

EVALUATION OF BIOCHEMICAL CHANGES IN ENDOGENOUS INTOXICATION IN DIABETIC COMPLICATIONS

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Annotation. Study of the effect of the new drug "Rheomannisol" on vital organs, taking into account of diagnostics and prevention of pathophysiological aspects in the complex treatment of experimental diabetic foot syndrome.

Key words: experimental model of diabetic foot, experimental animals, diabetes mellitus, alloxan, surgical debridement, reomannisol.

Introduction. Diabetes mellitus is accompanied by the development of complications, including diabetic foot syndrome (DFS), one of the leading clinical symptoms of which is the persistence of an ulcer on the skin of the lower extremities [4,5].

Delayed wound healing is one of the complications of the disease due to multiple factors including poor circulation [4,5,12,17], prolonged inflammation, and hyperglycemia. It is a common cause of morbidity and mortality in patients with DM [2,5,15,16]. When the wound becomes chronic, it is prone to developing foot ulcers, including neuropathy and foot deformities [6,13,17,18]. Foot ulcers in DM are the cause of more than 50% of all non-traumatic leg amputations [3,7,15]. Evidence has shown that hyperglycemia is one of the main factors contributing to slow wound healing by increasing cell apoptosis and decreasing cell survival in diabetic wounds. It has been shown to inhibit endothelial cell and fibroblast proliferation in humans [9], up to 75% slower in adult mice with DM compared to control mice [10].

Aim of the study. Study of the effect of the new drug "Rheomannisol" on endogenous intoxication and wound healing, taking morphological aspects into the complex treatment of experimental diabetic foot syndrome.

Materials and research methods. The work was done on experimental material. Healthy rats were selected for the experiment. Experimental studies were carried out on 140 outbred male rats weighing 220-250 g, kept in the Tashkent Medical Academy (TMA) vivarium. The rats were kept under optimal conditions, all rats lived in a room with a 12-hour light-dark cycle and a constant temperature of 22-25°C, with free access to water. All rats were given a sufficient amount of a normal rodent diet ad libitum. (diet for rodents, State standard No. GOST R50258-92) and tap water daily. Operations and all manipulations with animals were carried out using general anesthesia, in compliance with the principles of humanity outlined in the directives of the European Community (86/609/EEC) and the Declaration of Helsinki, by the "Rules for working with experimental animals". The experimental animals were divided into 4 groups: the 1st group was intact; 2nd group –the creation of an experimental model of alloxan diabetes mellitus; 3rd control group - against the background of alloxan diabetes, the creation of an experimental model of a diabetic foot using traditional complex treatment; 4th experimental group - on an experimental model of diabetic foot - traditional treatment and reomannisol.

After a 24-hour fast, the rats were weighed. A 2% solution of alloxan diluted in 0.9% saline was administered intraperitoneally as a single dose, corresponding to a dose of 20, 15, 12 mg of alloxan per 100 g of animal weight. Food and water were given to animals only 30 minutes after drug administration. On the 3rd day, the level of glucose in the blood was assessed.

Results. Thus, judging from Table 1, high content of MWM products, which cause the development of endotoxemia, was found in the blood. It was revealed that at the beginning of the experiment, the content of MWM in blood plasma and erythrocytes in animals of both groups was approximately 1.7-2 times higher than in the intact group (see Table 3). It can also be said, reliably given by this table, that the numbers of the toxemia index in plasma and erythrocytes are higher than those in the intact group. The peptide component of MWM is represented by the content of oligopeptides in plasma and erythrocytes in both groups, which also significantly exceeded by 1.6–2.4 times the value in the group of relatively intact animals. This may indicate the activation of pathological proteolysis processes. After the use of reomannisol, the experimental group showed a tendency to reduce all indicators of endogenous intoxication. By the 7th day, the indices of MWM, OP of plasma (pl.) and erythrocytes (eryt.) in the control group were on average 1.2 times higher than those of the experimental group. At 10, 14 days in the experimental - fix the values of indicators corresponding to the intact

group and the normalization of the pathological process in the body. Animals that received only traditional treatment, EI indicators remain elevated on average 1.2 times than in the experimental group, and the state of intoxication persists until the end of the experiment.

Table 3. Dynamics of change in indicators of endogenous intoxication.

	Serum				Erythrocytes			
	Medium weight molecules (MWM) of plasma, Conv. unit	Oligopeptides (OP) of plasma, g/l	Toxemic index (TI) of plasma, conv. unit	Intoxication index (II) conv. unit	Medium weight molecules (MWM) of eryt., conv. unit	Oligopeptides (OP) of eryt., g/l	Toxemic index (TI) of eryt, conv. unit	SCE, %
Intact group	3,6±0,24	0,45±0,04	1,81±0,20	3,57±0,36	3,5±0,21	0,68±0,04	2,28±0,40	7,8±0,43
Control group Day 1	6,1±0,22*	0,78±0,06***	4,41±0,55*	12,04±0,62*	7,3±0,25**	1,16±0,07***	7,79±0,62**	12,8±0,67**
Main group Day 1	6,1±0,17*	0,77±0,04***	4,20±0,21*	11,54±0,67*	7,0±0,16**	1,12±0,07***	7,44±0,36**	12,7±0,47**
Control group Day 3	5,6±0,16*	0,70±0,05***	3,73±0,45*	10,64±0,46*	6,4±0,19**	1,02±0,06***	7,21±0,22**	11,7±0,35**
Main group Day 4	5,3±0,09*	0,69±0,05**	3,36±0,28*	8,71±0,99***	5,9±0,08**	0,96±0,06***	5,54±0,65**	10,4±0,44**
Control group Day 7	5,3±0,11*	0,67±0,05**	3,09±0,22*	8,51±0,35***	5,6±0,11**	0,92±0,05**	5,79±0,32**	9,6±0,31**
Main group Day 7	4,0±0,11 ^{^^}	0,58±0,02*	2,15±0,26 [^]	5,61±0,62 ^{^^^}	4,1±0,11 ^{^^}	0,78±0,04 [^]	3,46±0,36 ^{^^}	8,3±0,17 ^{^^}
Control group Day 10	4,9±0,10*	0,56±0,03*	2,83±0,23*	6,84±0,31***	5,2±0,11**	0,85±0,05*	4,64±0,23**	9,3±0,21**
Main group Day 10	3,7±0,14 ^{^^}	0,48±0,05	1,86±0,22 [^]	3,65±0,24 ^{^^^}	3,7±0,12 ^{^^}	0,72±0,05 [^]	2,43±0,17 ^{^^}	8,0±0,23 ^{^^^}
Control group Day 14	4,2±0,11*	0,52±0,03	2,39±0,15*	5,56±0,24***	4,2±0,10**	0,77±0,04	3,30±0,16*	8,7±0,17*
Main group Day 14	3,5±0,18 ^{^^}	0,45±0,04	1,80±0,23 [^]	3,55±0,37 ^{^^^}	3,2±0,17 ^{^^}	0,68±0,02	2,30±0,22 ^{^^}	7,8±0,43 [^]

Note: *- significantly compared with the intact group (*-P<0,05; **-P<0,01; ***-P<0,001)

[^] - significantly compared with the control group ([^]-P<0,05; ^{^^}-P<0,01; ^{^^^}-P<0,001).

The study of the sorption capacity of erythrocyte membranes was carried out on erythrocytes from 10 practically healthy rats. The mean SCE in this group was 7.8% ± 0.43. After the administration of alloxan to the body of rats, in both groups on the first days, a regular increase in SCE was observed on average by 1.6 times, intoxication index was 3.3 times that in the intact atop. The redistribution of the toxic load between plasma and blood erythrocytes is a necessary part of the body's natural detoxification [2, 10]. Endotoxins bind to the

transmembrane protein of erythrocytes - glycoporphin, and in this form are transported to the detoxification organs.

As a result, the use of reomannisol intraperitoneally in rats of the experimental group improved the condition of the animals, reduced the EI of the body. By 10, 14 days in the control group Intoxication index (II) 6.84 ± 0.31 ; 5.56 ± 0.24 and SCE 9.3 ± 0.21 ; 8.7 ± 0.17 , respectively, were, on average, 1.7 (II) and 1.1 (SCE) higher than the values of the experimental group - II 3.65 ± 0.24 ; 3.55 ± 0.37 and SCE 8.0 ± 0.23 ; 7.8 ± 0.43 (see table No. 3). This is due to the fact because the qualities of an antioxidant that improves blood rheology, a detoxifying effect (enterosorbent), and a diuretic, which have the effect of "biochemical sanitation" and restores the physiological functions of cells for the biotransport of endotoxins.

Conclusions

After using the drug reomannisol intraperitoneally at a dose of 1 ml / 100 g 1 time per day for 5 days, there was a sharp decline in EI numbers. On the 10th day, the EI values in the experimental group returned to normal, similar to those in the intact group. The drug reomannisol performs "biochemical rehabilitation", due to its inherent qualities: antioxidant, improves blood rheology, detoxification, and diuretic. In rats of the control group, the EI numbers remain at high levels until the end of the experiment.

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