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CLINICAL AND CARDIOMETABOLIC EFFICACY OF FRUCTOSE-1,6-DIPHOSPHATE (NEOSTIN) THERAPY IN PATIENTS WITH COMORBID CARDIOVASCULAR DISEASES AND TYPE 2 DIABETES MELLITUS

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Annotation

The article presents the results of a comparative evaluation of the clinical and cardiometabolic efficacy of fructose-1,6-diphosphate (Neostin) in patients with cardiovascular diseases and comorbid type 2 diabetes mellitus. The study included 203 patients who were divided into a main group (n=152), receiving Neostin in addition to standard cardiological and glucose-lowering therapy, and a control group (n=51), receiving conventional therapy. Neostin was administered intravenously at a dose of 5 g once daily for 10 days. The patients were followed for 6 months, with assessment of metabolic, lipid, hematological, coagulation, hemodynamic, functional, echocardiographic, and Holter monitoring parameters. The results demonstrated significant improvements in the main group, including reductions in fasting glucose, HbA1c, total cholesterol, triglycerides, LDL cholesterol, and NT-proBNP levels. Significant improvements were also observed in blood pressure, heart rate, frequency of angina attacks, exercise tolerance, left ventricular ejection fraction, ventricular volumes, left ventricular myocardial mass index, and pulmonary artery systolic pressure. Holter monitoring demonstrated a marked reduction in ventricular and supraventricular extrasystolic activity. Compared with standard therapy, the addition of Neostin was associated with significantly greater positive changes in metabolic control, cardiovascular function, myocardial remodeling, and electrical stability. The findings indicate that fructose-1,6-diphosphate may have a favorable cardiometabolic effect and may be considered as a component of comprehensive therapy in patients with cardiovascular diseases and comorbid type 2 diabetes mellitus.

Keywords: fructose-1,6-diphosphate; Neostin; cardiovascular diseases; type 2 diabetes mellitus; cardiometabolic efficacy; diabetic cardiomyopathy; myocardial metabolism; heart failure; NT-proBNP; glycemic control; lipid profile; endothelial function; myocardial remodeling; left ventricular ejection fraction; arrhythmia; Holter monitoring.

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Introduction

One of the most pressing global challenges in modern medicine is the comorbid course of cardiovascular diseases (CVDs) and type 2 diabetes mellitus (T2DM). According to statistical data, mortality among patients with comorbid cardiovascular diseases and type 2 diabetes mellitus is 2–4 times higher than that observed in the general population [1]. Myocardial involvement in the setting of diabetes mellitus, known as diabetic cardiomyopathy, is closely associated not only with atherosclerotic processes but also with profound metabolic alterations in cardiomyocytes. Under conditions of chronic hyperglycemia and insulin resistance, myocardial energy metabolism undergoes substantial changes: glucose utilization is impaired, and cardiomyocytes shift almost completely, by up to 90–95%, toward ATP production through the β-oxidation of free fatty acids [2, 3]. This metabolic shift markedly increases myocardial oxygen demand, contributes to mitochondrial dysfunction, promotes lipotoxicity, and induces pronounced oxidative stress associated with the accumulation of reactive oxygen species [4, 5]. Under ischemic and hypoxic conditions, intracellular lactate accumulation leads to intracellular acidosis, which in turn promotes intracellular calcium (Ca^{2+}) accumulation and apoptosis of cardiomyocytes [6, 7]. Fundamental studies conducted in recent years have demonstrated that even during short-term optimal glycemic control in patients with type 2 diabetes mellitus, the development of microvascular complications affecting the vascular endothelium and myocardium may persist. This phenomenon, known as "metabolic memory," is primarily associated with chronic mitochondrial oxidative stress and ATP deficiency [8]. From this perspective, the inclusion of metabolic agents such as fructose-1,6-diphosphate in conventional treatment regimens appears pathogenetically justified, as these agents may directly modulate cellular metabolic processes and potentially interrupt the mechanisms underlying "metabolic memory" [9, 10]. One of the most relevant areas of contemporary cardiology and endocrinology is the development of effective treatment algorithms for patients with comorbid conditions, particularly those with cardiovascular diseases occurring in the setting of type 2 diabetes mellitus [1].

In view of the above, evaluating the clinical efficacy of Neostin (fructose-1,6-diphosphate) as part of the comprehensive treatment of cardiovascular diseases in patients with comorbid type 2 diabetes mellitus, as well as assessing its effects on myocardial contractility, endothelial function, and metabolic parameters, represents an important scientific and practical objective.

Aim of the study: To comparatively evaluate the clinical and cardiometabolic efficacy of Neostin (fructose-1,6-diphosphate) over a 6-month follow-up period in patients with cardiovascular diseases and comorbid type 2 diabetes mellitus.

Materials and Methods: A total of 203 patients with type 2 diabetes mellitus (T2DM) and comorbid cardiovascular diseases (CVDs) were enrolled in the study. Patients were divided into two groups according to their clinical status, laboratory parameters, and treatment approaches.

The **main study group** consisted of 152 patients who received Neostin (fructose-1,6-diphosphate) as metabolic infusion therapy in addition to standard cardiological and glucose-lowering treatment. The drug was administered intravenously by infusion at a dose

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of 50 mL (5 g) once daily for 10 days. The group included 82 (53.9%) male and 70 (46.1%) female patients.

The **control group** consisted of 53 patients who received only conventional standard cardiological and endocrine basic therapy. Neostin was not administered to patients in this group. The control group included 27 (52.9%) male and 24 (47.1%) female patients.

The **inclusion criteria** were: a confirmed diagnosis of type 2 diabetes mellitus, the presence of comorbid cardiovascular diseases, informed consent to participate in the study, and availability of complete clinical and laboratory data. The **exclusion criteria** included type 1 diabetes mellitus, severe hepatic or renal insufficiency, acute infectious diseases, malignant neoplasms, and non-compliance with the study protocol.

The obtained data were subjected to statistical analysis. Quantitative variables were expressed as mean ± standard deviation (M±SD). Between-group differences were assessed using Student's t-test or the Mann–Whitney U test, as appropriate. Categorical variables were compared using the chi-square (χ^2) test. Differences were considered statistically significant at $p<0.05$. Statistical analysis was performed using SPSS Statistics version 26.0.

Results of the study

Analysis of the baseline clinical and demographic characteristics of patients in the main and control groups demonstrated that the groups were comparable. The mean age was 58.4±4.2 years in the main group and 57.9±4.6 years in the control group (p=0.478). This finding indicates homogeneity between the groups with respect to age and supports the validity of subsequent comparative analyses.

In the main group, 82 (53.9%) patients were male and 70 (46.1%) were female. In the control group, the corresponding figures were 27 (52.9%) and 24 (47.1%), respectively (p=0.901). These findings demonstrate a comparable sex distribution between the study groups and suggest that sex-related differences were unlikely to substantially influence the results of the comparative analysis.

Table 1. Comparative Clinical and Demographic Characteristics of Patients in the Main and Control Groups

Indicator	Main Group (Neostin, n=152)	Control Group (n=51)	p
Mean age, years (M±SD)	58,4 ± 4,2	57,9 ± 4,6	0,478
Men, n (%)	82 (53,9)	27 (52,9)	0,901
Women, n (%)	70 (46,1)	24 (47,1)	0,901
Duration of T2DM, years (M±SD)	6,8 ± 1,4	6,5 ± 1,5	0,213
Body mass index, kg/m² (M±SD)	29,3 ± 2,2	28,9 ± 2,4	0,294
Stable angina pectoris, FC II, n (%)	76 (50,0)	26 (51,0)	0,896

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Stable angina pectoris, FC III, n (%)	76 (50,0)	25 (49,0)	0,896
Chronic heart failure, stage I, n (%)	84 (55,3)	29 (56,9)	0,842
Chronic heart failure, stage IIA, n (%)	68 (44,7)	22 (43,1)	0,842

The duration of diabetes mellitus was virtually identical in both groups: 6.8 ± 1.4 years in the study group and 6.5 ± 1.5 years in the control group (p=0.213). Analysis of body mass index (BMI) revealed a tendency toward overweight and obesity in the majority of patients. Mean BMI was 29.3 ± 2.2 kg/m² in the study group and 28.9 ± 2.4 kg/m² in the control group (p=0.294). The distribution of patients according to the functional class of effort angina was also comparable between the groups. In the study group, 50.0% of patients were classified as Functional Class (FC) II and 50.0% as FC III, whereas in the control group, these figures were 51.0% and 49.0%, respectively (p=0.896). Regarding the stages of chronic heart failure, Stage I was observed in 55.3% (n=84) of the study group and Stage IIA in 44.7% (n=68), while the corresponding figures for the control group were 56.9% (n=29) and 43.1% (n=22) (p=0.842).

Analysis of the study results demonstrated that patients in the study group receiving combination therapy showed significant improvement in metabolic status, cardiovascular functional state, and hemodynamic parameters. The observed positive changes were significantly superior to the trends seen in the control group, confirming the high clinical and pathogenetic efficacy of the treatment method employed (Table 2). Specifically, fasting glucose levels in the main group decreased from 9.2 ± 1.8 mmol/L at baseline to 7.1 ± 1.3 mmol/L at the end of the study, representing a 22.8% reduction from the initial value ($p_1 < 0.001$). A positive trend in this parameter was also observed in the control group—a decrease from 9.0 ± 1.7 mmol/L to 8.2 ± 1.5 mmol/L ($p_2 = 0.041$); however, the magnitude of the change was significantly smaller compared to the results recorded in the main group ($p_3 < 0.001$).

Table 2. Changes in metabolic parameters, lipid profile, and NT-proBNP levels during treatment

Indicator	Main group (n=152) Before	Main group After	p_1	Control group (n=51) Before	Control group: After	p_2	p_3
Fasting glucose, mmol/L	9,2±1,8	7,1±1,3	<0,001	9,0±1,7	8,2±1,5	0,041	<0,001
HbA1c, %	8,4±0,9	7,3±0,7	<0,001	8,3±0,8	7,9±0,8	0,067	<0,001

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Total cholesterol, mmol/L	5,9±0,8	5,1±0,7	<0,001	5,8±0,9	5,5±0,8	0,081	<0,001
Triglycerides, mmol/L	2,3±0,5	1,8±0,4	<0,001	2,2±0,4	2,0±0,4	0,093	0,002
LDL cholesterol, mmol/L	3,7±0,6	3,0±0,5	<0,001	3,6±0,6	3,3±0,6	0,076	<0,001
NT-proBNP, pg/mL	486±95	342±81	<0,001	472±89	425±85	0,058	<0,001

Note: p_1 — difference in values before and after treatment in the study group; p_2 — difference in values before and after treatment in the control group; p_3 — statistical significance of the difference in changes between the study and control groups.

Analysis of HbA1c levels—an integrated marker of glycemic control—revealed a significant improvement in carbohydrate metabolism in the study group. Specifically, this parameter decreased from 8.4 ± 0.9% at the start of treatment to 7.3 ± 0.7% by the end of the study, representing a significant positive change of 13.1% relative to the baseline value ($p_1 < 0.001$). A certain reduction in HbA1c levels was also observed in the control group—from 8.3 ± 0.8% to 7.9 ± 0.8% ($p_2 = 0.067$). A comparative analysis between the groups demonstrated that the magnitude of the HbA1c reduction was significantly greater in the study group than in the control group, confirming the high efficacy of the administered therapy in improving long-term glycemic control ($p_3 < 0.001$).

Analysis of lipid profile parameters demonstrated the high efficacy of the administered therapy in correcting lipid metabolism. Specifically, total cholesterol levels in the study group decreased from 5.9 ± 0.8 mmol/L at the start of treatment to 5.1 ± 0.7 mmol/L, representing a significant positive change of 13.6% ($p_1 < 0.001$). In the control group, this parameter decreased from 5.8 ± 0.9 mmol/L to 5.5 ± 0.8 mmol/L; however, the observed change did not reach statistical significance ($p_2 = 0.081$).

Triglyceride concentrations in the study group also showed significant improvement: the level decreased from 2.3 ± 0.5 mmol/L to 1.8 ± 0.4 mmol/L, representing a 21.7% reduction relative to the baseline value ($p_1 < 0.001$). In the control group, triglyceride levels decreased from 2.2±0.4 mmol/L to 2.0±0.4 mmol/L; however, this change did not reach statistical significance ($p_2=0.093$). A comparative analysis between the groups showed that the magnitude of the reduction in triglyceride levels in the study group was significantly greater than in the control group ($p_3=0.002$), confirming the high efficacy of the administered therapy in resolving atherogenic dyslipidemia.

Furthermore, LDL-cholesterol levels in the study group decreased from 3.7±0.6 mmol/L to 3.0±0.5 mmol/L ($p_1<0.001$), whereas in the control group, they decreased from 3.6±0.6 mmol/L to 3.3±0.6 mmol/L ($p_2=0.076$). The difference between the groups was statistically significant ($p_3<0.001$).

Analysis of the NT-proBNP biomarker—which is crucial for the early diagnosis and severity assessment of heart failure—revealed a positive effect of the administered

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therapy on myocardial functional status. Specifically, in the study group, NT-proBNP levels fell from 486±95 pg/mL at the start of treatment to 342±81 pg/mL at the end of the study, representing a significant 29.6% reduction from baseline ($p_1<0.001$). This trend indicates a substantial reduction in hemodynamic load on the heart walls and in myocardial stress.

A trend toward reduced NT-proBNP levels was also observed in the control group—decreasing from 472±89 pg/mL to 425±85 pg/mL—but this change did not reach statistical significance ($p_2=0.058$). A comparative analysis between the groups demonstrated that the magnitude of the reduction in NT-proBNP levels was significantly greater in the study group compared to the control group ($p_3 < 0.001$) (Table 2).

These results confirm the important role of the administered therapy in reducing neurohumoral activation, slowing myocardial remodeling processes, and improving the clinical course of heart failure. Furthermore, the significant reduction in NT-proBNP levels serves as a key indicator associated with improved patient functional status and long-term cardiovascular prognosis.

Upon completion of the study, patients in the study group exhibited significant positive changes in several complete blood count parameters compared to the control group. Specifically, hemoglobin levels in the study group rose from 132.4 ± 11.8 g/L to 136.7 ± 10.6 g/L, representing a statistically significant positive change ($p_1 = 0.018$). In the control group, this parameter increased from 133.1 ± 10.9 g/L to 134.2 ± 10.4 g/L; however, this change did not reach statistical significance ($p_2 = 0.412$). Comparative analysis between the groups revealed that the changes in hemoglobin levels were significantly more pronounced in the study group ($p_3 = 0.041$). Erythrocyte counts in the study group also increased from 4.42 ± 0.38 × 10^{12}/L to 4.56 ± 0.35 × 10^{12}/L, indicating a statistically significant positive trend ($p_1 = 0.026$). In the control group, this parameter remained virtually unchanged ($p_2 = 0.571$). The difference between the groups was statistically significant ($p_3 = 0.048$) (Table 3).

Table 3. Changes in complete blood count parameters during treatment

Indicator	Main group (n=152) Before	Main group After	p_1	Control group (n=51) Before	Control group: After	p_2	p_3
Hemoglobin, g/L	132,4±11,8	136,7±10,6	0,018	133,1±10,9	134,2±10,4	0,412	0,041
Erythrocytes, ×10^{12}/L	4,42±0,38	4,56±0,35	0,026	4,45±0,36	4,48±0,34	0,571	0,048
Leukocytes, ×10^9/L	8,1±1,4	6,9±1,2	<0,001	8,0±1,3	7,6±1,2	0,084	<0,001
Platelets, ×10^9/L	248±38	241±35	0,214	245±36	243±34	0,698	0,389
Neutrophils, %	66,8±6,2	61,2±5,8	<0,001	66,1±5,9	64,4±5,7	0,137	<0,001

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Lymphocytes, %	24,1±4,3	29,6±4,7	<0,001	24,8±4,1	26,3±4,2	0,118	<0,001
Monocytes, %	6,3±1,2	6,7±1,1	0,083	6,2±1,1	6,3±1,2	0,744	0,216
ESR, mm/h	18,4±5,7	12,8±4,3	<0,001	17,9±5,2	15,6±4,8	0,091	<0,001

The leukocyte count—a key laboratory marker of inflammatory processes—decreased in the study group from 8.1±1.4×10⁹/L to 6.9±1.2×10⁹/L, representing a significant positive change of 14.8% ($p_1<0.001$). A downward trend was also observed in the control group, but the change did not reach statistical significance ($p_2=0.084$). The difference between the groups was highly significant ($p_3<0.001$).

Analysis of the platelet count revealed no substantial changes in either group. In the study group, this parameter shifted from 248±38×10⁹/L to 241±35×10⁹/L ($p_1=0.214$), while in the control group, it went from 245±36×10⁹/L to 243±34×10⁹/L ($p_2=0.698$). No statistically significant intergroup differences were found ($p_3=0.389$).

Analysis of the leukocyte differential count showed that the proportion of neutrophils in the study group decreased from 66.8±6.2% to 61.2±5.8%, a statistically significant reduction ($p_1<0.001$). In the control group, the decrease in this parameter did not reach a significant level ($p_2=0.137$). Meanwhile, the proportion of lymphocytes in the study group increased from 24.1±4.3% to 29.6±4.7%, indicating an improvement in immunological status ($p_1<0.001$). In the control group, the change in lymphocyte levels did not reach statistical significance ($p_2=0.118$). Intergroup differences for both indicators were highly significant ($p_3 < 0.001$).

Analysis of the monocyte fraction in the study group showed an increase from 6.3 ± 1.2% to 6.7 ± 1.1%; however, this change did not reach statistical significance ($p_1 = 0.083$). No significant changes were observed in the control group either ($p_2 = 0.744$). The intergroup difference was also not significant ($p_3 = 0.216$).

Erythrocyte sedimentation rate (ESR)—a key integrated indicator of inflammatory activity—decreased in the study group from 18.4 ± 5.7 mm/h to 12.8 ± 4.3 mm/h, representing a highly significant positive trend ($p_1 < 0.001$). A trend toward decreased ESR was also observed in the control group, but the change did not reach statistical significance ($p_2 = 0.091$) (Table 3). The intergroup difference was significant, indicating much more effective control of inflammatory processes in the study group ($p_3 < 0.001$).

Thus, complete blood count results confirmed that the administered therapy led to reduced inflammatory activity, normalization of immunological markers, and improvement in several hematopoiesis parameters. The findings demonstrated both clinical and laboratory efficacy of the treatment method used in the study group.

Analysis of coagulation parameters revealed an improvement in the hemostatic system during treatment, as well as a reduction in hypercoagulable changes. By the end of the study, patients in the study group showed positive changes in several blood coagulation parameters; these changes were significantly more pronounced than those observed in the control group. Specifically, prothrombin time (PT) in the study group decreased from 14.2

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± 1.6 s to 13.4 ± 1.3 s, representing a statistically significant change ($p_1 = 0.002$). In the control group, this parameter changed from 14.0 ± 1.5 s to 13.8 ± 1.4 s; however, this trend did not reach statistical significance ($p_2 = 0.327$). A comparative analysis between the groups showed that the changes in PT in the study group were significantly more pronounced ($p_3 = 0.018$) (Table 4).

A positive trend was also observed in the analysis of the prothrombin index (PTI). In the study group, the PTI level increased from 88.6 ± 9.4% to 94.8 ± 8.1%, a highly significant change ($p_1 < 0.001$). In the control group, this parameter increased from 89.2 ± 8.7% to 91.0 ± 8.3%, but this change did not reach statistical significance ($p_2 = 0.214$). The intergroup difference was significant, confirming a more pronounced normalization of hemostatic parameters in the study group ($p_3 = 0.006$).

The International Normalized Ratio (INR) in the study group decreased from 1.14 ± 0.12 to 1.06 ± 0.10, demonstrating a statistically significant positive trend ($p_1 < 0.001$). In the control group, the INR decreased from 1.13 ± 0.11 to 1.10 ± 0.10; however, this change did not reach statistical significance ($p_2 = 0.119$). The results of the intergroup comparison showed that the changes in the study group were more effective compared to the control group (p_3=0.011) (Table 4).

Таблица 4. Динамика показателей коагулограммы на фоне лечения

Indicator	Main group (n=152) Before	Main group After	p_1	Control group (n=51) Before	Control group: After	p_2	p_3
Prothrombin time (PT), sec	14,2±1,6	13,4±1,3	0,002	14,0±1,5	13,8±1,4	0,32	0,018
Prothrombin index (PTI), %	88,6±9,4	94,8±8,1	<0,001	89,2±8,7	91,0±8,3	0,21	0,006
International Normalized Ratio (INR)	1,14±0,12	1,06±0,1	<0,001	1,13±0,11	1,10±0,1	0,11	0,011
Fibrinogen, g/L	4,3±0,8	3,6±0,6	<0,001	4,2±0,7	4,0±0,7	0,083	<0,001
aPTT, sec	30,8±4,2	32,6±3,8	0,004	31,1±4,0	31,6±3,9	0,452	0,027

In the study group, the level of fibrinogen—an important marker of plasma acute-phase proteins and thrombogenesis—decreased from 4.3 ± 0.8 g/L to 3.6 ± 0.6 g/L, representing a significant reduction of 16.3% ($p_1 < 0.001$). In the control group, this parameter decreased from 4.2 ± 0.7 g/L to 4.0 ± 0.7 g/L, but statistical significance was not reached ($p_2 = 0.083$). The difference between the groups was highly significant ($p_3 < 0.001$), indicating a substantial reduction in inflammatory and thrombogenic risk in the study group.

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Activated partial thromboplastin time (aPTT) in the study group increased from 30.8 ± 4.2 s to 32.6 ± 3.8 s, a statistically significant change ($p_1 = 0.004$). In the control group, this parameter changed from 31.1 ± 4.0 s to 31.6 ± 3.9 s, but the difference was not significant ($p_2 = 0.452$). The intergroup comparison also revealed a significant difference ($p_3 = 0.027$) (Table 4).

Thus, the analysis of coagulation parameters demonstrated the high efficacy of the therapy administered to the study group in normalizing the hemostatic system, reducing hypercoagulability, and lowering the risk of thrombosis. In particular, the favorable changes in fibrinogen, INR, and prothrombin index (PTI) confirm the anticoagulant and antithrombotic effects of the treatment.

Positive dynamics were also observed in the analysis of hemodynamic parameters. Systolic blood pressure in the study group decreased from 148 ± 12 mmHg... ...to 129±8 mmHg ($p_1<0.001$), and in the control group—from 147±11 mmHg to 136±10 mmHg ($p_2=0.032$). Diastolic blood pressure changed from 92±7 mmHg to 81±5 mmHg ($p_1<0.001$) and from 91±8 mmHg to 86±6 mmHg ($p_2=0.048$), respectively. Superiority of the study group was confirmed for both parameters ($p_3<0.001$). Heart rate in the study group decreased from 84±9 bpm to 72±6 bpm ($p_1<0.001$), and in the control group—from 83±8 bpm to 77±7 bpm ($p_2=0.041$). The intergroup difference remained significant ($p_3<0.001$) (Table 5).

Table 5. Dynamics of hemodynamic parameters, clinical symptoms, and functional status during treatment

Indicator	Main group (n=152) Before	Main group After	p_1	Control group (n=51) Before	Control group: After	p_2	p_3
Systolic BP, mmHg	148±12	129±8	<0,001	147±11	136±10	0,032	<0,001
Diastolic BP, mmHg	92±7	81±5	<0,001	91±8	86±6	0,048	<0,001
Heart rate, bpm	84±9	72±6	<0,001	83±8	77±7	0,041	<0,001
Angina attacks (per week)	5,8±1,4	2,3±0,9	<0,001	5,6±1,3	4,2±1,1	0,037	<0,001
NYHA functional class	2,8±0,4	1,9±0,3	<0,001	2,7±0,5	2,4±0,4	0,071	<0,001
6-minute walk test, m	312±48	398±52	<0,001	318±46	352±49	0,044	<0,001

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Note: p_1 — difference in parameters before and after treatment in the study group; p_2 — difference in parameters before and after treatment in the control group; p_3 — statistical significance of the difference in changes between the study and control groups. BP — blood pressure; HR — heart rate; NYHA — New York Heart Association..

Analysis of the clinical symptom dynamics revealed a significant reduction in the ischemic syndrome during treatment. Specifically, the frequency of angina attacks in the study group decreased from an average of 5.8±1.4 to 2.3±0.9 per week, representing a 60.3% reduction relative to baseline ($p_1<0.001$). This result reflects a substantial decrease in myocardial ischemia episodes and the high efficacy of the anti-anginal therapy.

A certain reduction in the frequency of angina attacks was also observed in the control group—from 5.6±1.3 to 4.2±1.1 per week ($p_2=0.037$). However, this positive trend was significantly less pronounced than the changes recorded in the study group. A comparative analysis between the groups showed that the reduction in the number of angina attacks in the study group was statistically significantly greater than in the control group ($p_3<0.001$).

The results confirm the significant clinical value of the administered therapy in improving myocardial perfusion, reducing ischemic symptoms, and increasing patients' tolerance for daily physical activity. The significant reduction in the frequency of angina attacks is a key indicator of improved patient quality of life and clinical prognosis.

Results from the 6-minute walk test, which assesses patients' functional status, also demonstrated significant improvement. In the study group, the distance covered increased from 312±48 m to 398±52 m—an increase of 86 m, or 27.6% ($p_1<0.001$). In the control group, this parameter increased from 318±46 m to 352±49 m ($p_2=0.044$). The intergroup difference was statistically significant, indicating a substantially greater recovery of functional capacity in the study group ($p_3 < 0.001$) (Table 5).

In our study, an analysis of echocardiographic parameters revealed a positive effect of the administered therapy on the structural and functional status of the heart. Specifically, left ventricular ejection fraction (LVEF) in the study group increased from 49.2 ± 4.8% to 54.8 ± 4.1%, representing a significant positive change of 11.4% ($p_1 < 0.001$). In the control group, this parameter increased from 49.7 ± 5.1% to 51.6 ± 4.9%, but the change did not reach statistical significance ($p_2 = 0.084$). The intergroup difference was statistically significant, indicating a much more pronounced improvement in myocardial pumping function in the study group ($p_3 < 0.001$) (Table 6).

Table 6. Dynamics of echocardiographic parameters during treatment

Indicator	Main group (n=152) Before	Main group After	p_1	Control group (n=51) Before	Control group: After	p_2	p_3
LVEF, %	49,2±4,8	54,8±4,1	<0,001	49,7±5,1	51,6±4,9	0,084	<0,001
EDV, ml	146,3±18,4	136,7±15,2	<0,001	144,8±17,9	141,2±16,8	0,172	0,003
ESV, ml	74,6±11,2	62,8±9,4	<0,001	73,8±10,8	69,9±10,2	0,094	<0,001

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SV, ml	71,7±9,6	74,9±8,7	0,011	71,0±8,9	72,1±8,4	0,438	0,041
Left atrial size, mm	42,1±3,8	39,8±3,2	0,003	41,7±3,5	40,9±3,3	0,217	0,018
LVMI, g/m²	128,4±14,6	119,2±12,1	<0,001	126,7±13,8	123,5±13,2	0,183	<0,001
PASP, mmHg	34,8±6,2	29,4±5,3	<0,001	34,1±5,8	32,7±5,4	0,194	0,002

Note: p_1 — difference in parameters before and after treatment in the study group; p_2 — difference in parameters before and after treatment in the control group; p_3 — statistical significance of the difference in changes between the study and control groups. LVEF — left ventricular ejection fraction; EDV — end-diastolic volume; ESV — end-systolic volume; SV — stroke volume; LVMI — left ventricular myocardial mass index; sPAP — systolic pulmonary artery pressure.

Left ventricular end-diastolic volume (EDV) in the study group decreased from 146.3±18.4 ml to 136.7±15.2 ml (p_1<0.001), whereas in the control group, it decreased from 144.8±17.9 ml to 141.2±16.8 ml (p_2=0.172). The intergroup difference was significant (p_3=0.003), indicating a reduction in left ventricular dilation and a favorable change in remodeling processes.

Left ventricular end-systolic volume (ESV) in the study group also decreased from 74.6±11.2 ml to 62.8±9.4 ml (p_1<0.001), while the change in this parameter in the control group did not reach statistical significance (p_2=0.094) (Table 5). Intergroup comparison revealed a significant difference favoring the study group (p_3<0.001).

Analysis of stroke volume (SV) also indicated an improvement in myocardial pump function. In the study group, this parameter increased from 71.7±9.6 ml to 74.9±8.7 ml (p_1=0.011), while in the control group, it went from 71.0±8.9 ml to 72.1±8.4 ml (p_2=0.438). The intergroup difference reached statistical significance (p_3=0.041).

Left atrial size in the study group decreased from 42.1±3.8 mm to 39.8±3.2 mm (p_1=0.003), whereas no significant change in this parameter was observed in the control group (p_2=0.217). The intergroup difference was statistically significant (p_3=0.018), indicating a reduction in the pressure load on the cardiac chambers.

Left ventricular myocardial mass index (LVMI) in the study group decreased from 128.4±14.6 g/m² to 119.2±12.1 g/m², indicating regression of myocardial hypertrophy (p_1<0.001). No significant changes in this parameter were observed in the control group (p_2=0.183). The intergroup difference was highly significant (p_3<0.001).

Pulmonary artery systolic pressure (PASP) decreased from 34.8±6.2 mmHg to 29.4±5.3 mmHg (p_1<0.001) in the study group, and from 34.1±5.8 mmHg to 32.7±5.4 mmHg (p_2=0.194) in the control group. The intergroup difference was statistically significant (p_3=0.002), indicating a reduction in the severity of pulmonary hypertension and an improvement in pulmonary hemodynamics (Table 6).

Thus, the analysis of echocardiographic parameters confirmed the high efficacy of the administered therapy in improving systolic cardiac function, slowing pathological remodeling processes, reducing myocardial hypertrophy, and stabilizing hemodynamic

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status. The results demonstrate a significantly greater degree of recovery of the heart's structural and functional status in the study group compared to the control group. According to the study results, a statistically significant and clinically meaningful reduction in arrhythmic activity was observed in the main group of patients receiving fructose-1,6-diphosphate (Neostin) during a 10-day treatment course. Analysis of Holter monitoring data showed that the number of ventricular extrasystole episodes in the main group decreased from 1,840 ± 210 to 580 ± 95, representing a relative reduction of over 68% ($p_1 < 0.001$). Furthermore, the incidence of supraventricular extrasystoles decreased significantly from 620 ± 88 to 260 ± 60, demonstrating a marked positive trend ($p_1 < 0.001$).

Certain positive changes were also observed in the control group receiving standard therapy; however, the magnitude of these changes remained relatively modest. Specifically, the number of ventricular extrasystole episodes decreased from 1,810 ± 195 to 1,380 ± 170, and supraventricular extrasystoles decreased from 610 ± 85 to 420 ± 72 ($p_2 < 0.05$) (Table 7).

Table 7. Dynamics of daily arrhythmic episodes during therapy with fructose-1,6-diphosphate (Neostin) (results of 10-day Holter monitoring)

Indicator	Main group (n=152) Before	Main group After	p_1	Control group (n=51) Before	Control group: After	p_2	p_3
Ventricular extrasystoles, n/day	1840±210	580±95	<0,001	1810±195	1380±170	<0,001	<0,001
Supraventricular extrasystoles, n/day	620±88	260±60	<0,001	610±85	420±72	0,021	<0,001

The results of the comparative analysis between the groups confirmed that the antiarrhythmic efficacy of therapy incorporating fructose-1,6-diphosphate (Neostin) is significantly superior to standard treatment ($p_3 < 0.001$). This indicates that the drug exerts its clinical effect by improving myocardial electrical stability and reducing the activity of ectopic impulse generation.

Conclusions

The inclusion of fructose-1,6-diphosphate (Neostin) in the standard treatment regimen for patients with cardiovascular disease and type 2 diabetes mellitus resulted in a significant improvement in clinical and cardiometabolic parameters. In the study group, fasting glucose levels decreased by 22.8% and HbA1c levels by 13.1%, ensuring effective control of carbohydrate metabolism.

A 29.6% reduction in NT-proBNP levels—a marker reflecting myocardial functional status—demonstrates Neostin's ability to reduce hemodynamic load on the heart walls, limit neurohumoral activation, and ameliorate the course of heart failure.

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The use of Neostin enhanced the anti-anginal efficacy of the therapy: the frequency of angina attacks decreased by 60.3%, and the patients' functional status improved significantly. Performance on the 6-minute walk test improved from 312±48 m to 398±52 m, indicating a recovery of exercise tolerance.

Echocardiographic analysis confirmed the cardioprotective effect of Neostin. Left ventricular ejection fraction increased from 49.2±4.8% to 54.8±4.1%; end-diastolic and end-systolic volumes (EDV and ESV) and the left ventricular mass index (LVMI) decreased, and a reduction in systolic pulmonary artery pressure was observed. These changes indicate a slowing of myocardial remodeling and a restoration of cardiac pumping function.

Fructose-1,6-diphosphate (Neostin) demonstrated high antiarrhythmic efficacy. The 24-hour count of ventricular extrasystoles decreased by 68.4% (from 1,840 to 580), and that of supraventricular extrasystoles by 58.1%, confirming the drug's important role in restoring myocardial electrical stability.

Overall, the inclusion of fructose-1,6-diphosphate (Neostin) in the standard regimen of cardiac and hypoglycemic therapy resulted in a comprehensive improvement of metabolic, hemodynamic, functional, and structural-functional parameters in patients with cardiovascular disease and comorbid type 2 diabetes mellitus, thereby demonstrating its high cardiometabolic efficacy and the advisability of its use in clinical practice.

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