Drugs in Elderly

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Aging is a process that involves biological, emotional, social and financial changes that affect a person's overall health. Disease and mental attitude do determine the tempo of the aging process. Persons over age of 65 differ widely in their ability to carry out daily activity. How do we explain this disparity among older people? Age is less a chronological marker than a combination of factors that determine the overall functioning of people in their mid-sixties and beyond. Firstly, genetics plays an important part in the aging process.[1] Aging is associated with the development of chronic diseases such as high blood pressure and glucose intolerance that may contribute to morbidity. Most of them develop chronic conditions because they have a genetic predisposition to the disorder. Dyslipidemia, ischaemic heart disease, cancer, diabetes and other problems may "run in families". Human body's immune system is also on progressive decline by gradual aging, gradually losing its ability to recognize outside threats, a virus, for example and hence putting them at greater risk of infectious diseases.

Emotional and psychological issues have a major impact on overall health and the aging process. Even though an older person is well physically, he may still be at risk for organic and mental illnesses such as Alzheimer's disease, depression and anxiety. The aged especially elderly men are more likely to commit suicide than the rest of the population, but most do not seek professional help. Despite the fact that over one million elderly have some sort of abnormal memory loss (senility or dementia); they may tend to be too embarrassed or too ill to seek help. Old age is characterised by multiple diseases.

In India at the beginning of this century 12 million Indians were aged 60 years or more. Expectancy of life at birth has gone up from 49.7 years during 1970-75 period to 60.3 years during the period 1991-95. 45% of the elderly have a chronic disease. Top ten common diseases are hypertension, cataract, osteoarthritis, chronic obstructive airway disease, ischemic heart disease, diabetes, benign prostatic hypertrophy, dyspepsia, constipation and depression. The five top killer diseases in rural elderly are bronchitis, pneumonia, ischemic heart disease stroke, cancer and TB.[2]

When it comes to drugs, the elderly use like everyone else, only more so. They tend to have more health problems and are therefore likely to consume more medicines, both prescribed and over-the-counter get more side effects, and possibility of more deaths from improper use.[3] In fact, some two-thirds of all people over age 65 take medication regularly. Today more elderly live longer, better lives than ever because of the many new drugs such as platelet antiaggregants, antiosteoporotic and antioxidants. In fact, those over age 65 are among the main beneficiaries of the revolutionary advances in medicine during the twentieth century. Three key developments have especially helped the aging population have healthier and more productive lives: anti-cardiac failure and antihypertensives, anti-inflammatory and medications that overcome the mental disorders encountered in the aged. Medications like oral hypoglycemic agents, ACE inhibitors, ARBs have also benefited the elderly. Along with better nutrition and low cholesterol, low sodium diets, the development of drugs that help us as we age have reduced death rates from CAD, CV strokes and suicides significantly in the past few decades. But medications used by any aging person are truly the proverbial double-edged sword, since as many as 80 percent of the elderly are on multiple-drug regimens.

PRESCRIBING IN THE ELDERLY

The action and interaction of drugs is dependant on their "Pharmacokinetics" and "Pharmacodynamics". The term "pharmacokinetics" refers to absorption, distribution, metabolism and elimination of drugs and their metabolites. Pharmacodynamics is interaction between agonists and antagonists at drug receptors. In the elderly, both these components of drug metabolism are altered. Table 1 summarizes physiologic changes in the elderly that affect these processes.

The rate and extent of drug absorption are not severely affected by age. However, some commonly prescribed drugs (e.g. anticholinergics, laxatives, calcium channel blockers, agents used to decrease gastric emptying) affect gastrointestinal motility. For

Table 1: Physiologic changes in the elderly that affect pharmacokinetics

Decreased
1. Creatinine clearance
2. Hepatic blood flow
3. Lean muscle mass
4. Renal blood flow
5. Serum albumin level
6. Total body water
Increased
1. Total body fat

example, hepatic function is decreased in the elderly, so drugs that are mainly transformed into active metabolites by the liver may have limited bioavailability after absorption.

Drug distribution is also affected by the 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.[4] Thus, the volume of distribution is reduced for water-soluble drugs (e.g., digoxin), cimetidine, resulting in increased plasma concentrations. The volume of distribution is increased for lipid-soluble drugs (e.g. diazepam), chlordiazepoxide (Librium) resulting in a prolonged half-life. Serum albumin level is decreased in the elderly, so for protein-bound drugs (e.g. propranolol hydrochloride (Inderal), the unbound moiety is increased and drug action is prolonged and enhanced.

1. Kidneys and liver do not eliminate fluids and toxins in the same efficient manner
2. Xerosis making them more vulnerable to bruises.
3. Pulmonary capacity diminishes (on PFT decreased FEV_1, FEV_1/FVC, ↓DLCO, ↑FRC, ↓VC, ↓PaO_2, ↓SaO_2), which increases risk of pneumonia and diseases caused by smoking or air pollution (emphysema).[5]
4. Weakness of muscles, joints, tendons and ligaments leading to injury to hips joints, knee joints and wrists more likely from even a simple fall.
5. The cardiovascular system looses peak efficiency (decreased CO, increased HR, increased PVR, decreased EF and decreased LVEDV).
6. The special senses they depend on like hearing, sight, taste-change subtly and affect mobility (driving a car).
7. The body's weight (increased fat and decreased muscle mass) changes, so that "usual" doses of medication require adjustments.
8. Immune systems declines, making them more vulnerable to both infection and cancer.
9. Cognitive functions may deteriorate due to atherosclerosis that affects blood vessels.

All of the above contribute to the potential harm that medications can cause in the aging body. If a kidney can not eliminate a drug after it has done its work, it remains in the body longer, perhaps causing an overdose or an adverse effect. If a patient is amnestic on medication that regulates the heart or blood pressure, a stroke or heart attack could be the result. Any person over the age of 65 who is taking medications in the following categories should be aware of the potential for increased side effects, overdose and diminished efficacy.[7]

1. Antibiotics (Penicillin, Cephalosporins, Macrolide)
2. Antihistamines (Chlopheneramine maleate, fexophenadine)
3. Antihypertensives (Ca channel blockers, ACE inhibitors, β-blockers, α-blockers)
4. Antiulcer medicines (Ranitidine, Cimetidine, PPI)
5. Antiplatelets (Aspirin, Clopidogrel)
6. Bronchodilators (β stimulants, theophylline derivatives)
7. Calcium or potassium supplements
8. Antianginal, anti-CHF (Vasodilators, Nitrates)
9. Corticosteroids
10. Estrogens
11. Over-the-counter (OTC) drugs containing alcohol (cough and cold medications) or caffeine
12. Analgesics, anti-inflammatory (NSAIDs, COX II inhibitors)
13. Psychiatric medications – Antidepressants, antianxiety
14. Skin medications and creams – Topical steroids

DRUG INTERACTIONS

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.[6]

Drugs commonly prescribed for elders

1. Diuretics given to increase the amount of urine produced. Side effects: Alteration of body salt balance, loss of bladder control, falls due to drop in BP. Advice: Unless otherwise directed, should be taken only in the morning.
2. Sedatives help people to sleep. Side effects: Confusion, falls due to unsteadiness, loss of bladder and bowel control and dependence on the drug. Advice: Avoid if possible, by using other means to sleep e.g. relaxation techniques massage etc.
3. Anti-depressant lifts the mood in depression. Side effects: Confusion, drop in BP (Leading to falls), decreased bowel movements, dry mouth. Advice: Try to use other means such as counselling.
4. Antihypertensives decrease the blood pressure. Side effects: Increased fall in BP (Leading to giddiness and falls), depression and impotence. Advice: Non-drug therapy where possible.
5. Anti-Parkinson's drugs reduce tremor and rigidity. Side effects: Nausea, poor appetite, confusion. See : Parkinson's
6. Analgesics relieve pain. Side effects: Some of them cause acidity, gastro-intestinal bleed and ringing in the ears. Some of them cause constipation and dependence. Advice: When the drugs cause problems, other pain relieving measures have to be tried.
7. Antibiotics given in infections. Side effects: Diarrhoea, skin rash. Advice: Antibiotics should be taken as a full course as prescribed by the clinician.
8. Steroids reduce reactions and in turn inflammation. Side effects: Confusion, gastro-intestinal bleeding. Though they are very useful, they should be taken strictly as advised.

Table 2 : Common Side Effects

1. ACE inhibitors	Cough (dry hacking, continuing), rash, dizziness, lightheadedness, headache.
2. Alpha blockers	Chest pain, dizziness or fainting (more likely if you drink alcohol), fatigue, fluid retention, vision problems)
3. Beta blockers	Anxiety, depression, constipation, diarrhoea, dizziness, dry eyes, fatigue, headache, impotence, insomnia, itching, muscle cramps, nausea, rash, swelling, stuffy nose, vivid dreams.
4. Calcium channel blockers	Constipation, dizziness, fatigue, flushing, gastrointestinal problems, gum problems, insomnia, nausea, swollen extremities, urination problems.
5. Diuretics	Diarrhoea, dizziness, headache, impotence, increased sun sensitivity, loss of appetite or libido, rash, upset stomach.

AGING, MENTAL HEALTH AND MEDICATIONS

Among the first signs that a drug may not be working properly in an older person is a change in mood, energy, attitude or memory. Too often, these alternations are overlooked, ignored or chalked off to "old age" or senility. Older people may themselves perceive that their blue mood is caused by something external such as the death of a friend or simply by boredom. Nothing could be farther from the truth. Virtually every cardiac drug, antihypertensive agent, sedative and tranquilizer has been known to trigger depression symptoms.

When a psychological symptom appears in an older person, it is necessary to examine his or her medication or drug used first. Consider, too, factors like alcohol intake, poor nutrition, and hormone imbalance. It is never advisable to dismiss the possibility that a real psychological problem has developed and may itself require medication. Any older person with feelings of hopelessness, worthlessness, unexplained, crying, thoughts of suicide and similar symptoms could be among the five percent of elderly who have a treatable, reversible depression.

Likewise up to 15 percent of the aging population suffers from the symptoms of dementia: viz. memory loss, disorientation, and confusion. Dementia could be drug-induced. It may also be related to hypertension or conditions like Huntington's disease (a genetic disorder), Parkinson's disease (involuntary tremors), or Creutzfeldt-Jakob disease (a viral infection). Treatment of these can, to some extent, reverse the dementia. However, some 60 percent of those with symptoms of dementia have Alzheimer's disease, a slow progressive mental deterioration that, so far, can't be cured.

Alzheimer's disease is a particularly tragic disorder. It can affect people in their forties, but is more common among the elderly.[7] Among the first signs of Alzheimer's is loss of short-term or recent memory- forgetting to shut-off a light or the stove, or pick up the kids on time. As the condition deteriorates patient tends to become lost more easily and begins to forget how to do simple tasks like adding up number or reading the newspaper. Later on, all mental functions may deteriorate, although the body is usually spared.

Treatment today consists largely of keeping the patient nourished, reducing agitation through tranquilizers, and helping the family cope through support groups.

AGE AND CARDIOVASCULAR SYSTEM

Antihypertensive medications and possible side effects

CHF is the most common indication for hospitalization among adults over 65 yrs of age. The rate of readmission is about 29 to 47%, which can be prevented by multidisciplinary treatment strategy.[8]

DRUGS AND GASTROINTESTINAL SYSTEM

Drugs which are prescribed inappropriately and without proper attention to side effects, they note "failure to identify side effects can lead to use of other drugs to treat the symptoms, rather than adjustment of the dose of the drug responsible".

Some side effects can be mistaken for the effects of old age and aged-related illness. This is particularly the true of anticholinergic side effects, which are among the most common drug-related effects experienced by elderly people living in nursing and residential homes.

In addition, the number of drugs with anticholinergic potential available without prescription is increasing, making it more difficult to monitor the situation. For example, histamine (H2) antagonists such as cimetidine, famotidine, ranitidine could be bought over-the-counter in some countries for indigestion.

Other over-the-counter (OTC) drugs that could cause anticholinergic side effects include cold and flu medicines, hypnotics and anti-diarrhoea treatments. Since many elderly patients take several medications at once, this increases the likelihood of 'anticholinergic load'. The elderly were also more at risk because their metabolism was often less efficient. It is essential to be alert to the possibility that dry mouth, constipation and blurred vision may be caused by medication. Changes in intellectual function should also be investigated, particularly in patients who already have cognitive impairment. Constitution leading to prolonged passage time of drug leading to increase side effects.[9]

For most drugs with anticholinergic potential an alternative is available. Combination of drugs with strong anticholinergic activity, such as thioridazine and amitriptyline, should obviously be avoided.

AGE AND THE KIDNEY

A progressive loss of nephron units with age has been well documented; between ages 40 and 80, the kidney loses about 20% of its mass. This natural involutionary process is represented histologically by a decrease in the renal vasculature (especially in the renal cortex), an increase in the number of obsolescent glomeruli, tubular atrophy and dilatation interstitial scarring. In spite of compensatory hyperfiltration and hyperfunction by the remaining nephron units, the glomerular filtration rate (GFR) declines with age, beginning about age 35 to 40.[10] A yearly

decline of about 0.8 to 1mL/min continues thereafter. However, the serum creatinine level (an index of skeletal muscle mass) remains within the normal range because of decreased muscle mass with age.

Creatinine clearance (in mL/min) in men may be determined by using the following Cockcroft Gault formula; in women, multiply the result by 0.85.[11]

$$\frac{(140\text{-age}) \times \text{body weight (kg)}}{72 \times \text{serum creatinine (mg/dL)}}$$

As can be seen, a serum creatinine level of 1.5 mg/dL in two men who both weight 81 kg. (180 Ib.) represents creatinine clearance of about 45 mL/min if the man is 80 years old but 90 mL/min if the man is 20 years old.

In general, tubular function is also altered in elderly persons.[12] 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, which helps explain the common symptom of nocturnal polyuria. Because they are closely linked to water disorders, sodium disorders are common in the elderly.[13] Also, aging kidneys have problems with distal tubular acidification, which contributes to acid-base disturbances in elderly patients.

NSAIDs may harm kidneys of elderly: Older adults who use over-the-counter or prescription medications containing nonsteroidal anti-inflammatory agents such as ibuprofen may be at greater risk of developing kidney damage.[13]

Blood tests in elderly patients taking regular doses of nonsteroidal anti-inflammatory drugs (NSAIDs) showed higher levels of laboratory values that indicate kidney dysfunction than those not taking the drugs.[14] NSAIDs are commonly prescribed to older adults to control pain and inflammation. While frequent use of NSAIDs can affect kidney function in patients of all ages, it may be particularly damaging in older adults due to declining renal function that accompanies age.

AGE AND JOINTS

Osteoporosis is common in males and females. Risk factors are post-menopausal women, long-term corticosteroids, smoking, alcohol and physical inactivity.[15] Osteoarthritis is a common problem in elderly. NSAIDs are prescribed for chronic arthritis, which can lead to GI bleed, ulcers, renal failure. Post-menopausal women can be treated with HRD. COX 2 inhibitors are better than NSAIDs for arthritis.[16]

NUTRITION SUPPORT IN ELDERLY

In elderly annual decline in lean body mass of 1 – 2% and an increase of fat by 0.5% to 1.5% which start around the age of 30. Cardiac, renal, pulmonary functions decrease with ageing. Poor dentition, esophageal motility problems, decreased gastric emptying, diminished gastric acid production and decreased colonic motility occurs with ageing.

Protein caloric deficits are common. The causes can be remembered by mnemonic WEIGHT LOSS.

W – Wandering and forgetting to eat
E – Emotional problems
I – Insufficient funds
G – Gastrointenstinal tract problems
H – Hypo or hyperthyroidism or other endocrine problems
T – Tremors or other neurological problems interfering with feeding
L – Low salt and other unappetising diet.
O – Oral problems
S – Swallowing problems
S – Shopping and food preparation difficulties

Guidelines for geriatric patients in USA have been recently released. The requirement of all nutrients including electrolytes, vitamins and trace elements are altered in disease states such as cardiac, pulmonary or hepatic insufficiency and needs to be altered depending on known principles.[17]

SAFE MEDICATION USE FOR THE AGED

Safe medication use for the elderly demands vigilance on the part of the older person and those assisting him. It is especially important to keep track of maintenance drugs and make sure they are taken regularly. For a chronic condition such as hypertension or diabetes mellitus, these medications are a key to maintaining good health.

It is worthwhile to remember, that perfectly ordinary drugs really can lead to unexpected results especially in the elderly. It is vise to be alert for gradual changes that may signal an unwanted side effect. It is necessary to guard against harmful drug interactions by making sure the physician knows about all the medicines the older patient is taking, including those prescribed by other practitioners and any over-the-counter drugs.

CONCLUSION

Physicians who treat elderly patients must be aware of the declines in renal function that accompany the aging process. Glomerular filtration rate decreases steadily, starting in middle age. Muscle mass also decreases with age, so an apparently low serum creatinine level may translate into creatinine clearance in the normal range in an elderly person. Evaluation of elderly patients should include careful consideration of possible fluid and electrolyte disturbances and of prescription and over-the-counter medications that may be contributing to the disturbances. Physiologic changes of aging also affect pharmacokinetic processes. Therefore, before a drug is prescribed, consideration must be given to the available volume of distribution, metabolism and elimination capabilities, and other functional factors that characterize elderly patients. So careful and cautious prescription of drugs in the elderly is extremely important in clinical practice.

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