



Risk of Adverse Drug Reactions in Older Adults - in the Elderly

DK Brahma*

Associate Professor, Department of Pharmacology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Mawdiangdiang, Shillong, India

***Corresponding Author:** DK Brahma, Associate Professor, Department of Pharmacology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Mawdiangdiang, Shillong, India.

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Abstract

The demographic transition is a global phenomenon and India is not an exception to it. The number of the elderly population is increasing rapidly in our country. The elderly population consumes more medication in comparison to the younger groups of the population. Increased use of drugs raises the risks of adverse drug reactions (ADR) including drug interactions. It is important to minimize or prevent the ADRs for quality drug care to this special frail people. Every healthcare professional has roles to play in the identification and prevention of ADRs in the older people. However, accurate identification of ADRs in older people has been a challenge for the clinicians, pharmacists, nurses or any other healthcare personals. This challenge is going to be tougher in the coming decades in India due to the paucity of quality research and accurate drug safety data in elderly. Moreover, geriatric care in our country is still in its infancy and more urbanized in nature. There is an urgent need of the capacity building for different groups of healthcare personnel on geriatric care and Pharmacovigilance in India at all levels of the healthcare system.

Keywords: Elderly; Adverse Drug Reactions; Drug Safety Data

Introduction

In India, according to the population census reports nearly 104 million are elderly persons above 60 years of age, out of which 53 million are females and 51 million are males. The process of population aging is taking place rapidly in India where the percentage of the elderly people above 60 years of age is projected to share almost one fifth (19%) of the total population by 2050 from 8.6% in 2011 [1]. Under these circumstances the total number of the elderly population will be around 300 million by 2050 from around 100 million at present. The main causes of this demographic transition being experienced in India along with other parts of the world are due to the low birth rates, steady increase in life expectancy, reduction in fertility rates and more importantly better healthcare facilities [2].

The consequence of population aging contributes to the increase in the prevalence of multiple chronic diseases (CD) due to the fact that age is a known non-modifiable risk factor for many of these disorders, e.g. cardiovascular disease, diabetes, cancer and chronic respiratory disease. The developed countries globally, particularly Europe are already experiencing the problem and burden of these

NCDs as leading cause of mortality [3]. Developing countries like India having just recovered from the burden of communicable diseases, will have to face the important challenges of these NCDs in the coming years. This is reaffirmed in the recently released data by World Health Organization (WHO) on India stating that nearly 61% of deaths in India are now attributed to non-communicable diseases (NCDs), including heart disorders, cancer and diabetes.

Pharmacotherapy plays crucial role in geriatric health and it is well established that this frail, special group of people with CDs and multiple other factors including multimorbidity with decreased physiological reserves consumes a greater number of drugs [4,5]. Increased use of drugs raises the risks of adverse drug reactions including drug interactions [6]. It is important for each and every health care provider to ensure quality use of medicines in older people by minimizing the adverse drug reactions.

Extent of ADRS in elderly

Studies from around the world have shown a definite correlation between the prevalence of ADRs and elderly people, although

varying rate and extent. Lazarou, *et al.* found incidence of serious ADRs in the general hospitalized population of the USA to be 6.7%, even after excluding errors in the drug administration, noncompliance, overdose, drug abuse, therapeutic failures, and possible ADRs [7]. In a systematic review by Alhawassi, *et al.* found the median prevalence of ADRs in elderly leading to hospitalization to be 10% (95% CI:7.2% -12.8%) and the prevalence of ADRs occurring in hospital to be 11.5% (95% CI:0%-27.7%) [8]. For Indian settings, although there is definite scarcity of data on ADR studies in the elderly, Harugeri, *et al.* in a hospital setting found that the prevalence of ADR-related hospital admissions was 5.9% [9]. while in other two studies it was found to be 6.7% and 10% [10,11]. However, these studies contain relatively small numbers of participants and may not reflect the actual data.

Thus, it is a well-known fact that there is an integral association between the old age and increased in the rate of ADRs. A number of other factors also contribute to the increased risks of ADRs in elderly. Older age frequently accompanied by polypharmacy, comorbidity and frail with age-related pharmacodynamics and pharmacokinetic changes.

Nature of ADRS in elderly

Accurate identification of ADRs in older people has been a challenge for the clinicians, pharmacists, nurses or any other health-care personals due to a number of reasons. It is often complicated in the elderly that symptoms and problems are already prevalent in the elderly e.g. dizzy spells, falls or confusion etc. may themselves be due to ADRs [12]. These symptoms may get overlooked resulting in cascade of events of ADR where one drug is used to treat adverse effects of another.

The term “geriatric syndrome” is a clinical condition in older people which are by their nature non-specific and do not fit into a single deficit diagnosis. The commonly encountered such syndromes are delirium, falls, dizziness and urinary incontinence etc. requiring rational use of medications. Studies have indicated that delirium, oversedation and falls are the most commonly occurring adverse events among the elderly [13].

Falls

The incidence of fall-related injuries is common in older people with subsequent decline in functional status, increased likelihood of hospitalization and greater use of medications. Even if the falls are not serious in nature, the risk of hospitalization increases due to the loss of confidence leading to functional decline [14]. It is es-

timated that one-fifth of the falls require medical attention. Hip fractures are the most common and serious form of fall-related injuries and a significant number of people among them die within 1 month. However, these deaths are not necessarily related to fall only, but may be due to multimorbidity conditions. Polypharmacy also contributes to the increased risk of falls [15]. Studies have shown that increased rate of falls are commonly associated with the use of hypnotic or sedatives, neuroleptics and antipsychotics, antidepressants, benzodiazepines and antihypertensives [16]. This fact has been further validated by the evidences of the reduction in the incidence of falls in older people after withdrawal of these medications [17].

Delirium

Confusion and delirium can be very common in the elderly and is associated with increased mortality, poor functional and cognitive recovery and increased length of hospital stay [18]. Delirium is often multifactorial, medications especially polypharmacy or inappropriate prescribing can be contributing in combination with several factors, e.g. infections, structural, metabolic, or environmental causes [19]. However, sometimes drugs may be the sole cause of delirium in many instances. Delirium caused by drugs may be of any of the three types, e.g. hyperactive, hypoactive and mixed [20]. Studies have shown that medication-induced delirium are commonly associated with the drugs like opioids, benzodiazepines, dihydropyridine calcium channel blockers and antihistamines [21].

Clostridium difficile infection

Clostridium difficile is a ubiquitous, anaerobic, spore-forming, gram-negative bacterium and its infection is now recognized as a major cause of gastrointestinal infections globally. The major victim of *Clostridium difficile* infection (CDI) is the elderly population [22,23]. There is definite and proven association of CDI with the use of antibiotics. The common clinical manifestation of CDI is diarrhoea. However, it may sometimes lead to life-threatening conditions such as pseudomembranous colitis, toxic megacolon, organ failure and death [24]. Studies have shown that prescription of proton pump inhibitors (PPI) increases the risk of diarrhoea among the hospitalized patients and this risk is increased by two folds if PPIs are co-prescribed with antibiotics [25].

Antipsychotics

Behavioural and psychological symptoms are very common symptoms in dementia among elderly people and therefore antipsychotics are frequently prescribed. However, antipsychotics in

older people are reported to be associated with increased risk of fall, over sedation, parkinsonism, cerebrovascular accidents and ultimately death. Risperidone, olanzapine and aripiprazole are useful in bringing down aggressive symptoms in Alzheimer's disease. However, these drugs, risperidone in particular are reported to be associated with significant increase in cerebrovascular events [26].

Urinary incontinence

Older adults are commonly affected by the problem of urinary incontinence and medications may exacerbate the problem. Multiple medications use particularly increases the risk of urinary incontinence [27]. The medications mostly involved are the ones causing polyuria, decreased sensory input and decreased bladder contractility [28].

Nutrition

Poor nutritional status is also a major concern among the elderly. Higher medication use and polypharmacy contributes to poorer nutritional status. Increased in number of medications may lead to decreased intake of soluble and nonsoluble fibre, vitamins and minerals. There may be increased in the intake of cholesterol, glucose and sodium. There is evidence that patients receiving polypharmacy are at the higher risk of malnourishment in comparison to the patients without polypharmacy [29].

Common drugs causing ADRS in elderly

ADRs have been classified into two major subtypes: Type A or predictable and type B or bizarre reactions [30]. Majority of ADRs in elderly is of predictable and potentially avoidable type A reactions. Type B bizarre reactions may be idiopathic and uncommon, but sometimes may cause serious toxicities. Various drugs or groups of drugs are involved in causation of ADRs in older patients. In a reported study, the drug classes involved were antipsychotics, anticoagulants, diuretics and antiepileptics [31]. A systematic review found antiplatelets, diuretics, NSAIDs, and anticoagulants as major groups involved in preventable adverse drug reactions causing hospital admissions [32]. In another systematic review anticoagulants, anti-infectives/antibiotics, antihyperglycemic agents, analgesics (including opioids and NSAIDs) and cardiovascular drugs (antihypertensive agents, diuretics and digoxin) were reported to be the major drug classes involved in causing adverse drug events (ADEs) during hospital stays [33].

Prevention of adverse drug reaction in the elderly

The term inappropriate medications may be defined as medications or medication classes that should be avoided in persons

65 years or older because they are either ineffective or they pose unnecessarily high risk for older persons and a safer alternative is available. There is an integral relationship between inappropriate prescription (IP) and ADRs. A significant association also found to be existing between IP, ADEs, acute hospitalization, death and higher healthcare costs [34-36]. The Beers criteria [37-39] is the most frequently and globally used clinical tool to identify ADRs in the elderly. The STOP/START (Screening Tool of Older Persons Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria is another tool for medication review in the elderly [40].

Every healthcare professional has roles to play in the identification and prevention of ADRs in the older people. There is a need of enhancement of communications between different healthcare providers [41]. Diagnosis and management of ADRs in older patients requires physician's knowledge of physiology and pharmacology of aging. There are certain general measures for promoting good prescribing in older adults which include careful identification and documentation of diagnoses, medication and history of previous ADRs. Physicians should suspect for ADR in all older patients who develop new symptoms after starting or dose adjusting a medication, or in those presenting with cognitive or functional decline. Physicians should consider ADRs as a cause of new symptoms in older patients with renal impairment, falls, orthostatic hypotension, heart failure, delirium, polypharmacy and previous history of ADR [42]. Careful and proper time should be dedicated in clinical assessment, detailed medication review (prescription and over-the-counter drugs) and any collateral history. Comorbid illness should be considered while assessing the medication list. There should be no therapeutic duplication, unnecessary medications should be discontinued, and dosing frequency of continued drugs should be optimized. Clear therapeutic goals should be set with the dates for review of efficacy and ADRs. Drug doses should be titrated carefully from low starting dose and patients actively monitored for development of adverse effects.

In recent time, it has been observed and documented that greater involvement of pharmacists, particularly emergency departments have been shown to reduce inappropriate therapies, as defined by Beers criteria. The pharmacists can educate prescribers, by developing notices for patient on which drug combinations to be avoided. This procedure can be implemented by computerized prescriber data entry and by giving feedback to prescribers on their performance [43]. Researchers showed that the application of Beers criteria identified elderly patients needing an alternate level of care who subsequently experienced an ADR.

Application of Beers criteria can be very helpful to the pharmacists in the screening of elderly patients for prescribing of inappropriate medications and thereby ensuring attention to the most needed ones. Pharmacists can also take the help of the other evidence-based STOP/START criteria to identify patients needing evaluation of their drug therapy [44]. Researchers have shown that the application of STOP/START screening criteria has been shown to improve the appropriateness of prescribing and reduce subsequent drug-related readmissions. Some investigators even found STOP/START more effective over Beers criteria in identifying potentially dangerous drugs having risks of ADR in the older patients [45,46]. Some researchers found that pharmacists significantly improved prescribing and reduce subsequent ADRs by use of structured approach in identifying and interviewing patients for assessing their drug therapy. Frailty index is another tool which can be utilized by the pharmacists in the selection process of drugs in very old people [47]. It is a simple assessment score based on only 5 clinical variables (> 8 medications, hyperlipidemia, elevated white blood cell count, use of antidiabetic agents, and hospital length of stay >12 days) which of the very i.e. > 80 years of age are likely to experience an ADR [48].

Conclusion

Increasing number of the elderly population has social, economic and political implications with strains on the healthcare and social care systems for a country. Our country India is not an exception to it. The increase in the number of older persons will increase the disease burden and a corresponding increase in medication utilization with consequent increased risk of ADRs. Geriatric medicine is still in its infancy in India and presently most of the geriatric out-patient department services are available at tertiary care hospitals only. Most of the other facilities of geriatric care are till now urban-based in our country. Moreover, the pharmacovigilance system in our country is still in its infancy. There is definite shortage of good quality data on ADRs and drug safety data in our country, particularly for the elderly patients. Therefore, it is anticipated that ADRs in the elderly is going to be huge challenge in our country in coming decades to deal with and will definitely be a hindrance in providing quality medical care to our elder people. Time has come for us to realize this and to develop strategies to deal with such scenario. Capacity building for different groups of healthcare personnel is the need of the hour. Training of medical officers, pharmacists and other health workers at all level of health care system should be emphasized more now. Inclusion of more

chapters on geriatric medicine and ADRs in the academic curriculum of the various academic programs in the country is needed.

Competing Interest

No competing interest to declare.

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