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## INFLUENCE OF OZONE THERAPY ON FIBRINOLYSIS, PROTEOLYSIS INDICES IN BLOOD OF EXPERIMENTAL RATS WITH PYOINFLAMMATORY PROCESSES AGAINST THE DIABETES BACKGROUND

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**Key words:** *diabetes, pyoinflammatory complications, fibrinolysis, protective properties, ozone therapy.*

**Abstract.** *Experimental study of 35 white rats with pyoinflammatory processes against the background of diabetes using ozone therapy revealed improvement of the regulation indices of blood aggregation state, decrease of hypercoagulation manifestations: increase of time of plasma recalcification, activated partial thromboplastin time, prothrombin time, thrombin time, activation of thrombocyte-vascular hemostasis; significant protective properties with decreased azoalbumin lysis, total nonenzymatic fibrinolytic activity and proteinase activity by Kunitz in blood plasma are detected.*

### Introduction

Diabetes topicality is caused by the fact that in more than 30-70% of patients pyoinflammatory processes develop and 50% of hospitalized patients need surgical care for purulent-necrotic complications [2, 5]. The rapid progression of purulent-necrotic foci is caused by the development of polymorphic aerobic and anaerobic non-clostridial infection, which is often irresponsive to most antibiotics [3, 5]. Purulent infection and diabetes complicate the course of one another. Mortality caused by DM with purulent surgical infection, as well as a few decades ago, remains high - from 6 to 44.4% [1, 4].

Thus, pyoinflammatory complications of soft tissues in patients with diabetes are a complex surgical problem. That is why the course of pyoinflammatory processes of soft tissues in diabetic patients requires further study to optimize its correction.

### Objective

To study experimentally the influence of ozone therapy on the course of pyoinflammatory processes in diabetes.

### Material and methods

The experimental study was conducted on 35 white mature rats. The control group numbers 8. Diabetes was simulated by subcutaneous administration of alloxan (100mg per kg of body weight). Rats of the first experimental group (10) received subcutaneous administration of fecal suspension (pool of 20 animals' feces was diluted with 0.9% sodium chloride solution) at a dose of 0.5 ml per 100g of body weight. On the 14th day after alloxan administration the animals of the second

experimental group (9) were injected 10% feces suspension subcutaneously. The animals of the third group (8) with simulated DM were administered fecal mixture subcutaneously and during the next three days ozonized 0.9% sodium chloride solution was administered intraperitoneally once a day at the rate of 1.0ml per 100g of body weight.

Ozonation of sterile 0.9% sodium chloride solution was carried out by the apparatus "Boson" until the concentration of ozone in isotonic sodium chloride solution was 20 mg/ml.

### Discussion of the results of the study

Assessment of the system of unlimited proteolysis, fibrinolysis activity and average weight molecules of blood plasma under conditions of purulent processes of skin and subcutaneous tissue in mature rats revealed increase of azocasein lysis and average weight molecules concentration in blood plasma (Table 1).

Assessment of regulation system of aggregation state of blood under conditions of purulent processes development in mature rats revealed (Table 2) decrease of time of plasma recalcification, thrombin time, increase of adhesive thrombocytes percentage and index of platelets spontaneous aggregation, indicating activation of platelet-vascular hemostasis and coagulation system of plasma.

Decreasing of time of Hageman-factor-dependent fibrinolysis was ineffective in opposition to the specified changes of hypercoagulation activation.

Diabetes significantly complicated the course of purulent processes. That was indicated by a significant increase of proteolysis by azoalbumin lysis, azocasein, azocollagen, increased total nonenzymatic

Table 1

**State of system of unlimited proteolysis, fibrinolysis activity and average weight molecules of plasma under conditions of pyoinflammatory processes of soft tissues in mature rats ( $x \pm Sx$ )**

Indices	Control (n=8)	Main Fecal suspension administration (n=10)
Azoalbumin lysis, mg/ml $\Phi$ hour	2,24 $\pm$ 0,351	2,39 $\pm$ 0,329
Azocasein lysis, mg/ml $\Phi$ hour	1,87 $\pm$ 0,227	3,00 $\pm$ 0,209
Azocollagen lysis, mg/ml $\Phi$ hour	0,77 $\pm$ 0,137	1,14 $\pm$ 0,176
Total fibrinolytic activity, mg/ml $\Phi$ hour	4,23 $\pm$ 0,486	4,78 $\pm$ 0,489
Nonenzymatic fibrinolytic activity, mg/ml $\Phi$ hour	1,88 $\pm$ 1,05	1,11 $\pm$ 0,175
Proteinase activity by Kunitz – caseinolytic units, calibrated by trypsin	0,19 $\pm$ 0,029	0,27 $\pm$ 0,031
Average weight molecules concentration, arbitrary units	0,12 $\pm$ 0,015	0,18 $\pm$ 0,018

p– probability of differences compared with control, n – number of observations

Table 2

**State of regulation system of blood aggregation state under conditions of purulent processes of soft tissues in mature rats ( $x \pm Sx$ )**

Indices	Control (n=8)	Main Fecal suspension administration (n=10)
Time of plasma recalcification, sec	101,5 $\pm$ 2,38	90,8 $\pm$ 2,33
Activated partial thromboplastin time, sec	42,5 $\pm$ 2,32	35,8 $\pm$ 2,35
Prothrombin time, sec	16,4 $\pm$ 1,38	13,2 $\pm$ 1,37
Thrombin time, sec	14,5 $\pm$ 0,97	10,9 $\pm$ 1,07
Concentration of fibrinogen in blood plasma, g/l	4,48 $\pm$ 0,179	4,80 $\pm$ 0,175
Antithrombin activity III, %	98,2 $\pm$ 3,53	104,6 $\pm$ 3,37
Activity of blood clotting XIII factor, %	94,9 $\pm$ 3,74	96,5 $\pm$ 3,35
Percentage of adhesive thrombocytes by Mishcheiko method, %	2,69 $\pm$ 0,362	4,90 $\pm$ 0,358
Index of thrombocytes spontaneous aggregation by Tacolla method, %	28,3 $\pm$ 1,91	34,4 $\pm$ 1,90
Hageman-factor-dependent fibrinolysis, min	16,9 $\pm$ 0,68	13,4 $\pm$ 0,66
Plasminogen potential activity, min	15,8 $\pm$ 1,26	12,4 $\pm$ 1,19
Antiplasmins, %	93,0 $\pm$ 4,75	100,6 $\pm$ 4,48

fibrinolytic activity and proteinase activity by Kunitz (Table 3). Increase of average weight molecules indicated growth of the intoxication degree. Diabetes also caused significant disorders in hemostasis system under the conditions and presence of purulent processes. Thus, a significant increase of blood plasma hypercoagulation was revealed by the decrease of time of plasma recalcification, activated partial thromboplastin time, prothrombin time, thrombin time. Decrease of fibrinogen concentration in blood plasma denoted its use in the hypercoa-

gulation process. Activation of thrombocyte-vascular hemostasis under these conditions was confirmed by the increase of adhesive thrombocytes percentage and index of platelets spontaneous aggregation.

The use of ozone therapy in conditions of pyoinflammatory processes in mature rats with diabetes discovered significant protective properties, indicated by azoalbumin lysis decrease, total nonenzymatic fibrinolytic activity and proteinase activity by Kunitz in blood plasma (Table 3).

Таблиця 3

**State of system of unlimited proteolysis, fibrinolysis activity and concentration of average weight molecules in blood plasma in condition of pyoinflammatory processes in soft tissues in mature rats with diabetes against the background of ozone therapy ( $\bar{x}\pm Sx$ )**

Indices	Fecal suspension administration with DM (n=9)	Fecal suspension administration with DM against the background of ozone therapy (n=8)
Azoalbumin lysis, mg/ml hour	4,64±0,443	3,08±0,282 p<0,02
Azocasein lysis, mg/ml hour	5,95±0,744	4,41±0,735 p<0,01
Azocollagen lysis, mg/ml hour	3,57±0,743	1,84±0,351 p<0,01
Total fibrinolytic activity, mg/ml hour	9,84±0,838	6,34±0,709 p<0,01
Nonenzymatic fibrinolytic activity, mg/ml hour	7,55±1,495	1,42±0,198 p<0,01
Proteinase activity by Kunitz – caseinolytic units, calibrated by trypsin	0,89±0,103	0,31±0,142 p<0,01
Average weight molecules concentration, arbitrary units	0,30±0,034	0,32±0,039

Ozone therapy also improved the indices of regulation of blood aggregation state under conditions of purulent processes presence in diabetic mature rats. This was detected by the decrease of hypercoa-

gulation manifestations, indication of which was an increase of plasma recalcification time, activated partial thromboplastin time, prothrombin time, thrombin time (Table 4). The decrease of pathogenic inf-

Таблиця 4

**State of regulation system of blood aggregation state under conditions of pyoinflammatory processes in soft tissues in diabetic mature rats against the background of ozone therapy ( $\bar{x}\pm Sx$ )**

Indices	Feces suspension administration (n=9)	Feces suspension administration using ozone therapy (n=8)
Plasma recalcification time, sec	67,7±4,39	84,8±2,01 p<0,01
Activated partial thromboplastin time, sec	21,3±1,73	37,1±2,39 p<0,001
Prothrombin time, sec	9,31±0,869	14,0±1,38 p<0,01
Thrombin time, sec	7,11±0,579	10,9±0,77 p<0,01
Fibrinogen concentration in blood plasma, g/l	2,99±0,161	3,55±0,225 p<0,05
Antithrombin activity III, %	99,1±6,90	116,3±5,35 p<0,05
Concentration of soluble fibrin monomer complexes in blood, mg/l	3,25±0,403	7,57±0,693 <0,001
Activity of blood clotting XIII factor, %	88,8±7,61	91,9±5,48 p<0,05
Percentage of adhesive thrombocytes by Mishcheko method, %	11,95±0,558	8,60±0,687 p<0,01
Index of thrombocytes spontaneous aggregation by Tacolla method, %	45,7±2,07	33,8±2,46 p<0,01
Hageman-factor-dependent fibrinolysis, min	9,67±0,758	11,8±1,06 p<0,01
Plasminogen potential activity, min	10,3±0,69	8,33±0,810 p<0,01
Antiplasmins, %	112,9±5,36	115,9±5,10

fluence of thrombocyte-vascular hemostasis activation indicated the decrease of adhesive thrombocytes percentage by Mishchenko and index of thrombocyte spontaneous aggregation by Tacolla method. Additional anticoagulating properties under these conditions were revealed by an increase of concentration of soluble fibrin monomer complexes.

Such changes in mature rats can be considered positive in the course of pyoinflammatory processes: decrease of intoxication, increase of protective properties, decrease of hypercoagulation manifestations against the background of chronic forms of diabetes.

### Conclusions

1. The use of ozone therapy under conditions of abscesses of soft tissues in diabetic mature rats reveals significant protective properties with decreased azoalbumin lysis, total nonenzymatic fibrinolytic activity and proteinase activity by Kunitz in blood plasma.

2. Ozone therapy improves the regulation indices of blood aggregation state under conditions of pyoinflammatory processes in diabetic mature rats with decrease of hypercoagulation manifestations: increase of time of plasma recalcification, activated partial thromboplastin time, prothrombin time, thrombin time.

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### ВПЛИВ ОЗОНОТЕРАПІЇ НА ПОКАЗНИКИ ФІБРИНОЛІЗУ, ПРОТЕОЛІЗУ КРОВІ ЕКСПЕРИМЕНТАЛЬНИХ ЩУРІВ ПРИ ГНІЙНО-ЗАПАЛЬНИХ ПРОЦЕСАХ НА ФОНІ ЦУКРОВОГО ДІАБЕТУ

*С.Ю. Каратєєва, Т.О. Лобанова, О.К. Головачук*

**Резюме.** Експериментальні дослідження на 35 білих щурах із гнійно-запальними процесами на фоні цукрового діабету із застосуванням озонотерапії виявили покращення показників регуляції агрегатного стану крові, зменшення проявів гіперкоагуляції: зростання часу рекальцифікації плазми крові, активованого парціального тромбoplastинового часу, протромбінового часу, тромбінового часу, активації тромбоцитарно-судинного гемостазу, виявлено істотні протекторні властивості зі зниженням лізису азоальбуміну, сумарної, неферментативної фібринолітичної активності та активності протеїназ за Кунітцом у плазмі крові.

**Ключові слова:** цукровий діабет, гнійно-запальні ускладнення, фібриноліз, протекторні властивості, озонотерапія.

### ВЛИЯНИЕ ОЗОНОТЕРАПИИ НА ИЗМЕНЕНИЯ ПОКАЗАТЕЛЕЙ ФИБРИНОЛИЗА, ПРОТЕОЛИЗА КРОВИ ЭКСПЕРИМЕНТАЛЬНЫХ КРЫС ПРИ НАЛИЧИИ ГНОЙНО - ВОСПАЛИТЕЛЬНЫХ ПРОЦЕССОВ НА ФОНЕ САХАРНОГО ДИАБЕТА

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**Резюме.** Экспериментальные исследования на 35 белых крысах с гнойно - воспалительными процессами на фоне сахарного диабета с применением озонотерапии обнаружили улучшение показателей регуляции агрегатного состояния крови, уменьшение проявлений гиперкоагуляции: рост времени рекальцификации плазмы крови, активированного парциального тромбoplastинового времени, активации тромбоцитарно-сосудистого гемостаза, выявлены существенные протекторные свойства со снижением лизиса азоальбумину, суммарной, неферментативной фибринолитической активности и активности протеиназ по Кунитцу в плазме крови.

**Ключевые слова:** сахарный диабет, гнойно-воспалительные осложнения, фибринолиз, протекторные свойства, озонотерапия.

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