

CLINICAL PHARMACOLOGY OF THYROID AND ANTITHYROID MEDICATION, ANTIDIABETICS, GLUCOCORTICIDS

A.Actuality

The implementation of new diagnostic and treatment methods in medical practice is dictated by the increasing influence of various environmental factors and drugs on the body, including the endocrine system. Elucidation of pathogenetic mechanisms of endocrine disorders and pathological conditions caused by hormone insufficiency or hypersecretion opens new perspectives in the development of drug preparations capable of annihilating the changes that have occurred. Knowing the pharmacodynamic and pharmacokinetic properties of hormonal preparations is necessary for clinical endocrinology to solve the problems of diagnosis and treatment of endocrine diseases, emergency states and complications caused by them.

In the last few decades, the number of hormonal and, especially, anti-hormonal preparations has rapidly risen. Elucidation of molecular mechanisms of action opens new perspectives for their use as substitution, suppression, for normalization or stimulation of endocrine glands secretion. In addition, hormonal preparations are prescribed to the patient for vital purposes in major emergencies (various types of shock, hypotension, stroke, etc.).

B.Training aim

Acquiring the clinical and pharmacological principles to justify the prescription, use, dosage regimen of hormonal and anti-hormonal drugs.

C.Teaching objectives

The student should be able:

- a) to choose a minimum complex of investigation methods to assess the pharmacodynamic effect of hormonal and anti-hormonal drugs;
- b) to analyze and appreciate the results of pharmacodynamic studies of hormonal and anti-hormonal medicinal preparations, obtained by laboratory and instrumental methods;
- c) to predict possible complications and side effects of medications in these groups;
- d) to predict adverse reactions depending on the dosage regimen of these drugs and the functional state of organs and systems of the body;
- e) to apply contemporary methods of pharmacological and non-pharmacological correction of adverse reactions caused by hormonal and anti-hormonal drugs.

D. Knowledge from previously studied disciplines and related subjects

Medical-biological disciplines. Endocrine glands and regulation of their function. Classification of biologically active hormones and substances. Structure of biochemical compounds. Cell Structure. The role of mitochondria, ribosomes in

providing vital metabolic processes in the cell. Hormonal regulation of lipid, protein and carbohydrate metabolism.

Endocrinology. Etiology, pathogenesis of the main forms of endocrine pathologies. Clinical manifestations of endocrine disorders. Functional and laboratory tests applied in endocrinology.

Pharmacology. Classification of hormonal medicinal preparations by structure and mechanism of action. Mechanisms of action, effects, indications and contraindications, side effects of hormonal preparations of the thyroid gland, pancreas, corticoadrenals.

E. Questions for self-training

1. Thyroid hormone drugs. Particularities of the mechanism of action, pharmacological effects and their manifestations, pharmacokinetics, indications and dosing principles, contraindications, adverse reactions.
2. Antithyroid medication. Classification. Particularities of the mechanism of action and pharmacological effects, pharmacokinetics, indications and dosing principles, contraindications, adverse reactions of thioamides, iodine preparations, beta-adrenoblockers, lithium preparations etc.
3. Drugs used in the treatment of diabetes mellitus. Characterization of human insulin preparations according duration of action and type of action. The metabolic effects of insulin. Absolute and relative indications. Human insulins, pharmacodynamic and pharmacokinetic particularities, indications. Insulin analogues (rapid-acting – aspart, lyspro, glulisine; long-acting – glargine, detemir, degludec). Basal and biphasic insulin. The principles of insulin dosing in diabetes. Hyper and hypoglycemic coma, choice of medication and their dosing. Adverse reactions: their manifestations and prophylaxis. Insulin resistance. The pharmacokinetics of insulin preparations, routes of administration.
4. Oral antidiabetics. Classification according mechanism of action and influence on blood glucose.
5. Sulfonylureas derivatives: the particularities of the hypoglycemic effect, other pharmacological effects, indications and dosing principles, contraindications, adverse reactions, pharmacokinetics.
6. Biguanide derivatives: the particularities of the hypoglycemic effect, other pharmacological effects, indications and dosing principles, contraindications, adverse reactions and manifestation peculiarities, pharmacokinetics.
7. Thiazolidinediones: the particularities of the hypoglycemic effect, the indications and principles of dosing, contraindications, adverse reactions and manifestations, pharmacokinetics.
8. Meglitinides: the particularities of the hypoglycemic effect, indications and dosing principles, contraindications, adverse reactions and manifestations, pharmacokinetics.
9. Tetrasaccharides and aldoreductase inhibitors: the particularities of the antihyperglycemic features, indications and dosing principles, contraindications, adverse reactions, pharmacokinetics.

10. GLP-1 receptor agonists: the particularities of the antihyperglycemic effect, indications, dosage principles, contraindications, adverse reactions, pharmacokinetics.
11. DPP-IV inhibitors: the particularities of the antihyperglycemic effect, dosage indications, dosage principles, contraindications, adverse reactions, pharmacokinetics.
12. Sodium-glucose cotransporter-2 inhibitors - gliflozins (dapagliflozin, canagliflozin, empagliflozin, etc.): particularities of the antihyperglycemic effect, indications and principles of dosing, contraindications, adverse reactions, pharmacokinetics.
13. Glucocorticoids, classification according activity, duration of action, anti-inflammatory and mineralocorticoid effect, way of administration. Genomic and non-genomic mechanism of action. Pharmacological effects (anti-inflammatory, anti-allergic, immunodepressive and anti-shock effects), the influence on organs and systems. Mechanisms of anti-inflammatory and immunodepressive action. Metabolic effects of glucocorticoids and their mechanism. Pharmacokinetics. Indications of glucocorticosteroids. Dosing depending on the nature and severity of the disease, the functional status of the liver, kidneys, adrenal cortex function. Interaction with other drugs. Cortico-dependence, clinical manifestations, prophylaxis and treatment.
14. Drugs used in endocrine emergencies (thyrotoxic crisis, myxedema coma, hyperglycemic coma, hypoglycemic coma, acute cortico-adrenal insufficiency).

F. Individual work (the 1.1 and 1.2 sequences are to be done in writing form):

1.1. Indicate the pharmacological groups and drugs used in (for): thyrotoxic crisis; myxedema; hyperthyroidism; radiation protection of the thyroid gland, hyperthyroidism and allergy to thioamides; hypothyroidism; diabetes mellitus type 1, diabetes type 2 and pregnancy; diabetes type 2 and obesity; diabetes type 2-combined treatment; diabetic ketoacidosis coma; hypoglycemic coma; acute adrenal insufficiency; chronic adrenal insufficiency; adrenogenital syndrome in children, cytokine storm in SARS CoV-2 infection.

1.2. For each indication, write the prescription(s) for the drug(s) of choice (from the list of mandatory drugs); the form of delivery and the dosage regimen should be appropriate for the respective pathology: Levothyroxine, liothyronine, thiamazole, potassium iodide, propranolol, regular human insulin, insulin aspart, insulin glargine, isophane (NPH) insulin, glibenclamide, glimeperide, repaglinide, acarbose, sitagliptin, metformin, hydrocortisone, prednisolone, methylprednisolone, dexamethasone, fluocinolone, budesonide, fluticasone.

2. Tests. Tests on Clinical Pharmacology (for faculty of medicine), Chisinau-2004, page 74.

G. Interactive activity

1. The didactic instructional work and the patient's discussion.

2. Clinical-pharmacological selection and use of drugs in endocrine disorders:

- Principles for the selection and use of drugs in diabetes mellitus type 1;
- Principles for the selection and use of drugs in diabetes type 2 and obesity;
- Principles for the selection and use of drugs in diabetes type 2 during pregnancy;
- Principles for the selection and use of drugs for combined treatment of diabetes type 2;
- Principles of selection and use of drugs for hypothyroidism and cardiovascular diseases;
- Principles of selection and use of drugs for radiation protection of the thyroid gland;
- Principles of selection and use of drugs in diffuse toxic goiter.

3. Clinical cases. *Clinical cases in Clinical Pharmacology*, Chisinau-2017, page 162.

4. Personal Drug (P-Drug) and personal treatment (P-treatment) selection according to the criteria of efficacy, safety, acceptability and cost.