Hemostasis disturbances in patients with acute pancreatitis and the ways of their correction

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Acute pancreatitis (AP) is characterized by a range of symptoms - from local inflammation to a heavier form (acute necrotizing pancreatitis), which is associated with systemic inflammatory response and high mortality. The development of acute necrotizing pancreatitis usually associated with necrosis of pancreatic acini. Apoptosis acinar cells release cytokines, activation of coagulation, tissue ischemia and necrosis are key factors in the deterioration and the development of appropriate ekstrapankreatychnyh complications [8].

Acute pancreatitis induces severe inflammatory response in experimental animal models and humans, and this is independent of the initiating factor damage acinar cells [47]. The pathophysiologic mechanisms of this disease include premature activation of trypsinogen activation, followed by coagulation and inflammation cascade systems, resulting in damage to acinar pancreatic cells and activated leakage of enzymes and pro-inflammatory compounds perypankreatychni tissue [19]. Bold pro-inflammatory mediators in general circulation causes a systemic inflammatory response syndrome [47]. The main mediators of inflammation AP is a tumor necrosis factor-α (TNF-α), interleukin (IL) 1, 6 and 8 and chemokines platelet activating factor [61].

Mediators of inflammation, in turn, may affect hemostasis. Ways of inflammation and coagulation are closely related. For example, proinflammatory cytokines (TNF-α, IL-1β) are avtokrynno and paracrine activating neutrophils and monocytes. These cytokines also activate endothelial cells, increasing the synthesis of adhesion molecules, including P- and E-selectin and chemokines. This leads to the selection of leukocytes to the site of injury. Activated monocytes and endothelial cells express tissue factor (TF), which initiates the coagulation cascade and may also be expressed by cells damaged pancreas. The complex TF / factor VIIa activates factor X to Xa (or factor XI to XIa), a complex of factor Xa / factor Va converts prothrombin to thrombin. Thrombin not only forms a fibrin clot, but also is a potent stimulator of receptor-1 protease activated. Activation of this receptor is proinflammatory responses, including the secretion of cytokines and growth factors, and increases the synthesis of adhesion molecules. While clotting associated with inflammation in inflammatory processes, proteases, derived from inflammatory infiltrate cells, activated pathways involved in coagulation and fibrinolysis [42].

The degree of systemic disorders of hemostasis at AP ranging from subclinical activation of coagulation, which can only be detected using sensitive markers of activated coagulation factors to lightning syndrome, disseminated intravascular coagulation (DIC), which is characterized by multiple systemic microvascular thrombosis and profuse bleeding from different areas. Multiple organ dysfunction syndrome and DIC - serious complications and the main factors that contribute to high mortality in the AP [75]. These complications are the result of micro-circulating disorders and microvascular thrombosis that caused damage endothelial cells of blood vessels and hypercoagulation [72]. Ultrastructural changes in the pancreas in the AP in humans include infiltration of polymorphonuclear leukocytes stroma and parenchyma, intra- and extravascular accumulation of platelets and mikrotrombov in blood vessels [21].

When AP disturbances in coagulation system / fibrinolysis are closely associated with the severity of the disease and dysfunction of organs. Value of coagulation and fibrinolysis in the AP depends on complex interactions activators and inhibitors of clotting and fibrinolysis, as well as the reactions of other proteolytic mechanisms that interact with them. In practice, these complex interactions lead to the prevalence of a process at different stages of the AP, and which one will prevail - difficult to predict.

Changes in hemostasis with pancreatitis may have prognostic value, and the data of animal studies suggest that inhibition of hemostasis can affect the severity of the disease [58].

Inflammation can initiate coagulation at several points in the primary and secondary hemostasis systems. Inflammatory cytokines - key mediators of the immune system, among them IL − 6 may stimulate platelet production [110]. Platelets, which are produced in response to inflammation are more thrombogenic, with increased sensitivity to platelet agonists [32]. Infectious agents and numerous inflammatory mediators may be platelet activators, including bacterial endotoxin, thromboxane $A_{2,}$ platelet activating factor and cathepsin G (an enzyme that is released by neutrophils). To activate platelets, which is caused by inflammation, may further aggravate the inflammatory response in two ways. First, activated platelets aggregated to provide a negatively charged phospholipid surface is necessary for secondary hemostasis. The end result of secondary hemostasis - formation of thrombin. Thrombin is traditionally seen as a catalyst for the conversion of fibrinogen to fibrin, but by itself it is a potent agonist of platelets and inflammatory mediators [53]. Thrombin modulates the inflammatory system by binding to specific cell surface receptors group known as proteazaktyvovani receptors [91]. Second, activated platelets interact with endothelial cells, stimulating adhesion and recruitment of inflammatory leukocytes. Activated

platelets can synthesize IL-1β, which increases the adhesive properties of endothelial cells [100].

The adhesion of platelets to sites of vascular damage is a multistage process that involves interactions between receptor and platelet adhesion ligands subendotelialnymy [90]. The initial attachment of platelets to collagen mediated subendotelialnoho Willebrand factor - a large multimeric protein secreted by activated endothelial cells and platelets [71]. Level Willebrand factor significantly increased after induction of severe acute pancreatitis in rats [107].

Sticky platelets are activated and change shape, becoming spherical and ekstruzuyuchy long filopodiyi that enhance platelet-platelet interaction. Activated platelets release ADP from their dense granules and synthesize and release thromboxane $_{A2}$ [51]. Released ADP and thromboxane $_{A2}$ binding to different receptors on adjacent platelets and activate them, thereby attracting additional platelets at the site of injury. Activated platelets also secrete the content of their alpha granules (eg Willebrand factor, platelet-derived growth factor, coagulation cofactors V and VIII) [80]. Finally, activated platelets contribute to blood clotting using phosphatidylserine expression negatively charged phospholipid which is usually found on the inside of the cell membrane of platelets [34]. The concentration of clotting factors on the surface activated platelets leads to explosive thrombin generation.

Evidence of increasing platelet activation associated with pancreatitis has been demonstrated in experimental animal models. The introduction of rabbits ascites of patients with chronic pancreatitis caused aggregation and platelet activation [77]. When AP platelets were activated and their indexes (average volume of platelets, the ratio of large platelets, platelet distribution width) - increased between onset and remission AP [12]. The average volume increased platelet AP at [11]. However, other authors point to the decline of this indicator [62]. In AP patients during hospitalization observed increased platelet activation, as reflected in the increasing number of large platelet concentrations of markers of degranulation (platelet factor 4 and β-trombohlobulin) expression of glycoprotein IIb / IIIa [78].

Increased platelet response characteristic of AP patients easy, while reducing the number of platelets (due to the increased consumption of platelets) observed in severe AP. Low levels of platelets in the plasma of patients with AP also associated with poor clinical outcome [16]. Changes of platelet aggregation activity in severe Ass related to the development of renal, hepatic insufficiency and Thrombocytopathy [2].

Simultaneously with the activation of platelet coagulation occurs in three steps, overlapping: initiation, amplification and propagation [46]. Cloth factor is the "spark" that triggers blood clotting. Under normal conditions it is not expressed

by cells that are in direct contact with the blood. [23] After TF wall endothelial damage, however, enters the bloodstream, where it can freely communicate with factor VIIa plasma, forming a complex of TF / factor VII [60].Tissue factor is also expressed by macrophages and monocytes after stimulation of inflammatory mediators [63].

Numerous mediators and products of inflammation are prokoahulyatsiynyy effect on secondary hemostasis, including TNF-α and other proinflammatory cytokines, lipoproteins, C-reactive protein, bacterial endotoxins, as well as the activation of complement [56]. These mediators initiate clotting by increasing the expression of tissue factor on endothelial cells, circulating monocytes and macrophages [41]. Induction of tissue factor promotes coagulation via an external way; coagulation progresses through a common pathway of coagulation (conversion factor X to factor Xa), which leads to the formation of thrombin [42, 106].Rolls develop after the formation of thrombin. Mediates inflammation and coagulation using a mechanism that is independent of tissue factor path, monocytes, activated inflammation can directly activate factor X to catalyze the conversion of prothrombin to thrombin [68].

Tissue factor forms a complex with a small amount of circulating activated factor VII (FVIIa) and acts as a cofactor for improving the ability of F VIIa convert FX to FXa and FIX into FIXa on the cell surface [60]. FXa activates FV and together they convert small amounts of prothrombin to thrombin [96]. This is known as the initiation stage clotting. During the amplification phase small amount of thrombin generated initiating positive feedback tion by further activating FV and thus increases the formation of thrombin [69]. Large-scale generation of thrombin complex formation begins with Tanase (tenase complex) (consisting of FVIIIa and FIXa) complex and prothrombinase (FXa and consists FVa) on the anion surface of activated endothelial cells or platelets [46]. It is thrombin burst, further generates fibrin from fibrinogen. The rapid formation of thrombin activates Factor XIII and trombinaktyvovanyy fibrinolysis inhibitor (Taif). Factor XIIIa then able to sew a thread of fibrin to support and stabilize the fibrin meshwork, while protecting Taif clot formed from plazminoposeredkovanoho fibrinolysis [95].

The level of TF in the plasma of patients with AP is higher than in healthy people, although no statistically significant difference in the level of TF depending on the severity of the disease [36]. Plasma concentrations of TF in alcoholic AP with severe necrotizing pancreatitis significantly higher than in severe alcoholic AP or without pancreatic necrosis with nonalcoholic AP with severe necrotizing pancreatitis. These results confirm that the increase in plasma TF may be associated with the development of pancreatic necrosis with severe alcoholic AP. However, E. Andersson et al. [101] indicate that tissue factor may be an early marker of severe AP.

High levels of tissue factor inhibitor in patients with severe combined AP in violation of thrombin formation and development associated with organ dysfunction and the risk of death [99].

Other measurements of blood clotting is prothrombin time (PT) and activated partial thromboplastin time (APTT) that control external and internal ways of curtailing respectively. Clinical studies have shown elevated in patients with PT SE [29]. However, there were no reports of significant deviations in APTT or F1 + 2 levels in patients with AP [99]. However, in another study, PT and APTT were extended at AP was reduced level of fibrinogen [4].

Despite the fact that these measurements confirm hemostatic disorders earlier in the AP, their usefulness in predicting the disease is limited. Clinical studies in which measure other parameters (especially D-dimer and antithrombin III - AT III) showed better sensitivity and specificity in predicting the course than PT or APTT.

Acute pancreatitis is also characterized by impaired fibrinolysis. On the one hand, there are conditions for activation of fibrinolysis Inland way as activation of factor XII (Hageman factor) in the area of contact of blood with damaged endothelium. Moreover, the conditions of synthesis endotoxemia significantly activated endothelial tissue plasminogen activator (tPA), which leads to marked activation of fibrinolysis. On the other hand, inflammatory mediators (IL-1 and TNF-α) dramatically increases the activity of plasminogen activator inhibitor, thereby inhibiting the fibrinolytic potential of blood.

If AP is a severe coagulopathy, mainly by reducing the total number of platelets and fibrinogen concentration in plasma, especially as a result of activation of fibrinolysis [3]. However, it was shown that in patients with severe AP hypercoagulable state associated with the growth of production at constant fibrin fibrinolysis [105].

First, during inflammation increases fibrinolysis by increasing the release of plasminogen activators of epithelial and endothelial cells, monocytes and neutrophils [52]. Tissue plasminogen activator converts plasminogen to plasmin, which is responsible for the dissolution of fibrin intravascular rolls. [70] In the extracellular matrix urokinaznyy plasminogen activator (ALM) and its receptor are also to initiate fibrinolysis through activation of plasminogen to plasmin [67]. Inflammation then reduces the fibrinolytic system through significantly increased production of plasminogen activator inhibitor type 1 (PAI-1), which acts as a strong inhibitor of TAP and the UAP. Regulation of PAI-1 mediated inflammatory cytokines (such as TNF-α) and C-reactive protein [93]. Fibrinolysis also suppressed by generating zymohenu trombinaktyvovanoho inhibitor of fibrinolysis. TAIF activation depends on a large number of the generation of thrombin and thrombin's ability to complexing with thrombomodulin. Activating

TAIF inhibits fibrinolysis by reducing indirect plasminogen activation, which leads to lower generation of plasmin [93].

Fibrinolytic system prevents the deposition of fibrin, preventing thus excessive accumulation of fibrin in the field of vascular injury and restore blood flow. Plasmin, an enzyme that dissolves the fibrin clots formed in the presence of plasminogen TAP or ALM. Plasmin breaks down fibrin, which results in the production of fibrin degradation products (eg, D-dimer) [9].

Established that the level of performance of internal combustion engines (low levels of platelets and AT III, hi-cue level of D-dimer) and complex thrombin / antithrombin III at admission associated with increased severity and poor prognosis AP [16]. Fourfold increase in D-dimer levels were complicated AP marker [24]. Patients with severe AP who died had significantly higher levels of D-dimer, and PAI-1 than those who survived. [33] High concentrations of D-dimer, and PAI-1 in patients with AP show hypercoagulable and microvascular coagulopathy that can lead to the formation mikrotrombov strengthen and multiple organ failure.

Some researchers confirm that the levels of D-dimer and antithrombin III can be used as indicators of severity AP and its consequences [28, 79].

In patients with severe AP marked activation of intravascular coagulation [1]. In hemostaziohrami was reduced clotting time, prothrombin index and increased concentration of fibrinogen in the blood, shortened activated partial thrombin time and also increased the amount of soluble fibrin monomer complexes.

Trombinaktyvovanyy inhibitor of fibrinolysis is carboxypeptidase 58 kDa which is synthesized in the liver and circulates in the plasma as zymohenu activated in the main complex of thrombin / thrombomodulin and becomes activated enzyme (TAIF) [22]. TAIF acts as a tissue plasminogen activator inhibitor type-dependent fibrinolysis [74]. This reduces the formation of plasmin by cleavage of lysine residues on the surface of fibrin (and can be a bridge between coagulation and fibrinolysis) [18]. In addition to suppression of fibrinolysis, TAIF may also be involved in inflammatory processes [7]. TAIF role as a natural anti-inflammatory molecule study indicating its ability to inhibit activated complement factors - C3a and C5a, and proinflammatory mediators - bradykinin and thrombin cleaved osteopontin. [55] Given the unique biochemical activity of TAIF, he may participate in inflammation AP.

Trombinaktyvovanyy fibrinolysis inhibitor increases with AP [73]. Its assessment of patients with AP in combination with other markers of inflammation may provide additional information to assess the severity of the disease.

Increased blood clotting in the AP and can contribute to shortage of natural anticoagulants.

There are three main endogenous anticoagulant inhibitors path of tissue factor (ISHTF), antithrombin III and protein S (PS) [54]. Inflammatory conditions causing a reduction in the expression and function of antithrombin III and activated protein C (APS), while the concentration ISHTF sequence does not change [108]. In patients with severe AP was marked by low levels of platelets, AT III and PS [99].

Antithrombin III, an inhibitor of plasma serine protease (serpin), is synthesized and secreted by the liver, has a wide inhibitory activity for enzymes in the coagulation cascade, particularly thrombin and factor Xa [64]. Inhibition of enzyme antithrombin III is slow but accelerating about 1000 times in the presence of negatively charged polysaccharides, such as heparin pharmacological and heparansulfat, which is found on the surface of endothelial cells [25]. Stimulatory effect of heparin and heparansulfatu pentasaharydnoyu mediated by a unique sequence that binds with high AT III affinity. Binding of this sequence is pentasaharydnoyi conformational change in AT III, which facilitates its interaction with FXa but not thrombin. To accelerate the inhibition of thrombin antithrombin III, heparin must bind together with antithrombin III and thrombin, a process that connects with the enzyme and inhibitor in triple complex [25]. Antithrombin III also has anti-inflammatory properties by inducing the release of prostacyclin from endothelial cells, inhibition of the interaction of leukocyte-endothelium (eg rolinhu and adhesion), inhibition of pro-coagulating cellular signaling pathways and changes in the expression of cell receptors that modulate the release of lysosomal proteases interleukins and soluble intercellular adhesion molecules [42].

In inflammatory lesions antithrombin III consumption and inactivated by proteolysis; in severe conditions of its functional activity decreased to 50% of normal [39]. Endogenous heparynopodibni endothelial glycosaminoglycans, which increase the activity of antithrombin III, reduce product release of neutrophils and inflammatory cytokines [39], leading to a further reduction of antithrombin III.

In patients with low AP AT III (<69%) showed at the hospital, which was associated with a poor prognosis. [16]

The second aircraft is a natural anticoagulant, vitamin K-dependent glycoprotein that is synthesized in the liver. Way PC provides anticoagulant response "on site" and "on demand" when thrombin generated [40, 43]. Damage to blood vessels triggers a cascade of coagulation, which ultimately leads to the formation of thrombin and formation of blood clots. Then excess thrombin binds to thrombomodulin - a receptor that is found on the surface of endothelial cells of blood vessels. Binding of thrombin with thrombomodulin is crucial for effective activation of protein C [50], and that this interaction is a significant change in the specificity of thrombin, which increases the speed of splitting of protein C in ~ 1000. Convert to PS aPC increases about 20 times *in vivo* receptor protein C

endothelial cells (EPCR - endothelial cell protein C receptor) [66]. EPCR binds circulating protein C and presents it in a complex of thrombin / thrombomodulin. Activated protein C in combination with its cofactor protein S spoils clotting cofactors Va and VIIIa on the surface of negatively charged phospholipids (eg, activated platelets) [84].

Inflammation way inhibits protein C, primarily due to inhibition of thrombomodulin receptors and transcription of endothelial cells to protein C, which reduces the ability to generate aPC [39, 83]. Neutrophil elastase cleaves thrombomodulin on endothelial cells, thereby significantly reducing the activity of thrombomodulin. While other ranks, reducing the concentration of protein C in severe inflammation is to increase consumption and weakened ability to synthesize protein due to hepatic dysfunction [39].

Significant changes of PC was found in experimental AP and AP in humans [17]. In rabbits rapid decline in aircraft observed after induction of acute necrotizing pancreatitis [82]. Consistent definition of PS AP patients showed differences between patients, survivors and dead patients. In patients who survived, watched a progressive normalization of plasma SS, while not dead, he was promoted [33]. Reducing aircraft may reflect an increase in consumption, vascular leakage or breach of PS synthesis in the liver [57]. Activate but insufficient to generate aPC may be associated with the development of multiple organ failure in severe AP [103].

The third natural anticoagulant - an inhibitor of tissue factor path (TFPI - tissue factor pathway inhibitor), an inhibitor of serine protease Kunitz-type, produced by monocytes, macrophages, liver and endothelial cells [59]. It is stored mainly in three different areas of the body: blood platelet cytoplasm bound to the endothelium [31]. TFPI forms a quaternary complex with TF, FVIIa and factor Xa, thereby further preventing the production of factor Xa and IXa using complex TF / VIIa and thrombin generation more blocking factor Xa. [37]

ISHTF anti-inflammatory effects include decreased activation of leukocytes and expression of TNF-α [86].

T. Yasuda et al. [75] investigated the level ISHTF patients AP. The blood plasma of patients with AP it was significantly higher than in healthy volunteers and in severe concentration ISHTF AP was higher than in the light. Increase ISHTF probably positively correlated with the severity, the degree of necrosis and frequency of organ dysfunction.

Modulation hemostasis can be an attractive strategy for treating AP. Animal models include administration of activated protein C to improve microcirculation (lower mikrotromboutvorennya) and reduce inflammation. Other strategies aimed at pro-coagulating factors such as platelet activating factor (TFF), platelets and factor VIIa.

Recombinant human aPC (Drotrecogin alfa activated; Xigris®) is the first biological agent to improve survival of patients with severe sepsis associated with AP [35, 45]. The study of protective properties *in vivo* and *in vitro* have shown that aPC has not only anticoagulant, but cytoprotective effect on the signaling molecules involved in inflammation, apoptosis and vascular permeability [48]. The protective effect of APS in severe sepsis probably reflects its ability to modulate the complex changes associated with pathophysiological mechanisms of sepsis.

The importance of protein C in antykoahulyatsiynyh mechanisms in AP first studied in rabbit models. Induction grave AP resulted in a marked decrease in APS [82]. P. Chen et al. [5] found aPC effects on coagulation mechanisms at AP. When AP in rats caused tauroholatom sodium previous administration of 50 mg / kg APS led to a significant reduction in serum TNF-α, IL-8, pancreatic matrix metalloproteinase − 9 (MMP − 9), an enzyme that breaks down a wide range of components of the extracellular matrix (eg, collagen, fibronectin, gelatin). In addition, the introduction of APS rats resulted in a significant increase thrombomodulin and EPCR in the pancreas receptors are important for the activation of protein C was shown to increase endotoxins sheddinh membrane to produce soluble EPCR EPCR using MMP-9 [38], which responds to increasing inflammatory cytokines [109]. It is assumed that aPC treatment inhibits the expression of MMP-9, thus reducing sheddinh EPCR EPCR for increased expression of endothelial cells in the pancreas. The use of activated protein C in experiments with AP reduced levels of IL − 8 and increased expression of thrombomodulin [6]. Aktyvovanyy antykoahulyatsiynymy protein C has anti-inflammatory properties and depending on its relationship with receptors on endothelial cells. If aPC is separated from the receptor, it can form a complex with protein S cofactor for proteolytic inactivation of cofactors Va and VIIIa, to provide anticoagulant effect [42]. When aPC is bound to the receptor, generated by intracellular signals that inhibit apoptosis, reduce the expression of nuclear factor κB, and adhesion molecules induced TF [42]. These cell responses are used to directly reduce inflammation.

Positive therapeutic effects of APS in the AP has been demonstrated in different models [5, 30, 94], but other researchers have noted a positive effect on the survival APS [104]. Thus, research to verify the therapeutic effects of aPC treatment in animal models of AP gave different results.

The use of activated protein C in the clinic at the AP had failed [15]. However, given that this randomized clinical trial 16 patients received only APS requires further evaluation of efficacy [65].

Modulation of platelet activating factor also studied at the AP in the experiment [97]. FAT is a vasodilator and retseptorozv'yazuvalnyy lipid that activates basophils, endothelial cells, platelets and neutrophils. Inhibition of TFF

using antagonist or an enzyme that accelerates its degradation (acetylhydrolase), reduces inflammation, reduces proinflammatory cytokines [76], activation of pancreatic enzymes [87], and improves survival [27], hemodynamics [88]. However, the clinical use of antagonists TFF had a positive effect [44].

Also studied the therapeutic effect of reducing the inflammatory activity of platelets while maintaining their hemostatic properties. Inflammatory role of platelet-prodemon strovano in a study where the introduction of the supernatant platelet deficiency mice restored normal platelet recruitment of leukocytes [98]. In tseruleyinoviy model AP depletion of platelets because of antibody (anti-GP1bα) reduced many tokens serious AP, including amylase, necrosis of acinar cells, interstitial hemorrhage in the pancreas, inflammatory infiltration of neutrophils, myeloperoxidase pancreatic inflammatory protein-2 of macrophages during gastric cancer (MIP-2), circulating leukocytes and neutrophils [89]. This study, along with others, has shown that platelets have a proinflammatory effect, causing the synthesis of chemokine MIP-2 in cells of the pancreas (macrophages and acinar cells) [85, 92], the main signal for the infiltration of neutrophils and chemotaxis [20, 26]. So focus on the inflammatory nature of platelets may have therapeutic potential in reducing damage to the pancreas and severity AP [89].

The effect of inhibiting FVIIa AP in experimental conditions was investigated by infusion taurodeoksyholatu [102]. Introduction inhibitor FVII and N-acetylcysteine for 90 minutes before induction AP caused a significant reduction in myeloperoxidase in distant organs such as the lungs and ileum, and reduced in plasma levels of IL-6 and MIP-2 [102]. This study confirms that koahulyantni mediators may be a potential therapeutic target for reducing the severity of AP.

However, given that the use of recombinant FVIIa significantly improves the coagulation in patients with severe AP and reduces the risk of bleeding in nekrsekvestrektomiyi [10]. However FVIIa does not improve internal coagulation and does not reduce mortality.

In tauroholatindukovanomu experimental pancreatitis in rats high doses of AT III improved survival [81]. In tseruleyinindukovanomu AP in rats AT III slowing down the release of HMGB1 (high mobility group box 1 protein), and other pro-inflammatory cytokines and NO [14]. When antithrombin III binds to endogenous glycosaminoglycans endothelial cells, it conveys anti-inflammatory effects, such as increased formation of prostacyclin, decrease the activation of nuclear factor κB, and reduced activation and leukocyte adhesion to endothelial cells [42]. This anti-inflammatory effect disappears when antithrombin III heparin binds to exogenous [49]. However, the analysis randomized studies have confirmed the effectiveness of AT III in reducing total mortality in critically ill patients [13].

These results indicate that disturbances in coagulation is a characteristic feature in the AP and associated with the severity of the disease. The results of experimental animal studies and in clinical confirm that modulation of hemostasis may provide a therapeutic target for the treatment of AP. Inhibition of coagulation cascade can prevent intravascular coagulation and inflammation in the pancreas and distant organs, thereby preventing the occurrence of systemic complications in patients with acute pancreatitis.

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Hemostasis disturbances in patients with acute pancreatitis and the ways of their correction

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Key words: acute pancreatitis, platelets, coagulation, fibrinolysis, anticoagulants

The literature review imposed the experimental and clinical data on the changes in the hemostatic system at acute pancreatitis. The reasons of hemostatic disorders and possible ways of its correction were identified. Disturbance in the coagulation is a feature at acute pancreatitis and is associated with disease severity. The results of experimental studies in animals and clinical studies suggest that modulation of hemostasis can provide a therapeutic target for the treatment of this disease. Inhibition of the coagulation cascade can prevent intravascular coagulation and inflammation in the pancreas and distant organs, thereby preventing systemic complications in patients with acute pancreatitis.