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Drugs Acting on Blood Coagulation system and their Mechanism of Action: A review

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Review Article

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ABSTRACT

This review mainly explains about the different classes of the drugs which affects the blood coagulation and mechanism of action of the drugs on the coagulation of the blood system. The mechanism of blood coagulation is explained. The impact of different drugs on the blood coagulation system, their way of action on blood clots, the inhibition action on the receptors is clearly discussed.

INTRODUCTION

Coagulation is the process of blood clotting, which is mainly used to heal an injury or lesion or wound which finally stops bleeding. The body should have ability to control the flow of blood. The process of blood clotting and then the subsequent dissolution of the clot and repair of the injured tissue is termed as haemostasis. Coagulation involves platelet association and coagulation factor [1-6]. Usually, the process of coagulant is under the inhibitory control of several inhibitors that limit the clot formation, thus avoiding the thrombus propagation. Anticoagulants are agents are used to prevent the formation of blood clots. The mechanism of action of anticoagulation varies from drug to drug. This thrombohaemmorhagic balance is maintained in the body by complicated interactions between coagulation and the fibrinolytic system as well as platelets and vessel wall. It is important to maintain the haemostatic system. This balance sometimes may be disturbed by surgery, trauma or infectious agents [7-13].

Anticoagulants therapy is used for the prevention of coagulation and treatment of thrombosis [14-17]. The drugs like heparin, fondaparinux, and warfarin are commonly used anticoagulants; they are used as thrombin inhibitors. Novel oral anticoagulants have been invented in clinical development to treat blood coagulation disorders. Hemorrhage is the adverse effect with all anticoagulants [18-22].

BLOOD COAGULATION

It is the process by formation of blood clot to stop bleeding. This process is called hemostasis, which is the very process for survival [23-24].

Mechanism of Blood Coagulation

The first step in the process of the blood coagulation is the vascular constriction, which limit the blood flow in the injured area. Then the platelets are activated by thrombin, then these platelets and aggregate at the site of injury, forming a temporary, loose platelet plug [25-28]. Then these platelets clump by binding to collagen, finally these platelets release the nucleotide, ADP and the eicosanoid, TXA2 serotonin, phospholipids, lipoproteins, and other proteins important for the coagulation cascade. Then fibrin mesh forms and entraps the loose plug to make it

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stable. If the plug contains only platelets it is called as white thrombus, if contains red blood cells, it is called a red thrombus [29-32].

DIFFERENT CLASSES OF THE DRUGS WHICH ACT ON BLOOD COAGULATION SYSTEM

Drugs which Inhibit Platelet Function (Anti Platelet Drugs)

Platelets aggregate and form platelet to platelet adhesion. After adhesion of platelets, these platelets are activated by number of agonists such as adenosine diphosphate (ADP) which are present at the sites of vascular injury [33-37].

When a blood vessel wall is injured, platelets adhere to the collagen and von Willebrand factor in the wall via platelet receptors which leads to platelet activation [38-45]. Activated platelets release the contents of their granules including ADP and secrete TXA2 → activates nearby platelets to produce further accumulation of more platelets, then platelet aggregate and forms a platelet plug [46-51].

After this platelets are stimulated to aggregate, arachidonic acid is released from platelet phospholipids, which is converted to thromboxane A2 by the cyclooxygenase and thromboxane synthetase. As this occurs, platelet levels of cyclic AMP decrease, and ADP is released [51-59]. Both ADP and thromboxane A2 are potent stimuli for platelet aggregation [60-61]. Anti-platelet drugs acts in three ways.

Drugs act inhibiting cyclooxygenase

These drugs inhibits platelet cyclooxygenase-1, which is the key enzyme involved in the synthesis of thromboxane A 2 and there by decrease the action of aggregation of platelets [62-68]. e.g., Aspirin.

Drugs act by Inhibiting Phosphodiesterase

These drugs inhibits phosphodiesterase in platelets, thereby increase in cAMP concentration in cells which prevents the synthesis of thromboxane A 2, thereby decrease in platelet aggregation [69-73]. e.g., Dipyridamole.

Drugs act by inhibiting ADP-mediated aggregation

These drugs blocks purinergic receptors for ADP in platelet membranes thereby inhibits the ADP-induced expression of glycoprotein (GP) IIb/IIIa receptors in platelet membrane decrease in platelet aggregation [74-79]. e.g., Ticlopidine.

Drugs act by expanding plasma

These drugs are plasma expanders which lead to decrease in the vascular stasis, there by decrease platelet adhesiveness [80-86]. e.g., Dextran.

Drugs which Decrease Fibrin Formation (Anticoagulants)

These are the drugs which act by Inhibit clotting mechanism or by fibrin formation.

Drugs act Activation of anticlotting factors especially antithrombin III

These drugs binds to the antithrombin III , a protease inhibitor that complexes with activated clotting factors II, IX, X and XI and enhances the action Antithrombin III which inhibits clotting factor proteases, by forming stable complexes. Thereby prevents platelet binding [87-90]. e.g., Heparin

Drugs act by fibrin formation

These drugs act by binding to thrombin thereby by inhibiting fibrin formation. There by stops coagulation. e.g., Hirudin

Drug act by Inhibition of synthesis of blood coagulation factor precursors

These drugs act by interfering with the synthesis of Vitamin k by inhibiting epoxide hydrase. This leads to inhibition of activation of vitamin K-dependent clotting factors (II, VII, IX, X). e.g., Warfarin [91-95]

Drug Act by Activation of Fibrinolysis (Thrombolytic Drugs)

These are the drugs act by stimulating the conversion of endogenous plasminogen to plasmin, degradation both of fibrin and fibrinogen which leads stemic activation of fibrinolysis which thereby causes the dissolution of the thrombus [95-99]. e.g., Streptokinase, urokinase.

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Drugs which are Used to Affect Hemostasis

Aminocaproic acid, tranexamic acid, Desmopressin, Dihydroergotamine mesylate and Pentoxifyllin.

CONCLUSION

The vast research studies have been conducted to understand the mechanisms of different drugs which act on blood coagulation system, which helped in invention of many anticoagulant therapies. These therapies helped to improve the management of the bleeding in patient. The mechanism of the action still more drugs should be discovered and more anticoagulant drug should be invented to improve the quality of therapies.

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