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VENOTROPIC (PHLEBOTROPIC) DRUGS

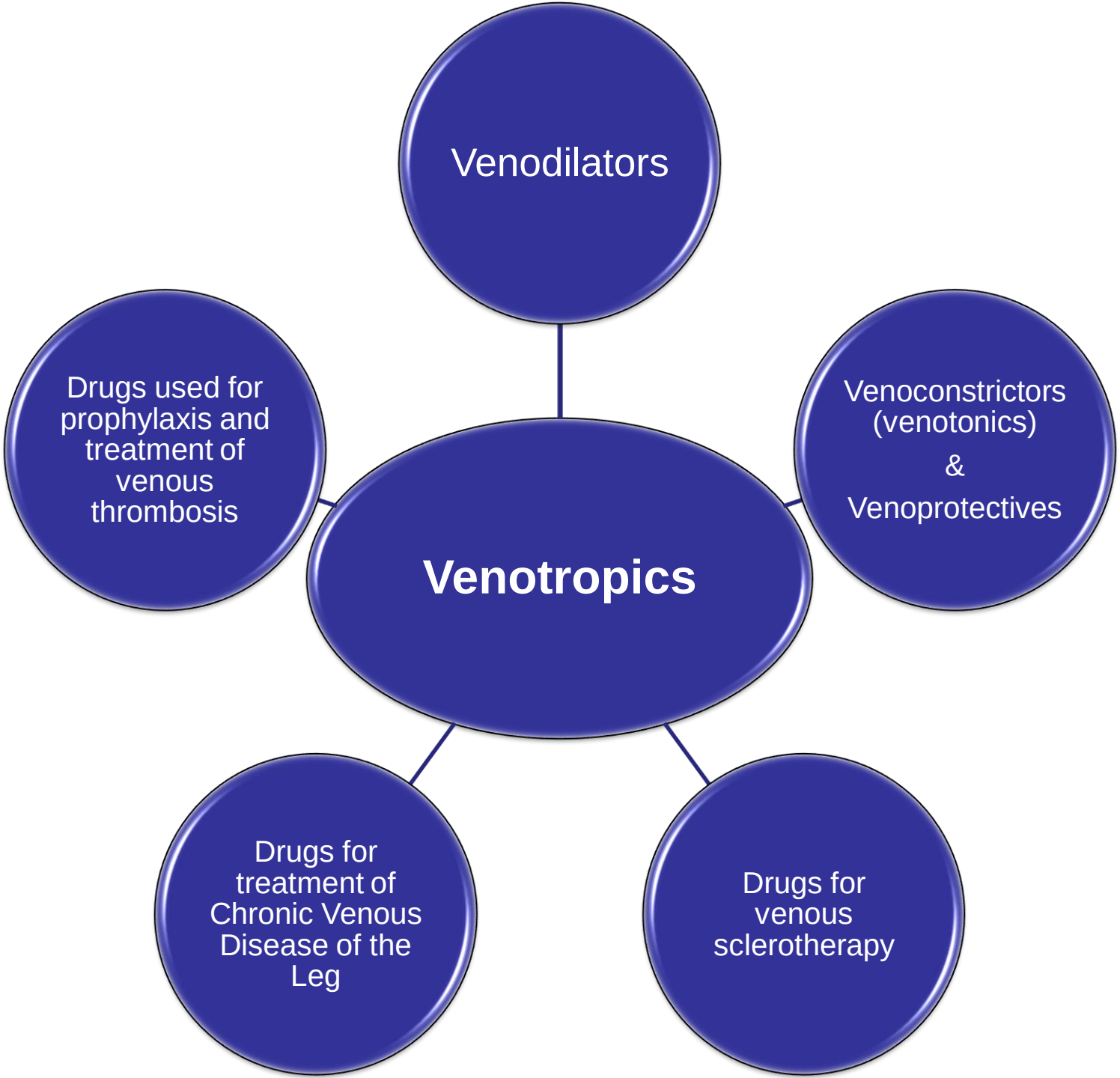
OVERVIEW

- Point prevalence of venous disease - 50%
- Classification - CEAP (clinical, etiologic, anatomic, pathophysiological)
- Symptoms - pain, oedema, itching and heaviness
- Treatment - vein surgery, endothermal ablation or foam sclerotherapy, compression stockings, pharmacological

CEAP (Clinical, Etiologic, Anatomic, Pathophysiological) Classification of Chronic Venous Disease

C Class	Description
C0	No visible or palpable signs of venous disease
C1	Telangectasia or reticular veins
C2	Varicose veins
C3	Oedema
C4a: C4b:	Skin pigmentation and / or eczema Lipodermatosclerosis and/or atrophie blanche
C5	Healed venous ulceration
C6	Active venous ulceration

Eklof B, Rutherford RB, Bergan JJ, Carpentier PH, Gloviczki P, Kistner RL, *et al.* Revision of the CEAP classification for chronic venous disorders: consensus statement. J Vasc Surg 2004; 40: 1248-52.


Venodilators
Drugs used for prophylaxis and treatment of venous thrombosis
Venoconstrictors (venotonics)
&
Venoprotectives
Venotropics
Drugs for treatment of Chronic Venous Disease of the Leg
Drugs for venous sclerotherapy

Venotropic drugs

- a group of naturally occurring or synthetic drugs that act on capillary permeability or venous tone and may therefore have a beneficial effect in patients with chronic venous hypertension.

Gohel MS, Davies AH. Pharmacological agents in the treatment of venous disease: an update of the available evidence. Curr Vasc Pharmacol. 2009 Jul;7(3):303-8. doi: 10.2174/157016109788340758. PMID: 19601855.

Venodilators

- Nitrates
- Alpha-adrenoblockers
- Sympatholytics

Venoconstrictors (venotonics) and Venoprotective drugs

- Venoconstrictive drugs increases the tone of the smooth muscles of the veins.
- Venoprotective drugs:
  - reduce or prevent damage of veins,
  - decrease the permeability of venules,
  - prevent the development of edema, inflammation, microcirculation disturbances, and subsequent destruction of surroundig tissues.

Venoconstrictors (venotonics) & Venoprotective drugs

Classification (1)

- Venoconstrictors:
  - Alpha-adrenomimetics – ethylephrine, midodrine
  - Dihydrated ergot alkaloids – dihydroergotamine, dihydroergotoxine, dihydroergocriptine

Venoconstrictors (venotonics) & Venoprotective drugs

Classification (2)

- Venoprotective:
  - Rutin & derivatives (bioflavonoids, rutosides, oxerutines) – rutin (rutoside), troxerutin (troxevasin)
  - From Ginko biloba tree – bilobil, ginkio, memoplant, gincor forte
  - Synthetics (dioxibensoles) – calcium dobesilate

Venoconstrictors (venotonics) & Venoprotective drugs

Classification (3)

- Mixed:
  - Bioflavonoids: detralex (diosmin+hesperidin), daflon (micronized purified flavonoid fraction, diosmin), diovenor (diosmin), phlebodia
  - From horse-chestnut tree: escin, reparil, eskuzan, esflazin, venoplant, anavenol (compound dr.)
  - From Ruscus aculeatus root: cyclo-3 forte (vegetal extract+hesperidine+vit.C)
  - Grape seed extract: endotelon
  - Synthetic drugs: tribenozide

Mechanisms of action of venotropics

- Improve venous tone
- Decrease white cell activation
- Decrease release of inflammatory mediators
- Decrease capillary fragility and permeability
- Decrease blood viscosity

Calcium dobesilate

- Increase lymphatic drainage
- Increase venous tone
- Improves oedema, symptoms of disease and lymphatic drainage

Oxerutins and rutosides

- Mixture of flavonoid derivatives
- Decrease capillary permeability
- Reduce free radicals
- May be used locally or systemically
- Reduce the symptoms of venous disease
- Improve haemodynamic venous function
- Rutosides - varicose veins in pregnancy

Bioflavonoids: detralex (diosmin+hesperidin), daflon (micronized purified flavonoid fraction, diosmin), diovenor (diosmin), phlebodia

- Inhibition of noradrenaline degradation by catechol-Omethyltransferase and thus indirectly increasing venous tone
- Inhibition of leukocyte adhesion and activation and therefore reducing inflammation
- Inhibition of platelet function
- Increased lymphatic drainage

Side effects of phlebotropics

- 5% of patients
  - Gastrointestinal:
    - nausea, vomiting, colicky abdominal pain
  - CNS - insomnia, drowsiness and headaches
- The use of multiple venoactive drugs at the same time is generally discouraged

Drugs for venous sclerotherapy

- **Hypertonic saline (23,4%)**
- **Detergents:**
  - **Sodium tetradecyl sulfate**
  - **Polidocanol**
  - **Chromated glycerin**
  - **Sodium morrhuate**
  - **Ethanolamine Oleate**

Vein sclerotherapy

- Sclerotherapy - endovenous chemical ablation
- Detergents - disrupt vein cellular membrane (protein theft denaturation)
- Indications – telangiectasias, reticular veins, nonsaphenous varicosities, saphenous varicosities

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Regional (antiischemic) VASODILATORS

vasodilator agents with predominant action on cerebral vessels, brain energy potential, blood rheology and platelet aggregation, as well as some broad-spectrum antispasmodics

ANTIISCHEMIC VASODILATORS

I. MYOTROPIC VASODILATORS

1. Vinca minor alkaloids

- Vincamine – vinpocetine - vincapan

2. Xanthine derivatives

- pentoxifylline - xanthinol nicotinate -aminophylline

3. Calcium channel blockers

- Nimodipine - flunarizine - cinnarizine

4. Broad profile antispasmodics

- Papaverine - papazol - nicoverine
- Drotaverine - bencyclan

ANTIISCHEMIC VASODILATORS

II. NEUROTROPIC VASODILATORS

1. Ergot alkaloids
   - Ergotamine - dihydroergotamine - dihydroergotoxine
2. Alpha-adrenolytics
   - Nicergoline - tolazoline
3. Beta-adrenomimetics
   - Isoxuprine - Bufenin - Bametan
4. Antiserotoninics
   - Cinnarizine - naphthydrofuryl - methysergide
   - Cyproheptadine - lisuride etc.
5. GABA derivatives:
   - Gamalon –aminalon -picamilon

MEDICINES USED IN THE COMPLEX TREATMENT OF CEREBRAL AND PERIPHERAL CIRCULATION (VASCULAR) DISORDERS

- In the treatment of cerebral circulation disorders, are mainly used myotropic vasodilators, preparations that influence cerebral metabolism and blood coagulability.
- Neurotropic vasodilators, xanthine derivatives, anticoagulants and antiaggregants are prioritized in the treatment of peripheral vascular disorders.

MEDICINES USED IN THE COMPLEX TREATMENT OF CEREBRAL AND PERIPHERAL CIRCULATION (VASCULAR) DISORDERS

Medicines with influence on cerebral metabolism

1. Nootropics
   - Piracetam,
   - Pyritinol
   - Gamma-aminobutyric acid and gamma-aminobutyric nicotinoyl
   - Meclofenoxate
   - Fezam (cinnarizine+piracetam), etc.;
2. Various preparations that influence cerebral metabolism
   - Instenon
   - Tanakan
   - Cerebrolysin
   - Citicoline
   - Choline alfoscerate
   - Orocetam, etc.

Medicines with influence on blood coagulability and fibrinolysis

1. Anticoagulants:
   - Direct
     - heparin, nadroparin, enoxaparin, dalteparin, reviparin, bivalirudin, rivaluridine, etc.;
   - Indirect
     - acenocumarol, warfarin, phenindione, etc.;
2. Antiplatelet agents:
   - acetylsalicylic acid, alprostadil, ticlopidine, clopidogrel, prasugrel
   - daltroban, abciximab, sulotroban etc.;
3. Fibrinolytics:
   - streptokinase, urokinase, alteplaseetc.;
4. Antifibrinolytics:
   - aprotinin, aminocaproic acid, tranexamic acid, aminomethylbenzoic acid

ALKALOIDS FROM VINCA MINOR

The mechanism of action

- Vasodilatory effect, caused by the inhibition of phosphodiesterase (10-100 times stronger than theophylline) with the increase of cAMP concentration in the smooth muscles of the vessels.
- Decrease the uptake of adenosine by various cells, including erythrocytes, with an increase in its blood concentration.
  - Adenosine causes vasodilatation effect, as well as influences the function of the formed blood elements and can be responsible for hemodynamic and metabolic effects, especially specific for the brain.

ALKALOIDS FROM VINCA MINOR

Effects

1. Increase brain blood flow.
   - Selective arteriodilation and increase of the tone of brain veins.
   - The dilation of arterial vessels leads to an increase in cerebral flow, a reduction in vascular resistance with the redistribution of blood in favor of ischemic areas.
   - Almost does not change arterial pressure, minute volume, peripheral vascular resistance.
   - Toning the cerebral veins increases venous outflow from the brain, reducing intracranial pressure and, possibly, cerebral edema, especially during the acute period of ischemic stroke.

ALKALOIDS FROM VINCA MINOR

Effects

2. Improvement of microcirculation.
   - Caused by the blocking of adenosine uptake by erythrocytes with the increase of their elasticity and deformation, which favors their passage through capillaries with more adequate tissue oxygenation.
   - Moderately inhibits platelet adhesion and aggregation with the improvement of blood rheological properties.
3. Intensification of metabolism in the brain.
   - As a result of vasodilatation, improvement of microcirculation and rheological properties of the blood – the metabolic and energetic processes in the brain are improved.
   - The use of oxygen and glucose is intensified, which contributes to increasing the resistance to hypoxia.
   - The antihypoxant effect makes the aerobic glucose splitting reactions predominate with the prevention of acidosis.

ALKALOIDS FROM VINCA MINOR

Indications

1. Acute and chronic cerebral insufficiency:
   - transient brain ischemic disorders;
   - CVA
   - residual phenomena after stroke;
   - chronic cerebrovascular insufficiency.
2. Neurological disorders of a non-ischemic nature:
   - acute hypertensive encephalopathy;
   - sequelae of cranio-cerebral trauma;
   - postoperative treatment of neurosurgical patients;
   - migraine, headache, vertigo;
   - psychobehavioral disorders in the elderly, caused by trophic changes and/or cerebral atherosclerosis;
   - neurological and mental symptoms (aphasia, dizziness, memory disorders, motor activity, etc.).

ALKALOIDS FROM VINCA MINOR

Indications

3. Otolaryngology:

- cochlear neuritis;
- auditory disorders (sensory or transmission deafness) of an ischemic or toxic nature;
- deafness in the elderly;
- Menier's disease;
- tinnitus, headache of labyrinthine origin.

4. Ophthalmology:

- ophthalmic diseases accompanied by atherosclerosis or angiospasm of retinal vessels (angiopathy and retinopathy);
- thrombosis, embolism of retinal arteries and veins;
- degenerative changes of the corpus luteum and retina;
- secondary glaucoma;
- chorioretinitis.

ALKALOIDS FROM VINCA MINOR

- Adverse reactions
  - transient hypotension;
  - tachycardia (sometimes);
  - allergic skin reactions.
- Contraindications
  - severe ischemic heart disease;
  - heart rhythm disorders and sequelae of myocardial infarction;
  - pregnancy;
  - brain tumors.

CALCIUM CHANNEL BLOCKERS
Nimodipine

- Dihydroperidine derivative.
- Prevents or removes the spasm caused by various vasoconstricting substances (serotonin, prostaglandins, histamine etc.).
- Possesses neuro- and psychopharmacological effects

CALCIUM CHANNEL BLOCKERS
Nimodipine

- Mechanism of action
  - Blocks L-type Ca2+ channels in SMC and neurons and inhibits Ca2+ influx.
- Effects
  - Influences both the cerebral circulation and the neuronal activity: it intensifies the cerebral blood flow, more pronounced in the affected regions than in the healthy ones; this effect manifests itself especially in the case of vessel spasms after subarachnoid hemorrhages;
  - Reduces fibrosis, lipid infiltration and thickening of the basal membrane in the small cerebral vessels;
  - Exerts a cerebroprotective effect, stabilizing the functional state of neurons;
  - Has a positive effect on memory and the ability to concentrate.

CALCIUM CHANNEL BLOCKERS
Nimodipine

Indications

- transient disorders of cerebral circulation;
- CVA;
- vascular spasms after subarachnoid hemorrhages;
- dyscirculatory encephalopathy with dementia;
- sequelae after ischemic stroke and subarachnoid hemorrhage, after surgical interventions in subarachnoid hemorrhage;
- migraine prophylaxis;
- cerebral circulation disorders in elderly patients (reduced memory and concentration, emotional lability, etc.).

CALCIUM CHANNEL BLOCKERS
Nimodipine

Contraindications

- Serious liver diseases, including liver cirrhosis (for tablets);
- Pregnancy, breastfeeding period (for tablets);

CALCIUM CHANNEL BLOCKERS
Nimodipine

Adverse reactions

- Cardiovascular : sudden decrease in blood pressure, tachycardia, peripheral edema, facial hyperemia, feeling of heat, sweating. When administered intravenously: bradycardia, extrasystole, collapse (rare), phlebitis.
- GIT and liver: dyspeptic disorders; increase of transaminases, alkaline phosphatase, gammaglutamyltransferase.
- CNS: sleep disturbances, increased psychomotor activity, aggressiveness, hyperkinesis, depression.
- Kidneys: renal disorders with the increase of urea and/or creatinine in the serum.

XANTINIC DERIVATIVES
Xanthinol nicotinate, aminophylline

- Mechanism of action
  - blocks A1 and A2 adenosine receptors;
  - inhibits phosphodiesterase and increases the level of cAMP and its duration of action;

- Effects
  - has a non-selective vasodilator action on cerebral vessels with increased blood flow in both ischemic and healthy areas;
  - improve the rheological properties of blood and improve microcirculation by reducing platelet aggregation;
  - amplifies the energy potential of the brain by increasing the supply of energy substances (glucose, phosphate) and intensifies their oxidation;
  - improves blood circulation in other vascular regions - of the eye, inner ear and limbs.

XANTINIC DERIVATIVES
Pentoxifylline

- Mechanism of action
  - blocks adenosine receptors;
  - inhibits phosphodiesterase and increases cAMP levels;
  - probably alpha-1-adrenoblocking and/or beta-2 adrenomimetic.

XANTINIC DERIVATIVES
Pentoxifylline
Effects

- No selectivity for specific vascular regions;
- Dilate arteries of the brain, limbs, retina and inner ear, except renal and coronary arteries;
- No important changes of systemic hemodynamics;
- Weak positive inotropic effect;
- Improvement of blood rheology and microcirculation:
  - Antiplatelet effect
    - In low doses, stimulates the formation of prostacyclin in the vascular wall and inhibits platelet aggregation.
    - High doses block platelet phosphodiesterase – inhibit synthesis of thromboxane A2;
  - Inhibit erythrocyte aggregation and ↑plasticity.
- RBC - ↑ glycogenolysis → ↑2,3-diphospho-glycerate → ↑ dissociation of oxyhemoglobin → ↑tissue oxygenation;
- ↓fibrinogen in the plasma;
- ↑ tone the cerebral veins and venous outflow from the brain.

XANTINIC DERIVATIVES
Pentoxifylline

Indications

A. Cerebral circulation disorders:

- consequences of cerebral atherosclerosis (vertigo, dizziness, memory disorders, incoherence, encephalopathy, etc.);
- CVA, including consequences;
- dyscirculatory encephalopathy.

B. Organic and functional peripheral arterial and venous circulation disorders of atherosclerotic, diabetic and inflammatory nature:

- acute peripheral ischemia; arteritis;
- chronic peripheral ischemia syndrome (endarteritis obliterans with intermittent claudication, diabetic angiopathy, etc.);
- postthrombotic syndrome, trophic ulcers of the calf, gangrene, paresthesias, acrocyanosis, etc.;
- Raynaud's disease, frostbite.

C. Acute, subacute and chronic ophthalmic circulation disorders, retinal ischemia.

D. Circulatory disorders of the inner ear with deafness.

XANTINIC DERIVATIVES
Pentoxifylline

Contraindications

- acute or recent myocardial infarction;
- severe hemorrhages (especially recent in the brain and retina);
- pregnancy;
- advanced cerebral and coronary atherosclerosis with hypertension;
- liver or kidney failure;
- hypersensitivity.

XANTINIC DERIVATIVES
Pentoxifylline

Side effects

- dizziness, headache;
- nausea, vomiting, feeling of heaviness in the epigastrium, diarrhea;
- allergic reactions: itchy rashes, hives; sometimes - anaphylactoid or anaphylactic reactions, including - angioneurotic edema, bronchospasm;
- rarely – cardiac arrhythmias, anginal pain, weakness, hypotension, feeling of heat;
- increases the level of transaminases;
- intrahepatic cholestasis, thrombocytopenia, hemorrhages.

ERGOT ALKALOIDS
Ergotamine hydrotartrate

Mechanism of action

- alpha-adrenoblocking action (partial agonist);
- blocks the reuptake of noradrenaline in noradrenergic synapses;
- acts directly on the vascular wall;
- strong serotonin antagonist.

ERGOT ALKALOIDS
Ergotamine hydrotartrate

Effects

- Increases the peristalsis of the intestines and potentiates the effect of neostigmine;
- Dual effect on blood vessels, depending on the initial tone of the vessels:
  - high vascular resistance – vasodilation
  - low vascular resistance – vasoconstriction;
- Higher rise in vascular resistance in the external carotid artery and less in the internal one;
- Venoconstriction;
- In therapeutic doses, blood pressure increases moderately;
- Sedative effect on the CNS;
- Decreases basal metabolism, tachycardia in Bazedov's disease and of sympathetic origin;
- Increases the tone of the uterine muscles.

ERGOT ALKALOIDS
Ergotamine hydrotartrate

Indications

- Postpartum uterine bleedings;
- Prophylaxis and treatment of migraine attacks;

Side effects

- nausea, vomiting, diarrhea;
- paresthesias, convulsions;
- intermittent claudication (with long-term use);
- worsening of angina pectoris, increase in blood pressure;
- transient tachycardia;
- edema.

Contraindications

- arterial hypertension; angina pectoris;
- atherosclerosis;
- Peripheral vascular diseases;
- septic conditions;
- pregnancy;
- hypersensitivity to the preparation;
- myocardial infarction.

ALPHA-ADRENOBLOCKERS
Nicergoline (sermion, nicelin)

Mechanism of action

- blocks the alpha-1 and alpha-2 adrenoreceptors;
- direct musculotropic vascular relaxing effect;
- stimulates adenylate cyclase and inhibits phosphodiesterase.

ALPHA-ADRENOBLOCKERS
Nicergoline (sermion, nicelin)

EFFECTS

- decreases the tone of the cerebral and peripheral arteries;
- decreases cerebrovascular resistance and increases blood flow, especially in the ischemic area;
- inhibits platelet aggregation;
- improves microcirculation;
- amplifies the energy potential of the brain;
- intensifies the uptake of glucose and oxygen by the neurons, and conversion of adenylates into macroergic nucleotides;
- improves the function of cell membranes, positively influences the hydro-electrolytic metabolism and increases the level of cAMP;
- intensifies DNA methylation and synthesis processes, which contribute to improving memory and learning processes;
- blood flow increases in the upper and lower limbs;
- lowers blood pressure in patients with high blood pressure.

ALPHA-ADRENOBLOCKERS
Nicergoline (sermion, nicelin)

INDICATIONS

- acute and chronic cerebral and/or peripheral circulatory disorders;
- acute and subacute ischemic stroke;
- transient ischemia;
- dyscirculatory encephalopathy;
- cerebral atherosclerosis;
- deafness and tinnitus in the elderly;
- migraine;
- thrombosis and embolism of cerebral vessels, thrombosis of retinal veins and arteries, senile disorder of the macula;
- diabetic retinopathy;
- ischemic edema of the papilla of the optic nerve;
- endarteritis obliterans;
- Raynaud's syndrome.

ALPHA-ADRENOBLOCKERS
Nicergoline (sermion, nicelin)

Side effects

- Cardiovascular:
  - dizziness, feeling of heat and hot flashes, flushing;
  - transient hypotension, postural hypotension.
- CNS:
  - drowsiness or insomnia.
- GIT:
  - anorexia, epigastric pain;
  - vomiting, gastric colic.

Contraindications

- hypersensitivity;
- arterial hypotension;
- acute hemorrhages.

BETA-ADRENOMIMETICS
Isoxuprine

Mechanism of action

- stimulation of beta-2 adrenoreceptors (less);
- direct relaxation of the vascular smooth muscles.

Effects

- improves peripheral and cerebral circulation;
- has positive inotropic and chronotropic effects;
- tocolytic action;
- Weak bronchodilator.

Indications

- peripheral circulation disorders: diabetic angiopathy, endarteritis obliterans, Raynaud's syndrome, vascular spasms, etc.;
- chronic cerebral insufficiency of atherosclerotic origin;
- retinal vascular diseases: atherosclerosis of the retinal arteries, etc.;
- Abortion prevention.

Contraindications

- recent hemorrhages;
- arterial hypotension;
- angina pectoris;
- hyperthyroidism.

Adverse reactions

- tachycardia, arrhythmias, arterial hypotension;
- dizziness, hot flashes;
- angina pains;
- restlessness, tremors;
- nausea, vomiting;
- skin rash

ANTI-SEROTONICS
Cinnarizine

Mechanism of action

- blocks slow calcium channels
- serotoninolytic, antihistaminic, cholinolytic and direct myotropic.

Effects

- Decreases vasoconstriction caused by epinephrine, norepinephrine, angiotensin and serotonin;
- Increases brain, peripheral and coronary blood flow;
- has a greater affinity towards cerebral vessels;
- reduces the influx of calcium into erythrocytes, as a result the latter are more easily deformed and circulate more easily through the capillaries while maintaining blood fluidity;
- increases tissue oxygenation;
- facilitates glucose assimilation;
- inhibits pathological vestibular reactions.

ANTI-SEROTONICS
Cinnarizine

Indications

- chronic cerebrovascular insufficiency;
- ischemic stroke;
- sequelae of hemorrhagic stroke and brain trauma;
- cerebrovascular disorders (dizziness, headaches of vascular origin, memory disorders, inability to concentrate, irritability, ringing in the ears;
- dyscirculatory encephalopathy;
- migraine (attack prevention);
- motion sickness (with prophylactic purpose);
- vestibular disorders (dizziness, tinnitus, nystagmus, nausea, vomiting of labyrinthine origin);
- peripheral vascular disorders (acrocyanosis, endarteritis obliterans, diabetic angiopathy, intermittent claudication, Raynaud's disease, trophic and varicose ulcers, paresthesias, nocturnal vascular spasms of the limbs, etc.).

Contraindications

- hypersensitivity.

ANTI-SEROTONICS
Cinnarizine

Adverse reactions

- GIT:
  - dyspeptic disorders;
  - dry mouth.

- CNS:
  - headache, drowsiness;
  - in elderly patients with long-term use – extrapyramidal disorders, depression.

- Miscellaneous:
  - weight gain;
  - sweating;
  - skin rashes;
  - cholestatic jaundice;
  - lichen ruber planus.

CLASIFICATION of DRUGS USED in MIGRANE

I. Drugs used to relieve migraine attacks

Ergot alkaloids

- Ergotamine
- Dihydroergotamine

Indol derivatives

- Sumatriptan (imigran)

Non-opioids analgezics

- Paracetamol
- Acetylsalicylic Acid
- Naproxen
- Indometacin
- Ibuprofen

Antiemetics

- Metoclopramide

II. Migraine treatment (for prophylaxis of attacks)

- Serotonergic agonists (triptans, indole derivatives)
  - Sumatriptan –Rizatriptan –Zolmitriptan –Almotriptan –Frovatriptan
- Analgesics-antipyretics
  - Acetylsalicylic acid -Paracetamol -Metamizole -Ibuprofen etc.
- Ergot Alkaloids – Ergotamine - Dihydroergotamine
- Methylxanthines - Caffeine
- Antiserotoninergic agents
  - Cyproheptadine –Pizotifen
- Isothiourea derivative - Ravimig
- ß-adrenolytics
  - Propranolol –Metoprolol –Atenolol
- Calcium channel blockers
  - Verapamil –Nimodipine –Flunarizine -Cinnarizine
- Central α-2-adrenomimetics -Clonidine
- Tricyclic antidepressants
  - Amitriptyline –Protriptyline –Doxepin
- ACE inhibitors
  - lisinopril, enalapril
- Angiotensin receptors antagonist
  - candesartan, losartan
- Combined agents
  - Vazobral -Cafergot

ISOTHIOUREA DERIVATIVES WITH ANTIMIGRAINE PROPERTIES
Ravimig

Pharmacodynamics

- inhibits NO-synthase;
- selectively constricts the carotid arteries without affecting cerebral blood flow;
- Onset of action – 20-30 minutes, relief of symptoms in 0.5-1 hour.

Idications

- treatment of migraine attacks with or without aura;
- treatment of migraine attacks associated with the menstrual period in women (algodysmenorrhea);

Side effects

- transient increase in blood pressure;
- bradycardia or tachycardia, arrhythmias;
- sensation of chest constriction;
- fatigue or drowsiness, fatigue, vertigo, nausea, vomiting;
- pain or tingling sensations, heat;
- heaviness or pressure in any part of the body;
- allergic reactions: skin rashes, urticaria, dyspnea, angioneurotic edema.

Principles of treatment of CVA

I. Support of systemic hemodynamics

- Vasopressors and cardiotonic agents
- Norepinephrine, phenylephrine increase the tone of cerebral vessels less than peripheral ones, therefore they increase, but do not reduce cerebral flow.

II. Increasing the brain's resistance to hypoxia

- The use of antioxidants - amtizole 100 - 150mg intravenously in acute and subacute strokes.

III. Rehabilitation therapy after 5 – 7 days of ICU treatment

- Nootropics (piracetam, pyritinol);
- Cerebrolysin (hydrolyzate from brain tissue with protein fixation).

Principles of treatment of CVA

IV. Improvement of microcirculation in the ischemic area

1. Combating tissue edema:
   - moderate doses of glucocorticoids (30-40 mg), which stabilize the membranes and reduce their permeability;
   - cautious use of diuretics (furosemide or osmotic diuretics (except ureea).
2. Improving the rheological properties of blood (reducing viscosity, aggregation):
   - dextran-40;
   - pentoxifylline – 100 – 200 mg intravenous infusion;
   - vinpocetine – 30 mg intravenously in 3 doses.
3. Restoring and improving the venous blood flow:
   - intensification of the work of the heart, improuvement of the microcirculation and removal of edema;
   - pentoxifylline and vinpocetine.