AGENTS REGULATING VASCULAR TONE AND BLOOD PRESSURE

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ANTIHYPERTENSIVES

ARTERIAL HYPERTENSION

- **is the syndrome of increasing of blood pressure in essential hypertension and symptomatic arterial hypertensions.**

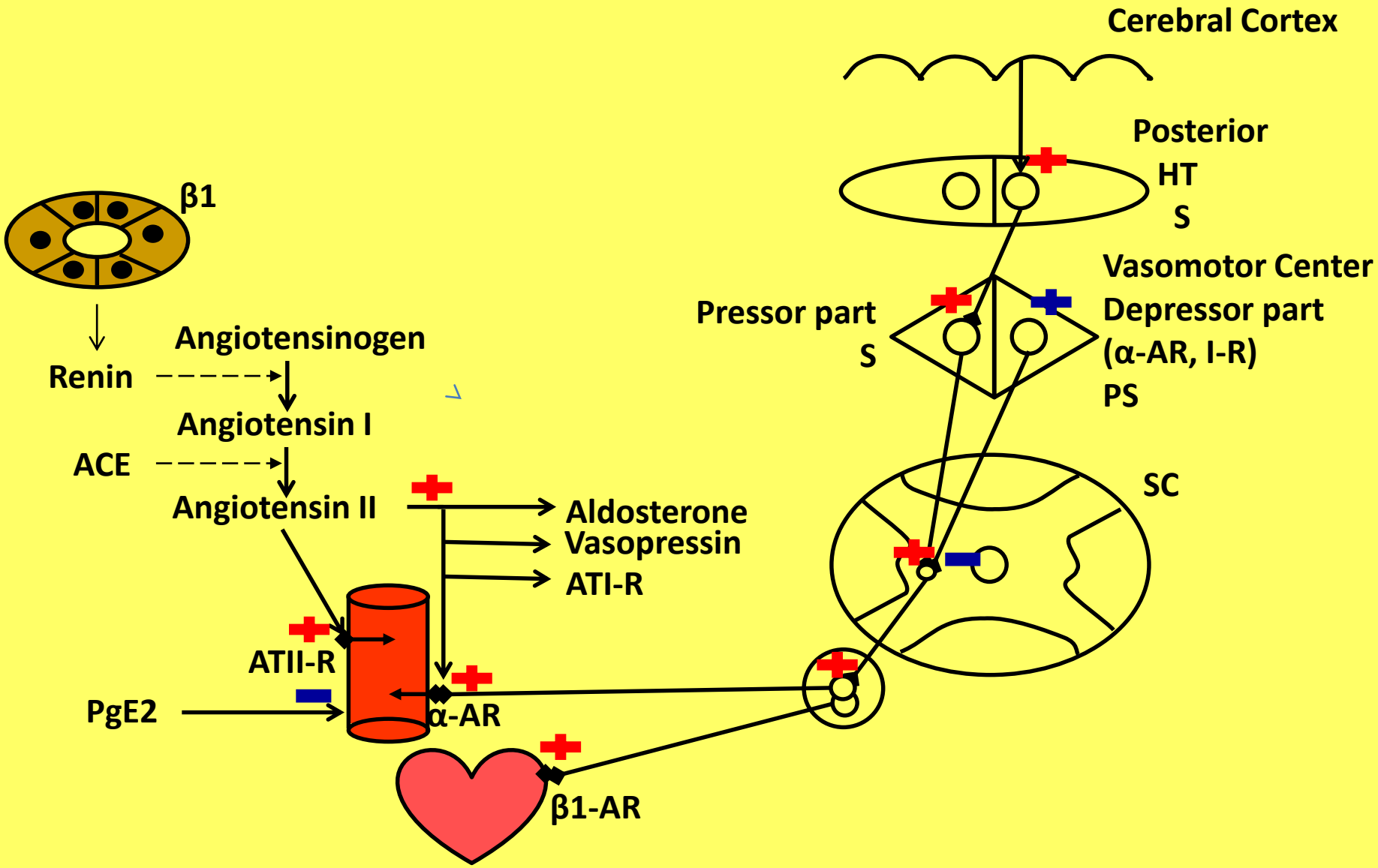
The level of blood pressure in hypertension:

SBP ≥ 140 mm Hg; DBP ≥ 90 mm Hg (anything less – optimal, normal, high normal BP)

Criteria of elevated BP are largely conditional, because there is a direct link between the level of BP and CVD, starting from the values of 115/75 mm Hg.

The GFCF. Prevention, diagnostics and treatment of arterial hypertension. Russian recommendations (second revision), 2004

SCHEME OF REGULATION OF BLOOD PRESSURE



CLASSIFICATION

I. SUPPRESSING SYMPATHETIC ACTIVITY

1. PREDOMINANTLY CENTRAL ACTION

A. AGONISTS of α2-ADRENERGIC AND I1-IMIDAZOLINE RECEPTORS

Clonidine, Methyldopa (Dopegit)

B. AGONISTS of I1-IMIDAZOLINE RECEPTORS

Moxonidine, Rilmenidine

2. PREDOMINANTLY PERIPHERAL ACTION

A. GANGLIONIC BLOCKERS

Hexametonium bromide (Benzohexonium), Azamethonium bromide (Pentamin), Trepirium iodide (Hygronium)

B. α-BLOCKERS

Phentolamine, Prazosin

C. β1-BLOCKERS

Propranolol, Atenolol, Metoprolol

D. SYMPATHOLYTICS

Reserpine, Guanetidine (Octadine), Rauwolfia alkaloids (Raunatine)

CLASSIFICATION

II. PERIPHERAL VASODILATORS

1. DONATORS OF NITRIC OXIDE

- Sodium nitroprusside

2. DIFFERENT DRUGS

- Hydralasine (Apressin), Bendazol (Dibazolum), Magnesium sulfate, Papaverine (Papaverine hydrochloride)

III. BLOCKERS of CA++ CHANNELS

- Verapamil, Diltiazem, Nifedipine, Amlodipine

IV. DIURETICS

- Watch classification of diuretics

CLASSIFICATION

V. INHIBITORS OF THE RAAS

1. ACE-INHIBITORS

A. 1st GENERATION

Captopril

B. 2nd GENERATION

Enalapril, Ramipril, Lisinopril (Diroton)

2. BLOCKERS of AT-RECEPTORS

Losartan

3.DIRECT INHIBITORS OF (SECRETION) RENIN

Aliskiren

Clonidine

MECHANISM OF BLOOD PRESSURE REDUCTION

(Watch «Scheme of regulation of blood pressure»)

It permeates through the BBB, accumulates in neurons of the depressor part of the VMC; by stimulating α2-AR it stimulates the depressor part of the VMC, which inhibits neurons of lateral horns of the SC regulating vascular tone; occurs inhibition of sympathetic effects on :

a) α-AR of vessels, vasodilation;

b) β1-AR of the myocardium, reduction of myocardial activity, a decrease of cardiac output, stroke and minute volumes;

c) β1-AR of the JGA, inhibition of the RAAS, inhibition of renin secretion.

Clonidine

Features

1.Little effect on the tone of peripheral veins.

- 2.Hypotensive response is accompanied by increased reabsorption of sodium and water, increased CBV, decreasing of hypotensive action. Clonidine is prescribed with diuretics.

3. Has a sedative and hypnotic action.

Application*

1.Hypertensic crisis.

2. Essential hypertension.

3. Other hypertensions.

SIDE EFFECTS

1.Orthostatic hypotension up to collapse (rarely).

2. Abstinence syndrome.

3. Sleepiness, fatigue, negative emotions.

* Rarely used

Prazosin

MECHANISM OF BLOOD PRESSURE REDUCTION

(Watch «Scheme of regulation of blood pressure»)

Blocks α-AR of smooth muscle layer of blood vessels, reduces the stimulating effect of NA to α-AR, vasodilation (including dilatation of renal blood vessels; increasing filtration and decreasing reabsorption of sodium and water; increasing in diuresis; reduction in CBV*).

FEATURES

1.Has an antiatherogenic effect (reduces blood levels of LDL, VLDL).

2. Positive effect on kidney's function (watch<< mechanism of blood pressure reduction >> effect on renal vessels).

3. After the first dose of the drug may occur a sharp drop in blood pressure up to collapse (a phenomenon of the first dose)**.

APPLICATION

1. Essential hypertension.

2. Other hypertensions.

SIDE EFFECTS

1.The phenomenon of the first dose (see above).

*As a result there is also a reduction of edema.

**The patient must be in a horizontal position; later – adaptation of organism.

PROPRANOLOL, ATENOLOL

MECHANISM OF BLOOD PRESSURE REDUCTION

(Watch «Scheme of regulation of blood pressure»)

Block β1-AR:

A) of myocardium, reduction of myocardial activity, a decrease in cardiac output, stroke and minute volumes;

B) of the JGA, inhibition of the RAAS, inhibition of the renin secretion.

FEATURES

1.Have a pronounced cardiodepressive effect (also used in the treatment of bradyarrhythmias, angina).

2. Nonselective β-blockers (propranolol) block β2-AR of the bronchi, causing bronchospasm.

3. Has an atherogenic effect (increases blood levels of LDL, VLDL).

PROPRANOLOL, ATENOLOL

APPLICATION

1.Essential hypertension.

2.Other hypertensions.

3.Atrial and ventricular tachyarrhythmias.

4.Prevention of angina.

SIDE EFFECTS

1.Bradycardia.

2.Hypotension.

3.Atrioventricular heart block.

4.Bronchospasm (propranolol).

5.Atherogenic effect.

6.Abstinence syndrome.

7.Hypoglycemia.

RESERPINE

MECHANISM OF BLOOD PRESSURE REDUCTION

(Watch «Scheme of regulation of blood pressure»)

1.Reduces the activity of adrenergic synapses in peripheral vessels; tone reduction and vasodilation.

2.It permeates through the BBB, accumulates in the posterior (sympathetic part) hypothalamus; decreasing of activating effect on neurons of the pressor part of the VMC, which activates neurons of the lateral horns of SC, regulating vascular tone; occurs an inhibition of sympathetic effects on:

a) α-AR of vessels, vasodilation;

b) β1-AR of the myocardium, reduction of myocardial activity, a decrease in cardiac output, stroke and minute volumes;

c) β1-AR of the JGA, inhibition of the RAAS, inhibition of renin secretion.

RESERPINE

FEATURES

1.Little effect on the tone of peripheral veins.

2.Hypotensive response is accompanied by increased reabsorption of sodium and water, increased CBV, edema (prolonged administration) and reduction of the therapeutic (hypotensive) action. Reserpine is prescribed with diuretics.

3.Has a sedative and hypnotic effect (before now were treated neuroses, psychoses).

4.Cardiodepressive effect.

RESERPINE

APPLICATION*

1.Essential hypertension.

2.Other hypertensions.

SIDE EFFECTS

1.Orthostatic hypotension up to the collapse.

2.Edemas.

3.The suppression of the psychoemotional sphere (sleepiness, fatigue, negative emotions, depression).

4.Cardiodepressive effect.

5. Bronchospasm, exacerbation of PUD and duodenum ulcer (the predominance of anterior (PSNS) HT due to the suppression of posterior (SNA) HT.

6.Provoking breast cancer*.

7.In males – gynecomastia, reduced libido*.

Now is not recommended*

CAPTOPRIL, ENALAPRIL

MECHANISM OF BLOOD PRESSURE REDUCTION

(Watch «Scheme of regulation of blood pressure»)

Inhibits ACE; reduces the content of AT II; elimination of the effect on AT II-R; dilatation of peripheral blood vessels.

FEATURES

1.With prolonged administration it decreases hypertrophy of LV and myocytes of walls of resistive type arteries, prevents the progression of heart failure and slow down a progression of LV dilatation.

2.Increases coronary and renal blood flow (e.g. it's reduced a HT of myocytes of walls of resistive type arteries). Improves blood supply to ischemic myocardium. Increases diuresis.

3.After the first dose of captopril it may occur sudden drop in blood pressure up to the collapse (first dose phenomenon).

4.There is an accumulation of bradykinin (painful cough, allergic reactions).

CAPTOPRIL, ENALAPRIL

APPLICATION

1.Essential hypertension.

2.Other hypertensions.

3.Hypertensic crisis (taken sublingually).

4.Diabetic nephropathy.

SIDE EFFECTS

1.Painful cough.

2.Angioedema.

3.The phenomenon of the 1st dose (captopril).

LOSARTAN

MECHANISM OF BLOOD PRESSURE REDUCTION

(Watch «Scheme of regulation of blood pressure»)

Specific antagonist of angiotenzin II-receptors (subtype AT1); vasodilation, decreased SVR.

FEATURES

1.Reduces the concentration in blood of adrenaline and aldosterone.

2.Reduces pressure in the pulmonary circulation, afterload.

3.Has a diuretic effect (reduce the dose when taken with diuretics).

4. Prevents the development of myocardium HT, increases tolerance to physical load in patients with CHF.

5.Doesn't prevent the destruction of bradykinin, so allergic reactions (including angioedema) are rare.

6.In patients with hypertension (without concomitant diabetes) with proteinuria reduces proteinuria, the excretion of albumin and immunoglobulins G.

7.Stabilizes the level of urea in the blood plasma.

8.No effect on the autonomic reflexes.

9.No effect on the level of TAG, total cholesterol, HDL in patients with hypertension; glycemia.

LOSARTAN

APPLICATION

1.Essential hypertension.

2.Other hypertensions.

3.Chronic heart failure.

4.Reduced risk of developing CVD (including stroke) and mortality in patients with hypertension and HT of LV.

5.Diabetic nephropathy.

SIDE EFFECTS

Side effects are rare, usually transient and don’t require discontinuation of the drug.

HYPERTENSIVES

CLASSIFICATION

I NEUROTROPIC PRESSOR ACTION

- **1. CENTRAL ACTION (depressing the depressor department of VMC)**
- **Cordiamine, Camphor, Ephedrine (Ephedrine hydrochloride), Caffeine (Caffeine-sodium benzoate, Coffein)**
- **2.PERIPHERAL ACTION**
- **A. INCREASES PERIPHERAL VASCULAR TONE (α-agonists)**
- **Norepinephrine, Phenylephrine (Mesaton)**
- **B. INCREASES CARDIAC OUTPUT (β1-adrenergic agonist)**
- **Isoprenaline (Izadrin), Dobutamine (Dobutamine hydrochloride)**
- **C. INCREASES PERIPHERAL VASCULAR TONE AND CARDIAC OUTPUT (α and β1-adrenergic agonists)**
- **Epinephrine, Ephedrine (Ephedrine hydrochloride), Amphetamine (Phenaminum)**

II MYOTROPIC PRESSOR ACTION

- **Angiotensinamide**

THANK YOU FOR YOUR ATTENTION!