 9.4% participants experienced 55 ADRs in the past 6 months. Insulin/Anti-diabetic agents and cardiovascular agents were leading causative agents for ADRs in 32.72% cases each. The most frequently observed complaints were regarding hypoglycemia and gastrointestinal upset in 12.72% cases each. According to the WHO-Uppsala Monitoring Centre causality assessment scale, 69% reactions were classified as probable, 32.63% were classified as certain/definite, and 7.27% were classified as possible. **Conclusions:** Geriatric patients require close monitoring for ADRs to avoid clinically significant harmful consequences. Antidiabetic agents and cardiovascular agents caused the highest number of ADRs in our study which indicates that adequate caution, proper care, and continuous monitoring and good communication among doctor and patient must be implemented.

KEY WORDS: Geriatric Population; Adverse Drug Reaction; WHO-Uppsala Monitoring Centre Scale

INTRODUCTION

As the growth of the elderly population continues, the burden on the health-care system and society has also increased. Chronic diseases such as hypertension, coronary artery disease, diabetes mellitus, stroke, arthritis are more prevalent in elderly. These patients are likely to be treated for some or all of their conditions with drug therapies. When used appropriately, drugs may be the single most important intervention in the care of an older patient, but when used inappropriately, they may even endanger the health of an older patient and make them vulnerable to develop adverse drug reactions (ADRs).[1] ADRs are one of the leading cause of repeated hospitalization and adversely affects the quality of life.[2] The prevalence of ADRs is 5% higher among geriatric as compared to adults.[3] The possible reasons for the higher prevalence of ADRs in geriatric patients are other comorbidities, polypharmacy, and age related alteration in pharmacokinetics and pharmacodynamics.[4]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2020.10.04083202001052020	

The majority of ADRs (80%), occurring during the course of treatment, are type A reactions. They are predictable and potentially avoidable in nature, as they are related to the accentuation of known pharmacological effects of the drug. They are dose-related and usually mild, but few of them may be serious or even fatal (such as intracranial bleeding from warfarin). Type B ("bizarre" or idiosyncratic reactions) ADRs are usually uncommon, but rarely may sometimes cause serious toxicities (e.g., hepatotoxicity in association with flucloxacillin or the antibiotic combination, amoxicillin plus clavulanic acid). Such reactions are usually due to inappropriate dosage, especially when drug elimination is impaired.[5]

In England, 0.9% of the total hospital admissions were due to ADRs during the year 1999–2008. ADRs are common in the Australian health-care system also and they contribute to 1% of hospital admissions. In the United States of America, ADRs contribute 3.4–7% of hospital admissions.[6] The incidence of ADR reported by various studies across the world is 6–20%, whereas, in India, it is up to 3%.[7]

This study was conducted to observe type and pattern of ADRs among the geriatric population.

MATERIALS AND METHODS

A cross-sectional study was conducted on the geriatric population of Anand district, Gujarat, after taking approval from the institutional ethics committee; the data of 500 patients were collected between November 2017 and August 2019. Participant of either gender who has completed 65 years of age and who were on medication was included in the study.

The participants, who were willing to take part in the study, were interviewed at their homes at their convenient time. Before collecting data, eligible participants were explained about the study in details and their informed consent was taken. Information regarding demography (age, gender), disease (disease from which participant was suffering/ investigations done in past 1 year), and drugs (number of drugs, generic name, route of administration, frequency and duration of medications, and ADRs experienced and reported by patients) were taken and entered into the case record form. Participants were asked to show treatment-related documents, prescriptions, medications, and relevant questions were also asked.

Reported ADRs experienced by patients within the past 6 months, was confirmed by their treating physicians (it was also mentioned in treatment-related documents), by asking detailed history about developed ADRs from participants and by correlating with past laboratory investigations.

Suspected and reported ADRs were assessed for causality by WHO-Uppsala Monitoring Centre (UMC) scale. Categories for the WHO-UMC scale entails: (a) Certain, (b) probable/ likely, (c) possible, (d) unlikely (e) conditional/unclassified, and (f) unassessable/unclassifiable.

RESULTS

Of 500 participants, 55.2% were males and 44.8% were females. Of total 500 participants, the majority of participants were in the age group of 65–74 years, 73.6% followed by age group of 75–84 years 23.2% and the lowest number of participants 3.20% was in the age group of more than 85 years.

Among 47 (9.4%) participants, 55 ADRs were observed. These reported ADRs were experienced by the patients within the last 6 months.

The details of medications responsible for causing ADRs are showed in Table 1. The number of drugs causing ADRs in this study were Insulin/antidiabetic drugs 18 (32.72%), cardiovascular drugs 18 (32.72%), nonsteroidal anti-inflammatory drugs (NSAIDs) 6 (10.90%), antidepressants, anti-manic, and sedative-hypnotics 4 (7.27%), bronchodilator agents 4 (7.27%), and vitamins and minerals 3 (5.45%). In addition, the least number of ADRs were seen with steroids and anticancer drugs 1 (1.81%) each.

Figure 1 shows the frequency distribution pattern for patients experiencing ADRs versus their suspected precipitant

Table 1: Frequency of ADRs and causative drug groups

Causative drug groups	Frequency (%)
Insulin/antidiabetic agents	18 (32.72)
Cardiovascular agents	18 (32.72)
NSAIDs	06 (10.90)
Antidepressants, anti-manic, and sedative-hypnotics	04 (7.27)
Bronchodilator agents	04 (7.27)
Vitamins and minerals	03 (5.45)
Steroid	01 (1.81)
Anticancer agents	01 (1.81)
Total	55 (100)

ADR: Adverse drug reaction, NSAIDs: Nonsteroidal anti-inflammatory drugs

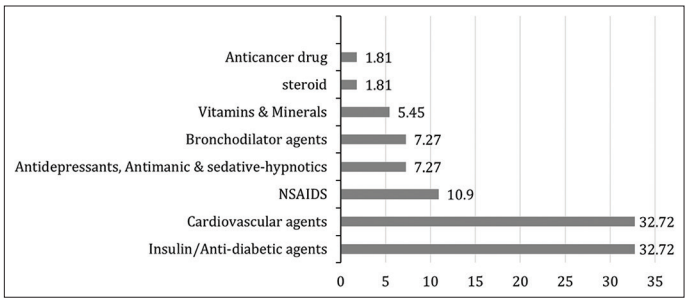

Figure 1: Frequency-wise distribution of adverse drug reactions

drugs. Insulin/antidiabetic agents and cardiovascular agents caused ADRs in the most number of patients, 18 (32.72%) each. NSAIDs were next in the frequency of causation in 6 (10.90%).

The clinical manifestations observed as ADRs are shown in Table 2. The most frequently observed complaints were regarding hypoglycemia and gastrointestinal upset in 7 (12.72%) participants each. This was followed by tremors and pedal edema in 6 (10.90%) participants each. Besides that, acute kidney injury in 5 (9.09%) and gastritis in 4 (7.27%) participants were observed. Furthermore, constipation, cough, and postural hypotension were equally observed in 3 (5.45%) patients each. The urticaria, photodermatitis, atrial fibrillation, hyperkalemia, hypokalemia, insomnia, pleural effusion, dryness of mouth, and encephalitis were equally identified in 1 (1.81%) patients each. In this study, it was observed that ADRs often affected multiple body systems in a patient.

A list of observed ADRs with their causality assessment are shown in Table 3. Overall, 23 drugs are responsible for causing 55 ADRs. Suspected drugs and associated clinical manifestations are mentioned in table. Among them, most of ADRs which are classified as "certain" (metformin, warfarin, digoxin, valproate, lithium, and spironolactone) and few of "possible" (steroid, dasatinib) are responsible for hospitalization or either prolongation of hospitalization. Hence, it can be considered as a serious type of ADRs.

According to the WHO-UMC scale, 69% of the ADRs were falling in the probable category while 23.63% were belonged to certain/definite category. Others (7.27%) were classified as possible type of ADR [Figure 2].

DISCUSSION

This study was designed to highlight and observe the pattern of medications most frequently involved in ADRs among the geriatric population of Anand district. A total of 55 ADR were reported in 47 participants (9.4%). Out of 55 adverse drug reactions, hypoglycemia due to Insulin/Anti-diabetic agents and adverse drug reactions due to cardiovascular agents were most frequently reported, followed by ADRs due to NSAIDS. The common causality association with suspected drugs was probable (69.09%) or certain/definite (23.63%), while remaining (7.27%) were classified as possible. Frequently causality assessment has been a challenge due to lack of information on dechallenge and rechallenge, simultaneous starting of multiple drugs, and existence of comorbidities with similar symptoms. Thus, causality association comes down to lower "possible" grade. However, this does not undermine the importance of causal association with suspected drug and causality assessment per se.

The observed incidence of ADRs in 9.4% is quite similar to the study done in Nigeria[8] and Chandigarh,[9] in which 10% of the geriatric population develop ADRs during the course of their treatment. A recent study has reported the ADRs related hospitalization rate as 6–12% among the elderly.[10] Insulin/antidiabetic, cardiovascular agents, and NSAIDs were leading causative groups for ADR in this study. The almost similar pattern seen in the study done in Nigeria in which maximum number drugs causing ADRs of frequency were insulin (27.5%), NSAIDs (19.6%), and antihypertensives (15.7%). The most commonly affected system by ADRs was the central nervous system, probably because two of the first three topmost implicated classes of medications causing ADRs manifest with symptoms referable to the central nervous system. For example,

Table 2: Pattern of ADR observed

Clinical manifestations	No. of events (%)
Hypoglycemia	7 (12.72)
Gastrointestinal upset	7 (12.72)
Tremor	6 (10.90)
Pedal edema	6 (10.90)
Acute kidney injury	5 (9.09)
Gastritis	4 (7.27)
Constipation	3 (5.45)
Cough	3 (5.45)
Postural hypotension/giddiness	3 (5.45)
↑PT/INR	2 (3.63)
Urticaria	1 (1.81)
Photodermatitis	1 (1.81)
Atrial fibrillation	1 (1.81)
Hyperkalemia	1 (1.81)
Hypokalemia	1 (1.81)
Insomnia	1 (1.81)
Pleural effusion	1 (1.81)
Dryness of mouth	1 (1.81)
Encephalitis	1 (1.81)
Total	55 (100)

ADR: Adverse drug reaction

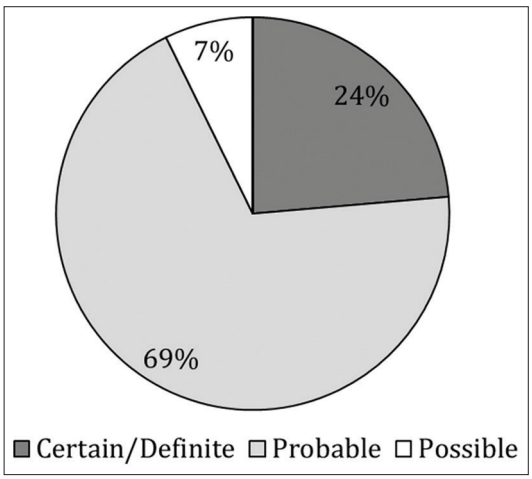

Figure 2: Causality assessment by to WHO-Uppsala Monitoring Centre scale

Table 3: Observed ADRs with their causality assessment

Name of drug	Total no. of events observed	Clinical manifestations	Causality assessment WHO-UMC scale
Metformin	4	Acute kidney injury ↑se S.Crt	Certain
Warfarin	2	↑se PT/INR, petechial hemorrhage	Certain
Digoxin	2	↑se therapeutic concentration > 2.56 nmol/L Atrial fibrillation with fast ventricular rate	Certain
Valproate	1	↑se concentration >350 μmol/L, Tremor, involuntary micturition, defecation	Certain
Lithium	1	Tremor, hyperreflexia, ataxia, vomiting raised concentration >1.5 mEq/L	Certain
Prazosin	1	Postural hypotension, giddiness	Certain
Spironolactone	1	Hyperkalemia	Certain
Furosemide	1	Hypokalemia	Certain
Amlodipine	6	Pedal edema	Probable
Insulin	8	Hypoglycemia, giddiness, mental confusion, sweating	Probable
Enalapril/Ramipril	3	Dry cough	Probable
Beta-blocker	1	Bradycardia, giddiness	Probable
Voglibose	6	G.I. upset	Probable
NSAIDs	6	Gastritis, acute kidney injury, photodermatitis	Probable
Salbutamol	3	Tremor, tachycardia	Probable
Formoterol/Budesonide	1	Dryness of mouth	Probable
Iron	2	Constipation	Probable
Benzodiazepines	1	Insomnia	Probable
Fluoxetine	1	Tremor	Probable
Steroid	1	Encephalitis	Possible
Dasatinib	1	Pleural effusion	Possible
Tamsulosin	1	Giddiness	Possible
B- complex	1	Urticaria	Possible

ADR: Adverse drug reaction, UMC: Uppsala Monitoring Centre, NSAIDs: Nonsteroidal anti-inflammatory drugs

insulin leads to impair consciousness due to hypoglycemia, while antihypertensives manifest mainly with postural dizziness and headache due to postural hypotension. The next most common system involved was the gastrointestinal system, and this may be related to the fact that NSAIDs which constituted the third most common class of medications involved in ADRs usually manifest with problems referable to the gastrointestinal system. According to Amin *et al*.[11] and Pauldurai *et al*.,[12] the most common body system affected was gastrointestinal followed by neurological and skin and appendageal disorders in geriatric patients. This may be because most of the suspected drugs were administered orally and most frequently in those studies.

The ADRs were reported spontaneously while doing data collection from the community, so it can be assumed that these ADRs were not reported by others.There was recall bias pertaining to age-related amnesia and other psychological problems. Despite this limitation, we believe that our study has revealed various important aspects of ADRs in the geriatric population.

CONCLUSIONS

The results of our study conclude that elderly patients should be closely monitored for ADRs to avoid clinically significant harmful consequences. ADRs further increase patients' morbidity, mortality, and length (duration) of hospitalization. Antidiabetic agents and cardiovascular agents caused the highest number of ADRs which indicate that adequate caution, proper care, and continuous monitoring must be implemented during the course of treating patients with these drugs to optimize their clinical efficacy and prevent the occurrence of ADRs in them.

Regular medication review, potentially aided by the use of prescribing indicators or electronic prescription systems, can help in the optimization of prescriptions to benefit patients from their medicines. Good communication between health-care providers, patients, and caretakers is key to managing medicines well.

REFERENCES

1. Beyth R, Shorr RI. Epidemiology of adverse drug reactions in the elderly by drug class. Drugs Aging 1999;14:231-9.
2. Davies EC, Green CF, Taylor S, Williamson PR, Mottram DR, Pirmohamed M. Adverse drug reactions in hospital in-patients: A prospective analysis of 3695 patient-episodes. PLoS One 2009;4:e4439.
3. Occurrence of Adverse Drug Reactions in Elderly Population (PvPI Newsletter); 2014. Available from: http://www.ipc.

gov.in/PvPI1/Newsletter_April_issue.pdf. [Last accessed on 2016 Sep 10].
4. Alomar MJ. Factors affecting the development of adverse drug reactions (Review article). Saudi Pharm J 2014;22:83-94.
5. National Agency for Food and Drug Administration and Control. Safety of Medicines in Nigeria-A Guide for Detecting and Reporting Adverse Drug Reactions. Nigeria: National Agency for Food and Drug Administration and Control/ National Productivity Council/The National Insurance and Guarantee Corporation Limited; 2004. p. 1.
6. Kalaiselvan V, Thota P, Singh G. Pharmacovigilance programme of India: Recent developments and future perspectives. Indian J Pharmacol 2016;48:624-8.
7. Singh P, Agrawal M, Hishikar R, Joshi U, Maheshwari B, Halwai A. Adverse drug reactions at adverse drug reaction monitoring center in Raipur: Analysis of spontaneous reports during 1 year. Indian J Pharmacol 2017;49:432-7.
8. Akhideno PE, Fasipe OJ, Isah AO. The incidence and prevalence of adverse drug reactions among medical inpatients in a Nigerian University Teaching Hospital. J Curr Res Sci Med 2018;4:86-93.
9. Mandavi SD, Sachdev A, Tiwari P. Adverse drug reactions & their risk factors among Indian ambulatory elderly patients. Indian J Med Res 2012;136:404-10.
10. Hartholt KA, Van Der Velde N, Looman CW, Panneman MJ, Van Beeck EF, Patka P, *et al*. Adverse drug reactions related hospital admissions in persons aged 60 years and over, the Netherlands, 1981-2007: Less rapid increase, different drugs. PLoS One 2010;5:e13977.
11. Amin S, Shah S, Desai M, Shah A, Maheriya KM. An analysis of adverse drug reactions in extremes of age group at tertiary care teaching hospital. Perspect Clin Res 2018;9:70-5.
12. Pauldurai M, Kannaaiyan D, Rao R. Adverse drug reaction monitoring in geriatric patients of rural teaching hospital. Der Pharm Lett 2015;7:187-93.

How to cite this article: Dalwadi ZP, Gajjar BM, Mirza NY. Pattern of adverse drug reactions among geriatric population of Anand district, Gujarat, India. Natl J Physiol Pharm Pharmacol 2020;10(08):614-618.

Source of Support: Nil, **Conflicts of Interest:** None declared.