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*RESEARCH ARTICLE*

# GERIATRIC PHARMACOLOGY: OVERVIEW

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## *Abstract*

Global population ageing is an important challenge and opportunity to be taken virtually by all the countries. Ageing is associated with progressive decline in physiological functions as well as cluster of diseases, which alter the pharmacological response to a drug. In advanced age, the pharmacokinetics and pharmacodynamics of many drugs are altered. In addition, pharmacotherapy may be complicated by difficulties with obtaining drugs or complying with drug regimens. Safe and effective pharmacotherapy remains one of the greatest challenges in geriatric medicine. This review deals with the principles of geriatric pharmacology.



## Introduction:-

Global population ageing is an important challenge and opportunity to be taken virtually by all the countries. Medical society has identified persons aged over 65 as elderly while those above 75 as geriatric population. By 2050 the worldwide elderly population is expected to reach 1.4 billion which means that one out of ten people will be more than 65 years of age [1]. Ageing is associated with progressive decline in physiological functions as well as cluster of diseases. These age's related changes are associated with reduced income and loneliness; further worsen their health [2]. Pharmacokinetics and pharmacodynamics changes in elderly population which leads to a reduction in physiologic reserves. In addition, differences in receptor numbers and binding affinities [3] changes in target organ responses and impaired compensatory reflexes e.g. autonomic blood pressure control also result in less predictable outcomes [4,5]. Under appreciation of these changes may contribute to inappropriate dosing, inadequate monitoring and increased adverse drug reactions [6,7]. Hence it is mandatory for physicians to be aware of normal age related physiological and pharmacological changes taking place in old people. This will help to avoid irrational prescribing, minimize adverse drug reactions and maximize benefits of drugs in elderly patients. In this review, we attempt to draw together the principles of ageing and geriatric pharmacology in order to guide prescribing in older people.

**Pharmacological changes in elderly:**

Age related physiological and pathological changes play a major role in altering the pharmacological actions of a drug. These changes impaired hepatic and renal functions play a significant role in decreasing absorption, distribution, metabolism and excretion of drugs. These pharmacokinetic changes alter free drug concentration which is a major determinant of a drug's potency and duration of action. Apart from these changes, ageing is also associated with pharmacodynamic changes like altered organ response to drugs. These changes are vital as they contribute to the variations in drug response.

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**Pharmacokinetic changes:**
All aspects of pharmacokinetics are affected by ageing. The change in absorption is often not a major clinical problem, but significant changes can be observed in distribution, metabolism, and excretion of drugs. The most significant pharmacokinetic change in ageing is related to the decreased hepatic mass, uptake, and blood flow and to decreased renal function, impairing the clearance of many drugs and their metabolites [8,9]. In addition ageing is associated with changes in body composition, including a reduction in total and lean body mass, and a relative increase in fat mass, which may affect the volume of distribution and loading dose of drugs.

Ageing can cause changes in the absorption process of the drug. These age-related changes include decreases in the intestinal blood flow, alterations with the time needed for gastric emptying, and variations with the mucosal cell absorbing area, gastric pH, gastrointestinal motility, intestinal permeability, drug transporters, and gastrointestinal blood flow, which might delay or reduce absorption [10]. Pharmacokinetic studies on the effect of ageing on drug absorption have provided conflicting results. While some studies have not shown significant age-related differences in absorption rates, the absorption of vitamin $B_{12}$, iron and calcium through active transport mechanisms is reduced [11] whereas the absorption of levodopa is increased because its absorption may increase due to a reduction in dopa-decarboxylase in the gastrointestinal mucosa causing an increase in drug levels in the blood [12]. Changes in body composition in older adults are characterized by a progressive reduction in total body water and lean body mass, resulting in a relative increase in body fat. This change can affect the volume of distribution of the drug. The main effect of the increased volume of distribution is a prolongation of half-life [13]. Thus, water soluble drugs like digoxin have increased concentration, whereas lipid soluble drugs like diazepam, chlordiazepoxide, thiopentone sodium have a greater volume of distribution and longer half life (t ½).The results of these changes are that the elderly are more susceptible to toxicity and are more prone to side effects of the drug. Interindividual variability in drug metabolism is common in the elderly. The liver plays an integral role in biotransformation; age-related changes in liver function will affect the efficiency of this process. The main age-related change in the physiology of the liver is a decrease in the size, substantial reduction in blood flow of about 40% [14]. Some studies on human liver tissue showed that cytochrome (CYP) P450 enzyme activity is maintained even with advanced age [15]. Although enzymes are usually unchanged by ageing, many drugs are metabolized more slowly in older people due to a reduction in hepatic blood flow. This decreased metabolism of the drug may cause a buildup of the drug and result in toxic effects. Orally administered drugs with large flow–dependent first-pass effects (e.g., labetalol, propranolol, verapamil, and morphine) should be used with caution because the reduction in hepatic blood flow could lower the first-pass effect and increase drug concentrations in the elderly. Ageing is associated with a significant reduction in renal mass and number of nephrons. Glomerular filtration rate, tubular secretion and renal blood flow decrease by 0.5, 0.5 and 1 percent per year respectively over the age of 20 years [16]. Tubular secretion and glomerular filtration may not decline in parallel. A variable decline in renal clearance occurs with ageing. It may affect drugs eliminated primarily by the kidney e.g. aminoglycosides, atenolol, lithium and digoxin. The effect of changes in the kidney is an overall reduction in excretion and the accumulation of drugs and drug metabolites in the body.

**Pharmacodynamic changes:**
Pharmacodynamic changes with age include drug receptor alterations that are changed in receptor number and affinity, impaired signal transduction and decreased homeostatic regulation, physiologic reserve and in response to injury [11]. However, these changes have not been characterized in ageing the pharmacokinetic changes. The enhanced sensitivity is seen with commonly used drugs like NSAIDs, opioids, benzodiazepines, antipsychotics and antiparkinsonian drugs. Similarly, a greater anticoagulant response to a coumarin anticoagulant is observed in elderly patients than young patients. Elderly people have reduced sensitivity to some drugs like beta-adrenergic blockers and beta-agonists, there are decreased receptors and more significant in the elderly due to physiological decline and co-morbidities. Hence care should be taken to reduce or alter the dose while prescribing these drugs in elderly. Mildly nephrotoxic drugs like NSAIDs may have disastrous consequences in elderly individuals with impaired renal function at baseline due to blunting of baroreceptor reflex. Postural hypotension in elderly is aggravated by antihypertensives as well as by neuroleptics, benzodiazepines and antiparkinsonian drugs. Neurotransmitters in the CNS decrease with age. Drug related confusion increases in elderly with theophyllines, beta-blockers, anticholinergics and hypnotics. Alcohol, barbiturate and neuroleptics potentiate hypothermia, while anticholinergics aggravate hyperthermia. Many pharmacodynamic studies have focused on primarily healthy older people. In older people with disease, the pathophysiology of the disease itself may be different from younger people, thereby altering the pharmacodynamic response and therapeutic outcome.

**Table 1:-** Pharmacokinetic and pharmacodynamic changes in the elderly.

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|---|---|---|
| Absorption/first pass | Unchanged absorption Reduced first pass metabolism | Same amount of medication absorbed, but increased bioavailability of some drugs (e.g. metoprolol, nortriptyline) |
| Volume of distribution | Increased body fat Decreased body water | Prolonged half life of lipid soluble drugs (e.g. diazepam) Increased serum concentrations of water soluble drugs (e.g. digoxin, paracetamol) |
| Protein binding | Lower serum albumin in frail or unwell elderly | Increased free concentrations of protein bound drugs (e.g. warfarin, phenytoin) |
| Metabolism | Reduced oxidative metabolism (liver) Unchanged conjugative metabolism (liver) | Prolonged half life, higher steady state concentrations of some drugs (e.g. diazepam, metoprolol, phenytoin) |
| Excretion | Reduced with decreased glomerular filtration rate (GFR) and tubular excretion | Prolonged half life, higher steady state concentrations of some drugs or metabolites (e.g. digoxin, cephalexin, morphine) |

## Conclusion:-

Age-related changes in pharmacokinetics and pharmacodynamics and numerous comorbidities further contribute to the complexity of drug therapy. Older people are the major recipients of drug therapy, increased research and a better evidence base is an imperative to guide clinicians who manage geriatric patients. The goal of medical intervention in older patients is to improve the quality of the remainder of their life. Drug therapy is the most important intervention directed toward this goal. Clinical pharmacology, drug efficacy, and drug safety differ in elderly patients compared with their younger counterparts. Therefore, a different approach is necessary to provide optimal care to these complex patients.

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