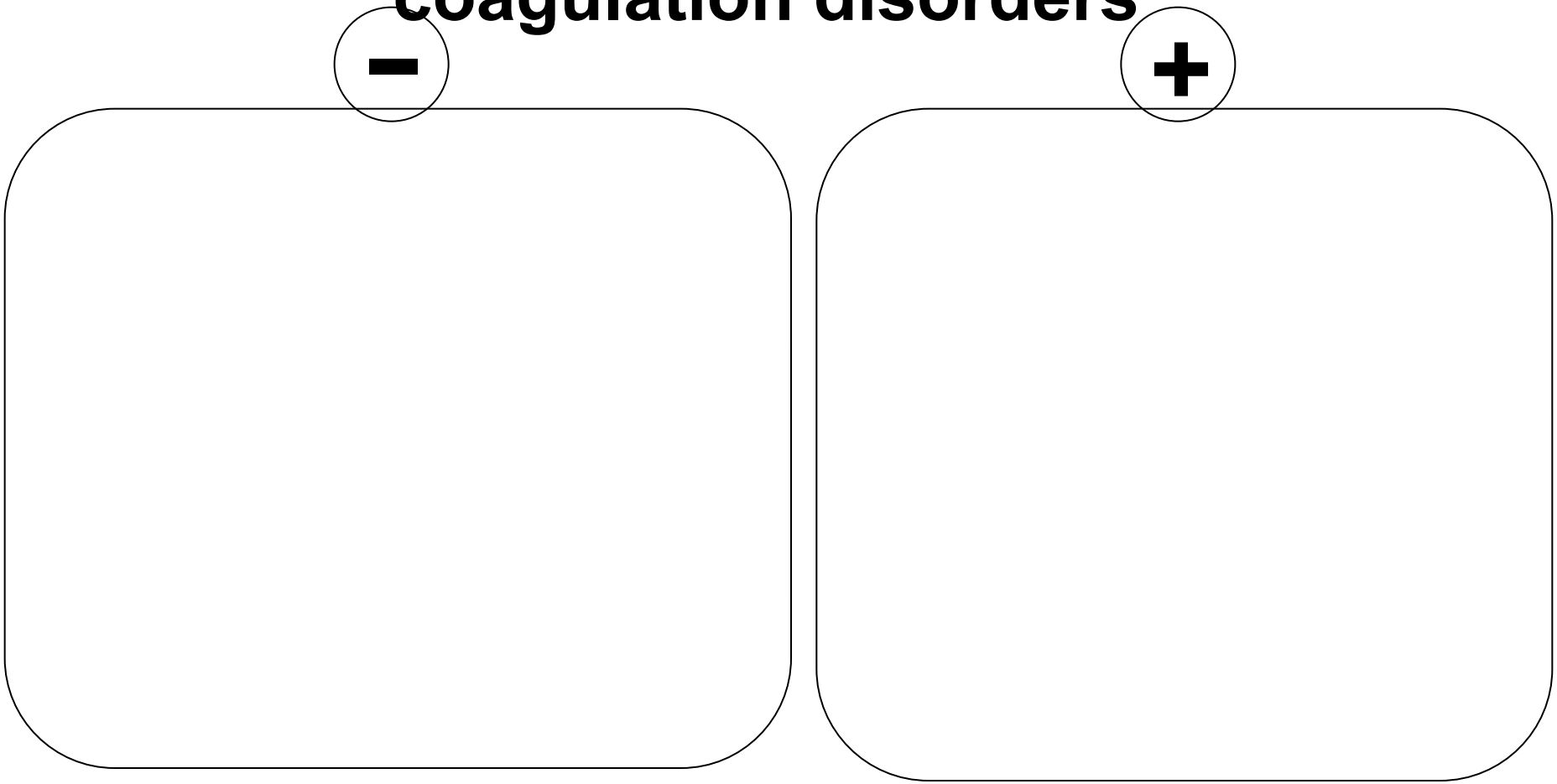
DRUGS FOR BLOOD COAGULATION DISORDERS

This study material is recommended specifically for practical courses from Pharmacology II for students of general medicine and stomatology. These brief notes could be used to prepare for the lesson and as a base for own notes during courses. Addititonal explanations and information are given in single lessons.

Drugs for the blood coagulation disorders



Anticoagulants

- drugs inhibiting blood coagulation

- monitoring of their efficacy usualy necessary - APTT orPT (INR)

Direct

- heparin and its derivatives

Indirect

- oral anticoagulants

Direct anticoagulants

Heparin

MofA: speeds up antithrombine III interactions

I: deep vein thrombosis, pulmonary embolia – therapy and prophylaxis....

CI: bleeding or risk of bleeding

AE: bleeding – GIT, urinary tract, trombocytopenia

Protamine sulphate = specific antagonist

Direct anticoagulants

Low molecular weight heparins (LMWH)

• produced by standard heparin degradation

MofA: block of Xa factor (coagulation early phase)

Nadroparin, enoxaparin, dalteparin, parnaparin, reviparin, sulodexide

• subcutaneous administration (exceptionally iv.)

Direct anticoagulants - heparinoids

- saccharide polysulphuric i.e. heparansulphate

Direct anticoagulants Sulphonated pentasaccharide

- **fondaparinux**, indraparinux

Direct anticoagulants – thrombine inhibitors

Antitrombine III

Hirudin

- lepirudin, desirudin, bivalirudin

Melagatran/ximelagatran (pro-drug), dagibatran

Indirect anticoagulants

MofA: - vit. K competitive antagonists
- induction of structurally incomplete coagulation factors

• effective in vivo only
• gradual onset of effect

AE: - bleeding
- rarely small intestine and skin necrosis

I: thrombembolism prophyklaxis

CI: - gastrointestinal ulcerations
- thrombocytopenia
- malign hypertension

Indirect anticoagulants

Warfarin
– common drug-drug interactions = ↑ risk of bleeding

Dicoumarol

Ethyl biscoumacetate

Fenprocoumon

Fibrinolytics (thrombolytics)

MofA: plasminogen activators (PA)

I. generation

non-selective→ their effect is linked with systemic fibrinolysis

- streptokinase
- urokinase

II. generation

selective firbrinolysis locally on the thrombus

- t-PA
- anistreplase
- saruplase

Fibrinolytics (thrombolytics) nonselective

Streptokinase

Urokinase

Fibrinolytics (thrombolytics) selective t-PA

- high binding capacity for fibrin
- recombinant origin

- **alteplase**
- **duteplase**
- **reteplase**
- **tenecteplase (TMK-tPA)**

Fibrinolytics (thrombolytics) selective

Anistreplase ASPAC

Fibrinolytics (thrombolytics) selective

Saruplase (rscu–PA)

Defibrinogating agents

- snake venoms

MofA: fibrinogen to fibrin conversion → consumption

Ancrod (ancrodum)

Batroxobin

Antifybrinolytics

MofA: block plasmin to fibrin binding

AE: nausea
CI: DIC

- **kyselina ε-aminocaproic acid (EACA)**
- **tranexamic acid**
- ***p*-aminomethylbenzoic acid (PAMBA)**
- **aprotinin**

Antiaggregants (antiplatelet drugs)

Modes of action

1. **inhibition of thromboxane A2 production -** COX inhibition

2. **. inhibition of thromboxane A2 production by increase of cAMP levels in thrombocytes**
   - phosphodiesterase inhibition
   - adenylate cyclase stimulation

3. **inhibition of fibrinogen bounds formation**
   - inhibition of ADP receptors
   - inhibition of IIb/IIIa receptors

Antiaggregants

Acetylsalicylic acid

MofA: ireversible COX inhibition

- dose dependant effect,usualy administered chronicaly once daily in the dose of 50-100 mg

I: AIM, nonstableAP
AIM prevention
ischemicstroke

AE: app. 20 % of patients
10-20% are ASA resistant

Antiaggregants - NSAIDs

- reversible COX inhibition

Sulfinpyrazone

Indobufen

Picotamide

Antiaggregants– pentoxyphylline

Antiaggregants– dipyridamole

Antiaggregants– tienopyridiny ticlopidin a clopidogrel

Ticlopidine

Clopidogrel

Prasugrel – 3.generation

Antiagregační (protidestičkové) látky

TXA2 antagonists

sulotroban, ditazole, dextransulphate

IIb/IIIa Rc antagonists

trigramine – from snake venom

eptifibatide, tirofiban, lamifiban

amidoximes

abciximab

Hemostatics

Local:

With vasoconstringent activity
etamsylate
ornipressin
terlipressin
desmopressin

Without vasoconstringent activity
gelatine
gelatine sponge
collagen

Systemic: frozen plasma, human fibrinogen, thrombine, coagulation factors

Therapy of anemia and hematopoietic factors

Anemy therapy– with regard to cause

Pharmacotherapy:

Iron deficiency

– **ferrous sulphate** p.o.

- malabsorption **Fe-dextrane or Fe- sorbitol** intramusculary

Folic acid deficiency

→ oral supplementation

Vitamin B12 deficiency (cobalamine)

→ **hydroxycobalamine** intramusculary

Hematopoietic growth factors

- controls proliferation, maturation and differentiation of blood cels

Erythropoietin – released from kidneys, hypoxia or massive blood loss induce relase

Thrombopoietin

CSF – regulates myeloid white cell line proliferation, produced during infections

Colony stimulating factors

G-CSF – granulocytes CSF → **filgrastim, lenograstim**

GM-CSF – granulocytes-macrophages CSF → **molgrasmostim**

Use:

- to reduce neutropenia during cytotoxic therapy
- oncology– to stimulate release of progenitor cells to peripheral blood for collection and subsequent therapeutic use after chemotherapy
- AIDS