

48 Drugs and Elderly

Abstract: Before writing a prescription, physicians should ponder 'Is drug therapy required?' and drug regimen should be reviewed regularly so that unnecessary drugs are discontinued.

Is a particular drug that is satisfactory for younger patient suitable for the elderly? For example is there increase likelihood of side effects? Which preparation should be used? Consider dosage form. In general use smaller doses than are normally given to younger adults. For example initial doses of CNS active drugs should be about 50% of the dose appropriate to younger patients. The dose can be increased thereafter on the basis of response.

Drug prescribed should be clearly labeled in large print and packaged in readily openable containers. Supervision of therapy may sometimes be desirable.

Aging population has been rising globally and India is no exception. Since independence, India's population has more than doubled, life expectancy has risen to 65 in 2001 from 32 during British rule.¹

India is one of the few countries in the world where men outnumber women in all ages till about 70 years and only in very old age (80+) there are more women than men. One of the main social effect of extension of life in later years is the extended period of widowhood for women mainly due to cultural practice of men marrying younger women and widow marriage as well as divorce being uncommon. However, death rates in female are lower than males at all ages but there is a paradox in that although women outlive men they are much more likely to become disabled in old age (Fig. 1).

Studying relationship between drug treatment and older people, a number of factors have become clear. Firstly, the elderly are major consumers of drugs. Secondly, the rational use of drugs has been hampered by lack of knowledge of the natural history of disease in old age. Thirdly, diagnosis is often difficult in old because of atypical symptoms and multiple pathology. Additionally access to modern diagnostic facility tends to be less easily arranged. Fourthly, the adverse drug reactions (ADRs) occur more frequently than in younger people.

Polytherapy is often mandatory in the management of most of the common ailments affecting patients in the geriatric age group. Diseases like hypertension, heart failure, cancer, certain infections etc. require multiple drug therapy. The goal in these cases is to improve therapeutic effectiveness.⁵

DRUG PRESCRIBING IN ELDERLY

Treatment of the elderly patients presents the physician with a great challenge, the challenge for all those involved in treating the elderly is to maximize the benefits of medication and to minimize the risk. This responsibility falls on physicians as they alone can prescribe drugs. The first of these is the epidemiology of drug prescribing and various other aspects of drug consumption. Secondly, what happens to drugs in the body after they are administered - the pharmacokinetics. There are important changes in pharmacokinetics with aging and depending on which drug, one is concerned with, they may be of sufficient magnitude to affect the response observed. Finally, there are some examples of altered responsiveness to drugs in the elderly; for a given amount of drug at the site of action, there is an altered magnitude or duration of response.

Clearly, the end result of the doctor writing a prescription is determined by many factors - some physiological others psychological and yet others sociological.

The elderly receive the greatest number of prescriptions per person and there is an increase in the prescribing of psychotropics. Most frequently prescribed groups of drugs are diuretics, analgesics, antipyretics and psycho-tropic drugs. However, recently it has been shown that elderly patients suffering from epilepsy receive potentially inappropriate anti-epileptic drugs.² It has been suggested that better doctor-patient and doctor-doctor relationships and systems for transferring information between care setting will increase the appropriate use of medicine in elderly people.³ Still recently, it has been reported that analgesic, psychotropic and anticholinergic drug use is more among older women than among older men.⁴ The practice of repeat prescriptions exposes the elderly to unnecessary risk and it was estimated that out of 755 prescriptions given to elderly patients most are repeat prescription often given without the patient seeing the doctor.

Pharmacokinetics

The action and interaction of the drugs is dependent on their pharmacokinetics and pharmacodynamics. However, rate and extent of drug absorption are not significantly affected by age⁵ but drug distribution is affected by aging process. The distribution of drug in elderly subjects is altered due to reduction in lean body mass, serum albumin, total body water content and increase in percentage of body fat. Thus the volume of distribution is reduced for water soluble drugs e.g. digoxin, cimetidine etc resulting in increased plasma concentration. The volume of distribution is increased for lipid soluble drugs e.g. diazepam, chlordiazepoxide, etc. resulting in a prolonged half life. Serum albumin level is decreased in the elderly for protein bound drugs e.g. propranolol. The unbound moiety is increased and drug action is prolonged and enhanced.

However, difference in body composition between male and female regardless of age may be as marked as those between young and elderly. Consequently, female show more extensive distribution of highly lipid soluble drugs than males do and less extensive distribution of relatively water soluble drugs. Table 1 shows average changes in body composition and function (male and female).

Metabolism: There is some evidence for lesser susceptibility to enzyme induction in the elderly. However, elderly smoke less which may contribute to less enzyme induction. Hepatic drug metabolism has been classified into phase 1 (oxidation-reduction) reactions mediated by the mixed -function oxidase system and phase 2 (conjugation) reactions. The clearance of some drugs (chlordiazepoxide and diazepam) oxidized by phase 1 reactions is retarded with age but conjugation reaction remains unim-paired.⁶

Hepatic clearance of metabolized drugs depends on two factors, hepatic blood flow and the activity of drug metabolising enzymes - intrinsic hepatic clearance. Elimination of most drugs such as, diazepam and phenylbutazone is dependent mainly on intrinsic hepatic clearance because these drugs have a small hepatic excretion ratio. Drugs with a moderate or high hepatic extraction ratio undergo extensive first pass metabolism in the liver after oral administration and thus their bioavailability is low.

The bioavailability of chlormethiazole, propranolol and labetalol is greater in elderly indicating that presystemic hepatic extraction declines with age. Recently, it has been reported that aging is associated with a decline in drug elimination.⁷

Renal Elimination

Age related changes in renal function are well documented. Glomerular filtration rate (GFR) declines predictably in old age with a mean 35% in elderly (> 65 years) compared with young (<

30 years) individuals. Renal flow also decreases. If a kidney cannot eliminate a drug after it has done its work, it remains in the body longer causing an adverse effect.

In general, tubular function is also altered in elderly. The kidney's ability to maximally concentrate urine after water deprivation is decreased and its ability to excrete maximally diluted urine after water loading is lost. This tubular dysfunction is accentuated during the night, usually may explain the common symptom of nocturnal polyuria. Because they are closely linked to water disorders, sodium disorders are common in elderly.

Drugs eliminated by renal tubular secretion such as penicillin and aminoglycosides are also affected by the age associated decline in renal mass and loss of nephrons.⁶

The response to an acid load is impaired and maximum rate of secretion of hydrogen ions falls. Changes in blood pH in response to an acid load are therefore greater in magnitude and longer in duration than in younger people. Response to antidiuretic hormone is reduced and water conservation less efficient. Average renin and aldosterone levels diminishes with age with consequent impairment of Na conservation.

Pharmacodynamic effects: Age associated increases in the effects (including adverse effects) of some drugs are not readily explicable in term of gross pharmacokinetic changes and pharmacodynamic effects at receptor level have been proposed. Such effects may contribute to the increased susceptibility of older people to benzodiazepines and warfarin and to the age associated reduction in sensitivity of beta receptors to adrenergic beta blockers. The susceptibility of older people to gastric complications of non-steroidal anti-inflammatory drugs may also have a pharmacodynamic element.⁶

Cardiovascular System

Interpretation of changes in cardiovascular function in old age is made difficult by age-associated increase in prevalence of ischemic heart disease.⁸ Peripheral Arterial Disease (PAD) in elderly can be (1) asymptomatic, (2) associated with intermittent claudication or (3) critical limb ischemia and are at increased risk for all cause mortality from Coronary Artery Disease (CAD).⁹ Hypertension, diabetes mellitus dyslipidemia and hypothyroidism should be treated and smoking should be stopped.

Blood Pressure: Older people are more susceptible to the risk of hypovolemia, postural hypotension is also common in older population and may be a constraint in management of hypertension. When assessing older people taking medication that may affect blood pressure, lying and standing blood pressure should be used routinely.

A recent dramatic increase in number of elderly patients with hypertension has made the proper management of the disease in this population more important since Quality of Life (QOL) is greatly affected in elderly patients with hypertension, as a lifestyle disease. It has been shown that treatment of hypertension could affect QOL and given the major role of stroke in deterioration of QOL, it was demonstrated that calcium channel blockers are effective in reducing risk of stroke, as their effect is not limited to blood pressure reduction.¹⁰

Respiratory System

The interpretation of changes in respiratory functions with age is complicated by prevalence of cigarette smoking which is less common in Indian elderly. Although total lung volume does not alter, vital capacity falls and residual volume increases with age. However, ventilatory capacity falls with age at a lower rate in non-smokers.

The principles of management of respiratory disease do not vary with age of the patient. Cough due to left ventricular failure or to esophageal reflux disease may become more common and more likely to be affected due to industrial exposure to asbestos and coal dust.⁶

Endocrine System

Diabetes: Clinical presentation of diabetes in old age may differ from that of younger patients. There is now sufficient evidence to justify trying to control hyperglycemia in elderly. Dietary treatment and oral hypoglycemic agents are first line treatment but insulin should not be withheld, if it is necessary for control of hyperglycemia. Short acting oral hypoglycemic drugs should be preferred over long acting anti-diabetic agents.

Diabetes mellitus interacts with other risk factors for cardiovascular disease. Diabetic patients of any age should be persuaded to give up smoking. Control of blood pressure is very important with evidence to support the use of ACE inhibitors in preference to other classes of drugs. Hypercholesterolemia should be reduced. Currently, sub-optimal use of cardioprotective drugs in newly treated elderly individuals with Type 2 diabetes has been found.¹¹

Drugs and GI Tract

Older people are liable to the full range of gastrointestinal disorders even coeliac disease may present for the first time in old age.⁶ Gastrointestinal hemorrhage is common and frequently associated with ingestion of nonsteroidal anti-inflammatory drugs. Constipation is a common complaint among older people; when chronic constipation is a problem, daily intake of 10-20 grams of dietary fiber should be aimed at, with a necessary stool softening agent such as lactulose. Doses of stimulant more, laxatives such as senna may be necessary but should be avoided as much as possible.

Locomotor System

Age and joints: Osteoporosis is common in elderly in males as well as females. Risk factors are postmenopausal women, long term cortico-steroids, smoking, alcohol and physical inactivity,⁵ NSAIDs prescribed for chronic arthritis can lead to GI bleeding, ulcers and renal failure. Postmenopausal women can be better treated with COX-2 inhibitors than NSAIDs for arthritis.

Falls: Falls and fear of falls are important causes of morbidity among older people. From cardiovascular health study it was demonstrated that 7.3% of women and 4.9% of men were frail, thereby men in this cohort are almost half as women to be frail.¹² Falling especially if associated with inability to rise again is an extremely unpleasant experience and may suffer the additional problems arising from a long lying. These include hypothermia, pressure sores, rhabdomyolysis which may lead to acute renal failure. Significant hemorrhage following falls is an increasing problem as more older people are being prescribed anticoagulants for atrial fibrillation. A history of fall is a relevant issue in deciding whether an older person should be established on anticoagulants.

Warfarin dose requirement drops by about 50% as age increases from 30 to 75 years. Also the anticoagulant response to single dose of warfarin changes with advancing age (Fig. 2), possibly due to changed receptor sensitivity and a greater Vitamin K₁ clearance in elderly in the absence of warfarin or greater accumulation of vitamin K₁ oxide in the elderly in the presence of warfarin.

Central Nervous System

The elderly seem to have an inordinate number of adverse effects to CNS active drugs such as barbiturates, benzodiazepines, cimetidines, methyl dopa, metoclopramide, opiates, propoxyphene and tricyclic antidepressants. Perhaps such qualitative and quantitative changes in response relate to changes in the brain. Marked loss of cells and synapses is seen in senile dementia of Alzheimer type and there is significant reduction in choline acetyl transferase activity and ability of tissue to synthesize acetylcholine. As a rule of thumb the initial dose of CNS active drugs in elderly should be one half of that given to younger patients. On the other hand dementia could be drug induced, it may also be related to hypertension or conditions like Huntingtons' disease (a genetic disorder), or Parkinsons' disease. Treatment of these can to some

extent reverse the dementia but not due to Alzheimers' disease, a slow progressive mental deterioration. However, several transdermal delivery systems are currently under investigation for the treatment of Parkinson's disease. Alzheimers disease and neuropathic pain.¹³

Prevention of Adverse Drug Reaction

It is unlikely that prescribing physicians can be improved. In one study it was found that 23.7% of elderly people in medical or geriatric wards received drugs which were contraindicated because of disease, concomitant medication or previous adverse drug reaction. They also considered that in 65.5% cases the prescription of indenting drugs was avoidable. According to another investigation 3.7% patients were taking drugs that were seriously contraindicated and most frequent contraindication was the prescription of beta blockers in patients with obstructive airway disease, peripheral vascular disease or congestive heart failure. Reports from independent monitoring systems demonstrate an overall increased frequency of adverse drug reactions associated with increased patient age (Table 2).

Drug Compliance

In chronic diseases, compliance with treatment regimen is the major determinant of outcome. However, most studies of the influence of age on compliance do not find any association with age and decreasing compliance.

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MULTIPLE CHOICE QUESTIONS

- 1. A 60 year old with mild Type 2 Diabetes lives half of the time in hotels with problems of maintaining suitable diet with restaurant meals can take any of the following drugs *except*:**
 - A. Glipizide
 - B. Nategliride
 - C. Glyburide
 - D. Repaglinide
 - E. Acarbose
 - 2. Adverse effects resulting from the administration of furosemide include all the following *except*:**
 - A. Hypercalcemia
 - B. Hyperuricemia
 - C. Hypokalemia
 - D. Ototoxicity
 - E. Alkalosis
 - 3. Which of the following agents would bring rapid heart rate (120 beats/minute) back to normal:**
 - A. Isoproterenol
 - B. Phentolamine
 - C. Propranolol
 - D. Phenoxy Benzamine
 - E. Edrophonium
 - 4. All the following untoward effects are commonly associated with cancer chemotherapy *except*:**
 - A. Alopecia
 - B. Teratogenesis
 - C. Leukopenia
 - D. Nausea
 - E. Exfoliative dermatitis
 - 5. The maximum effect achieved by a drug is a measure of:**
 - A. Potency
 - B. Efficacy
 - C. The quantal response
 - D. Antagonist magnitude
 - E. Therapeutic Index
 - 6. India is the only country where men outnumber women *except*:**
 - A. All ages
 - B. Above 50 years
 - C. Above 60 years
 - D. Above 70 years
 - E. Above 80 years
 - 7. In elderly subjects:**
 - A. Death rate is more in females than in males
 - B. Death rate is mores in males than in females
 - C. Death rate is males and females is equal
 - D. Death rate is males is half of femals
 - 8. The first pass effect occurs most often after which route of administration?**
 - A. Oral
 - B. Sublingual
 - C. Intravenous
 - D. Intramuscular
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1. D 2. A 3. C 4. E 5. B 6. E 7. B 8. A