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Chapter

Approach to Minimize Adverse Drug Reactions in Elderly

Hima Bindu Gujjarlamudi

Abstract

The elderly, above the age of 65, are heterogeneous population with increased morbidity. They are more exposed to medication due to multiple health problems. The natural physiological changes and alterations in homeostatic regulation alter drug response and increase the risk of adverse drug reactions in them. Multi-prescription, polytherapy also increases the incidence of adverse reactions. It is difficult to diagnose adverse reactions in the elderly as they often present with nonspecific symptoms and to differentiate whether they are due to medications or not. Most of the hospital admissions due to adverse reactions are predictable and 50% among them are preventable Type A reactions as most of the errors occur during prescribing or monitoring of drugs. Prescribers should review the medication list regularly and be cautious in prescribing new medicines. Physicians’ awareness of the physiology and pharmacology of aging can reduce adverse reactions that help in promoting better health care for older adults.

Keywords: elderly, adverse reactions, polytherapy

1. Introduction

The population of the elderly is increasing worldwide. India is going to be the highest in Asia with people aged 60 years and above. In 2020, there are an estimated 727 million persons aged 65 years or above worldwide. It may be doubled by 2050, nearing to more than 1.5 billion persons. The share of older persons in the global population is expected to increase from 9.3 percent in 2020 to 16.0 percent in 2050 [1]. As age advances, they are more exposed to multiple diseases in addition to the increased incidence of other illnesses such as Alzheimer’s disease, Parkinson’s disease, vascular dementia, stroke, arthritis, and fractures [2]. So, medications play a crucial role in geriatric health care as they treat chronic diseases, reduce pain, and improve quality of life [3].

The physiological changes that occur with aging alter the pharmacokinetics and pharmacodynamics of drugs, which increases the risk the adverse drug reactions (ADR) and drug interactions (DI). Multi-prescription, polytherapy, and inappropriate medication use also increase the incidence of ADR. A major threat to the health-related quality of life of older adults is ADRs. They can decrease functional status and increase the use of health services and costs, as well as mortality [4]. Hence this
article focuses on the prevalence and risk factors for ADR in older adults and the steps taken to minimize them.

2. Prevalence of ADR in older adults

ADR is defined as “an appreciably harmful or unpleasant reaction resulting from an intervention relating to the use of a medicinal product” [5]. Compared with younger patients, patients aged 65 years or older are seven times more likely to have an ADR requiring hospitalization [6]. ADRs are responsible for 5–28% of acute geriatric hospital admissions, and studies have indicated that more than half of them are preventable with only 19–28% of ADRs causing hospital admission in older patients considered unavoidable [7].

A study done by Harugeri et al. [8] in a hospital setting found that the prevalence of ADR-related hospital admissions was 5.9%, while in another study [9] in India, it was observed to be 6.7%. In-hospital incident ADRs cause a 9% increase in length of stay and a 20% increase in the cost of care encompassing bed consumption, laboratory, and treatment costs [10]. About 20% of ADR-related hospitalizations need blood products to treat gastrointestinal bleeding adding to extra cost on the patient [11].

3. Risk factors for ADR in elderly

Several factors contribute to the higher incidence of ADR. Table 1 highlights the list of risk factors for ADR in the elderly. Older people experience greater morbidity with a corresponding increase in medication utilization resulting in a higher risk of ADRs [12].

3.1 Physiological changes

The natural physiological changes that occur due to aging and alterations in homeostatic regulation alter drug response and increase the risk of ADR in them. Drug metabolism and clearance change with alterations in pharmacokinetics [13] further increasing the risk of ADRs. The decrease in total body water alters the volume of drug distribution prolonging the half-life of a drug and increasing the risk of toxicity [14, 15].

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<tr>
<th>S.No</th>
<th>Risk factor</th>
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Table 1.
List of risk factors for ADR.
The filtration capacity of the glomerulus reduces as age advances, which results in the decreased excretion of drugs and an increase in adverse reactions.

### 3.2 Polytherapy

Multi-prescription, polytherapy also increases the incidence of adverse reactions. It was estimated that more than 60% of the elderly take five or more drugs regularly. The risk of ADRs is increased with the increase in the number of medicines prescribed [16]. This has been estimated at 13% for two drugs, 58% for five drugs, and 82% for seven or more drugs [17].

### 3.3 Nonadherence

Complex medication regimens related to polypharmacy can lead to nonadherence in older adults [18]. Nonadherence can lead to serious sequelae, including disease progression, treatment failure, hospitalization, and adverse drug events [19].

### 3.4 Potentially inappropriate medications

The use of potentially inappropriate medications (PIMs) in the elderly has also been described as a potential cause of ADR [20]. PIMs use increases the risk of hospitalization, drug-related problems, and other adverse health outcomes by two to three folds [21]. For example, drug-related problems secondary to the inappropriate use of sedatives and hypnotics among older adults are found highly associated with the risk of falls, delirium, and hallucination [22].

### 3.5 Medication errors

Errors in medication administration and autonomous modification of medication schedules have also been reported to contribute to ADRs [23]. Another important risk factor for developing ADR is its previous occurrence. Re-exposure to offending drugs due to poor documentation can cause the same ADR.

### 3.6 Multiple diseases

The risk of ADRs also increases with an increasing number of chronic diseases. When medicine was given to treat one condition, it aggravates the signs or symptoms of another underlying disease. For example, beta-blockers taken for cardiovascular disease worsen asthma symptoms or metoclopramide for gastric dysmotility worsens motor symptoms of Parkinson’s disease [24].

### 4. Common drugs causing ADR in elderly

The majority of ADRs in older people are Type A reactions that is, they are attributable to a predictable known pharmacological effect of a drug. Type A adverse drug reactions are usually avoidable and typically involve commonly prescribed medications [25]. There are many drugs to be avoided or used with great caution in the elderly. The most frequently implicated drug groups causing ADRs in the elderly are antibiotics, cardiovascular drugs, steroids, loop diuretics, hypoglycemic,
antipsychotics, and antidepressants (Table 2) [26]. A systematic review of nine studies of ADRs as a cause of hospitalization found that 51% of preventable drug-related admissions were associated with antiplatelet agents (16%), diuretics (16%), NSAIDs (11%), or anticoagulants (8%) [27]. A drug combination may sometimes cause synergistic toxicity, which is greater than the sum of the individual toxicities used alone. The risk of the development of NSAID-induced peptic ulcers in the elderly may increase by 10% when used along with corticosteroids [28]. However, concurrent use of corticosteroids and NSAIDs had shown a risk of peptic ulcers, which was 15 times greater than that of non-users of either drug [29].

5. Steps to reduce ADR in older adults

The main factor in reducing ADR is its correct identification. It is difficult to recognize ADR in older people as they often present with nonspecific symptoms such as falls, fatigue, cognitive decline, or constipation. The inability to distinguish drug-induced symptoms from a definitive medical diagnosis often results in the addition of yet another drug to treat the symptoms, which increases drug-drug interactions and ADR, known as “the prescribing cascade” [30]. For example, anti-Parkinsonian drugs are prescribed to treat motor symptoms occurred due to prolonged antipsychotic therapy. The risk of ADR can be reduced by regular monitoring of the patient, prompt identification of symptoms, and the effect of medication on different organs. Hence, both the prescribers and patients play an equal contribution in reducing the risk of ADR in the elderly.

5.1 Role of prescribers

5.1.1 Examine the patient

A systematic approach to the patient will reduce ADR. The patient has to be examined thoroughly in a comprehensive view, not just focusing on symptoms alone.
As symptoms can be adverse reactions to the drugs or due to disease progression, patient’s treatment need has to be identified and documented by the diagnosis.

5.1.2 Maintain the record

All drugs used by the patient including non-pharmacological agents such as herbal preparations, supplements, or over-the-counter (OTC) medications are recorded because alternatives or herbals may interact with the present regimen, increasing the risk of adverse reactions. The most commonly used herbals and dietary supplements are glucosamine, extract of gingko biloba, St. John’s wort, and ginseng. A study in the United States found that out of 3072 ambulatory elderly patients, 82.5% used at least one supplement and 54.5% used three or more [31]. A record of all medications including herbals and other alternatives should be updated frequently with possible simplest regimens to reduce the duplication, unnecessary medication, and important drug interactions. It also reduces polypharmacy and the underuse of vital drugs.

5.1.3 Benefit-risk assessment

The elderly patient is evaluated for benefits and risks while prescribing the medication. This reduces the use of unnecessary medication or duplication, and polypharmacy and further reduce the cost burden on the patient.

5.1.4 Adjust the dose of the drug

Aging decreases the filtration capacity of the glomerulus because of a decrease in renal size, perfusion, and nephron function [32]. Glomerular filtration rate must be calculated for drugs eliminated through the kidney. The dose of the drug has to be adjusted for renal impairment by using Cockroft and Gault Equation to minimize the risk of ADR.

5.1.5 Inappropriate medications

The use of inappropriate medications is most common in elderly patients. Approximately 50% of the elderly take one or more medications that are not necessary [33]. The Beers criteria are the most commonly used criteria to guide prescribers in preventing ADR [34, 35]. This was recently revised in 2019 by an expert panel sponsored by the American Geriatric Society. Screening Tool of Older Person’s Prescriptions (STOPP) is another tool consisting of 65 STOPP criteria to represent common avoidable instances of inappropriate prescriptions [36]. “The Good Palliative–Geriatric Practice algorithm” for discontinuation of drug reduced polytherapy and improved morbidity and mortality in community-dwelling elders and nursing home inpatients [37]. These criteria consist of drugs to be avoided or used with caution in the elderly and reduce inappropriate prescribing and its related ADR. In the elderly, underuse of medicines is also prevalent. Prescribers may underuse the useful drug if the patient is not able to afford the medication. START (screening tool to alert doctors to the right treatment) is a tool designed specifically on the list of evidence-based useful medications but possibly omitted drugs in the elderly [38]. This can be reduced by documenting the patient’s condition and prescribing the medication for the current condition.
5.1.6 Start with a low dose

Aging alters the pharmacodynamic responses. So, the elderly are more sensitive to the effects of drugs than young adults even with standard doses. Drugs such as morphine and neuroleptics cause more confusion and warfarin increases the anticoagulation effect with a regular therapeutic dose. This can be minimized by starting with the lowest possible dose and gradually titrating the dose depending on the response by carefully monitoring the patient.

5.1.7 Drug frequency and dosing

The time of drug administration also plays a role in the development of ADRs. Chronotherapy is the delivery of a drug following biorhythm that prevents an overdosing of any class of drug [39]. Patients with osteoarthritis have less pain in the morning and more at night. NSAIDs reduce pain when given at least 4–6 hrs before the pain reaches its peak. So, it is given around noon or midafternoon [40]. The incidence of ADR can be reduced by administering the right drug at the right time.

5.1.8 Drug interactions (DI)

Drug-drug, drug-disease, and drug-food interactions should be considered while prescribing to the elderly. Co-morbidities and polytherapy in the elderly increase the risk of DI. The prevalence rate of DI-induced ADR-related hospitalizations was 22.2% and 8.9% for hospital admission and hospital visits, respectively [41]. The most important DI occurs with drugs that have serious toxicity and a low therapeutic index. Bisphosphonates are often co-prescribed with calcium supplements in the treatment of osteoporosis. Calcium binds to the bisphosphonates and reduces its absorption with the possibility of therapeutic failure [42]. This may be avoided by allowing a sufficiently long dosage interval; the possible approach is to give bisphosphonates for 2 weeks and calcium supplements for 10 weeks [43].

The risk of potential drug interaction increases from 39% to 100% when patients are on more than six medications compared to when they are on 2–3 medications [44]. Most of the DI can be reduced by choosing alternative medications that are not associated with DI. For instance, pantoprazole is given to patients on clopidogrel in place of omeprazole to avoid interaction between omeprazole and clopidogrel.

The risk of drug-disease interaction is also important as the elderly population suffers from more than one condition. The most common interactions were aspirin and peptic ulcer disease; calcium channel blockers and heart failure and beta-blockers and diabetes [45].

These interactions are of utmost importance as they decrease the efficacy of the drug or may increase the toxicity of a drug. Hence, prescribers must have knowledge on the pharmacology of drugs and their interactions to reduce DI-related ADR.

5.1.9 Economical alternative

Strict adherence to the medication is very important to reduce the progression of the disease, treatment failure, and further adverse effects. An increase in the cost of medications reduces adherence to the treatment. The pill burden can be reduced by using medications that can control two or three conditions and by choosing economical alternative drugs [46].
5.1.10 Patient education

Patients and their families should be educated about the effects of polytherapy and can stop the unnecessary medication if there is no benefit. Counseling is given on the probable adverse effects of the drugs, adherence to the therapy, and sudden stoppage of treatment. The plan of treatment, its effects, and follow-up visits should be clearly discussed with the patient and their families.

5.2 Role of patients/caregivers

Elderly patients or their caregivers play an equal role in reducing the incidence of ADR. In a study of 30,000 Medicare enrollees aged over 65 years followed for a 12-month period, 99 adverse drug events (23.5% of all adverse drug events) and 30 potential adverse drug events (13.6% of potential adverse drug events) were attributed to patient error [23]. Errors in medication administration, adherence to the treatment regimen, and modification of medication schedules are commonly encountered patient errors.

5.2.1 Information about medications

The elderly patients and their informal carers should obtain clear information about the effects of drugs, the timing of administration, and diet restrictions. They must have minimum knowledge of common side effects of their drugs and drug interactions so that they can inform their physician immediately when they occur for necessary action.

5.2.2 Improving the compliance

Poor adherence to the prescribed regimen is most common in the elderly, which compromises the efficacy of the drug. Dementia, decreased vision, financial constraints, and too frequent administration of medication further decrease compliance. Some patients decrease the dose of the drug or may even stop the drug because of undesirable effects without informing the physician. Strict adherence to treatment should be enhanced by using daily or weekly pill boxes, setting alarm clocks, and daily reminders.

5.2.3 Use of over-the-counter drugs (OTC)

The patient has to inform all the drugs they are using, including OTC, herbals, or other supplements, which helps the physician in identifying ADRs and DI. In a telephonic survey in North America, 34% cohort was taking at least one unintentional drug and 72% of them reported that they did not inform their clinician about this [47]. Herbal medications interact with the current regimen resulting in adverse effects. Severe bleeding with warfarin and ginkgo, garlic; exacerbation of extrapyramidal effects with neuroleptic drugs, and betel nut; potentiation of oral and topical corticosteroids by licorice are some of the examples [48].

5.2.4 Maintain the record of medications

A list of medicines should be updated regularly and brought to the clinician during the visits. All the duplicated medicines and unnecessary medications should be deleted.
6. Conclusion

Prescribing drugs in the elderly is a serious challenge as there is an increased possibility of drug interactions and ADR. It is difficult to balance beneficial therapy and inappropriate medication. Prescribers need to know what other prescriptions the patient is taking, including herbs and supplements, and the drug regimen is evaluated periodically to reduce polypharmacy. ADR is considered in every differential diagnosis. Good communication should be maintained among health care providers, patients, and caregivers. Physicians’ awareness of the physiology and pharmacology of aging can reduce adverse reactions, which helps in promoting better health care for older adults.

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