VOLUME-7, ISSUE-5, MAY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Pharmacy

A REVIEW ON PHARMACOTHERAPEUTIC CONSIDERATIONS IN GERIATRICS

K. Supriya*	Pharm D V Year, Department Of Pharmacy Practice, Santhiram College Of Pharmacy, Nandyal, Pin- 518501. *Corresponding Author
B. Aswani	Assistant Professor Department Of Pharmacy Practice , Sree Vidyanikethan College Of Pharmacy, A Rangampet, Sree Sainath Nagar , Tirupathi
K.V.C.H.Bramham	Pharm D V Year, Department Of Pharmacy Practice, Santhiram College Of Pharmacy, Nandyal, 518501.
K.Anjineyulu	Pharm D V Year, Department Of Pharmacy Practice, Santhiram College Of Pharmacy, Nandyal, 518501.
K.Anjineya	Pharm D V Year, Department Of Pharmacy Practice, Santhiram College Of Pharmacy, Nandyal, 518501.

ABSTRACT

The people greater than 65 years of age are considered as geriatrics. The united nation estimates that elderly people currently accounts for 11% of total population and an exponential increase is expected upto 2050. Elderly patients are prevalence of multiple coexisting chronic conditions and geriatric syndromes. Older people tend to take more drugs than younger people because they are more likely to have more than one chronic medical disorder. Older people are susceptible to the side effects of drugs for several reasons. Pharmacokinetic variations like absorption is not significantly altered when compared to adults, distribution is altered in geriatrics, metabolism and elimination is decreased in geriatrics. Pharmacodynamic variations like alterations in homeostatic reserve and age related changes in receptor and target site. Many symptoms that can be worsenedby drugs in older people. There are many reasons for non adherence in the elderly. Strategies to improve compliance and risk factors for drug related problems. Many drug interactions are seen in elderly. Patient compliance is a major factor in the geriatrics therapeutic management. Because there are lot of barriers for compliance in geriatrics, which negatively impacts the quality of life. In this present article we make an attempt to briefly describe the various factors and considerations in geriatric therapeutic management.

KEYWORDS : Geriatrics, Pharmacokinetics, Pharmacodynamics , Compliance.

Introduction:

The people greater than 65 years of age are considered as geriatrics .The 65 and older population jumped 15.1 percent between 2000 and 2010, compared with a 9.7 percent increase for the total U.S population. The observed Geriatric population in India was 8%. [1] Geriatrics is classified into three groups. They are elderly (age 65-74), aged (75-84) and very old (age 85 and more).

Demographic changes in geriatrics:

Demography aging is a global phenomenon. The United nation estimates that elderly peoples currently account for 11% of total population (800millions) and an exponential increase is expected upto 2050(about 2 billions), at which it will be as large as the population of children (0-14years).This historic crossover of an increasing share of older persons and a declining share of children will mark the first time that the number of children and the older persons are the same. Persons aged 60 or older comprise10 percent of the world population. The percentage is much higher in the more developed region (20 percent) than in the less developed regions (8 percent), which are at an earlier stage of the demographic transition. It is especially low in the least developed countries (5 percent). Among individual countries, the most aged are Greece and Italy, where 24 percent of the population is aged 60 or older in 2000.Many European countries, as well as Japan, have percentages nearly as high. By 2050, the older ages will make up a projected 22 percent of the world population,33 percent in the more developed regions, 21 percent in the less developed regions ad 12 percent in the least developed countries.[2]

Co-morbid conditions in geriatrics:

One of the hall marks of elderly patients in the increasing prevalence of multiple co-existing chronic conditions and geriatric syndromes, such as dementia, incontinence, falls and frailty. It has been estimated that more than two thousands of patients with heartfailure have two or more non cardiac comorbidities and more than25% may have 6 or more concomitant diseases. Common comorbidities include renal disfunction, anaemia, chronic lung disease, depression, arthritis, sensory and nutritional disorders.[3]

- Renal disfunction may be worsened by diuretics, angiotensin converting enzyme inhibitors and may contribute to volume over load in persons prone to heart failure. Reneal failure is associated with adverse outcomes, particularly in patients with heart failure.[4]
- Anaemia may be related chronic diseases, such as renal diseases, malignancies or may be the consequence of treatments (aspirin, nonsteroidal antiinflammatorydrugs, warfarin) or in adequate intake (iron,folate,vitaminB12).It may increase symptoms and confers poor prognosis.[5]
- Chronic lung diseases may contribute to increased dyspnoea and exercise intolerance in elderly patients with heart failure. Plasma brain natriuretic peptide may provide a reliable diagnostic tool to distinguish primary pulmonary symptoms.[6]
- Depression and social isolation (primarily because of the death of the spouse) may impair drug compliance and are associated with poor prognosis and increased hospitalization rates.[7]
- Arthritis is a leading cause of disability in elderly people and is mainly treated with NSAID that may enhance renal sodium and water retension, antagonize the effects of diuretic and ACE inhibitors, and be responsible for gastro intestinal bleeding.Sensory deprivation with decreased visual and auditory acuity, as well as taste and smell decline may interfere with the ability of patients to comply with the therapeutic advices.[8]

Pharmacokinetic and pharmacodynamic changes in geriatrics:

Conceptually there are two ways to envision the drug therapy in individual patients, what the drug does to the body and what the body does to the drug. Pharmacokinetics includes parameters as absorption of the drug, distribution of the drug to the various

organs and tissues in the body, metabolism of the drug into other compounds, and renal excretion of the drug and metabolites with subsequent elimination from the body. Pharmacodynamics describes the action of specific drug and the response of the patient.

Pharmacokinetic changes:

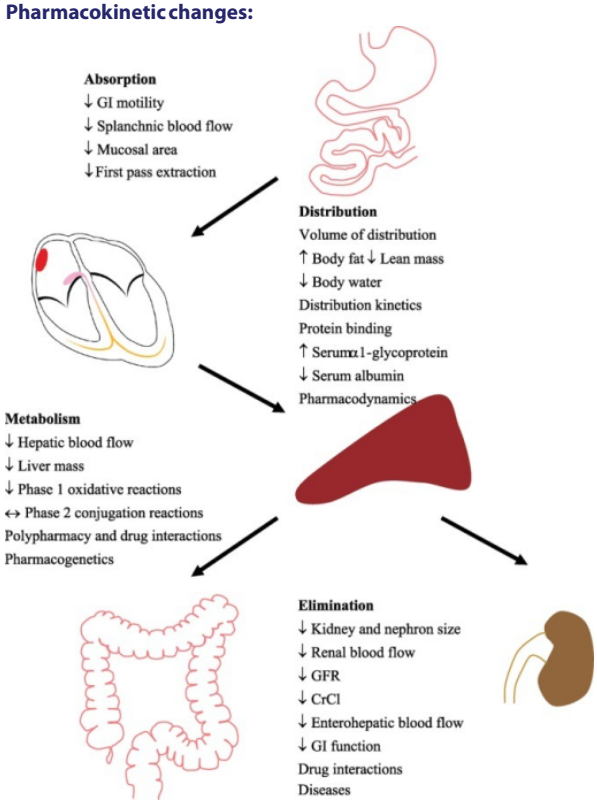

Figure.No.1: Pharmacokinetic variations in geriatrics

a)Absorption:

A number of changes in the GI tract occur with aging that can potentially affect the drug absorption after oral administration. The rate and extent of absorption of drug is influenced by a variety of factors, including changes in the GI physiology and function. Alterations in absorption will affect how much and how rapidly a dose will be absorbed. Physiological changes in the elderly that may potentially impact drug absorption include a slower rate of gastric emptying, a decrease in intestinal motility, a reduction in intestinal blood perfusion, and diminished intestinal mucosal surface area. In addition the extent of absorption may be increased in the elderly for drugs that undergo extensive first pass metabolism in the liver. This may be expected there is a decrease in the metabolic bio transformation of the drug resulting in a greater fraction of a dose entering the systemic blood circulation. The net effect of the above factors has proven difficult to predict and most frequently does not result in clinically relevant in drug absorption after oral administration. Reasons for this include the complex nature of the drug absorption process and bioavailability factors. However it is prudent to anticipate that the rate of drug absorption and the onset of action may be prolonged in the elderly and that the extent of absorption of drugs that undergo first pass metabolism may be greater than in younger persons. Geriatric patients may be prone to other factors that can alter drug absorption. These include swallowing difficulties, poor nutritional status, erratic meal patterns, and interactions with other prescription and non- prescription medications.[9]

b)Distribution:

The distribution of drugs in the body can significantly differ in geriatric patients as compared to younger adults. The difference reflects the various changes in body composition that normally occur as a person ages. In general, the total body weight of a person declines in old age particularly in the very old. Specifically there is a general decline in lean body mass, and an increase in the proportion body fat. This results in less drug distribution to muscle tissue for drugs such as Digoxin while fat soluble drugs such as diazepam have a relative increase in drug distribution. Additional changes in body composition in elderly a decrease in total body water, a general reduction in serum albumin concentration, and an increase in α-acid glycoprotein. Changes in total body water affect distribution of water soluble drugs such as lithium. A decrease in serum albumin concentration is significant for acidic drugs that are highly bound to this protein while basic drugs bind to α-acid glycoprotein. As the serum albumin concentration declines, the fraction of the free or unbound drug increases. Thus lower total (bound+unbound) drug concentrations area associated with greater pharmacological activity when the free fraction is increased , because the unbound drug is the active entity. This also complicates measuring serum drug concentrations for therapeutic drug monitoring purposes,because total concentration of the drug are most often measured. This necessitates making some adjustment in the value for proper interpretation. Using phenytoin as example, the proportion of free drug is normally 10 percent when the serum albumin concentration is 4.4 mg/dl, but it increases to 20 percent when the serum albumin concentration declines to 2.0 mg/dl. Thus for any given total serum phenytoin concentration, the pharmacological activity would essentially be twice as great when serum albumin concentration is 2.0 mg/dl versus the normal value of 4.4 mg/dl. When there is less drug distribution, smaller dosing of the loading medications are needed and the half life of the drug will be shortened. Failure to adjust the loading dose in response to a decrease in drug distribution will result in higher blood concentrations of the drug and places the patient at greater risk for toxicity and adverse effects. Conversly when drug distribution is expanded relatively higher loading doses are required to achieve desired blood concentrations and the half life of the drug is extended. Changes in the half life of a particular drug influences the frequency of dosing when designing dosage regimens. Generally the longer the half life, the less frequently a medication needs to be administered, because of the effect of the drug is prolonged. The shorter the half life, the shorter the duration of drug action and the medication will need to be administered more frequently.

c)Metabolism:

Many variables determine metabolic capacity, including nutritional status, diet, genetics, gender, alcohol intake, smoking, environmental factors, and the concomitant use of other medications. In the elderly, several physiological changes are associated with the altered drug metabolism including: a decrease in liver mass, a decrease in blood flow to the liver, and a reduction in the intrinsic activity of drug metabolizing enzymes. Several generalizations can be made in the geriatric patient. The rate of metabolism is diminished for drugs that are dependant upon hepatic blood flow, such as lidocaine, propranolol and meperidine. In addition, geriatric patients have been shown to have a reduced rate phase I metabolism of some drugs, which involves the oxidation, reduction, dealkylation or hydroxylation of compounds. Furthurmore, this difference may be gender related, with elderly women metabolizing some drugs (e.g., midazolam, doxylamine) as efficiently as younger adults. However no significant change has been observed in the rate of phase II metabolism in elderly, which consist of glucuronidation, acetylation, and sulfation of compounds. These age related differences in drug metabolism should be considered when selecting a drug and dosage regimen. For example, chlordiazepoxide, diazepam and flurazepam undergo phase I metabolism, and thus the rate of elimination will be slower than in younger adults. This may result in drug accumulation over time, potentially causing over-sedation, impaired psychomotor skills or confusion. Alternatively lorazepam, oxazepam, and temazepam are metabolized primarily by phase II reactions, which are not affected by the aging process. However while their shorter half life make these drugs less likely to accumulate . Older patients are often on multiple medications, there is a greater potential for some medications to alter the metabolism of other medications the

patient is taking. Moreover, there are some common conditions in the elderly(e.g., congestive heart failure) that also have a detrimental effects on metabolism of certain drugs. These factors must be taken into consideration when assessing drug therapy in this patient population.

d)Excretion:

It is well known that kidney function declines with advancing age. The level of decline varies significantly between individuals . Physiological changes associated with this age related decline in renal functions include diminished blood flow to the kidneys, a decrease in kidney mass, a reduction in the size and the number of functioning nephrons. Consequently, there is a reduction in the filtration, active secretion and tubular reabsorption of the drugs.

e)Pharmacodynamics in geriatrics:

Pharmacodynamics refers to the actions of a drug and the response that patients experience. With some medications, elderly patients often experience a different degree of response than in younger adults. It is difficult to determine if such differences are due to pure intrinsic pharmacodynamic changes or age related alterations in the pharmacokinetics. The normal aging itself may predispose patients to be more or less sensitive to particular medications, especially drugs that effect the cardiovascular and central nervous systems. It is postulated that this is a result of changes at the receptor site . Such difference may include changes in the binding affinity for the drug, changes in the number or density of active receptors at the organ, biochemical processes, homeostatic regulation, structural features and physiological processes. Additionally, changes in the anatomy and physiology in the older patient may render them more succesptible to the effects and side effects of medications. For example, elderly patients with impaired balance are at greater risk for drug induced falls, particularly when the medications cause dizziness or sedation. Age related changes at the receptor site may be responsible for an increase in sensitivity to warfarin, benzodiazepines, anti-cholinergics, and narcotic analgesics. Thus lower doses are generally required to achieve the same degree of effects as in younger patients. In contrast, the elderly have been shown to be less sensitive than younger adults to beta-adrenergic agonist(e.g.,isoproterenol), beta adrenergic antagonists (e.g.,propranolol), allopurinol and insulin. The anti hypertensive effect of calcium channel blockers (e.g., veerapamil) has also been observed to be greater in the elderly, where as the effect on cardiac conduction was less than in younger subjects studied. Age related changes occurring in the central nervous system may explain why dizziness, sedation and confusion are common adverse drug effects experienced by older patients. Similarly elder patients are more prone to orthostatic hypotension from medications that affect the cardiovascular system, because they often have a diminished capacity to quickly compensate for postural changes in blood pressure. Changes in pharmacodynamics in the elderly may be obscured by the age related changes in pharmacokinetics.[10]

Treatment challenges in geriatrics:

Older people tend to take more drugs than younger people because they are more likely to have more than one chronic medical disorder, such as high blood pressure, diabetes or arthritis. Most drugs used by older people for chronic disorders are taken for years. Nursing home residents are prescribed an average of 7 to 8 different drugs to take on a regular basis. Older people also take many non-prescription drugs. Many OTC drugs are potentially hazardous for older people[11].

Older people are more succesptible to the side effects of drugs for several reasons:

ØAs people age, the amount of drug in the body decreases, and the amount of fat tissue increases. Thus, in older people, drugs that dissolve in water reach higher concentrations because there is less water to dilute them, and drugs that dissolve in fat accumulate more because there is relatively more fat tissue to store them.

- As people age, kidneys are less able to excrete drugs in urine, and the liver is less able to metabolise many drugs. Thus druga are less readily removed from the body.
- Older people usually take more drugs and have more disorders.
- People who take more drugs and have more disorders.
- Older people are more likely to have chronic medical disorders that may be worsened by drugs or that may affect how the drugs work.

Table.No.1: Some disorders and symptoms that can be worsened by drugs in older people:(12)

Disorder / symptom	Drugs
Chronic kidney	NSAIDS(such as ibuprofen and naproxen), triamterene
Constipation	Diltiazem
Delirium, dementia or mild cognitive impairment	Verapamil, Chlorpromazine. Corticosteroids, Drugs with sedative effects(such as benzodiazepines, sedatives and sleep aids) or anti- cholinergic effects
Fainting / orthostatic hypotensi on	Chlorpromazine, donepezil, doxazosin, galantamine, olanzapine, some older anti- depressants (such as amitriptyline and imipramine), rivastigmine, terazosin, thioridazine, prazosin.
Hypotension	Use of more than one anti-hypertensive drug.
Heart failure	Cilastazol, diltiazem, disopyramide, dronedarone, NSAIDS and COX-2 inhibitors, pioglitazone, rosiglitazone, verapamil.
Insomnia	Caffeine, oral decongestants (such as pseudoephedrine and phenylephrine) stimulants (such as amphetamine, methyl phenidate and pemoline),theophylline.
Parkinson disease	Certain antinausea drugs (metoclopramide, prochlorperazine, promethazine) and most anti-psychotics except a few such as quetiapineand clozapine.
Peptic ulcer disease	Aspirin and most NASIDS.
Seizure disorders	Bupripion, chlorpromazine, clozapine, meperidine, olanzapine, thioridazone, thiothixene, tramadol.
Urinary incontinence	Doxazosin, estrogens taken by mouth or through the skin, prazosin terazosin.

Medication adherence in geriatrics:

Medication adherence is defined as the extent to which a person's behaviour agrees with the agreed medication regimen from a health care provider.[13] Adherence to medications has always been a problem patients. As the elderly are prone to multiple comorbidities, they are at higher risk of poly pharmacy, and therefore may present with higher risk of nonadherence to medications compared to younger population. This results in decreased therapeutic benefit for the patient, frequent hospital and physician visits due to deterioration of their medical condition, increased health care expenditure, and even over treatment of a condition. Reasons for nonadherence can be broadly classified into patient factors, medication factors, health care provider factors, health care system factors, and socioeconomic factors as per recommendation from Miller et al and the world health organization.[14]

Common drug interactions in elderly people:

It is impossible to rememder all the possible drug interactions. A number of drug interactions are frequently used but have the potential to cause significant harm if not managed appropriately.[15]

Table.No.2: Commonly observed drug interactions in geriatrics

Drug combination	Risk of harm	Prevention
Wafarin/ Phenytoin	Increased or possible decreased effects of warfarin. Phenytoin concentration possibly	Monitor phenytoin level and INR
Warfarin/NSAIDS	Increased risk of bleeding	Review need for NSAID consider paracetamol as an alternative.
Warfarin/ amiodarone		
Warfarin/ sulfa drugs		Monitor INR and adjust warfarin dose accordingly.
Warfarin/ macrolides		Use alternative antibiotic.
Warfarin/norfloxacin		
ACE inhibitors/ K supplements	Elevated potassium levels	Monitor potassium levels Discontinue k^+ supplements if not needed
ACE inhibitors/Spiranolactone	Elevated potassium levels Renal failure	Monitor potassium levels and renal function.
ACE inhibitors/ NSAIDS	Renal failure	Re-evaluate need for NSAID Monitor renal function Avoid hypovolaemia
Digoxin/Amiodarone	Digoxin toxicity	Decrease dose of digoxin by 50% when adding amiodarone and check digoxin levels weekly until stable.
Digoxin/Verapamil	Digoxin toxicity Bradycardia, heart block	Check ECG Re-evaluate need for these drugs
Theophylline/Norfloxacin and ciprofloxacin	Theophylline toxicity	Re-evaluate need for these drugs Monitor theophylline levels
Anticholinergic combinations e.g., TCA, sedating antihistamine, antipsychotic, oxybutynin, orphenadrine, benztropine, etc	Sedation, confusion, blurred vision, falls	Reduce numbers, strength or doses of these drugs
Drugs acting on the CNS Combinations of antiepileptics, Antipsychotics, analgesics, antidepressants, etc	Sedation, confusion, Falls	Reduce numbers, strength or doses of these drugs

Conclusion :

Therapeutic management in geriatrics is complex it required careful consideration of Pharmacokinetic, Pharmacodynamic parameters and patient compliance.

References:

1) Shamsher singh, Defining elderly in clinical practice guidelines for pharmacotherapy. Pharm practice. 2014;12(4): 489.
2) Barry Mirkin et al., The demography of population ageing. Journal of geriatrics. 2016; 12(1):415-420.
3) James W Davis et al.Prevalance of co-morbid conditions with ageing among patients with diabetes and cardiovascular disease. Hawai medical journal. 2011; 70(10): 209-213.
4) Claudia S. Oliveria et al.,Compensatory renal hypertrophy and handling of an acute nephrotoxicant in a model of ageing.Merck Manual.2016;75:16-23.
5) Tabea Geisel et al., An etiologic profile of anaemia in 405 geriatric patients.Hindawi publishing corporation.2014;11(2):111-118.
6) Kathleen M.Akgun et al., Epidemiology and management of common pulmonary diseases in older persons.The journal of gerontology.2012;67(3);276-291.
7) Barquawie et al.,Geriatric depression treatment. Journal of gerontology and geriatric research. 2015;12(8):2167-2182.
8) Nicholas A.De Angelo et al., Treatment of patients with arthritis related pain. The journal of osteopathic association.2004;104:2-5.
9) Sandra Jacobson et al., Effects of pharmacokinetic and pharmacodynamic changes in the elderly.2013;111:2-5.
10) J.Mark Ruscin et al., Pharmacodynamics in the elderly.Merck Manual.2015;78:15-18.
11) Michael Koron kowski et al., An update on geriatric medication safety and challenges specific to the care of older adults.Journal of geriatric medications. 2016; 24(3):37-40.
12) Paula A Rochon et al., Drug prescribing for older adults. Wolters kluwers. 2017;17(3):15-25.
13) Angela Frances yap et al., Medication adherence in the elderly. Journal of clinical gerontology and geriatrics.2015; 5:43-47.
14) John A.Sbarbaro et al.,Stratergies to improve compliance with therapy. The American journal of medicine. 2013;79(6): 34-37.
15) Maria Cristiana et al., Drug- drug interactions and adverse drug reactions in poly pharmacy among older adults. Journal of geriatrics. 2016;24:15-18.