

**WHY RATIONAL DRUG MANAGEMENT IN AN ELDERLY INDIVIDUAL?**H.Dilek Doğan<sup>1</sup>, Kadir Çalışkan<sup>2</sup>**Abstract**

Health requirements of the aging population, the importance of which is increasing with each passing day due to the changing population structure in the world and Turkey, has gained a place as the most important health policy today. In elderliness when several diseases can coexist simultaneously, it is very important to properly select among an increasing number of drugs and to use them in safe dose ranges. In elderly individuals, drug side effects, overutilization of drug, and cognitive problems such as forgetting and comprehension are common. It is therefore difficult to distinguish whether the symptoms observed in an elderly individual are drug side effects or the interaction between drug and disease. Rational drug management in the elderly includes starting treatments at a low dose and increasing the dose slowly, that is “start low, go slow”, and continuing with as low dose as possible to avoid unnecessary drug doses. In this context, clinical staff should be able to closely monitor the effects and side effects of drugs administered to elderly individuals, provide the required training to the patient and family, and be able to recognize cognitive changes early.

**Keywords:**

Aging, drug, pharmacodynamic and pharmacokinetic effect, rational drug use.

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## INTRODUCTION

Today, the world population is getting older in parallel with the factors such as benefiting from the opportunities of modern medicine more, developing economic and sociocultural conditions, and declining birth rate. According to the United Nations Population Fund (UNFPA) 2019 data, it is estimated that the population aged 60 years and older is over 900 million in the world and this number will reach 2.1 billion by 2050. In other words, it is reported that one in very five people in the world will be 60 years old and over in 2050. According to the Turkey 2019 data, the proportion of elderly population is 8.8%, and this rate is expected to increase to 10.8 per cent in 2023 and to 23.8 percent in 2050 (Kutsal,2019; Oztop et al., 2018; Turkish Council on Ageing 2019). These demographic changes in the elderly population affect health systems both socially and financially. In the most general sense, polypharmacy can be defined as the simultaneous use of one or multiple drugs. In terms of clinical significance, the use of 5 or more drugs can be considered as polypharmacy (Oztop et al., 2018; Turgeon et al., 2019). In a study conducted in Europe, it was found that 37.9% of individuals aged over 65 years had 4 or more chronic diseases and 50% of the patients were using 6 or more drugs a day, and one out of every two people were on psychotropic drugs with a high risk of side effects in the elderly (Oztop et al., 2018). In a 2008 study, the risk of developing drug side effects with the use of two drugs is 15% and this rate increases to 58% with the use of five drugs, and up to 82% with the use of seven or more drugs (Masodi, 2008; Yildirim and Kilic, 2017)

The most common used drugs in the elderly are central nervous system (CNS), cardiovascular system and gastrointestinal system drugs. The drugs that frequently cause side effects include those causing CNS depression, antibiotics, analgesics, anticoagulants, antihypertensives, bronchodilators, diuretics and oral hypoglycemics (Bahat et al., 2012; Oztop et al., 2018;). In the meta-analyses, it has been found that hospitalization and mortality rates due to predictable and preventable drug side effects are significantly increased in the elderly than in young adults. Moreover, the incidence of problems such as weight loss, fall, functional and cognitive decline, hip fracture, urinary incontinence has also been shown to increase (Beijer &Blaey, 2002).

## PURPOSE

In this review, the importance of safe drug use in elderly individuals and the correct selection of drugs increasing with aging is emphasized.

## WHY RATIONAL DRUG MANAGEMENT IN AN ELDERLY INDIVIDUAL?

There are age-related differences in the treatment of each disease or medical problem. Aging is a natural but risky life period that includes various disciplines. The increase in chronic diseases with aging causes excessive drug use. Pharmacokinetic and pharmacodynamic properties of drugs change with age. Therefore, rational drug management in an elderly individual will have a significant place in the preventive health services for elderly population both in the near and far future.



Therefore, the physiological and functional changes in the organism during the aging process should be known first.

### What is Aging?

Aging is a physiological process occurring over time at the level of cells, tissues and systems in the organism and comprising irreversible functional and structural alterations (Aslan and Hocaoglu, 2017; Turnheim, 2003). Aging begins with birth and continues by undergoing many changes until the death of each different organism (Aslan and Hocaoglu, 2017). It is not a stable period and shows differences between individuals. During this period, a decline in body functions, a decrease in organ reserves, difficulty in adapting to the environment and stressors, and a period vulnerable to diseases and injuries are experienced (Turnheim, 2003). The changes in the structure and functions of the human body are called biological aging and the changes in the organs are called physiological aging, while the change in lifestyle due to the individual's feeling himself or herself old is called social aging (Akin, 2006; Turnheim, 2003).

## **Physiological Changes and Disability in Aging**

### *Cardiovascular system*

Although aging itself directly affects the cardiovascular system, the occurrence of cardiovascular diseases may vary depending on age-related structural changes, presence of risk factors and concomitant diseases. The most common cardiovascular diseases in the elderly period are hypertension, heart failure, coronary artery diseases, atrial fibrillation, acute myocardial infarction, valve diseases and venous thrombosis. Therefore, the majority of cardiovascular deaths occur in the elderly population (Tiftik et al., 2012). Thickening and calcification of the heart valves, increase in the left ventricular thickness and left atrial size occur. On chest x-ray, the cardiac shadow appears slightly enlarged. The muscle structure undergoes atrophy and the cardiac output decreases due to the reduced volume of blood pumped at each contraction. The amount of adipose tissue around the heart increases and the pumping ability of the heart decreases by 1%. Heart rate and filling volume decrease and a fibrous tissue is formed in the sinoatrial node. The diameters of the lower extremity veins begin to expand and the activity of the baroreceptors decreases. During this period, the probability of arrhythmia increases and the circulation decreases due to the decrease in blood flow to all organs (Dedeli, & Karadakovan, 2011; Karadakovan & Arslan, 2011; Nalbant, 2008; Tiftik et al., 2012). Although the regeneration of the heart muscle and coronary arteries seems possible in the stem cell study, cardiovascular diseases continue to be an important health problem for both young people and the elderly (Nalbant, 2008).

### *Pulmonary System*

Pulmonary functions and vital capacity are reduced in the elderly due to decreased elasticity of lung, increased stiffness of chest wall and weakening of respiratory muscles. Very few changes occur in the bronchioles. The degeneration of the alveolar walls results in a reduction in the surface area for gaseous exchange. Acid base balance is disrupted. Posture change develops as a result of decreased rib cage flexibility. Alveolar membrane thickens, the cilia movements slow down and cough reflex decreases. The respiratory center slows down and the peripheral perfusion decreases. Oxygen saturation and

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respond to hypoxia are reduced. The efficiency of the respiratory system lowers and chest breathing is replaced by diaphragmatic breathing. While expiratory flow rate decreases, residual lung volume increases (Pehlivan and Karadakovan, 2012, Yildirim et al., 2013).

#### *Neurological System*

Brain weight and blood flow decrease with normal aging process. Nervous loss occurs in the Central Nervous System. As the blood circulation decreases, neuronal loss is more common in certain parts of the brain, while some parts are preserved. Sympathetic and parasympathetic system function losses. Concomitant reduction in various neurotransmitters and dendritic connections. Loss of sensitivity occurs in receptors. In addition to dementia, there is no decrease in cognitive functions despite the loss of advanced neurons in many regions. Many neurofunctional abilities decrease with age. A decrease in intellectual capacity is observed. Although within normal limits, most of the functions related to learning and memory may decelerate. With the delay of reflexes, the patient cannot protect himself against traumas, and intracranial hemorrhage is more common in motor vehicle accidents and other traumas. As mental disorders can be seen as agitation and laterji without trauma, caregivers can easily bypass the trauma (Pehlivan and Karadakovan, 2012; Ozkayar and Ariogul, 2007).

#### *Musculo-Skeletal System*

Aging decreases muscle mass and strength. Bone mineral loss increases and joint mobility decreases. As the body fat mass increases, the spine becomes round. In the musculo-skeletal system with aging; osteoporosis, osteoarthritis, degenerative joint diseases, rheumatoid arthritis, pelvic fractures and falls fractures. Studies have shown that the most common osteoporosis, lumbar, knee and cervical region degenerative diseases are seen (Pehlivan and Karadakovan, 2012). The muscle mass and strength are reduced. Decrease in muscle mass makes it difficult to perform daily activities and lowers the level of physical activity. Bone density and mineral losses occur in women between the ages of 30-35 and in men between the ages of 50-55 and 0.75-1%. The number and size of muscle fibers are reduced. An increase in the amount of intercellular fat is observed in muscle fibers. After 30 years, muscle strength decreases by 10-15% every 10 years and accelerates after 50 years. Therefore, the bones weaken and break easily. Degeneration of the intervertebral discs and calcification of cartilage and ligaments occur. Loss of elasticity in the joint and deterioration of cartilage occurs. Elderly, both in the posture and walking problems are experienced balance (Karadakovan and Arslan, 2011; Nalbant, 2008; Tiftik et al., 2012).

#### *Digestive System*

With aging, tooth loss is experienced and the sensitivity of taste and smell receptors is reduced. Absorption in the digestive system slows down and blood flow to the liver decreases. Chewing power is reduced, all secretions and enzymes are reduced. Pancreatic response decreases and sphincter tone decreases and metabolism slows down. Approximately 40% of healthy elderly patients complain of dry mouth. Basal salivary secretion probably decreases with age. Stimulated salivation is unchanged. Fecal incontinence can be seen due to loss of control of the anal sphincter. Elderly individuals due to changes in the digestive system; problems such as loss of appetite, indigestion, diarrhea, constipation, cachexia and obesity can also be seen. Appearance of foods should be made attractive, meals should be presented frequently and gradually, balanced and adequate nutrition should be provided. Since the inability to taste can cause excessive salt and sugar use, the family should be warned and controls should be performed.



Decreased sensitivity at the receiving nerve endings negatively affects appetite. If the use of prosthetics is added to this, nutritional problems may arise. In order to solve this problem, it is necessary to cooperate with the elderly and their families to prepare their favorite foods and to learn about their hot or cold eating habits and to consume foods that contain fiber, vitamins and minerals and prevent constipation. (Karadakovan and Arslan, 2011; Nalbant, 2008; Tiftik et al., 2011, Yildirim et al., 2012).

### **Physiological Changes That May Affect Drug Pharmacology In The Elderly**

#### ***Pharmacokinetic Effect in the Elderly***

Cognitive problems such as drug side effects, intoxications, drug-drug interaction, excessive drug use, forgetting and comprehension are common in elderly individuals. Polypharmacy causes drug side effects, drug interactions, nonadherence to treatment, increase in cost, hip fracture, weight loss, fall, cognitive impairment, prolonged length of hospital stay and death. Therefore, it is very difficult to distinguish whether the symptoms observed in the elderly are drug side effects or the interaction between drug and disease (Guc, 1997; Gulhan, 2013). Side effect refers to a possible expected event, while adverse effect refers to unexpected events (Yesil et al, 2012). Drug pharmacokinetic and pharmacodynamic change as a result of systemic and functional transformations in aging.

In the elderly period, the absorption of drugs, their distribution in the body, metabolism, excretion and response to drugs, which are pharmacokinetic properties, vary as a result of changes at the receptor level (Guc, 1997).

**1-Absorption:**Salivary secretion is reduced, which may affect the dissolution of drugs. With aging, the secretion of hydrochloric acid in the stomach is reduced. Although changes such as decrease in pepsin, pancreatic lipase and trypsin secretion, splanchnic blood flow and gastric motility occur, no significant change occurs in the absorption of drugs. Absorption may be affected due to the simultaneous use of multiple drugs. For example, congestive heart failure, one of the most common diseases in the age group of 65 and over, affects the absorption negatively by decreasing the splanchnic blood flow. However, active transport of vitamin B12, iron and calcium decreases, while the absorption of levodopa may increase as a result of decreased dopa decarboxylase enzyme activity in the gastric mucosa. As a general rule, it is stated that the amount of absorption does not change but the rate of absorption slows down. On the other hand, changes in nutritional habits in the elderly people and drugs used (such as antacids, anticholinergics, some herbal products) may change the rate of absorption (Aslan et al., 2017; Erenmeyenoglu, 2006)

**2-Distribution:** In aging, water and lean body mass decreases, while body fat percentage increases. This increases the plasma concentrations of water-soluble drugs such as gentamicin, digoxin, theophylline, lithium, ethanol. If this process cannot be compensated by excretion from the kidneys, it poses a risk especially for drugs with a narrow therapeutic index and leads to drug toxicity. Moreover, loading doses of drugs such as digoxin should therefore be reduced. Since the baroreceptor sensitivity decreases with the amount of body water in the elderly, orthostatic hypotension may develop as a result of using diuretic and vasodilator drugs. The distribution of water-soluble substances such as vitamin B is low. (Aydos, 2011; Erenmemisoglu,2006; Ozer & Ozdemir, 2009). Albumin is a plasma protein that is actively

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involved in the transport of drugs. In the elderly, the levels of albumin decrease and free (unbound) forms of drugs increase due to liver dysfunctions and malnutrition. The dose of free drug in circulation creates drug side effects and toxicity. When warfarin, sodium and oral hypoglycemic drugs, the drugs that bind to protein with albumin decrease, are used in combination, severe bleeding and hypoglycemia may develop, which are the side effects of the drugs (Ozer and Ozdemir, 2009).

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**3-Metabolism (Biotransformation):** With aging, a decrease in liver mass, a 12-40% decrease in liver blood flow and a decrease in enzyme activity occur. The liver is an organ that has high blood flow due to its vital functions, where the toxic substances and drugs in the organism are metabolized and made harmless. As the age progresses, the removal of toxic substances consequently decreases. In the elderly group, with the change in liver, a slowing in the elimination and metabolism of drugs such as barbiturates, warfarin sodium, diazepam, an increase in the plasma levels, and an increase in the incidence of side effects are observed (Erenmemişoğlu, 2006; Ozer and Ozdemir, 2009). The synthesis of vitamin K-dependent coagulation factors decreases and the sensitivity to anticoagulant drugs increases. Therefore, hemorrhage due to degenerative vascular diseases and anticoagulant therapy, may occur in elderly people (Ozer and Ozdemir, 2009).

**4-Excretion** The most important clinical factor that changes the drug's effect in the aging process is the kidneys. Renal blood flow may decrease by 30-40% (1% per year after age 50). With advanced age, nephron loss occurs and kidney mass decreases. Along with nephron loss, glomerular filtration rate and tubular secretion decrease up to 50%. Therefore, the elimination of water-soluble antibiotics, aminoglycosides, diuretics, digoxin, and lithium slows down, their half-lives prolong and the risk of toxicity increases. Creatinine clearance should be taken into consideration in the calculation of drug dose in the elderly (Erenmemişoğlu, 2006; Özer & Ozdemir, 2009).

**5-Receptor sensitivity:** It is the change in receptor number, change in receptor affinity, change in secondary messenger function, change in cellular response. In elderly people, sensitivity to drugs affecting the central nervous system has also increased. Therefore, drugs with sedative effect (eg diazepam) should be used in low doses in the elderly group. In addition, an increase in the undesired adverse effects of anticholinergic drugs such as confusion is seen with the decrease in cholinergic neurons and receptors in the elderly (Gelal, 2006; Kaya et al., 2017; Ozer and Ozdemir, 2009).



### *Pharmacodynamic Effect in Elderly Individuals*

Although pharmacokinetic changes are easily recognizable in the elderly, pharmacodynamic changes are more difficult to detect (Kaya et al., 2018) Pharmacodynamics is classically defined as 'dealing with what drugs do on the human body and how they do it'. More generally, pharmacodynamics is a branch of pharmacology that deals with the effects of drugs on physiological, biochemical and pathological events in humans and can be defined as the effect of drugs on the body. (Gelal, 2006; Kaya et al., 2018) Even if the drug level in the target tissue is the same, the effects of drugs may be increased or decreased in old age. Changes in tissue receptor sensitivity and/or homeostatic control mechanisms as a result of aging may change the effects of drugs (Gülhan, 2013). .Pharmacodynamic changes are primarily seen in drugs affecting the cardiovascular system and central nervous system. Drugs with aging-dependent increased sensitivity (warfarin, diazepam, morphine, etc.) should be chosen carefully as they can cause significant side effects. In cases where receptor sensitivity is decreased, higher doses of the drug may be needed for the drug to show its efficacy (Gelal, 2006). At the same time, in elderly individuals, some drugs produce different responses than expected, and sensitivity to drugs develops. For example, there is a decrease in sensitivity to beta receptors in the cardiovascular and respiratory system in the elderly, whereas there is a sensitivity increase to sedative-hypnotics, benzodiazepines, analgesics, opioids and neuroleptics in the central nervous system. Especially benzodiazepines, even at low doses, can cause significant sedation. Side effects of neuroleptics such as delirium, extra-pyramidal side effects, arrhythmia and postural hypotension are more common in the elderly. It has been found that anticholinergic side effects of tricyclic antidepressants, antihistamines, and antispasmodics such as dryness of the mouth, visual impairment, constipation, urinary retention, delirium are increased. While there may be severe hypotension at the beginning of the treatment with angiotensin converting enzyme inhibitors, long-term antihypertensive efficacy may not be successful. Decrease of the synthesis of vitamin K-dependent coagulation factors may also lead to increased sensitivity to warfarin and risk of hemorrhage. Therefore, it should be used at a lower dose (Gülhan, 2013).

### **Basic Rules For Rational Drug Use In The Old Age**

In 1985, the World Health Organization (WHO) defined rational drug use as "getting the most appropriate drug according to the clinical findings and individual characteristics of the patients, in the most appropriate doses that meet their individual needs, at a reasonable time, at the lowest cost for themselves and the community, and their easy access". When deciding the patient's treatment plan, targeted drug options should be evaluated in terms of effectiveness, safety, suitability, and cost (WHO, 1985; Gülhan, 2013; Kaya et al., 2018). When treating the elderly patients safely, using appropriate and reliable dosages of drugs is essential in terms of Rational Drug Management. Apart from the pharmacokinetic and pharmacodynamic changes caused by aging, the most common problems encountered in this group of patients are multiple drug use, namely polypharmacy, drug overdose, drug-drug interactions and difficulty in compliance and continuation of treatment (Gülhan, 2013; Gökçe, 2006; Kaya et al., 2018). Polypharmacy in the elderly increases the incidence of side effects of drugs, leads to the deterioration of compliance due to use, causes a decrease in quality of life and an increase in cost. In

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the studies carried out in order to determine the drug-related financial burden, drug expenditures have an important place in the general health expenses of the countries (Top & Tarcan, 2004; Ozer & Ozdemir, 2009). In the UK, although the elderly population aged 60 years and over constitutes only 1/5 of the total population, it is observed that 59% of the prescribed drugs are used by this population, and 20% of those over 70 years of age use 5 or more drugs (Milton, 2008). In randomized controlled studies with elderly individuals, generally, diseases such as hypertension and osteoporosis are focused on. However, there are more than one disease and drugs used that can interact with each other in the elderly. In the United States between 2002 and 2011, efficacy and safety data for the elderly patient group have been found to be sufficient in only 74 of the 214 drugs that can be used by the elderly patient group (Gülhan, 2013).

When the elderly people live holistically, physicians, nurses, pharmacists and all health workers have important roles and responsibilities in drug management. Especially doctors and nurses have ethical and legal responsibilities in drug administration. Elderly and his family need information and help to use therapeutic drugs safely and effectively. and notes. For elderly individuals with swallowing difficulties, solid form tablets should be used instead of liquid form or powder form. Rational drug management of the elderly; start-up and slow increase of treatment (startlow, goslow)”, continue as low as possible and avoid unnecessary use (Turkey aging workshop, 2015; Güç, 1997) Tablets can be crushed or liquid and so on. It should be questioned whether mixing with food makes any change in the effectiveness of the drug. The nurse should assess not only the disability and needs of the elderly individual, but also the resources and self-management strategy (Kaya et al., 2018; Pehlivan & Karadakovan, 2012; Ozer and Ozdemir, 2009).

Elderly people with visual problems should be informed about how to prepare and take their medicines in an illuminated environment. Medicine boxes and boxes of these elderly people should be written and labeled with big and colored pencils according to the requirement. Elderly individuals and their relatives should be informed about the storage of the drugs in suitable environments in terms of heat, light and humidity. Problems caused by drug use other than prescribed drugs should be explained to the elderly individual and family (Ozer and Ozdemir, 2009).

### **Basic Principles of Drug Use in Elderly**

1. When offering medication to the elderly patient, treatment should be individualized; o the most appropriate drug should be selected for the patient.
2. A diagnosis must be made before starting treatment; medication should not be recommended only for signs of disease.
3. Medical problems should be treated without medication as much as possible.
4. Other doctors should be asked if they have prescribed medication.
5. The drug should be started at the lowest possible dose.
6. If necessary, the dose of the drug should be increased in a controlled manner.
7. Sedation, sedative drugs should be recommended and used with caution as they may affect the person's daily activities.





8. Dose adjustment should be done carefully.
9. Drugs that may have side effects should be used and discontinued as soon as possible.
10. Drugs should be started after laboratory tests such as blood-urine examinations are necessary.
11. Drug treatment should be simplified.
12. In order to increase the patient's compliance with the treatment schedule, the usage schedule should be prepared and the medicine boxes should be clearly labeled.
13. Treatment should be reviewed regularly and unnecessary drugs should be removed
14. The treatment plan should be simplified as much as possible. (İskit, 2006; Ministry of elderly health diagnosis and treatment guide, 2010).

#### **Considerations For The Elderly**

1. The drug should not be taken immediately for each symptom or complaint.
2. He should bring all medicines used on his way to the hospital.
3. Always show your medication to your doctor.
4. Tell your doctor if you are smoking, drinking alcohol or drinking caffeinated beverages.
5. Use less medication as far as possible.
6. Take your medicine at the dose recommended by your doctor and try to comply with the treatment schedule.
7. If you have any problems or questions, always ask your doctor.
8. Always tell your doctor about any side effects related to the medications you use.
9. Tell your doctor if you have any difficulty using medication (for example, difficulty opening the lid of the medicine boxes, difficulty swallowing the drug, mixing tablets of the same color).
10. Make a mark on your calendar to remember details about drug use.
11. If you are going to use substances that are defined as if medicinal plants arasında among the people, be careful and think with your doctor that you may affect your current diseases or the dosage and efficacy of the drugs you are presently using. (Kutsal, 2019, İskit,2006; Ministry of elderly health diagnosis and treatment guide, 2010).

#### **CONCLUSION AND SUGGESTION**

As a result; the problems related to drug use in the elderly cause an increase in mortality and morbidity. It should be kept in mind that aging has its own characteristics and that every medical condition and application has important differences with respect to the elderly. The most important responsibility of the health care team and the nurse regarding drug treatments is that they have knowledge about pharmacodynamic and pharmacokinetic changes that develop with aging. In this period in which several chains of disease are seen together, every disability of the patient should be considered and the elderly

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individual should be evaluated as a whole. Rational drug management of the elderly; start-up and slow increase of treatment (startlow, goslow) ”, continue as low as possible, prevent unnecessary drug use. In this context, the nurse should monitor the effects and side effects of the drugs, provide education to the patient and the family, and closely monitor the mental state of the patient for cognitive changes.

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