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STATE AND TREATMENT OF THE HEMOSTASIS SYSTEM IN BURN SHOCK

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КУЙИШ ШОКИДА ГЕМОСТАЗ ТИЗИМИНИНГ ҲОЛАТИ ВА УНИ ДАВОЛАШ

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СОСТОЯНИЕ И ЛЕЧЕНИЕ СИСТЕМЫ ГЕМОСТАЗА ПРИ ОЖОГОВОМ ШОКЕ

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Резюме. Глобал миқёсда комбустиологияда гемостатик таъсирга эга имплантларни яратиш ва улардан фойдаланиш бўйича бир қатор илмий тадқиқотлар олиб борилмоқда, аутодермопластикадан кейин шикастланган фокус эпителиоцитларида репаратив регенерация жараёнларини рағбатлантиради [1]. Уткир куйиш токсикози босқичидаги ўлимнинг асосий сабаблари метаболик ва микробиал келиб чиқадиган эндоген интоксикатсия билан биргаликда йчрингли-септик асоратлардир [2]. Бу, айниқса, тана юзасининг чуқур куйиши билан эрта сепсис ривожланиш хавфини оширади. Барча турдаги жароҳатлар орасида куйиш частотаси 10-12% ни ташкил қилади. Шу билан бирга, оғир куйишларда ўлим даражаси ҳатто ихтисослаштирилган шифохоналарда ҳам юқори бўлиб қолмоқда ва унинг босқичига қараб ўзгариб туради [3, 4]. Ўлимнинг энг юқори фоизи (65 дан 95% гача) токсемия ва септикоксемия даврида содир бўлади. Куйиш касаллигида ўлимнинг бевосита сабаблари доимий сепсис, пневмония, тарқалган томир ичидаги коагулятсия ва уларнинг фонидида органлар етишмовчилигидир. Комбустиологияда куйишларни даволаш бўйича катта тажрибага қарамай, кўплаб беморлар ногирон бўлиб қоладилар ва шунинг учун жиддий тиббий ва ижтимоий муаммодир.

Калит сўзлар. Гемостаз, куйиш шоки, коагулятсион некроз, тарқалган интраваскуляр коагулятсия, тери ишемияси, аутодермопластика, некрэктомия.

Abstract. On a global scale, in combustiology, a number of scientific studies are being carried out on the creation and use of implants with a hemostatic effect, stimulating the processes of reparative regeneration in the epitheliocytes of a damaged focus after autodermoplasty [1]. The main causes of mortality in the stage of acute burn toxemia are purulent-septic complications in combination with endogenous intoxication of metabolic and microbial origin [2]. At the same time, the risk of developing early sepsis increases, especially with deep burns on the surface of the body. The frequency of burns is 10-12% among all types of injuries. At the same time, lethality among those who were severely burned remains high even in specialized hospitals and varies depending on its stage [3, 4]. The largest percentage (from 65 to 95%) of deaths occurs during periods of toxemia and septicotoxemia. The immediate causes of death in burn disease are constant: sepsis, pneumonia, disseminated intravascular coagulation and, against their background, developing multiple organ failure. Despite the vast experience in the treatment of burns in combustiology, a large number of victims become disabled, so they represent a serious medical and social problem.

Keywords. Hemostasis, burn shock, coagulative necrosis, disseminated intravascular coagulation, skin ischemia, autodermoplasty, necrectomy.

Introduction. Mortality among those with severe burns remains high even in specialized hospitals and varies depending on its stage. The largest percentage (from 65 to 95%) of deaths occurs during periods of toxemia and septicotoxemia. The immediate causes of death in burn disease are constant: sepsis, pneumonia, disseminated intravascular coagulation and, against their background, developing multiple organ failure [5]. Despite the vast experience in the treatment of burns in combustiology, a large number of victims become disabled, so they represent a serious medical and social problem. The introduction into medical practice of cheap, import-substituting, without side effects, effectively hemostatic and wound-healing drugs from local raw materials is important.

The aim this work is to assess the state of the coagulation, anticoagulant and fibrinolytic links of the hemostasis system in burn shock, acute burn toxemia and septicotoxemia.

Research methods. Methods of clinical, instrumental, laboratory studies and therapeutic measures in 217 victims with deep burns who were treated at the Samarkand branch of the emergency medical ambulance from 2017-2019. The observed patients, depending on the method of treatment used, were divided into 2 groups:

Group I (control) - in 105 (48.4%) patients with deep burns, homeostasis was corrected and early operations were performed without the use of a composite polymer material.

Group II (main) - 112 (51.6%) patients with homeostasis correction, prevention of blood loss during surgery, early surgical intervention with a composite polymer material in victims with deep burns.

Table 1. Distribution of victims according to the mechanism of injury (n=217)

Mechanism of injury	Total		1st group		2nd group	
	n	%	n	%	n	%
Boiling water	75	34.5	37	17	38	17.5
Fire	46	21.2	twenty	9.3	26	12
Explosion	63	29	31	14.2	32	14.7
Clothes on fire	33	15.2	17	7.9	16	7.4
Total:	217	100.0	105	48.4	112	51.6

Note: * - the difference between the signs is statistically significant ($p < 0.05$).

Table 2. The distribution of patients into groups in accordance with the Frank index

Frank index	I group		II group		Total	
	n	%	n	%	n	%
<30 units, favorable	ten	4.61	eleven	5.07	21	9.67
30-60 units, relatively favorable	75	34.56	78	35.94	153	70.51
61-90 units, doubtful	fifteen	6.91	17	7.83	32	14.75
>90u, unfavorable	5	2.30	6	2.76	eleven	5.07
Total:	105	48.39	112	51.61	217	100.0

Note: $p > 0.05$ means the statistical homogeneity of the compared groups.

Patients of both groups were representative in terms of age, total area of superficial and deep burns. Among the observed patients, there were 141 (65%) men and 76 (35%) women, aged 18 to 74 years.

The main etiological factors that led to thermal injury were boiling water (73; 33.6%), fire (51; 23.5%), flash (47; 21.6%) and clothing fire (30; 13.8%). The data available in Table 1 indicate that both groups were basically comparable in terms of the mechanism of injury.

In patients, the area of the lesion was assessed according to the generally accepted rule of "nine" proposed by AB Wallace, and according to the "palm" (I.I. Glumov, 1953), the depth of the lesion was determined in accordance with the 4-degree classification of A.A. Vishnevsky et al [7].

Most often, burns were localized in the area of the trunk and limbs (32.5%), head and limbs (27.2%), trunk (14.6%). Isolated lesions of the face and lower extremities were typical for contact burns. Multiple localization was observed in 26 (12%) patients who received flame or boiling water burns. Inhalation trauma combined with skin burns was observed in 28 patients (12.9%). Usually, they had a severe course of burn shock.

Concomitant diseases were revealed in 20.3% of the victims. These were mainly diseases of the cardiovascular system (13.8%) and were typical for persons of mature and elderly age.

We have studied the morphological manifestations of DIC in the internal organs of 19 people who died in the acute stage of burn disease. DIC was diagnosed in all patients during their lifetime by laboratory methods. Their age ranged from 18 to 75 years, the burn area was from 25 to 90% of the body surface ($64.6 \pm 4.8\%$ on average), the life expectancy after injury was from 1.5 to 12 days. The main causes of death were pneumonia, sepsis and burn shock.

We have developed a technique for modeling a deep thermal burn in rats using a hot liquid. Under general anesthesia with halothane vapor, under sterile conditions, the rat was fixed on the operating table in the prone position. Temperature control of the water at the point of contact with the skin, accurate fixation of the exposure time, tightness made it possible to reproduce identical burn wounds in terms of area and degree of burn. A 3rd degree burn was achieved with a contact time of 9 ± 1 sec.

Methods of treatment. The generally accepted complex of pathogenetic treatment of burn patients included infusion-transfusion therapy, administration of antibiotics, heparin, clinical nutrition, and symptomatic therapy. The main principle for the prevention and treatment of patients with DIC was the elimination of factors that caused the activation of intravascular coagulation (removal of foci of necrosis, which are the source of thromboplastin, elimination of intoxication, hypoxia, acidosis, correction of water and electrolyte disorders, treatment of infectious complications). In the hypercoagulable phase, therapy was started with the administration of heparin. The greatest anticoagulant effect of heparin was manifested against the background of a high content of AT-III. AT-III deficiency was replenished by transfusions of fresh frozen plasma. In the treatment of patients with DIC, preference was given to low molecular weight heparin (fraxiparin, clexane). To enhance the antithrombotic effect of heparin, antiplatelet agents (chimes, pentoxifylline), proteolysis inhibitors (gordox, contrycal) were used. Be sure to carry out infusion therapy with crystalloids and colloidal solutions. Of the colloidal preparations, amino starch derivatives were preferably used, because they have a pronounced disaggregation effect and do not cause the development of hypocoagulation. In the treatment of DIC in the stage of hypocoagulation, antiproteases (gordox, contrykal) and transfusions of fresh frozen plasma up to 1500 ml per day are indicated. Transfusion of fresh erythrocyte mass was performed when the hemoglobin content was less than 60-80 g/l, and platelet mass - if the number of platelets did not reach $40-60 \times 10^9/l$.

Operational interventions. Necrectomy operations (231 in total) were performed for III-IV degree burns in 209 patients (90.3%), of which early necrectomy (the first stage from days 1 to 7) - 120 patients, delayed - 97 (Table 3). In group II, 21 patients underwent multiple microperforation, and 91 patients underwent necrotomy. It should be noted that in the 2nd group with correction of hemostasis, early necrectomy was performed 2.87 times more often, and delayed necrectomy - 3.22 times less often.

Table 3. The nature of surgical interventions in burned patients (number of patients / number of operations)

Accompanying illnesses	Group I, n=105		II group, n=112		Total, n=217	
	n	%	n	%	n	%
Early necrectomy	31	29.5	89	79.5	120	55.23
Delayed necrectomy	74	70.5	23	20.5	97	44.7
Multiple microperforations	-	-	21	18.75	21	9.7
Osteonecrectomy	one	0.9	2	1.8	3	1.4
Amputation, disarticulation	1/2		2/3		3/5	
Autodermoplasty	118	112.4	113	100.9	231	106.4

The effectiveness of the ongoing therapeutic measures was evidenced by the lower frequency of repeated autodermoplasty : in the 1st group it was 112.4%, while in the 2nd group it was 100.9%.

With IV degree burns, 1 patient also underwent osteonecrectomy , and in 2 patients, disarticulation of the shoulder, amputation of the thigh (1), lower leg in the upper third (1), fingers and phalanges of the hand (5).

8 patients were not operated on (group 1 - 6 (5.1%) patients, group 2 - 2 (1.8%) patients), with extensive deep burns (more than 40% of b.t.) and thermal inhalation injury (TIT) due to the severity of the condition, who died from sepsis and multiple organ failure 3-15 days after the injury. Clinical, laboratory, instrumental and morphological research methods were used to study hemostasis disorders. Based on the treatment of victims of burn shock, we, like many researchers, believe that adequate infusion-transfusion therapy should be carried out on the day of admission of the patient, the necessary and qualitative composition of infusion therapy played a decisive role in the intensive care of burn shock. We have chosen the well-known Parkland formula as the base volume of one-day infusion therapy. In the control group of patients - 105 people (48.4%) with severe burns, homeostasis was corrected and early surgery was performed without the use of a composite polymer material. Necrectomy was performed in 105 (100%) patients, of which early necrectomy was performed in 31 patients (the first stage after 7 days), delayed necrectomy was performed in 74 patients. Starting from 2016, the system of early surgical treatment of burn patients in the burn department began to be more widely implemented. Surgical treatment of burn wounds is aimed at removing non-viable tissues in various ways at the earliest possible time. Subsequent restoration of the skin graft was performed immediately after necrectomy (immediately). In the absence of confidence in the stability of the achieved hemostasis and in the radical removal of non-viable tissues, skin grafting was performed after 24-48 hours of delay.

Upon admission to the hospital, we assessed the degree of burn shock by the deficit of circulating blood volume (BCV). The vast majority of patients (51.6%) had a deficit of BCC (plasma loss) from 20 to 30% of the initial significance, which corresponded to the II degree of burn shock. In contrast, (30.5%) patients were diagnosed with I-degree, 17.9% - with III-degree burn shock. In addition to the BCC deficiency, upon admission to the hospital, the Algovver index was studied , which had a direct dependence on the severity of plasma loss . According to the data obtained, for a severe degree of plasma loss , an increase in the Algovver index from 0.54 in the 1st degree to 1.45 in patients with the 3rd degree of plasma loss was characteristic . Therefore, these data point to deeper changes in the homeostasis system in patients with severe burn shock. The study of the state of the BCC and its components showed that the severity of the changes was directly proportional to the degree of burn shock. Upon admission to the hospital in patients with deep burns, there was a statistically significant decrease in the total BCC from 67.5±0.4 ml/kg to 53.9±0.4 ml/kg, respectively, I- and III-degree of shock. BCC deficiency also varied according to the severity of burn shock, amounting to 10.9±0.4% in I-degree, 22.0±0.3% in II- and 32.9±0.7% in III-degree. Structural indicators of BCC in patients with I-degree of shock did not differ significantly from those in the control group, although there were statistical differences between them. These changes were most clearly expressed in the group of patients with moderate and severe shock. This was evidenced by a decrease in circulating plasma volume (CVV), globular blood volume (GO), and circulating protein volume (CVV). After the therapeutic tactics, aimed at both correcting homeostasis disorders and complex anti-shock therapy, there were significant changes in the direction of improving BCC. Such a favorable trend was the most typical for patients with mild and moderate degree of burn shock. However, despite the positive dynamics of indicators, in the group of patients with severe shock, even after the measures taken, the worst indicators of BCC, VCP, BCG and GO remained.

Upon admission to the clinic of patients with deep burns of 20-25% of the body surface, there is a slight activation of the blood coagulation system, a decrease in hematocrit and suppression of fibrinolytic activity of the blood. In contrast, in patients with grade II shock, on admission to the clinic, an increase in the blood coagulation system was observed along with a continuing inhibition of fibrinolytic activity. This is evidenced by the lengthening of the PTI index to 94.6±3.8% (P<0.05) and the decrease in plasma heparin tolerance to 256.3±11.8 sec (P<0.05). Fibrinolysis statistically significantly decreases to 8.09±0.42% (P<0.05), and hematocrit to 33.1±1.4 due to intense loss of blood cells and hemoconcentration .

Research results . Studies of the hemostasis system parameters in 59 victims in the toxemia stage showed the development of DIC, manifested by thrombocytopenia, hypofibrinemia, against the background of accelerated clot lysis, a decrease in the level of AT-III, an increase in RFMK (Table 4).

The same changes in the parameters of the hemostasis system were also found in patients with deep burns of more than 30% of the body surface and those who underwent severe shock. However, due to high blood loss and a sharp decrease in VCP, the changes were more pronounced. Some activation of the hemostasis system was noted (heparin tolerance was 253.4±21.3 sec, thrombotest - 4.06±0.2, PTI decreased to 87.6±3.1%, P<0.05). Fibrinolytic activity was 6.58±0.69% (P<0.05), hematocrit decreased to critical values (19.1±2.1%, P<0.05).

In our opinion, the main screening test kit that allows you to quickly assess the course of DIC in burned patients is platelet count, prothrombin time, APTT, thrombin time, fibrinogen, AT-III, and fibrin monomer. It should be said that in a comprehensive assessment of the condition of the burned person, it is necessary to take into account other laboratory tests: hematocrit, hemoglobin level, red blood cell count, blood gas indicators, protein, electrolytes (potassium, sodium) and functional tests of the liver, kidneys.

The study of the influence of the severity of thermal injury in the stage of septicotoxemia on the nature of changes in the parameters of the blood coagulation system was carried out in 50 patients aged 18 to 75 years. The studies were carried out in 3 comparative groups: group 1 - 15 burnt patients with a Frank index (FI) up to 60 units ;, group 2 - 20 patients with IF from 60 to 90 units. and group 3 - 15 patients with IF over 90 units. The conducted studies showed that in 15 patients of the 1st group (sepsis) there was a shortening of the blood clotting time (5.5 ± 0.5 min), an extension of the plasma recalcification time to 66 ± 3.8 sec and 82 ± 4.2 sec to the end of the 1st - 3rd day. In the 2nd group of patients (severe sepsis with MOF), the time of blood clotting after the burn was 3.6 ± 0.3 min, the time of plasma recalcification was shortened to 40 ± 5.0 sec. and by the end of the third day was 76 ± 3.8 sec. In the 3rd group of burn patients (septic shock with refractory hypotension), the blood clotting time was 4.0 ± 0.4 min. and on the third day it increased to 5.8 ± 0.5 min. The plasma recalcification time was shortened to 33 ± 7.8 sec on the first day and remained reduced by the end of the third day. An increase in the concentration of fibrinogen was noted in the victims, both in the 2nd and 3rd groups already from the first day after the burn. In patients with the threat of burn sepsis, the initial period of the development of DIC was observed: thrombocytopenia, an increase in the level of RFMK against the background of a decrease in the activity of physiological anticoagulants. Timely detection of this life-threatening complication, adequate and early correction of the hemostasis system is the key to a favorable outcome of the disease.

Conclusions . In the acute period of burn disease, the initial period of the development of DIC is observed: thrombocytopenia, an increase in the level of RFMK against the background of inhibition of the anticoagulant mechanisms of the hemostasis system. In the stages of toxemia and septicotoxemia , the time of blood clotting, plasma recalcification , APTT, prothrombin and thrombin time are reduced, the concentration of AT-III drops sharply, and the concentration of fibrinogen increases by more than 2.5 times. Acceleration of the process of blood coagulation is carried out both by external and internal mechanisms.

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СОСТОЯНИЕ И ЛЕЧЕНИЕ СИСТЕМЫ ГЕМОСТАЗА ПРИ ОЖГОВОМ ШОКЕ

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Резюме. В мировом масштабе в комбустиологии проводится ряд научных исследований по созданию и применению имплантатов с гемостатическим эффектом, стимулирующих процессы репаративной регенерации в эпителиоцитах поврежденного очага после аутодермопластики [1]. Основными причинами летальности в стадии острой ожоговой токсемии являются гнойно-септические осложнения в сочетании с эндогенной интоксикацией метаболического и микробного генеза [2]. При этом возрастает риск развития раннего сепсиса, особенно при глубоких ожогах поверхности тела. Частота ожогов составляет 10-12% среди всех видов травм. В то же время летальность среди получивших тяжелые ожоги остается высокой даже в специализированных стационарах и варьирует в зависимости от ее стадии [3, 4]. Наибольший процент (от 65 до 95%) летальных исходов приходится на периоды токсемии и септикотоксемии. Непосредственные причины смерти при ожоговой болезни постоянны: сепсис, пневмония, диссеминированное внутрисосудистое свертывание и на их фоне развивающаяся полиорганная недостаточность. Несмотря на большой опыт лечения ожогов в комбустиологии, большое количество пострадавших становятся инвалидами, поэтому представляют собой серьезную медико-социальную проблему.

Ключевые слова. Гемостаз, ожоговый шок, коагуляционный некроз, диссеминированное внутрисосудистое свертывание крови, ишемия кожи, аутодермопластика, некрэктомия.