

## ANTIHYPERTENSIVE AND ANTIHYPOTENSIVE DRUGS

**A. Actuality.** According to WHO data, high blood pressure is among the disease that lead to disability and death. For the treatment of this pathology, a wide range of drugs is used, which requires deep knowledge of the pharmacological properties of antihypertensive drugs. The treatment of acute arterial hypotension, frequently encountered in practice, surgical interventions, etc., requires special attention and complex urgent treatment. Thus, a more thorough research of the existing medicinal drugs is necessary, as well as the development of new, more effective and more acceptable drugs in the medication of hypotensive states.

**B. The purpose of the training:** is to familiarize students with pharmacological properties of antihypertensive and antihypotensive drugs, with formation of the skills to select the most effective drugs in the treatment of different forms of blood pressure disorder.

### **C. Learning objectives:**

a) The student **must know:** classification, mechanisms of action, effects, indications, contraindications and adverse reactions of antihypertensive and antihypotensive drugs.

b) The student **must be able to:** prescribe the mandatory antihypertensive and antihypotensive drugs in all possible medicinal forms and doses; to indicate the groups and antihypertensive drugs or antihypotensive drugs in emergency situations and different forms of blood pressure disorders.

### **D. Knowledge of previous and related disciplines necessary for interdisciplinary integration.**

Human anatomy. Cardiovascular system (heart, arteries, veins and capillaries). Structural peculiarities of blood vessels. Arteries and veins of the large and small circuit. Congenital malformations of the major blood vessels.

Histology. The structure of the muscular, musculo-elastic and elastic arteries. The functional importance of muscular and fibrous (muscular) veins.

**Human physiology.** Hemodynamics. Blood circulation speed. Laminar and turbulent circulation. Blood pressure as a physiological constant of the body. Functional blood pressure self-regulation system. The afferent and effector influence of the vasomotor centers. The role of the vegetative nervous system and hormones in the mechanisms of extrinsic regulation of cardiac activity and the mechanisms of maintaining arterial pressure.

**Biochemistry.** Peculiarities of smooth muscle metabolism. The pathophysiology. The pathogenesis of essential hypertension, symptomatic hypertension. Acute arterial hypotension: collapse, shock.

**Semiology of internal diseases.** Hypertension. Notion about hypertension of the small circuit. Classification and clinical forms of arterial hypertension. General principles of treatment.

### **E. Self-training questions:**

1. Classification of antihypertensives (neurotropic, musculotropic drugs, drugs that regulate hydrosaline metabolism, inhibitors of the renin-angiotensin-aldosterone system).

2. Classification of neurotropic antihypertensive drugs.

a) Neurotropic antihypertensive drugs with central action: classification, mechanisms of action, pharmacological effects, indications, adverse reactions.

b) Neurotropic antihypertensive drugs with peripheral action: classification.

➤ Ganglioplegics: mechanism of action, antihypertensive effect, indications.

➤ Sympatholytics: mechanisms of action, antihypertensive effect, indications.

➤  $\alpha$ -adrenoblockers: classification, mechanism of action, effects, indications, adverse reactions.

➤  $\beta$ -adrenoblockers: classification, mechanism of action, effects, indications, adverse reactions.

- a,  $\beta$ -adrenoblockers: mechanism of action, effects, indications, adverse reactions.
- 3. Musculotropic antihypertensive drugs: classification.
  - a) Potassium channel activators: mechanism of action, effects, indications, adverse reactions.
  - b) Myotropic antihypertensives with direct action: classification. Arteriodilators: mechanism of action, effects.
  - c) Nitric oxide donors: mechanism of action, effects, indications, adverse reactions.
  - d) Calcium channel blockers: mechanism of action, effects, indications, adverse reactions.
- 4. Diuretics as antihypertensives: mechanism of action, indications, adverse reactions.
- 5. Antihypertensive drugs with influence on the renin-angiotensin-aldosterone system: classification.
  - a) Converting enzyme inhibitors: mechanism of action, effects, indications, adverse reactions.
  - b) Angiotensin receptor blockers: mechanism of action, effects, indications, adverse reactions.
  - c) Renin antagonists: mechanism of action, effects, indications, adverse reactions.
- 6. Drugs used in hypertensive crises and hypertensive emergencies. Characteristic.
- 7. The general principles of hypertension treatment.
- 8. Classification of antihypotensive (hypertensive) drugs according to the mechanism
- 9. Vasoconstrictor antihypotensives: classification.
  - a) alpha and alpha, beta-adrenomimetics: mechanism of action, antihypotensive effect, indications, adverse reactions.
  - b) isothiurea derivative: mechanism of action, effects, indications, contraindications, adverse reactions.
  - c) vasoactive peptides: mechanisms of action, effects, indications, adverse reactions.
  - d) vasoconstrictor drugs with central action: bulbar stimulants, particularities of action and use, adverse reactions.
  - e) CNS stimulants (methylxanthines): mechanism of action, influence on the heart, vessels, blood pressure, indications, adverse reactions.
- 10. Antihypotensive drugs with influence on the heart: classification.
  - a) dopaminomimetics: effects, indications, adverse reactions.
  - b) beta-1-adrenomimetics: effects, indications, adverse reactions.
- 11. Antihypotensives with permissive action: the particularities of the antihypotensive action of glucocorticoids.
- 12. Plasma volume substitutes: mechanism of action, effects, indications.

**F. Individual works for the student's** (points 1, 2, 3 and 4 is obligatory and is done in written form while preparing for the lesson)

**1) To prescribe** the following drugs in all possible medicinal forms:

1. Azamethonium. 2. Caffeine sodium benzoate. 3. Captopril. 4. Carvedilol. 5. Clonidine. 6. Dobutamine. 7. Dopamine. 8. Enalapril. 9. Epinephrine. 10. Phenylephrine. 11. Hydralazine. 12. Isoturon. 13. Labetalol. 14. Losartan. 15. Methyldopa. 16. Metoprolol. 17. Moxonidine. 18. Nebivolol. 19. Nifedipine. 20. Sodium nitroprusside. 21. Norepinephrine. 22. Prazosin. 23. Propranolol

<i>Nr.</i>	Name of the drugs	<i>Forms of delivery / dose</i>
1.	Azamethonium	Sol. 5% - 1 ml in ampoules
2.	Caffeine sodium benzoate	Tablets 0.1 Sol. 10% - 1 ml in ampoules

3.	Captopril	Tablets 0.025; 0.05; 0.1
4.	Carvedilol	Tablets 0.0125; 0.025
5.	Clonidine	Tablets 0.000075; 0.00015 Sol. 0.01% - 1 ml in ampoules;
6.	Dobutamine	Sol. 0.5% - 50 ml in ampoules Lyophilized powder 0.25 in vials
7.	Dopamine	Sol. 4% - 5 ml in ampoules
8.	Enalapril/ Enalaprilat	Tablets 0.0025; 0.005; 0.01 Sol. 0.125% - 1 ml in ampoules
9.	Epinephrine	Sol.0.1% - 1 ml in ampoules
10.	Phenylephrine	Sol.1% - 1 ml in ampoules Sol. 0.25% - 10 ml (nasal drops)
11.	Hydralazine	Tablets/ dragees 0.01; 0.025 Sol. 2% - 1 ml in ampoules
12.	Isoturon	Sol. 10% - 1 ml in ampoules
13.	Labetalol	Tablets 0.1; 0.2 Sol. 0.5% - 4 ml in ampoules
14.	Losartan	Tablets 0.05; 0.1
15.	Methyldopa	Tablets 0.25; 0.5
16.	Metoprolol	Tablets 0.025; 0.05; 0.1 Sol. 0.1% - 5 ml in ampoules
17.	Moxonidine	Tablets 0.0002; 0.0004
18.	Nebivolol	Tablets 0.005
19.	Nifedipine	Tablets/ Dragees/ Capsules 0.01; 0.02
20.	Sodium nitroprusside	Lyophilized powder 0.03 in ampoules Lyophilized powder 0.05 in vials
21.	Norepinephrine	Sol. 0.2% - 1 ml in ampoules
22.	Prazosin	Tablets 0.001; 0.002
23.	Propranolol	Tablets/ Capsules 0.01; 0.02; 0.04

**2.) List the groups and drugs used in (for):** hypertensive crisis; hypertensive emergencies; pheochromocytoma treatment; neurotropic drugs with central action in arterial hypertension; peripheral neurotropic drugs in arterial hypertension; musculotropic drugs in hypertension; inhibitors of renin-angiotensin-aldosterone system in arterial hypertension; converting enzyme inhibitors in arterial hypertension, arterial hypertension with arrhythmias, arterial hypertension with hyperaldosteronism, arterial hypertension with hyperreninemia, vasoconstrictors with central action in arterial hypotension; peripheral vasoconstrictors in arterial hypotension; cardiostimulators in arterial hypotension; hemorrhagic hypotension, cardiogenic shock with hypotension, hypotension resistant to sympathomimetics, orthostatic hypotension caused by ganglioblockers and alpha-adrenoblockers; hypovolemic shock, chronic arterial hypotension.

**3.) Tables** (knowledge consolidation)

*Table 1*

**The influence of hypotensive drugs on vascular tone, cardiac output and renin secretion**

Parameters	Vascular tone		Cardiac output	Renin secretion
	Arterial	Venous		
Clonidine				
Azamethonium bromide				
Reserpine				
Doxazosin				
Propranolol				
Hydralazine				
Minoxidil				
Nifedipine				
Verapamil				
Sodium nitroprusside				

Note: to complete the table use the following signs  
“↑” – increase, “↓” – decrease, “-” – absence of the effect.

Table 2

**Adverse reactions of myotropic hypotensives**

Adverse reactions	Hydralazine	Minoxidil	Sodium Nitroprusside	Nifedipine	Verapamil
Headache					
Skin hyperemia					
Tachycardia					
Bradycardia					
Orthostatic hypotension					
Edema of lower limbs					
Constipation					
Acute rheumatoid syndrome					
Hyperglycemia					
Rebound syndrome					

Note: mark the presence of the effect using the sign “+”.

Table 3

**The comparative characteristic of clonidine and moxonidine**

Comparative parameters		Clonidine	Moxonidine
Mechanism of action	Stimulation of central $\alpha_2$ -adrenoceptors		
	Stimulation of Imidazoline-I1central receptors		
Use	Control of hypertensive crises		
	Systemic therapy of hypertension		
Adverse reactions	Obvious sedative-hypnotic effect		

	Dry mouth		
	Rebound syndrome		

Note: mark the presence of the effect using the sign “+”.

Table 4

**The comparative characteristic of angiotensin converting enzyme inhibitors and angiotensin receptor blockers**

Comparative parameters		CEI	Angiotensin receptor blockers
Content in blood	Angiotensin II		
	Aldosterone		
	Norepinephrine		
	Bradykinin		
	Prostaglandin E2		
Use	Hypertension treatment		
	Treatment of heart failure		
Adverse Reactions	Dry cough		
	Skin rash		
	Angioneurotic edema (Quinke)		
	Vertigo		

Note: to complete the table use the following signs

“↑” – increase, “↓” – decrease, “-” – absence of the effect, “+” – presence of the effect

Table 5

**Medicines used in hypotension. Their mechanism of action**

Medicines	Acute hypotension	Chronic hypotension	Cardiogenic shock	Mechanism of action
Caffeine sodium benzoate				
Izoturon				
Dopamine				
Angiotensinamide				
Deoxycorticosterone acetate				
Epinephrine				

Note: mark the presence of the effect using the sign “+”.

**4.) Problems of situation**

**1) In experimental conditions, the following variants of arterial hypertension were modeled:**

- a) Immobilization of animals with development of stress
- b) Stimulation of sympathetic nerves with peripheral vasoconstriction and tachycardia
- c) Producing a vasoconstriction by administering substances with action on smooth muscles
- d) By stimulating the juxtaglomerular apparatus of the kidneys
- e) Development of an adrenal medulla tumor
- f) Administration of angiotensin II

**Which groups and drugs will you select for the treatment of high blood pressure?  
What is the mechanism of action of these drugs?**

**2) In experimental conditions, the following variants of arterial hypotension were modeled:**

- a) Decreasing the work of the heart;
- b) Vasodilatation through sympathetic denervation;
- c) Traumatic shock with hemorrhage;
- d) Administration of alpha-adrenoblockers.

**List the possible groups and drugs for treating hypotension.  
Explain the mechanisms of action of the selected groups.**

**5) Tests for self-training** (Guide for laboratory work in pharmacology).

**G. Interactive activity**

- 1. Experimental and virtual didactic movie** (elaboration of minutes, conclusions).
- 2. Clinical cases** (Guide for laboratory works in pharmacology).
- 3. Virtual situations** (Guide for laboratory works in pharmacology).