**SYSTEMIC VASOCONSTRICTOR AND VASODILATOR DRUGS**

**(antihypertensives, antihypotensives)**

 **A. Actuality.** According to WHO’s data, arterial hypertension is among the main diseases which lead to disability and death. A great variety of medication is used for treatment of this illness, which requires deep knowledge of pharmacological properties of antihypertensive drugs.

A special attention should be also paid to the treatment of acute and chronic hypotension, a pathologic state frequently encountered in therapeutic, surgical practice etc. And which requires a complex and emergency treatment. Thus, a more thorough investigation of existing medicines, as well as the development of new, more effective and acceptable drugs in the treatment of hypotensive conditions, is required.

**B. The purpose of the training:** To familiarize the students with the pharmacological properties of antihypertensive, antihypotensive drugs and develop the skills of selecting the most effective medication in the treatment of different forms of blood pressure disorder.

**C. Learning objectives:**

1) The student must **know**: the main antihypertensive and antihypotensive drugs, their general characteristics, classification, mechanism of action, drug forms and routes of administration, doses, indications, contraindications and adverse reactions.

2) The student must **be able to**: prescribe the necessary medicine and replace it if necessary with another one; to indicate vasodilator or vasoconstrictor drugs in various forms of blood pressure and emergencies.

**D. Initial level of knowledge required for interdisciplinary integration:**

 **Anatomy.** Cardiovascular system (heart, arteries, veins and capillaries). Structural features of blood vessels. The arteries and veins of the systemic and pulmonary circulation. Congenital malformations of magistral blood vessels.

 **Histology.** Structure of muscular, elastic-muscular and elastic arteries. Functional importance of muscular and fibrous veins (amuscular).

**Physiology**. Hemodynamics. Speed of blood flow. Laminar and turbulent flow. Arterial blood pressure as a physiological constant of the body. Functional self-regulation of the blood pressure (central and peripheral components analysis). Influence and effect of vasomotor centers. Vasomotor nerves (constrictors and dilators of blood vessels). The characteristics and particularities of baroreceptors of the vascular system. Humoral influence on vascular tone (adrenaline, vasopressin, renin, angiotensin, histamine and kinins).

**Biochemistry.** Particularities of smooth muscle metabolism.

**Pathophysiology**. Deregulation of blood pressure in case of damage of the receptors, centers and vascular wall properties. Pathogenesis of essential hypertension, symptomatic hypertension.

Acute and chronic circulatory insufficiency. The renin-angiotensin-aldosterone system. Hypotension.

**Semiology of internal diseases.** Hypertension. Concept of pulmonary hypertension. Classification of AHT, clinical forms of hypertension. General principles of treatment.

**E. Self-training questions:**

1. Classification of antihypertensive drugs (neurotropic drugs, musculotrope drugs, medicines regulating hydrosaline metabolism, inhibitors of the renin-angiotensin-aldosterone system).

2. Classification of neurotropic antihypertensive drugs that reduce sympathetic tone.

a) Centrally acting antihypertensive drugs. Mechanisms of action and pharmacological effects. Indications. Adverse reactions.

b) Ganglioblockers. Classification. Mechanism of action and effects. Indications. Complications of using and their prevention. Adverse reactions.

c) Sympatholytics: Mechanism of action. Effects. Indications. Contraindications. Adverse reactions and their prevention.

d) α-adrenoblockers: Classification, mechanism of action, effects. Indications. Adverse reactions.

e) β-adrenoblockers: Classification, mechanism of action, effects. Indications. Adverse reactions and their prevention.

f) α, β - adrenoblocks. Mechanism of action, effects. Indications. Adverse reactions.

3. Musculotropic antihypertensive medication. Classification.

a) Activators of potassium channels. Mechanism of action. Effects. Indications. Adverse reactions.

b) Nitric oxide donors: the mechanism of action. Effects. Indications. Adverse reactions.

c) Calcium antagonists. 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 of vasopeptidases. Mechanism of action. Indications. Adverse reactions.

a) Angiotensin converting enzyme inhibitors. Classification. Mechanism of action. Effects. Indications. Adverse reactions.

b) Angiotensin receptor blockers. Mechanism of action. Effects. Indications. Adverse reactions.

c) Vasopeptidase inhibitors. Mechanism of action. Effects. Indications. Adverse reactions.

d) Renin antagonists: Mechanism of action. Effects. Indications. Adverse reactions.

6. Drugs used in suppressing hypertensive crisis. Their characteristics.

7.General principles of hypertension treatment.

8.The principles of classification of antihypotension drugs (hypertensive).

9. Vasoconstrictors:

a) Sympathomimetics. Classification. Pharmacokinetics. Effects. Indications, contraindications, adverse reactions.Comparative feature.

b) Ergot alkaloids and their derivatives. Pharmacokinetics. Mechanism of action. Effects. Indications, contraindications. Adverse reactions.

c) Isothioureic compounds. Mechanism of action. Effects. Indications, contraindications. Adverse reactions.

d) Musculotrope vasoconstrictors. Pharmacokinetics. Mechanism of action. Effects. Indications, contraindications. Adverse reactions.

e) Psychostimulators. Analeptics. Pharmacokinetics. Mechanism of action. Effects. Indications, contraindications. Adverse reactions.

f) General tonizers. Mechanism of action. Indications, contraindications. Adverse reactions.

g) Particularities of action and local use of vasoconstrictors

10. Antihypotensives with complex mechanism. Pharmacokinetics. Pharmacodynamics.

11. Antihypotensives with permissive action. The particularities of their action.

12. Antihypertensive drugs that increase cardiac output. Pharmacokinetics. Mechanism of action. Effects. Indications, contraindications. Adverse reactions.

13. Plasma volume substitutes. Mechanism of action. Effects. Indications.

 **F. Independent work** (is done in written form while preparing for the lesson)

**1)Brief characteristics of compulsory drugs:**

**Down:** Drug name.1. Hydrochlorothiazide. 2. Captopril. 3. Diazoxide. 4. Hydralazine. 5. Sodium nitroprusside. 6. Losartan. 7. Moxonidine. 8. Enalapril. 9. Dextran-70. 10. Deoxychorticosterone acetate. 11. Angiotensinamide. 12. Izoturon.

***Medicines with action related to the topic, to be reviewed in the previous compartments***: 1. Clonidine. 2. Methyldopa. 3. Prazosin. 4. Propranolol. 5. Atenolol. 6. Nifedipine. 7. Azamethonium. 8. Nebivolol. 9. Labetalol. 10. Caffeine sodium benzoate. 11. Epinephrine. 12. Norepinephrine. 13. Phenylephrine. 14. Carvedilol. 15. Dopamine.16. Ergotamine.

 **Across:**1. Medicinal form. 2. Way of administration. 3. Doses (therapeutic, maximal for one intake and for 24 hours). 4. Spectrum of action 5. Mechanism of action. 6. Indications and contraindications. 7. Side effects.

**2) Questions on medical prescriptions.**

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

1. Clonidine. 2. Metildopa. 3. Azamethonium. 4. Propranolol. 5. Hydrochlorothiazide. 6. Atenolol. 7. Captopril. 8. Diazoxide. 9. Hydralazine. 10. Nifedipine. 11. Sodium nitroprusside. 12. Losartan. 13. Prazosin. 14. Nebivolol. 15. Enalapril. 16. Moxonidine. 17. Labetalol. 18. Carvedilol. 19. Epinephrine. 20. Norepinephrine. 21. Phenylephrine. 22. Ergotamine. 23. Caffeine sodium benzoate. 24. Dopamine. 25. Dextran-70. 26. Deoxychorticosterone acetate. 27. Izoturon. 28. Angiotensinamide.

**Drugs used in (for):** Hypertensive crisis, diagnosis of pheochromocytoma, treatment of pheochromocytoma, mild hypertension, severe hypertension, hypertension with arrhythmias, hypertension with hyperaldosteronism, hypertension with hyperreninemia, hemorhagic hypotension, hypotension caused by overdose of CNS depressants, cardiogenic shock with arterial hypotension, sympathomimetic resistant hypotension, orthostatic hypotension, hypovolemic shock, chronic hypotension.

**3.) Tests** (Guidelines for Laboratory Work in Pharmacology).

**4.) Clinical case** (Guidelines for Laboratory Work in Pharmacology).

**5.) Virtual situations** (Guidelines for Laboratory Work in Pharmacology).

**6.) Virtual didactic movie.**

**7.) Tables**

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 |  |  |  |  |
| Azamethoniu 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 antihypertensives**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Adverse reactions | Hydralazine | Minoxidil | Sodium Nitroprusside | Nifedipine | Verapamil |
| Headache |  |  |  |  |  |
| Skin hyperemia |  |  |  |  |  |
| Tachycardia |  |  |  |  |  |
| Bradycardia |  |  |  |  |  |
| Orthostatic hypotension |  |  |  |  |  |
| Edema |  |  |  |  |  |
| 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 α2-adrenoceptors |  |  |
| Stimulation of central Imidazoline-I1 receptors |  |  |
| Use | Hypertensive crisis |  |  |
| 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 | ACEI | 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 “+”.

**8.) Solve the case:**

In experimental conditions, have been modeled the following variants of hypertension:

a) Immobilizing animals with the development of stress

b) Stimulation of sympathetic nerves with peripheral vasoconstriction and tachycardia

c) Production of a vasoconstriction by administration of substances with action on smooth muscles

d) By stimulating the juxtaglomerular apparatus of the kidneys

e) Development of a tumor of the adrenal medula

f) Administration of angiotensin II.

What groups and drugs will you select for each case of hypertension?

What is the mechanism of action of these preparations?

  A patient who suffered a car accident was hospitalized in the intensive care department. The blood pressure was 60/20 mmHg, the frequency of cardiac contractions - 140 beats / minute, pO2 - 75%.

Prescribe the drugs that will increase the blood pressure.

Explain the mechanisms of action of selected drugs.