

Medication safety in elderly patients

Abstract

The present manuscript describes health problems that commonly affect elderly patients and explain which and why some drugs increase the risk of having problems related to drugs. The physiological changes that occur with ageing and how these impact on drug therapy are also explained. A brief detail of drugs that commonly cause adverse drug reactions (ADR's) are covered along with a plan for preventing them and improving the quality of life.

Keywords: health problems, quality of life, elderly, physiological changes

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Introduction

The statistics reports show that drug use in the elderly is very high. Patients over 65 years of age constitute 12% of the population and consume 31% of the prescribed drugs.¹ It is due to an increased severity of chronic illness, presence of multiple pathologies and excessive prescribing of drugs. During hospitalization 40% of admission medications are stopped and 45% of discharge medications are started. This poses high risk. Serious prescribing problems constitute 22% whereas other prescribing problems account to 66%. An average person over 65 takes an average of 4.5 prescription medications at a time plus 2 OTC medications.¹

Common diseases affecting the elderly include Osteoarthritis and osteoporosis, impaired mobility and falls, infectious diseases (Upper respiratory infections and urinary tract infections), chronic bronchitis, cardiovascular disorders including hypertension, ischemic heart disease, heart failure etc. and cerebrovascular diseases namely stroke, cancer and dementia.²

Increased prevalence of disease, polypharmacy, altered drug response inappropriate prescribing, adverse drug reactions, non compliance, pharmacokinetic changes with ageing, depression, constipation, visual and hearing impairment, malnutrition and related problems pose therapeutic challenges of prescribing for the elderly patients³ include.

Objectives

The main objectives of this article are:

1. To understand the Physiological changes that affect Pharmacokinetics of the drugs in the elderly.
2. To study the Physiological changes that affect Pharmacodynamics of the drugs in the Elderly.

Discussion

Changes in pharmacokinetics

The rate of absorption may be reduced due to increased gastric pH, decreased absorptive surface area, decreased gastric motility and delayed gastric emptying. Gastrointestinal disorders like enteritis, gastrectomy, malabsorption syndrome and concomitant use of drugs that affect GI function like laxatives, antacids and ion exchange

resins. may alter absorption. Distribution of drugs is changed due to increased body fat, decreased lean muscle mass, decreased serum albumin, decreased cardiac output and decreased total body water.⁴

Lipid soluble drugs are taken up into the tissues to a greater extent and have an increased volume of distribution and prolonged duration of action. Protein binding of highly bound drugs tends to be reduced in the elderly due to less albumin in the body. However binding of basic drugs is increased due to more Alpha 1- glycoprotein (primarily binds basic drugs) in the elderly patients.

Metabolism of drugs is reduced due to decreased: hepatic blood flow, hepatic mass and activity of hepatic enzymes. Excretion of drugs is affected due: to decreased renal blood flow, glomerular filtration rate, tubular secretion and number of nephrons.

Changes in pharmacodynamics in the elderly

Pharmacodynamic changes include increased drug sensitivity, changes in blood-brain barrier, alteration in receptor properties, increased adverse drug reactions, changes in homeostatic responses and altered receptor or tissue sensitivity.⁵ Central nervous system (CNS) becomes vulnerable to alterations in drug response. Adverse effects of benzodiazepines occur at lower drug concentrations in the elderly. Ageing brain loses a significant number of active cells and brain atrophy is common.

There is reduction in cerebral blood flow. There is selective decline in some nerve pathways and there is loss of cholinergic neurons resulting in memory loss, confusion and cognitive impairments. Monoamine oxidase activity increases with normal ageing whereas there is decline in noradrenaline and dopamine levels in brain. There is increased sensitivity to dopamine blocking agents (antipsychotic drugs). Excessive sedation, confusion, or behavioral disturbances e.g. agitation and aggression are also common in the elderly. Iatrogenic confusion and behavioral disturbances are more commonly reported. The elderly population is more sensitive to anticholinergic drug side effects outside the CNS. Other effects include urinary retention, constipation, blurred vision, dry mouth, tachycardia and aggravation of glaucoma.

There is an increased sensitivity to the effects of warfarin. Increased pharmacodynamic sensitivity due to age related is due to decline in hepatic synthesis of vitamin K dependent clotting factors. There is an altered homeostasis. Adverse effects result from impaired secondary

compensatory mechanisms (homeostasis). Postural hypotension results from impaired baroreceptor function reduced compensatory tachycardia and vasoconstriction in response to hypotension and failure of cerebral blood flow autoregulation. Patients with impaired cardiac output and taking diuretics are especially vulnerable. Benzodiazepines adversely affect balance and contribute to falls.⁶

Adverse Drug Reactions are 7 times more common in the elderly.⁷ They occur in about one in five hospitalized elderly patients. They account for 10-24% of hospital admissions and 50% of medication related deaths.⁷ The quality of life is affected. In ambulatory elderly 35% experience ADRs and 29% require medical intervention. In nursing facilities, 2/3 of residents, experience ADRs and 1:7 require hospitalization. Up to 30% of elderly hospital admissions involve ADRs. A number of Drug Interactions are reported in the elderly patients. Severe ADE's commonly reported have cardiovascular related problems (36%) whereas Acetylsalicylic acid contributes to only 7% problems.⁸

Factors that predispose elderly to ADRs:

These include self medication and little patient counselling. Drug accumulation occurs due to a reduced renal function which leads to adverse drug reactions. Other factors include polypharmacy, greater use of drugs with a low therapeutic index (i.e. digoxin) inadequate supervision of long-term therapy and poor patient adherence.^{3,9-11}

ADRs occur as a result of drug-drug interactions, drug-disease interactions, drug-food interactions, drug side effects and drug toxicity etc. The pharmacological parameters associated with ADRs in the elderly include altered free serum concentration of drug, diminished volume of distribution, altered renal drug clearance and prolonged absorption due to decreased gastric mobility.¹²

Following drug combinations are most commonly associated with ADRs in the elderly:

- a. Cardiovascular drugs, psychotropics and antibiotics
- b. Cardiovascular drugs, psychotropics and analgesics
- c. Gastrointestinal drugs, psychotropics and analgesics
- d. Gastrointestinal drugs, psychotropics and antibiotics

Drug-drug interactions: Are almost countless. Statins are known to interact with erythromycin and other antibiotics.

Angiotensin converting enzyme (ACE) inhibitors are known to increase the hypoglycemic effect of sulfonylureas. Patient non-compliance contributes to effects in the elderly. 40-50% of elderly patients in one US study were not compliant where as other studies showed it to be about 1/3. These interactions include wrong dose; wrong timing; wrong frequency; wrong way; not taking etc.

Drug-disease interactions occur too: Patients with Parkinson's disease have increased risk of drug induced confusion. Nonsteroidal anti-inflammatory drugs (and COX-2's) can exacerbate Congestive heart failure. Urinary retention is noticed in Benign prostatic hyperplasia patients who are on decongestants or anticholinergics. Constipation gets worsened by calcium, anticholinergics and calcium channel blockers. Neuroleptics and quinolones lower seizure thresholds. Drugs and Falls occur with the use of long acting benzodiazepines and other sedatives and hypnotics. Both serotonin reuptake inhibitors (**SSRIs** and Tricyclic antidepressant (TCAs) drugs are associated with increased risk of falling There is mild increase in risk of falling associated with the use of diuretics, type

IA anti-arrhythmics, and digoxin. Other examples about Geriatric drug interactions include NSAIDs. Acetaminophen is as effective as NSAIDs in mild osteoarthritis. NSAIDs side effects include GI hemorrhage and decline in Glomerular filtration rate. The effectiveness of diuretic anti-hypertensive agents has been reported to be decreased.¹³

Drug-food interactions in the elderly are common: Some of the examples include interaction of Warfarin and Vitamin K containing foods including green tea. Phenytoin and vitamin D metabolism, Methotrexate and folate metabolism etc. are also reported.

Drugs impact appetite more in the elderly population: Digoxin may cause anorexia whereas ACE inhibitors may alter taste in individuals. Poor drug adherence to medications in the elderly patients include multiple chronic disorders, multiple prescriptions, multiple doses, change in daily drug regime, cognitive or physical impairment, living alone, forgetfulness and visual impairment, impaired dexterity, inability to pay for drugs, presence of side effects and polypharmacy.¹⁴

Lots of discrepancies are reported in medications used in the elderly population: It is reported that 51% of times medication is not recorded, 29% medications are not taken by the patients and 20% errors happen due to dosage discrepancy.¹⁵

These are classified as:

1. Inappropriate prescribing

15 percent of elderly people are prescribed at least one inappropriate medication. There could be overprescribing, inappropriate drug selection and underprescribing Angiotensin converting enzyme inhibitors decrease morbidity and mortality associated with cardiac failure and are commonly underprescribed

2. Medication appropriateness

3. Overuse of a medication

Antibiotics, GI Medications and Sleep medications are commonly overused.

4. Misuse

This includes wrong dose and/or frequency

5. Underuse

This happens in chronic diseases and in preventative medications namely vaccines

6. High risk medications include following drug classes:

Analgesics

- NSAIDs
- Narcotics
- Muscle relaxants

Narrow therapeutic index

- Digoxin
- Phenytoin
- Warfarin
- Theophylline
- Lithium

Cardiovascular

Antihypertensives

Calcium channel blockers

Propranolol

Diuretics

Psychotropics

- Tricyclic antidepressants

- Antipsychotics

- Benzodiazepines

- Sedative/Hypnotics

Other High Risk Medications include H2 Blockers, Gastrointestinal Antispasmodics, Antibiotics (aminoglycosides) and Hypoglycemics. 70% of nonadherence is intentional.¹⁶

Personal health record

It is an important document that includes patient identifying information, doctors' contacts, caregiver contacts, past medical history and allergies, list of all medications, dose, reason they are taking it and whether it is new. This document will reduce polypharmacy and ADRs. It will keep record of multiple specialists involved in care transitions in care from independent living, hospitals, nursing homes and assisted living facilities. It is a great aid in emergency care and provides the patient with more peace of mind. The patient should bring this to every medical visit and present it to their provider. Each provider should update list with any changes

Use of over the counter drugs in the elderly

It is reported that elders take an average of 2-4 nonprescription drugs daily. Out of these laxatives are used in about one-third to about one half of the population even if they are not having constipation. Non-steroidal anti-inflammatory drugs, antihistamines, sedatives, and H2 blockers are all available as over the counter medications. They all may cause major side effects.

Herbals and supplements are sold and marketed without evidence of safety.¹⁷ Good manufacturing practices and standards are not followed in many countries for their sale. Some herbals and supplements are reported to have potential interactions with prescription drugs. SAME (S-Adenosyl-L-methionine) may increase homocysteine levels. St. John's wort and oral contraceptives interaction is well reported. Ginkgo is known to increase anticoagulant effects of acetyl salicylic acid, warfarin, nonsteroidal anti-inflammatory drugs and ticlopidine. Hence, the doctor must know what his patient is taking.

Drugs and dosages that should be avoided in elderly include Meperidine, Diphenhydramine, anticholinergic tricyclics like amitriptyline, doxepin, imipramine, diazepam, long acting NSAIDs like piroxicam, high dose thiazides (>25mg) etc. Iron in dose of 325 mg once daily is enough for the elderly population.

Principles for handling drugs in the elderly

During prescribing patients complete drug history, including intake of herbs and over the counter drugs should be taken. The cost of the medication is important especially if the patient has to pay for his medicines. The principle of "Start low, go slow, but get there" should be followed. The regimen should be kept simple. The instructions

should be written out clearly. The patients should be encouraged to bring in medications at each visit. Home visit, if needed should be followed. In case there is no benefit or there are side effects due to drug, they should be discontinued. The doctor needs to be careful with prescribing of newer drugs. In case newer drugs are to be used in the elderly, one must find out if clinical data is available and how does it compare with traditional therapy.

An Individualized drug therapy in the elderly is essential. Some of the Geriatric Rx Principles include considering non-drug therapies, matching drugs to specific diagnoses, reducing medicines whenever possible, reviewing medicines regularly (at least every 3 months), avoiding drugs with similar actions / same class, clearly communicating with patient and caregivers and considering cost of medicines. Automatic refills should be avoided. One must take caution with multiple providers. Don't use medications to treat side effects of other medicines. It is important to educate the patients by talking about potential ADRs, warning for potential side effects, educating the family and caregiver, asking pharmacist for help in identifying interactions and assisting the patient in making and updating a medication list. Personal medical record will reduce medication related risks. Beers Criteria includes strengths and limitations. Strengths are developed by 6 nationally known experts in geriatric care and pharmacology and are widely used to screen populations for possible drug-related problems. The limitations do not include identifying all cases of potentially inappropriate prescribing and medication reconciliation which includes comparing patient's medication orders to all medications that the patient has been taking.¹⁸

Medication Reconciliation for the elderly is a 5 Step Process which includes developing a list of medications, develop a list of medications to be prescribed, comparing the 2 lists, making clinical decision based on the comparison and communicating the new list to the appropriate caregivers and the patient

Conclusion

Measures to prevent ADRs in elderly include taking complete drug history including over the counter drugs and herbals, accounting for pharmacokinetic and pharmacodynamic changes that occur with aging, initiating therapy with low doses, monitoring clinical response and plasma drug levels, employing simplest regime possible, monitoring drug-drug interactions, periodically reviewing drug regimens, encouraging patient to dispose of old medications and promoting adherence to drug regime.

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Conflicts of interest

The authors declare no conflict of interest.

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