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AGE-RELATED ASPECTS OF CLINICAL PHARMACOLOGY AND THE CLINICAL SIGNIFICANCE OF RATIONAL MEDICINE USE.

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Abstract:

Background: Age is one of the key factors influencing the pharmacokinetics and pharmacodynamics of medicines. Physiological changes occurring throughout human development and ageing may significantly affect drug absorption, distribution, metabolism, and excretion, as well as the intensity of therapeutic and adverse effects.

Objective: This article aims to examine the age-related characteristics of clinical pharmacology and highlight the importance of individualized and rational pharmacotherapy in children, adolescents, adults, and older patients.

Methods: The study is based on a narrative review of scientific literature, international recommendations, clinical pharmacology textbooks, and publications addressing age-related changes in drug response and medication safety.

Results: The analysis demonstrates that age-related physiological differences have a substantial impact on drug response and treatment outcomes. In children, immature metabolic and excretory systems require careful dose selection. In older adults, reduced renal and hepatic function, altered body composition, increased pharmacodynamic sensitivity, and polypharmacy may increase the risk of adverse drug reactions. Individualized treatment, appropriate dose adjustment, regular monitoring, and consideration of drug interactions are essential components of safe pharmacotherapy across all age groups.

Conclusion: Understanding age-related aspects of clinical pharmacology is essential for improving treatment effectiveness and medication safety. Age-appropriate prescribing and individualized pharmacotherapy should be considered fundamental principles of modern healthcare and professional medical education.

Keywords: *clinical pharmacology, age-related changes, pharmacokinetics, pharmacodynamics, rational pharmacotherapy, pediatric patients, older adults, drug safety, adverse drug reactions, individualized treatment.*

Introduction. Clinical pharmacology is a medical discipline concerned with the study of the effects of medicines on the human body, their mechanisms of action, pharmacokinetic and pharmacodynamic properties, therapeutic effectiveness, and safety. One of the most important factors influencing the clinical response to medicines is the patient's age.

The human body undergoes continuous physiological and biochemical changes throughout life. These changes affect the functioning of organs and systems responsible for drug absorption, distribution, metabolism, and elimination. Consequently, the same medicinal product administered at an identical dose may produce different therapeutic effects and adverse reactions in patients belonging to different age groups.

Age-related characteristics are particularly important in pediatric and geriatric pharmacotherapy. Children cannot be considered simply smaller versions of adults, since their organs and regulatory systems are still developing. Similarly, older adults often experience physiological

changes that influence drug clearance, tissue distribution, receptor sensitivity, and overall treatment tolerance.

In modern healthcare, rational medicine use requires an individualized approach that considers not only the diagnosis but also the patient's age, body weight, organ function, concomitant diseases, and medications.

2. Aim and objectives of the study. The aim of this article is to analyze the age-related characteristics of clinical pharmacology and determine their significance for the rational and safe use of medicines. The objectives of the study are:

- to examine age-related changes in pharmacokinetic processes;
- to describe age-dependent differences in pharmacodynamic responses;
- to identify the main principles of pharmacotherapy in children and adolescents;
- to analyze the specific features of drug therapy in older adults;
- to highlight the risks associated with polypharmacy and adverse drug reactions;
- to formulate practical recommendations for individualized pharmacotherapy.

3. Age-related changes in pharmacokinetics. Pharmacokinetics describes the movement of a medicinal substance through the body and includes four main processes: absorption, distribution, metabolism, and excretion. Each of these processes may vary considerably depending on the patient's age.

3.1. Drug Absorption. Drug absorption is influenced by gastrointestinal function, gastric acidity, intestinal motility, blood flow, and the route of administration.

In newborns and infants, gastric acidity, gastrointestinal motility, and digestive enzyme activity differ from those of adults. These differences may affect the rate and extent of absorption of certain medicines.

In older adults, delayed gastric emptying, changes in gastrointestinal motility, and reduced splanchnic blood flow may influence the absorption of some medicinal products. However, the clinical significance of these changes varies depending on the medicine and its formulation.

3.2. Drug Distribution. Drug distribution depends on body composition, plasma protein concentrations, tissue perfusion, and the physicochemical properties of medicinal substances.

In newborns, total body water constitutes a larger proportion of body weight than in adults. This may increase the apparent volume of distribution of water-soluble medicines.

In older adults, total body water and lean body mass generally decrease, while the proportion of body fat may increase. These changes can alter the distribution and elimination of both water-soluble and lipid-soluble medicines.

Reduced plasma albumin concentrations in some older patients may increase the free fraction of highly protein-bound medicines, potentially increasing their pharmacological effects and toxicity.

3.3. Drug Metabolism. Drug metabolism occurs mainly in the liver and involves enzymatic systems responsible for the biotransformation of medicinal substances.

In newborns, hepatic enzyme systems are immature. Their activity develops gradually during infancy and childhood. Therefore, certain medicines may be metabolized more slowly in early life.

In older adults, hepatic blood flow and liver mass may decrease. These changes can reduce the clearance of some medicines, particularly those with extensive hepatic metabolism.

Consequently, the selection of a medicinal product and its dosage should take into account the patient's age, liver function, and relevant clinical characteristics.

3.4. Drug Excretion. The kidneys play a major role in eliminating many medicines and their metabolites.

Renal function is not fully developed at birth and gradually matures during childhood. In older adults, the glomerular filtration rate may decline with age, although the degree of decline varies considerably between individuals.

Reduced renal clearance may lead to drug accumulation and an increased risk of toxicity. This is particularly important for medicines that are predominantly eliminated through the kidneys.

Assessment of renal function and appropriate dose adjustment are therefore essential components of safe pharmacotherapy.

4. Age-related characteristics of pharmacodynamics. Pharmacodynamics refers to the biochemical and physiological effects of medicines on the body, including their mechanisms of action and interactions with receptors, enzymes, and other biological targets.

Age-related changes in receptor sensitivity, signal transduction, homeostatic regulation, and organ responsiveness may influence the clinical effects of medicines.

In pediatric patients, the developing nervous, cardiovascular, endocrine, and immune systems may respond differently to certain medicinal substances.

In older adults, increased sensitivity to some medicines may occur. For example, sedatives, hypnotics, opioids, and certain antihypertensive medicines may produce more pronounced clinical effects in susceptible patients.

Changes in cardiovascular regulation and reduced physiological reserves may also increase the risk of orthostatic hypotension, falls, confusion, and other adverse outcomes.

Thus, pharmacodynamic differences should be considered alongside pharmacokinetic changes when selecting treatment.

5. Clinical pharmacology in pediatric patients. Pediatric pharmacotherapy requires a particularly careful and individualized approach. The physiological characteristics of newborns, infants, preschool children, school-age children, and adolescents differ substantially.

5.1. Newborns and Infants. Newborns and infants have immature hepatic and renal functions, differences in body water distribution, and developing enzyme systems. These factors influence the pharmacokinetic behavior of medicines.

The following principles are important when prescribing medicines to this age group:

- selection of medicines with established safety information for the relevant age group;
- calculation of doses according to body weight or body surface area, when appropriate;
- consideration of gestational age and postnatal age in newborns;
- assessment of renal and hepatic function when clinically indicated;
- use of age-appropriate pharmaceutical formulations;
- monitoring for therapeutic effects and adverse reactions.

It is important to emphasize that dose calculation based solely on body weight does not guarantee safety. The pharmacological characteristics of the medicine, developmental maturity, clinical condition, and approved prescribing information must also be considered.

5.2. Children. During childhood, organ systems and metabolic processes continue to develop. Drug doses are often determined according to body weight or body surface area, but the method depends on the specific medicine and clinical indication.

Particular attention should be paid to medicines affecting the central nervous system, cardiovascular system, respiratory system, and endocrine regulation.

Parents and caregivers should receive clear instructions regarding the prescribed dose, administration interval, duration of treatment, and possible adverse reactions.

Self-medication and the use of adult formulations without appropriate dose adjustment may create significant risks.

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5.3. Adolescents. Adolescence is characterized by rapid physical growth, hormonal changes, and psychological development. Although many pharmacokinetic processes approach adult patterns during this period, individual differences remain important.

Medication adherence, lifestyle factors, nutritional status, and the possibility of unsupervised medicine use should be considered.

Healthcare professionals should provide age-appropriate information about responsible medicine use and the risks of inappropriate self-medication.

6. Clinical pharmacology in adults. In healthy adults, many pharmacokinetic processes are relatively stable. However, individual differences in body composition, genetic characteristics, liver and kidney function, lifestyle, and concomitant diseases may significantly influence drug response.

The following factors should be considered when prescribing medicines to adults:

- the patient's clinical diagnosis and disease severity;
- renal and hepatic function;
- body weight and body composition;
- pregnancy and lactation, where relevant;
- concomitant diseases;
- potential drug–drug interactions;
- the possibility of adverse drug reactions;
- adherence to the prescribed treatment regimen.

In patients with chronic diseases, long-term pharmacotherapy requires regular assessment of treatment effectiveness and safety.

7. Clinical pharmacology in older adults. Older adults represent a particularly vulnerable group in clinical pharmacology. Age-related physiological changes, multiple chronic diseases, and the simultaneous use of several medicines may increase the risk of medication-related problems.

7.1. Pharmacokinetic Changes in Older Adults. The most important pharmacokinetic changes include:

- decreased total body water;
- reduced lean body mass;
- increased proportion of body fat in many individuals;
- possible reduction in hepatic blood flow and metabolic capacity;
- age-related decline in renal function;
- changes in plasma protein concentrations.

These changes may affect drug distribution, metabolism, and elimination, potentially prolonging the duration of action of certain medicines.

7.2. Pharmacodynamic Changes in Older Adults. Older patients may demonstrate increased sensitivity to certain medicinal products. This is particularly relevant to medicines acting on the central nervous system and cardiovascular system. Potential clinical consequences include:

- excessive sedation and confusion;
- orthostatic hypotension;
- increased risk of falls;
- hypoglycemia in susceptible patients;
- bleeding complications associated with anticoagulant therapy;
- increased susceptibility to adverse drug reactions.

Treatment should therefore be individualized, and therapeutic outcomes should be monitored regularly.

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7.3. Polypharmacy and Medication Safety. Polypharmacy refers to the concurrent use of multiple medicines. Although the use of several medicines may be clinically justified in patients with multiple chronic conditions, it can increase the risk of drug interactions, inappropriate prescribing, medication errors, and adverse reactions. To reduce these risks, healthcare professionals should:

- regularly review the patient's medication list;
- identify unnecessary or duplicated medicines;
- assess potential drug–drug interactions;
- evaluate renal and hepatic function;
- consider non-pharmacological treatment options;
- simplify medication regimens when clinically appropriate;
- monitor treatment effectiveness and safety.

Medication review and individualized prescribing are important elements of comprehensive care for older adults.

8. Comparison of age-related pharmacological characteristics. The main age-related physiological characteristics and their clinical pharmacological implications are summarized in Table 1.

Table 1. Age-related physiological characteristics and clinical pharmacological considerations.

Age group	Main physiological characteristics	Clinical pharmacological considerations
Newborns and infants	Immature hepatic and renal functions; high proportion of total body water	Careful dose selection; consideration of developmental maturity; close monitoring
Children	Continuing development of organs and metabolic systems	Age- and weight-appropriate dosing; suitable pharmaceutical formulations
Adolescents	Rapid growth and hormonal changes	Individualized prescribing; attention to adherence and self-medication
Adults	Relatively stable physiological functions, with individual variation	Assessment of organ function, concomitant diseases, and drug interactions
Older adults	Possible decline in renal and hepatic function; changes in body composition and drug sensitivity	Dose adjustment when indicated; medication review; prevention of polypharmacy-related harm

The comparison demonstrates that pharmacological treatment should be adapted to the physiological and developmental characteristics of each age group. An individualized approach helps reduce medication-related risks and improve therapeutic outcomes.

9. Principles of rational pharmacotherapy across different age groups. Rational pharmacotherapy involves selecting the most appropriate medicine for an individual patient, using an effective and safe dose, for an appropriate duration, while considering clinical needs and potential risks. The following principles are essential:

1. Individualized treatment. Treatment should be selected according to the patient's age, diagnosis, physiological condition, and individual characteristics.

2. Appropriate dose selection. The dose should be based on approved prescribing information, clinical guidelines, organ function, and relevant patient-specific factors.

3. Assessment of renal and hepatic function. These organs play a central role in drug metabolism and elimination. Their function should be evaluated when clinically necessary.

4. Prevention of adverse drug reactions. Healthcare professionals should identify risk factors, monitor patients, and respond promptly to suspected adverse effects.

5. Assessment of drug interactions. The simultaneous use of several medicines requires careful evaluation of potential pharmacological interactions.

6. Patient education. Patients and caregivers should receive clear information about the purpose of treatment, dosage, administration, duration, and possible adverse reactions.

7. Regular monitoring. Treatment effectiveness and safety should be reviewed throughout the course of therapy.

10. Relevance to healthcare and professional medical education in Uzbekistan. The study of age-related clinical pharmacology is particularly relevant to the development of healthcare services and professional medical education in Uzbekistan.

Healthcare professionals working in hospitals, primary healthcare institutions, pharmacies, and medical educational institutions should understand how age-related physiological changes influence the effects and safety of medicines.

In professional medical education, clinical pharmacology should be taught not only as a theoretical discipline but also through practical clinical situations, case-based learning, prescription analysis, and medication safety exercises. Particular attention should be given to:

- rational pharmacotherapy in pediatric patients;
- safe prescribing for older adults;
- prevention of adverse drug reactions;
- identification of clinically significant drug interactions;
- appropriate use of medicines in patients with renal and hepatic impairment;
- patient counselling and medication adherence.

The integration of these topics into medical and pharmaceutical education can contribute to the development of professional competencies and improve the quality of pharmaceutical and medical care.

11. Conclusion. Age is a fundamental factor influencing the pharmacokinetics and pharmacodynamics of medicinal products. Physiological changes throughout human development and ageing affect drug absorption, distribution, metabolism, excretion, and pharmacological response.

Pediatric patients require careful consideration of developmental maturity and age-appropriate dosing. In older adults, changes in renal and hepatic function, altered body composition, increased sensitivity to certain medicines, and polypharmacy may increase the risk of adverse drug reactions.

Rational pharmacotherapy should therefore be based on an individualized approach that considers the patient's age, clinical condition, organ function, concomitant diseases, and medication profile.

The systematic application of age-related clinical pharmacology principles is essential for improving treatment effectiveness, reducing medication-related risks, and strengthening patient safety. These principles should also be an integral part of modern medical and pharmaceutical education.

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