CONTROL OF INDICATORS OF ENDOTOXICOSIS IN DIABETIC FOOT SYNDROME

Zokhirov Adkhamjon Rafiqovich
Tashkent Medical Academy

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.

Annotatsiya. Eksperimental diabetik oyoq sindromini yangi "Reomannisol" preparati bilan kompleks davolashdan keyin hayotiy organlarga ta'sirini o'rganish uchun patofiziologik diagnostika va profilaktikani olib borish.

Kalit so'zlar: diabetik oyoqning eksperimental modeli, tajriba hayvonlari, diabetes mellitus, alloksan, jarrohlik debridman, reomannisol.

Аннотация. Изучение влияния нового препарата «Реоманнисола» на жизненно-важных органов с учетом диагностики и профилактики патофизиологических аспектов в комплексном лечении экспериментального синдрома диабетической стопы.

Ключевые слова: экспериментальная модель диабетической стопы, экспериментальные животные, сахарный диабет, аллоксан, хирургическая обработка, реоманнисол.

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.

Determination of glucose concentration in the peripheral blood of animals. Diabetes was confirmed 3 days after the blood glucose concentration was determined. Peripheral blood glucose concentration was measured with an “AccuChek Active” glucometer (Roche Diagnostics, Germany), the linear measurement range was 0.6–33.3 mmol/L. Blood sampling to study the level of glycemia was performed from an incision in the tip of the tail. An experimental model of diabetes mellitus (type I diabetes) has been obtained. The day of verification of diabetes mellitus was considered the zero-day of its development.

Surgical procedure. On the day of verification, the skin surface of the right footpad was shaved and cleaned with a 70% ethanol wipe. On the skin of each rat’s right hind paw’s footpad, a full-thickness rectangular wound measuring 2 mm × 5 mm was created with a scalpel [3]. The scalpel and scissor wounds (Day 0) were of similar size and shape with minimal or no bleeding in all groups. Every day, the wounds were treated with the traditional method of treatment (5%

alcohol solution of iodine and levomekol ointment), until the end of the experiment, also for the experimental group, in addition to the local traditional method of treatment, a new drug Reomannisol (JV LLC REKA-MED FARM, Republic of Uzbekistan) was used, which was administered intraperitoneally once a day for 5 days, in single doses of the therapeutic range for humans, taking into account differences in relative body surface area [4]. In all cases, the average dose of the studied range was 1 ml of Reomannisol per 100 g of the calculated equivalent mean therapeutic dose (EMTD).

The development of the disease was assessed by the condition of the animals, lethality was recorded in groups, and recorded according to clinical symptoms (polyuria, polydipsia, polyphagia, weight loss, coat) and blood glucose levels. The wool of animals normally has a peculiar luster and is usually adjacent to the skin.

The amount of water drunk by the rats was determined individually by measuring its volume with a measuring cylinder before and after the animals took water. To assess the daily values of diuresis, an individual urine collection was performed using urinals.

Rats were taken out of the experiment by decapitation on days 1, 3, 7, 10, 14, blood was taken for laboratory examinations: biochemical analyzes (total protein, ALT, AST, glucose, creatinine, urea), products of lipid peroxidation (LPO) (malondialdehyde - MDA), indicators endogenous intoxication (MWM, SCE), morphological studies of tissues taken from the wound zone and the surrounding intact area were carried out. At each time, sampling for analysis was carried out in 10 animals of each group.

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***
Maingroup 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***
Maingroup 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**
Maingroup 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**
Maingroup 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*
Maingroup 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 - glycophorin, 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 becausethe 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

1. The best option for creating an experimental model of a diabetic foot is the introduction of alloxan intraperitoneally in a single dose of 12 mg per 100 g, in which moderate diabetes develops.
2. 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.
3. The results of biochemical studies demonstrate positive dynamics in experimental animals with a diabetic foot model when using the drug reomannisol. This was manifested by the fact that by the 10th day there was a decrease and normalization of the level of glucose in the peripheral blood, indicators of renal clearance (urea, creatinine), liver (ALT, AST, albumins).
4. An open, full-thickness wound of the foot, in rats with DM, had low blood circulation, prolonged inflammation, and was characterized by a violation of the inflammatory and proliferative phases of the healing process, which is associated with hyperglycemia. Thus, this model of the open foot in rats provides a good approach for studying the process of wound healing in DM, and this model can be regarded as creating an analog of the human diabetic foot syndrome in an experimental model of alloxan-induced diabetes mellitus.

References

1. Yusufjanovich E. U. et al. Evaluation of the lipid peroxidase index in diabetic complications //Conferencea. – 2023. – C. 68-73.
2. Yusufjanovich E. U. et al. Treatment of purulent-necrotic lesions of the lower extremities with modern drugs //Conferencea. – 2023. – C. 88-94.

3. Yusufjanovich E. U. et al. Assessment of the Process of Epithelialization After Complex Treatment of Diabetic Foot Syndrome //Texas Journal of Medical Science. – 2023. – Т. 16. – С. 19-23.
4. Ergashev U. Y., Zokhirov A. R., Minavarkhujaev R. R. Determination of changes in the lipid peroxidase index in purulent-necrotic lesions of the lower extremities. – 2022.
5. Ergashev U. Y., Zokhirov A. R., Minavarkhujaev R. R. Study and treatment of changes in biochemical processes in complications of diabetes mellitus. – 2023.
6. Ergashev U. Y., Zokhirov A. R., Minavarkhujaev R. R. The study of pathological physiology of indicators of endogenous intoxication in purulent-necrotic lesions of the lower extremities. – 2023.
7. Zohirov A. R., Ergashev U. Y., Ernazarov H. I. Qandli diabetda oyoqning yiringlinekrotik shikastlanishlarining patomorfologik jihatlarini kompleks davolashni o'rganish. International scientific forum-2022". June 2022. p132-136.
8. Ergashev U. Y. et al. The study of pathomorphological diagnosis of vital organs after modern treatment of diabetic foot syndrome. – 2022.
9. Ergashev U. Y. et al. The study of diagnostics and prevention of pathophysiological parameters after modern treatment of purulent-necrotic processes in diabetic. – 2022.
10. Ergashev U. Y. et al. Effective of Simultaneous Surgeries in Chronic Immune Thrombocytopenia //Jundishapur Journal of Microbiology. – 2022. – Т. 15. – №. 2. – С. 638-644.
11. Эрназаров Х. и др. Патоморфологическая картина жизненно важных органов при экспериментальной модели диабетической стопы. – 2022.
12. Каримов Ш. И. и др. Применение гибридных хирургических вмешательств у больных с критиче-ской ишемией нижних конечностей при мультифокальном атеросклерозе //Тиббиет янги куни. – 2019. – Т. 3. – С. 27.
13. Mustafakulov G. I. et al. Splenectomy for hairy cell leukemia //Central Asian Journal of Medicine. – 2021. – Т. 2021. – №. 4. – С. 160-167.
14. Ergashev U. Y. Ernazarov Kh. I., Zohirov AR, Alzabni ID 2022. Complex Treatment of Experimental Model of Diabetic Foot Syndrome //American Journal of Medicine and Medical Sciences. – 2022. – Т. 12. – №. 5. – С. 471-480.
15. Ergashev U. Y. et al. The role of minimally invasive technologies in the treatment of liver cavities //Frontiers in Bioscience-Landmark. – 2021. – Т. 8. – С. 82-89.
16. Зохиров А. Р., Абдусаломов Б. А., Моминов А. Т. Совершенствование комплексного лечения с учетом патофизиологических изменений гнойно-некротических поражений нижних конечностей при сахарном диабете. – 2022.
17. Зохиров А. Р., Эрназаров Х. И., Эргашев У. Ю. Патоморфологические особенности заживления ран при экспериментальной модели диабетической стопы. – 64-ой научно-практической конференции обучающихся «наука и здоровье» посвященная дню науки республики Казахстан с международным участием, 2022.

18. Эрназаров Х. и др. Патоморфологическая картина жизненно важных органов при экспериментальной модели диабетической стопы. – 2022.
19. Махмудова, Д. А., & Қарахонова СА, Х. К. (2015). Неврозларда фобия ва қўркув. Психиатрия журнали, (1-Б), 82.
20. Karakhonova, S. A., & Ishanhodjaeva, G. T. (2016). Cognitive disorders in Parkinsonism. Parkinsonism & Related Disorders, 22, e59.
21. Karakhonova, S. A. (2022). The Significance of the Application of Psycho-Correction Methods in the Treatment of Psycho-Emotional Disorder. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 2(12), 59-64.
22. Алишеровна, Қ. С., Сейткаримова, Г. С., & Юнусходжаева, Х. С. (2022). ЭФФЕКТИВНАЯ ПСИХОКОРРЕКЦИЯ ПРИ НЕВРОТИЧЕСКОМ РАССТРОЙСТВЕ. ЖУРНАЛ НЕВРОЛОГИИ И НЕЙРОХИРУРГИЧЕСКИХ ИССЛЕДОВАНИЙ, 3(1).
23. Ибодуллаев, З. (2022). EFFECTIVE PSYCHOCORRECTION IN NEUROTIC DISORDER.
24. Ибодуллаев, З. Р., Карахонова, С. А., & Сейткаримова, Г. С. (2021). Значение использования методов психокоррекции при лечении тревожно-фобического синдрома. ЖУРНАЛ НЕВРОЛОГИИ И НЕЙРОХИРУРГИЧЕСКИХ ИССЛЕДОВАНИЙ, (SPECIAL 1).
25. Karakhonova, S. (2019). Psychocorrection and optimal pharmacotherapy in anxiety-phobic syndrome. Psychosomatic Medicine and General Practice, 4(1), e0401175-e0401175.
26. Самигова, Н. Р. (2016). ИССЛЕДОВАНИЕ ФУНКЦИОНАЛЬНОГО СОСТОЯНИЯ СЕРДЕЧНО-СОСУДИСТОЙ СИСТЕМЫ У РАБОТАЮЩИХ ШВЕЙНОГО ПРОИЗВОДСТВА. ББК 28.903 я43, 203.
27. Шеркузиева, Г. Ф., Хегай, Л. Н., Самигова, Н. Р., Азизова, Ф. Л., & Курбанова, Ш. И. (2020). Результаты изучения острой токсичности пищевойсмеси “Мелла Круассан”. Журнал//Вестник, (1), 188-189.
28. Сушенок, М. В., & Замбржицкий, О. Н. (2018). Состояние профессионального здоровья медицинских работников. Молодежный сборник научных статей «Научные стремления», (24), 67-70.
29. Raimovna, S. N., Rikhsillayevna, M. M., & Ugli, B. F. I. (2017). Features of hygienic conditions of workers on poultry-farming complexes (Uzbekistan). European research, (4 (27)), 72-73.
30. Самигова, Н. Р., Шеркузиева, Г. Ф., Мусаев, Э. В., Рустамова, М. К. К., & Хаджаева, У. А. К. (2019). Особенности условий труда медицинских работников санитарно-гигиенических лабораторий. Academy, (2 (41)), 97-98.
31. Самигова, Н. Р., Мирсагатова, М. Р., & Нигматуллаева, Д. Ж. (2018). Экологические последствия урбанизации и индустриализации современности. In ДОСТИЖЕНИЯ ВУЗОВСКОЙ НАУКИ 2018 (pp. 249-252).

32. Самигова, Н. Р., & Мирсагатова, М. Р. (2017). Изучение динамики изменений в функциональном состоянии сердечно-сосудистой системы рабочих мебельного производства. Молодой ученый, (50), 126-129.
33. Самигова, Н. Р. (2005). Гигиено-физиологические основы оптимизации условий труда работников швейных производств Узбекистана (диссертация на соискание ученой степени кандидата медицинских наук).
34. Шеркузиева, Г. Ф., Самигова, Н. Р., Шайхова, Л. И., & Жалилов, А. А. (1999). Комплексная гигиено-токсикологическая оценка" Laktonorm-H". ИНФЕКЦИЯ, ИММУНИТЕТ и ФАРМАКОЛОГИЯ, 261.
35. Самигова, Н. Р., & Шеркузиева, Г. Ф. (2021). Использование модульной системы обучения как неотъемлемой части при подготовке клинических ординаторов профилактической медицины (Doctoral dissertation, Namangan).
36. Самигова, Н. Р., & Шеркузиева, Г. Ф. (2021). Использование модульной системы обучения как неотъемлемой части при подготовке клинических ординаторов профилактической медицины (Doctoral dissertation, Namangan).