

**DIABETES MELLITUS AND MENOPAUSE**

Khaydarova Zarrina Erkinovna
Khusainova Munira Alisherovna
Khaydarov Sanjar Nizamitdinovich
Samarkand State Medical University, Samarkand, Uzbekistan

Abstract

A study was performed to determine the effect of drospirenone, which is part of the low-dose drug Angelik, on carbohydrate metabolism and hemostasis in postmenopausal patients with type 2 diabetes mellitus.

50 patients with menopausal syndrome who are in natural menopause, duration of more than 2 years old, suffering from type 2 diabetes mellitus. 30 women who do not have contraindications are prescribed the low-dose drug Angelik. Indicators of carbohydrate metabolism were assessed by fasting glucose, C-peptide, insulin, insulin resistance was calculated by the Nomo index, hemostasis indicators by platelet level, coagulogram, D-dimer initially, after 3 and 6 months of treatment.

During treatment with Angelik, there was a significant decrease in glucose and insulin resistance by the 6th month of administration, and no effect on the state of the hemostasis system.

The obtained data allow us to recommend Angelik drug for hormone replacement therapy in postmenopausal patients suffering from type 2 diabetes mellitus as effective, safe and possessing a number of additional positive properties.

Keywords: menopausal syndrome, type 2 diabetes mellitus, hormone replacement therapy, carbohydrate metabolism, hemostasis.

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia. The vast majority of diabetes cases belong to the two most extensive etiopathogenetic categories: type 1 diabetes mellitus (DM1) with absolute insulin deficiency and type 2 diabetes mellitus 2 (DM2), in which chronic hyperglycemia develops due to a combination of insulin resistance and an inadequate compensatory insulin secret response. In relation to the menopausal period, DM 2 has the greatest clinical significance. It accounts for 90-95% of all DM patients. The incidence of diabetes mellitus increases significantly in older women 50 years old and, possibly, menopause has a certain effect on increasing its prevalence among older women. According to the register of diabetes in the Samarkand Territory, the prevalence of DM2 among women is 3.9%. Aged 40-49 years 1.1% of women have DM2, aged 50-59 years -2.2%, aged 60-69 years-8.7% of the female population, over the age of 70 years - 11.3% of women. It has been proven that sex hormones have multiple effects on various organs and tissues. The most significant consequences and clinical manifestations of estrogen deficiency,



which significantly affects the quality of life of women in peri – and postmenopausal age, include a high risk of atherosclerosis, arterial hypertension, coronary heart disease (3 times), acute circulatory disorders (7 times). These diseases occupy one of the leading places among the causes of death in postmenopausal women, with a sharp jump in the development of diseases occurring after menopause. But also sugar Diabetes is a classic model of micro- and macrovascular complications. Such a large-scale lesion of the entire vascular bed does not occur in any other disease. Type 2 diabetes mellitus is a disease of large vessels. Cardiovascular diseases and peripheral vascular diseases are the cause of significantly higher morbidity and mortality in patients with type 2 diabetes than the classical triad: nephropathy, neuropathy, retinopathy, although the risk of these diseases is also very high. The combination of menopausal syndrome and diabetes creates conditions for possible mutual encumbrance.

That is why it is important to identify type 2 diabetes during menopause and adequately treat it at the same time actively compensate for those hormonal changes that are characteristic of the menopausal period. For many years, there has been an opinion that women with diabetes are contraindicated in the appointment of hormone replacement therapy (HRT) for the treatment and prevention of menopausal disorders. The fundamental argument for this statement was the fact that most of the gestagens used in HRT provided negative effect on hemostasis, carbohydrate and lipid metabolism, minimizing the positive effect of estrogens.

The difficulties and problems that arise in the use of HRT in women with loss of ovarian function inevitably contribute to the development and improvement of this

method of treatment, the creation of new hormonal components and new effective and safe drugs based on them. These drugs include the drug Angelik (Schering, Germany), which is a modern means of continuous Low-dose combination therapy: each tablet contains 1 mg of estradiol hemihydrate and 2 mg of drospirenone. The use of drospirenone, which has an antiandrogenic effect, to a certain extent eliminates the adverse effect of androgens on metabolic processes. The elimination of excessive amounts of sodium under the influence of drospirenone contributes to better regulation of blood pressure. In addition, a positive effect is shown drospirenone affects the condition and function of the endothelium, increases the activity of nitric oxide, inhibits the conversion of angiotensin 1 to angiotensin 2, which also helps to reduce Blood pressure, improvement of myocardial function. Drospirenone has a good effect on the state of the lipid profile. The question arises about the effect of drospirenone on carbohydrate metabolism in postmenopausal patients with DM2, an important component of which is insulin resistance, and also whether its effect is associated with increased insulin resistance and an increase in the degree of glycemia.

Another problem is the effect of drospirenone on hemostasis, since HRT is attributed to one of the factors in the development of venous thrombosis.

These questions were the purpose of this study.

MATERIALS AND METHODS OF RESEARCH

The study included 50 patients with menopausal syndrome (CS) aged 45-57 years old (the average age of the study participants was 52 ± 0.5 years), who have been in natural menopause for more than 2 years, who suffer from DM2 and have abdominal type of obesity. The indication for the appointment of HRT in all cases was menopausal disorders, among which neurovegetative symptoms prevailed. A severe degree of menopausal disorders was



detected in 3 patients, an average degree in 20, and a mild degree in 27. Average score According to the menopausal modified index (MMI) assessment scale, it was 41 ± 2 points before the start of treatment. In order to correct menopausal disorders, 30 women who did not have contraindications were prescribed the low-dose drug Angelik). The examination revealed hypertriglyceridemia in 20 women, Therefore, an alternative treatment method is prescribed for this category of patients - Climadinone (phytoestrogen "Binorica") in combination with lipid-lowering therapy. In the case of normalization of triglyceride levels after 3 months of treatment, Angelik was prescribed to these women. HRT was prescribed for the compensation and subcompensation of diabetes mellitus. All the patients had self-control skills, they had training talks about the peculiarities of the dietary regime, and dosed physical activity was prescribed. Before starting HRT, it was mandatory examination: ultrasound of the mammary glands and pelvic organs, cytological examination of cervical smears, assessment of coagulation factors, blood pressure measurement, consultations with an optometrist, neurologist, nephrologist, cardiologist. CS was assessed using a modified menopausal index. To assess the degree of overweight or obesity, the body mass index (BMI) was calculated. The severity of abdominal obesity was determined by the size of the waist (FROM). Abdominal obesity was detected at a value of 80 cm or more (according to the IDF classification, 2005). Indicators of carbohydrate metabolism were assessed using the level of glycemia, immunoreactive insulin, and C-peptide. To determine insulin resistance, we calculated the Homa index. Hemostasis parameters were assessed using a coagulogram, Ddimer concentration. The entire diagnostic program was performed at the first treatment of women for menopausal disorders after three and six months of therapy.

THE RESULTS AND THEIR DISCUSSION

At the initial examination, overweight (BMI= 25.0-29.9 kg/cm²) was found in 15, grade I obesity (BMI 30.0-34.9 kg/m²) in 16, grade II obesity (BMI= 35.0-39.9 kg/m²) in 15, grade III obesity (BMI=40 kg/m²) in 4 patients. Everyone had an indicator FROM 80 cm, which indicated that they had abdominal obesity. BMI did not significantly change three and six months after the start of taking the drugs, although there was a distinct tendency to decrease body weight (BMI decreased from 32 kg/m² to 30.67 kg/m²). Stability of the indicator assessing the degree of abdominal obesity (AO), indicates not only the absence of a negative effect of the drug used on the severity of abdominal obesity, but also their restraining effect on body weight gain (AO decreased from $99.24 \text{ cm} \pm 1.9$ to $95.10 \text{ cm} \pm 1.8$) Taking the drug led to positive changes in carbohydrate metabolism. The tendency to decrease fasting glucose levels was revealed in the third month of HRT use and significantly decreased by the sixth month, and there was also a significant decrease in insulin resistance by the sixth month taking HRT. One of the widely discussed risk factors for HRT are deep vein thrombosis and thromboembolism of the main pulmonary artery or its branches. Attention to the problem of thrombosis on the background of HRT was attracted in 1998. Since that time, clinical studies have been initiated to identify significant risk factors for thrombosis: the study of drug administration routes, concomitant factors (obesity, hereditary thrombophilia, etc.), the quality of HRT products used, especially their progestogenic components.



In this study, the following was carried out evaluation of the coagulogram and concentration of Ddimer, the degradation product of insoluble fibrin. The study showed that in patients taking Angelik, the initial parameters of fibrinogen, PTI, APTV, platelets, as well as the concentration of D-dimer were within normal values. Taking the drug for six months did not affect the state of the hemostasis system. There was also no increase in concentration D-dimer.

CONCLUSIONS

The low-dose drug Angelik has good tolerability. In none of the cases were there complications on the background of HRT, which ensures the duration of administration, improving the course of CS: in 68% of women, the average severity of CS turned into a mild degree, in 40% of women, a mild degree of CS manifestation, in 1 woman, a severe degree of CS severity turned into an average degree. An important and newly established property of the drug associated with its constituent drospirenone is its positive effect on serum glucose, insulin, and C

- peptide. Other effects peculiar to drospirenone - the excretion of water and sodium, complement the importance of the drug. So, it helps to eliminate edematous syndrome, reduce body weight. It is possible that a decrease in body weight is also facilitated by a decrease in the concentration of insulin during the intake of Angelik: insulin enhances lipogenesis and inhibits lipolysis, therefore, reducing its level facilitates the destruction of adipose tissue. The drug does not affect the state of the hemostasis system. The data obtained allow us to recommend the drug Angelik for HRT in postmenopausal patients suffering from DM 2, as it is effective, safe and has a number of additional positive properties.

References

1. Khusainova, M. A., Eshmamatova, F. B., Ismoilova, K. T., & Mamadiyorova, M. M. (2023). METABOLIC SYNDROME IN RHEUMATOID ARTHRITIS AS A CRITERION OF CARDIOVASCULAR RISK. *Oriental renaissance: Innovative, educational, natural and social sciences*, 3(1), 331-339.
2. Khusainova, M. A. (2023). CYSTATIN C IS AN EARLY MARKER OF DECREASED KIDNEY FUNCTION. *Oriental renaissance: Innovative, educational, natural and social sciences*, 3(1), 485-490.
3. Khusainova, M. A. (2023). Comorbidity thyrotoxicosis with coronary heart disease. *Science and Education*, 4(5), 205-213.
4. Yarmatov, S., Khusainova, M., & Djabbarova, N. (2023). STUDY OF QUALITY OF LIFE INDICATORS IN PATIENTS WITH CORONARY HEART DISEASE USING THE SF-36 QUESTIONNAIRE. *Бюллетень студентов нового Узбекистана*, 1(7), 58-64.
5. Alisherovna, K. M. (2022). PSYCHOSOMATIC CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS AND GOUT. *Galaxy International Interdisciplinary Research Journal*, 10(5), 665-671.
6. Djamshedovna, K. D., & Alisherovna, K. M. (2024). CHANGES IN SOME SYSTEM INDICATORS IN PREGNANT WOMEN WITH GESTOSIS. *Spectrum Journal of Innovation, Reforms and Development*, 25, 111-115.
7. Khabibovna, Y. S., & Alisherovna, K. M. (2024). STRESS TESTING IN PATIENTS WITH CORONARY HEART DISEASE. *Journal of new century innovations*, 45(3), 28-33.



8. Alisherovna, K. M., Akramovna, I. K., & Yorkinovna, E. N. (2024). CLINICAL AND MORPHOLOGICAL CRITERIA OF COLITIS IN PATIENTS WITH CHRONIC ISCHEMIC DISEASE OF THE DIGESTIVE SYSTEM. *Ta'lim innovatsiyasi va integratsiyasi*, 18(6), 6-13.
9. Alisherovna, K. M., Akramovna, I. K., & Yorkinovna, E. N. (2024). CLINICAL AND MORPHOLOGICAL CRITERIA OF COLITIS IN PATIENTS WITH CHRONIC ISCHEMIC DISEASE OF THE DIGESTIVE SYSTEM. *Ta'lim innovatsiyasi va integratsiyasi*, 18(6), 6-13.
10. Alisherovna, K. M., Akramovna, I. K., & Kairatovna, R. A. (2024). THE EFFECTIVENESS OF TREATMENT OF PATIENTS WITH OSTEOARTHRITIS WITH CARDIOVASCULAR DISORDERS IN METABOLIC SYNDROME. *Ta'lim innovatsiyasi va integratsiyasi*, 18(5), 223-230.
11. Alisherovna, K. M., Ismatullayevich, M. A., & Nuriddinovna, E. N. (2024). FEATURES OF HEART FAILURE IN PATIENTS WITH CORONARY HEART DISEASE AND THYROTOXICOSIS. *Ta'lim innovatsiyasi va integratsiyasi*, 19(4), 52-61.
12. Alisherovna, K. M., Akramovna, I. K., & Baxtiyorovna, O. K. (2024). THE COURSE OF CHRONIC ISCHEMIC PANCREATITIS IN PATIENTS WITH CORONARY HEART DISEASE. *Ta'lim innovatsiyasi va integratsiyasi*, 18(5), 231-239.
13. Alisherovna, K. M., Davranovna, M. K., & Erkinovna, K. Z. (2024). CORONARY HEART DISEASE AND OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN. *Spectrum Journal of Innovation, Reforms and Development*, 26, 40-45.
14. Khabibovna, Y. S., Alisherovna, K. M., Nizamitdinovich, K. S., & Bakhtiyorovich, U. J. (2023). FEATURES OF OSTEOPOROSIS AND SARCOPENIA SYNDROMES IN RHEUMATOID ARTHRITIS. *Journal of new century innovations*, 38(2), 212-219.
15. Alisherovna, K. M., Habibulloyevna, I. M., & Voxidovna, R. F. (2024). STRUCTURAL AND FUNCTIONAL FEATURES OF THE LEFT VENTRICLE IN PATIENTS WITH HEART FAILURE IN ISCHEMIC HEART DISEASE AND THYROTOXICOSIS. *Ta'lim innovatsiyasi va integratsiyasi*, 19(4), 71-81.
16. Khabibovna, Y. S., Alisherovna, K. M., Nizamitdinovich, K. S., Tashtemirovna, E. M. M., Abdukadirovna, A. S., & Jasurovna, J. S. (2023). DEPRESSION, ANXIETY AND QUALITY OF LIFE IN PATIENTS WITH ATRIAL FIBRILLATION. *Journal of new century innovations*, 39(1), 185-189.
17. Alisherovna, K. M., Erkinovna, S. D., Duskobilovich, B. S., & Samandarovich, T. H. (2024). ARTERIAL HYPERTENSION IN THYROTOXICOSIS AND REMODELING OF THE LEFT VENTRICLE OF THE HEART. *Ta'lim innovatsiyasi va integratsiyasi*, 19(4), 114-121.
18. Alisherovna, K. M., & Djamshedovna, K. D. (2024). AFTER COVID-19 QUALITY OF LIFE. *Spectrum Journal of Innovation, Reforms and Development*, 25, 103-110.
19. Alisherovna, K. M., Mansurovna, M. D., Erkinovna, N. D., Farxodovna, X. R., Toxirovna, M. M., Tolibovna, R. D., & Yorkinovna, E. N. (2024). ARTERIAL HYPERTENSION AND THYROID STATUS IN PATIENTS OF DIFFERENT AGES. *Ta'lim innovatsiyasi va integratsiyasi*, 19(4), 122-129.
20. Alisherovna, K. M., Erkinovna, S. D., Yazdonkulovna, X. M., & Zafarovna, C. M. M. (2024). ATRIAL FIBRILLATION IN THYROTOXICOSIS—DETERMINANTS OF

- DEVELOPMENT AND CONSERVATION. Ta'lim innovatsiyasi va integratsiyasi, 19(4), 103-113.
21. Alisherovna, K. M., Yaxshiboyevich, U. M. R., & Yigitaliyevich, B. A. (2024). EVALUATION OF A NATRIURETIC PEPTIDE TO OPTIMIZE THE MANAGEMENT OF COMORBID PATIENTS WITH THYROTOXICOSIS AND HEART FAILURE. Ta'lim innovatsiyasi va integratsiyasi, 19(4), 62-70.
 22. Davranovna, M. K. D. K., Alisherovna, K. M., & Erkinovna, K. Z. (2024). CARDIAC ARRHYTHMIAS IN PATIENTS WITH RHEUMATOID ARTHRITIS. Spectrum Journal of Innovation, Reforms and Development, 26, 65-71.
 23. Erkinovna, K. Z., Alisherovna, K. M., & Davranovna, M. K. (2024). ARTERIAL HYPERTENSION AND ARRHYTHMIA. Spectrum Journal of Innovation, Reforms and Development, 26, 72-78.
 24. Alisherovna, K. M., Erkinovna, K. Z., Davranovna, M. K., & Pulotovna, Z. D. (2022). Positive Effect of Sorbitol in Patients with Chronic Renal Insufficiency. Miasto Przyszłości, 30, 214-217.
 25. Nizamitdinovich, K. S., Khabibovna, Y. S., Alisherovna, K. M., & Tashtemirovna, E. M. M. (2023). Spinal Injury for Rheumatoid Arthritis. Miasto Przyszłości, 40, 426-432.
 26. Baxtiyorovich, U. J., Alisherovna, K. M., & Mamasoliyevna, D. N. (2023). Features of cognitive impairment in patients with chronic kidney disease at predialysis stages. World Bulletin of Public Health, 22, 49-54.
 27. Alisherovna, K. M., Akmalovna, K. N., & Mamasoliyevna, D. N. (2022). Kidney dysfunction in chronic heart failure. Texas Journal of Medical Science, 13, 104-109.
 28. Alisherovna, K. M., Baxtiyorovich, Z. M., & Anvarovich, N. J. (2022). To Assess The Condition Of The Myocardium In Patients Chronic Heart Failure On The Background Of Rheumatoid Arthritis. Spectrum Journal of Innovation, Reforms and Development, 4, 210-215.
 29. Alisherovna, K. M., Toshtemirovna, E. M. M., Djamshedovna, K. D., & Maxammadiyevich, K. S. (2022). Endothelial Dysfunction in Patients with Chronic Heart Failure. Miasto Przyszłości, 30, 218-220.
 30. Nizamitdinovich, K. S., Alisherovna, K. M., & Erkinovna, K. Z. (2024). ASSESSMENT OF THE RISK OF DEVELOPING DIABETES MELLITUS FOR MEN. Spectrum Journal of Innovation, Reforms and Development, 26, 114-123.
 31. Mamasoliyevna, D. N., Akmalovna, K. N., & Alisherovna, K. M. (2022). Quality of Life Depending on Gender. The Peerian Journal, 11, 71-77.
 32. Mamasoliyevna, D. N., Alisherovna, K. M., & Totlibayevich, Y. S. (2023). Diabetes Mellitus and Non-Alcoholic Fatty Liver Disease: the Facets of Conjugacy. Miasto Przyszłości, 35, 166-173.
 33. Akramovna, I. K., & Alisherovna, K. M. (2024). CAUSES OF ARRHYTHMIA DURING PREGNANCY. Journal of new century innovations, 45(3), 34-41.
 34. Davranovna, M. K., Alisherovna, K. M., Erkinovna, K. Z., & Nizamitdinovich, K. S. (2022). Assessment of the quality of life of patients with coronary heart disease. The Peerian Journal, 11, 44-50.
 35. Nizamitdinovich, K. S., Alisherovna, K. M., Erkinovna, K. Z., & Davranovna, M. K. (2022). Heart Lesions in Rheumatological Diseases. Texas Journal of Medical Science, 13, 91-94.



36. Jamshedovna, K. D., Alisherovna, K. M., Erkinovna, K. Z., & Davranovna, M. K. (2022). LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN PREGNANT WOMEN WITH PRE-ECLAMPSIA WITHOUT PROTEINURIA. *Spectrum Journal of Innovation, Reforms and Development*, 10, 135-140.
37. Alisherovna, K. M., Akramovna, I. K., Bakhtiyorovich, U. J., Nizamitdinovich, K. S., Jasurovna, J. S., Kairatovna, R. A., & Abdukholikovna, E. S. (2023). Exacerbations of chronic obstructive pulmonary disease and coronary atherosclerosis. *Journal of new century innovations*, 39(1), 176-178.
38. Abdurasulovna, H. N., Akramovna, I. K., Rustamovna, A. K., & Egamkulovich, X. B. (2023). Inflammatory Activity And Renal Pathology In Lupus Nephritis. *Spectrum Journal of Innovation, Reforms and Development*, 13, 89-94.
39. Akramovna, I. K., & Rustamovna, A. K. (2023, November). ULTRATOVUSH TEKHIRUV USULINING ERTA RIVOZHLANGAN OSTEOARTHRISIS KASALLIGIDAGI DIAGNOSTIC AHAMIYATI. In *International Conference on Medicine and Life Sciences* (pp. 72-75).
40. Akramovna, I. K., & Xudoyberdiyevna, K. G. (2020). QANDLI DIABET KASALLIGI FONIDA YURAK QON TOMIR TIZIMI KASALLIKLARINING KLINIK KECHUV XUSUSIYATLARI. *Journal of cardiorespiratory research*, 1(3), 59-62.
41. Akramovna, I. K., & Rustamovna, A. K. (2024). Peculiarities of Rheumatoid Arthritis with Hereditary Predisposition. *American Journal of Bioscience and Clinical Integrity*, 1(1), 11-17.
42. Erkinovna, K. Z., Alisherovna, K. M., Davranovna, M. K., & Nizamitdinovich, K. S. (2022). Correction of Cytokine Imbalance in the Treatment of Stable Angina Pectoris. *The Peerian Journal*, 11, 64-70.
43. Alisherovna, K. M., Nizamitdinovich, K. S., Davranovna, M. K., & Erkinovna, K. Z. (2022). Kidney Condition in Patients with Myocardial Infarction. *Texas Journal of Medical Science*, 13, 85-90.
44. Alisherovna, K. M., Erkinovna, K. Z., Djamshedovna, K. D., & Nizamitdinovich, K. S. (2023). QUALITY OF LIFE PATIENTS WITH OSTEOARTHRITIS. *Journal of new century innovations*, 36(1), 164-175.
45. Toshtemirovna, E. M. M., Alisherovna, K. M., Erkinovna, K. Z., & Xudoyberdiyevich, G. X. (2022). DIAGNOSIS OF CIRRHOTIC CARDIOMYOPATHY. *Spectrum Journal of Innovation, Reforms and Development*, 10, 141-147.
46. Alisherovna, K. M., & Erkinovna, K. Z. (2022). Assessment of the Immune-Inflammatory Relationship in Patients with Chronic Heart Failure with Rheumatoid Arthritis. *Central Asian Journal of Medical and Natural Science*, 3(2), 373-377.
47. Erkinovna, K. Z., Alisherovna, K. M., Bakhtiyorovich, U. J., & Djamshedovna, K. D. (2023). METABOLIC SYNDROME IN RHEUMATOID ARTHRITIS. *Journal of new century innovations*, 38(2), 203-211.
48. Erkinovna, K. Z., Khabibovna, Y. S., & Abrorovna, V. N. (2023). MONITORING OF QUALITY OF LIFE IN PATIENTS WITH ARTERIAL HYPERTENSION OF OLDER AGE GROUPS. *Academia Science Repository*, 4(5), 276-285.
49. Khabibovna, Y. S., Alisherovna, K. M., Erkinovna, K. Z., & Djamshedovna, K. D. (2023). Gender Characteristics of the Course of Rheumatoid Arthritis. *Miasto Przyszłości*, 40, 438-442.