European Journal of Humanities and Educational Advancements (EJHEA)
Available Online at: https://www.scholarzest.com
Vol. 3 No. 05, May 2022
ISSN: 2660-5589

APPLICATIONS THE DRUG NICOMEX AT TREATMENT OF PATIENTS WITH CHRONIC HEART FAILURE AND TYPE 2 DIABETES MELLITUS

Normatov Murod Buribayevich
Samarkand State Medical University
Assistant of the Department of Propaedeutics of Internal Diseases,
Samarkand, Uzbekistan

Article history:

Received: 8th March 2022
Accepted: 10h April 2022
Published: 22th May 2022

Abstract:

An open prospective randomized 16-week study was conducted to study the effect of the drug Nicomex as part of combination therapy in patients with CHF and type 2 diabetes on structural and functional parameters of the liver. The hepatoprotective capabilities of the drug Nicomex have been demonstrated: a significant decrease in the severity of cytolysis, cholestasis, steatosis index, the ability to reduce the severity of structural changes in the liver according to ultrasound. The noted hepatoprotective effects are mediated by the effect of the drug Nicomex on the processes of lipid peroxidation, the activity of antioxidant defense enzymes, and a decrease in the manifestation of chronic systemic inflammation. The use of the drug Nicomex contributes to a more pronounced combined hypolipidemic effect, and also reduces the severity of insulin resistance. The noted hepatoprotective effects of the drug Nicomex improve not only metabolic processes in the liver, but also can significantly change the cardiovascular risk in this category of patients.

Keywords: chronic heart failure, type 2 diabetes mellitus, non-alcoholic fatty liver disease, Nicomex, hepatoprotection

CHF — chronic heart failure, DM — diabetes mellitus, IR — insulin resistance, ATP — adenosine triphosphate, HCV — chronic systemic inflammation, FFA — free fatty acids, OSSN — Society of Specialists in Heart Failure, NAFLD — non–alcoholic fatty liver disease, GB - hypertension, CHD — ischemic disease heart, alt — alanine aminotransferase, AST — aspartic aminotransferase, alkaline phosphatase, GGTP — γ—glutamyltranspeptidase, DC - diene conjugates, MDA — malone dialdehyde, IL — interleukin, LDL cholesterol — low—density lipoprotein cholesterol, HDL cholesterol — high—density lipoprotein cholesterol, IA — index atherogenicity, TG - triglycerides, PTI — prothrombin index, SOD — superoxide dismutase.

INTRODUCTION

In recent years, much attention has been paid to the violation of kidney function in cardiovascular diseases. The kidneys have a leading role in the formation and development of chronic heart failure (CHF), through the kidneys, the action of most pathogenetic agents for the treatment of CHF is realized. In addition, the risk of nephrotoxic effects of a number of drugs in patients with CHF is significantly higher than in the general population.

It is known that remodeling of the heart and structural and functional changes of the liver in CHF are closely interrelated, interdependent and manifest themselves regardless of the etiology, age and gender of patients. There are hemodynamic and ischemic mechanisms of liver damage in CHF, which is accompanied by the formation of ischemic hepatitis, congestive hepatopathy, and at advanced stages of CHF — cardiac fibrosis and cirrhosis of the liver. The liver is an independent target organ in type 2 diabetes. According to epidemiological studies, NAFLD in type 2 diabetes develops in 70-90% of cases. The pathogenetic basis for the development of NAFLD in patients with type 2 diabetes is the phenomenon of IR. Important pathogenetic links are disorders of glucose and lipid metabolism in adipose tissue. The liver acts as a center for the formation of IR. The main pathological phenomenon — an increase in the utilization of FFA as an alternative to glucose, leads, on the one hand, to compensatory hyperinsulinemia, and on the other — to a cascade of reactions leading to an intensification of the synthesis of atherogenic lipoprotein fractions. It should be noted that the liver is not only a passive target organ for CHF and type 2 diabetes, but also an active participant in maladaptive remodeling: with its defeat, there is a further increase in the risk of cardiovascular

complications, and the functional state of the liver has a significant impact on the prognosis and outcome of CHF. In addition, it should be taken into account that violations
biotransformation of drugs in patients with liver damage carried out by the n cytochrome P-450 system may lead to the development of hepatotoxicity of a number of drugs and changes in the pharmacokinetics and pharmacodynamics of drugs used in the treatment of CHF and type 2 diabetes. Thus, control over the functional state of the liver should be an integral component in the observation of a patient with CHF and type 2 diabetes, on the one hand. On the other hand, the use of "hepatoprotective" drugs in the complex treatment of this category of patients will reduce the risk of the expected adverse effects of taking a number of basic drugs, in particular statins. In accordance with modern principles of treatment of liver diseases, the program of complex therapy of such pathology includes etiotropic therapy, as well as adequate pharmacological correction of multifactorial and multi-temporal links of the pathogenesis of the disease [7]. Drugs that have a selective or preferential effect on the liver - hepatoprotectors — are used as means that affect the restoration of homeostasis in the liver, increase the resistance of the organ to the effects of pathogenic factors, normalization of functional activity and stimulation of reparative-regenerative processes in the liver. Considering that tissue hypoxia plays a significant role in the pathogenesis of hepatocyte damage, leading to disruption of mitochondrial functions, depletion of ATP reserves with activation of free radical processes, inclusion in combination therapy of patients with CHF and DM 2 types of drugs containing mitochondrial substrates — succinic acid (succinate), are promising both from the position of additional influence on the course of ischemic processes in cardiomyocytes and hepatocytes.
Of particular interest is a drug from the group of derivatives of 3-oxypyridine nicomex, which is characterized by a combination of two pharmacological properties — antihypoxic and antioxidant. As an antihypoxant, nicomex activates the succinate dehydrogenase pathway of glucose oxidation, which reduces the oxygen-intensive process of fatty acid oxidation (production of the same amount of ATP with less O2 consumption). The ability to directly increase the energy-synthesizing function of mitochondria by increasing the delivery and consumption of succinate by ischemic cells, to participate in the realization of the phenomenon of rapid oxidation of succinic acid by succinate dehydrogenase, as well as the activation of the mitochondrial respiratory chain, leading, as a result, to rapid ATP resynthesis, are realized in the effectiveness of the drug nicomex as a myocardial cytoprotector. The efficacy and safety of the additional use of the drug nicomex in the treatment of CHF, coronary heart disease, stable angina pectoris has been shown. At the same time, nicomex has a pronounced antioxidant activity, which makes it possible to reduce the clinical manifestations of oxidative stress when using it. However, there is no data on the possibility of using the drug nicomex in patients with CHF and type 2 diabetes from the point of view of the effect on the functional state of the liver in the available literature we did not meet.

The purpose of our study was to evaluate the hepatoprotective capabilities of the drug nicomex when used in combination therapy of patients with CHF and type 2 diabetes.

MATERIAL AND METHODS

An open prospective randomized 16-week study of the effect of the drug nicomex as part of combination therapy in patients with coronary heart disease and type 2 diabetes on the structural and functional state of the liver was conducted. The study included 60 patients aged 45-65 years, with CHF of functional classes I–II according to the classification of CHF (2002) and type 2 diabetes with a target level of glycated hemoglobin < 7.5%. All patients initially had a total cholesterol level > 5.0 mmol/l and TG > 1.7 mmol/l, HOMA index > 2.7, body mass index > 25 kg/m2. The patients included in the study had clinical and ultrasound signs of non-alcoholic liver steatosis. Patients with alcohol dependence (alcohol intake of more than 30 g per day) were not included in the study.
After randomization into two groups, patients of the 1st (main) group (30 people), in addition to basic therapy of coronary artery disease (angiotensin converting enzyme inhibitor, beta-blocker, antiplatelet agent, statin, the dose of which did not change during the study, if necessary calcium antagonists, nitrates), were prescribed nicomex at a dose of 0.4 g/day orally. The duration of the study was 16 weeks. The 2nd (control) group also included 30 people. Both groups were comparable in age, gender, severity of the disease, and the nature of basic therapy. The average dosages of basic therapy drugs in groups 1 and 2 did not significantly differ.
All patients underwent a physical examination, which included an assessment of their general condition, an office measurement of blood pressure on both hands in
sitting position according to the standard methodology, anthropometry. To verify the functional class of CHF, the criteria of the CHF (2002) and a test with a 6-minute walk were used. The assessment of the structural state of the liver was carried out on an ultrasound scanner with an assessment of the hepatic echogenicity of the parenchyma, vascular pattern, degree of attenuation of the echo signal to detect fatty degeneration on the Ergun ultrasound scale in the composition of Yilmaz and the allocation of ultrasound of the following classes: IA, IB, IC, II and III. To assess the functional state of the liver, the activity of ALT and AST, alkaline phosphatase and GGTP, total protein and albumin, total bilirubin, thymol test and prothrombin index in blood serum were studied according to generally accepted methods on a biochemical analyzer.
The state of the antioxidant system was assessed by determining the activity of antioxidant enzymes (catalase, superoxide dismutase) in the blood plasma and erythrocytes of patients. Catalase activity in erythrocytes was

determined by M.A. Korolyuk (1988) et al., superoxide dismutase activity was determined by V.A. Kostyuk et al. (1990). Lipid peroxidation was assessed by the content of DC and MDA. The level of DC was determined by the modified method of Z. Placer et al. (1976), MDA — using thiobarbituric acid by the modified method of I.D. Steel (1977). HCV syndrome was assessed by determining the level of C-reactive protein, IL-1β, IL-6 and tumor necrosis factor alpha (TNF-α) by enzyme immunoassay.

A number of metabolic indicators reflecting the state of carbohydrate (fasting blood glucose, basal insulin level with calculation of HOMA and QUICKI index), lipid (total cholesterol and its fractions, TG, IA) metabolism were studied.

RESULTS AND DISCUSSION

All patients included in the study had ultrasound signs of liver steatosis: diffuse hypoechoic echostructure, increased echostructure of the liver compared to the kidneys, blurred vascular pattern, distal attenuation of the signal, an increase in the ultrasound size of the liver. At the end of 16-week therapy with nicomex as part of the combination therapy of CHF in patients with type 2 diabetes, a decrease in liver size was noted in both groups 1 and 2. The observed changes were statistically insignificant in both groups.

The inclusion of the drug nicomex in combination therapy was accompanied by a significant decrease in the percentage of patients with initially higher class of structural changes according to ultrasound data: according to E. Yılmaz — IV, IC and II (76.6%), due to an increase in the percentage of patients with class IA at the end of 16-week therapy (73.3%). In the 2nd group, the indicators of the class on the E.Yılmaz scale practically did not change.

Under the influence of the drug nicomex as part of the combination therapy of CHF in patients with type 2 diabetes, a favorable dynamics of indicators reflecting the functional state of the liver was observed.

Initially, an increase in the activity of AST and ALT above normal values (but not more than three times the norm) was noted in 20% of cases in group 1 and in 23.3% — in the 2nd group. After 16 weeks of therapy with nicomex in as part of the combination therapy of CHF in patients with type 2 diabetes, hyperfermentemia was no longer registered in any patient in group 1, whereas in group 2, an increase in the level of AST activity remained in 10% of cases. The difference between the groups is statistically significant. In addition, there was a significant decrease in the activity of AST and ALT in the group of patients taking nicomex additionally (Δ,% = -39.06 and Δ,% = -26.93, respectively, vs Δ,% = - 4.1 and Δ,% = -0.98 in group 2). There was a decrease in the activity of both alkaline phosphatase and GGTP in patients receiving combination therapy with the inclusion of the drug nicomex. The activity of SCHF decreased by 22.7% in the 1st vs 0.34% in the 2nd group ($p < 0.05$), and GGTP by 41.86% vs 6.94 in the 1st and 2nd groups, respectively ($p < 0.05$). In addition, in the group of patients receiving nicomex as part of the combination therapy of CHF and type 2 diabetes, the percentage of patients with GGTP hyperfermentemia significantly decreased (from 26.7 to 0%), whereas in group 2, the increase in GGTP above 54 units/l in men and more than 35 units/l in women remained in 20% of patients. Noteworthy is a significant increase in PTI in group 1 (Δ,% = 7.54 vs Δ,% = -1.04 in groups 1 and 2, respectively, $p < 0.05$).

Laboratory parameters of hepatic cell insufficiency syndrome (total protein and albumin content in the blood), as well as mesenchymal inflammation syndrome (thymol test) under the influence of therapy did not undergo statistically significant changes.

The liver steatosis index in group 1 statistically significantly decreased by 9.43%, while in group 2 it increased by 2.46%, which may be due to a decrease in ALT and AST activity indicators, with the body mass index unchanged during the study in both group 1 and group 2.

The positive effect of the drug nicomex on the functional parameters characterizing the cytolysis and cholestasis syndrome noted in the course of the study is apparently mediated by the antioxidant effect of the drug. Initially, a significant intensification of lipid peroxidation processes was noted in both groups: an increase in the content of both primary (DC) and final peroxidation products (MDA), correlating with the severity of cytolysis syndrome. A positive correlation was revealed between the activity of ALAT and the level of DC ($r = -0.36$, $p < 0.05$), ALT and the steatosis index ($r = -0.53$, $p < 0.05$).

The inclusion of the drug nicomex in the combination therapy of patients with CHF and type 2 diabetes was accompanied by a decrease in the content of DC by 29.3% ($p < 0.05$), MDA by 33.2% ($p < 0.05$), while changes in these indicators in group 2, respectively, were Δ,% = – 9.8% and Δ,% = – 6.0%, respectively ($p > 0.05$).

In the study conducted against the background of 16-week therapy with nicomex as part of the combination therapy of patients with CHF and type 2 diabetes, a positive effect of the drug on the activity of antioxidant defense enzymes was noted.

The activity of the initially significantly reduced erythrocyte SOD in group 1 during 16-week therapy with nicomex increased by 20.6% ($p < 0.05$), and during

The 2nd group was only 3.8% ($p > 0.05$). There was a significant increase in the activity of erythrocyte catalase in groups 1 and 2 by 17.3% vs 12.3%, respectively.

The difference between the groups is statistically insignificant.

Many enzymes, including superoxide dismutase and catalase, are characterized by cross-regulation of activity. In addition, according to the literature, this type of multidirectional change in activity the antioxidant protection enzymes discussed are characteristic of hypoxia. There is an opinion that the reduction of hydrogen peroxide can serve as an additional source of molecular oxygen. Catalase, performing an antioxidant function, compensatorily increases the

efficiency of exogenous oxygen for energy purposes due to the partial return to the metabolic chains of oxidative phosphorylation of the molecular oxygen that is restored in the body by a single-electron pathway.
Immuno-inflammatory reactions with increased expression of proinflammatory cytokines play an important role in the formation of cytolysis and cholestasis
syndromes. The study initially showed a statistically significant increase in the content of all determined proinflammatory cytokines (CRP, IL-1β, IL-6, TNF-α), the most significant changes were undergone by CRP and TNF-α, correlating with activity ALT ($r = 0.36$, $p < 0.05$; $r = 0.32$, $p < 0.05$, respectively). At the end of the 16-week appointment the drug nicomex as part of the combined therapy of patients with CHF and type 2 diabetes showed a significant decrease in the content of IL-1ß and TNF-α by 46.5 and 32.73%, respectively, vs 12.95 and 11.4% in the control
group. The content of IL-6 in both groups did not undergo statistically significant changes.
The beneficial effect of the drug was revealed nicomex as part of the combination therapy of patients with CHF and type 2 diabetes for metabolic parameters characterizing carbohydrate and lipid metabolism. By the 16th week of the study, glycosylated hemoglobin in patients receiving nicomex as part of combination therapy decreased by 13.35% ($p < 0.05$) compared to that in group 2 (Δ,% = -0.83, $p > 0.05$). The differences between the groups are statistically significant. The results of our study indicate a significant decrease in the severity of IR in the 1st group of patients using the drug nicomex as part of combination therapy. The Homa index in group 1 decreased by 15.5% vs 11.6% in group 2 ($p < 0.05$), and the Quicki index increased in group 1 by 28.98% ($p = 0.05$) vs Δ,% = -0.69% in Group 2 (the difference between the groups is statistically significant).
The positive effect of the drug nicomex as part of the combined treatment of CHF in patients with type 2 diabetes for 16 weeks on the lipid profile was primarily expressed in a significant decrease in blood TG levels in group 1 patients by 25.89% ($p < 0.05$), which correlated with changes in the ultrasound class according to Yilmaz ($r = -0, 45$, $p < 9.05$). In addition, in group 1, a decrease in the percentage of patients with hypertriglyceridemia was noted by more than 2 times - from 56.7 to 26.7%. In group 2, the TSH level increased by 1.94% ($p > 0.05$), which may have a negative value for patients with CHF and type 2 diabetes not only due to the role of excess TG in the formation of NAFLD, but also cardiomyocyte steatosis, prognosis of fatal and non-fatal complications of coronary heart disease.
A statistically significant decrease in LDL cholesterol was noted in the group of patients taking nicomex as part of combination therapy of coronary heart disease (Δ,% -5.84 vs 2.61% in the control, $p < 0.05$). This hypolipidemic effect may be mediated by the above -mentioned decrease in the severity of IR, which determines
the development of atherogenic dyslipidemia in patients with DM 2 types. The change in other parameters of the lipid spectrum (IA, HDL cholesterol) was statistically insignificant both in the 1st and in the 2nd group.

CONCLUSIONS

Thus, the ability of the drug nicomex to have a significant effect on IR, the severity
of manifestations of oxidative stress and markers of CHF, lipid-lowering effect when used in combination therapy of CHF and type 2 diabetes causes its hepatoprotective capabilitiesin patients with NAFLD. The noted effects of the drug nicomex improve not only metabolic processes in the liver, but also can significantly reduce cardiovascular risk in patients of this category of patients.

LITERATURE

1. Alisherovna K. M., Davranovna M. H., Nizametdinovich K. S. Chronic Heart Failure in Women //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2022. – Т. 3. – №. 1. – С. 21-25.
2. Alisherovna M. K. 24-Hour Abp Monitoring Of Blood Pressure In Patients With Chronic Heart Failure And The State Of Kidney Function //Central asian journal of medical and natural sciences. – 2021. – Т. 2. – №. 1. – С. 197-204.
3. Alisherovna M. K., Erkinovna Z. K., Tatlibayevich S. Y. Liver Diseases in Pregnant Women, Principles of Treatment //Eurasian Research Bulletin. – 2022. – Т. 4. – С. 48-51.
4. Alisherovna M. K., Tatlibayevich S. Y. Prevention of the progression of chronic kidney disease by decompensation of chronic heart failure //Euro-Asia Conferences. – 2021. – Т. 4. – №. 1. – С. 54-58.
5. ALISHEROVNA M. K., XUDOYBERDIYEVICH G. X. Treatment of Chronic Heart Diseases Insufficiency Depending On the Condition of the Kidneys. – 2021.
6. Bekmuradova M. S., Khaydarov S. N. THE RELATIONSHIP BETWEEN INCREASED PULSE PRESSURE AND NATRIURETIC PEPTIDE //Journal of cardiorespiratory research. – 2022. – Vol. 3. – No. 1.
7. Buribayevich N. M. Treatment of Chronic Heart Failure in Patients with Type 2 Diabetes Mellitus //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2022. – Т. 3. – №. 1. – С. 183-186.
8. Khabibovna Y. S., Buribaevich N. M. STUDY OF PARAMETERS OF CENTRAL HEMODYNAMICS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS //Достижения науки и образования. – 2020. – №. 13 (67). – С. 57-59.
9. Khusainova M. A., Yarmatov S. T. CARDIAC ARRHYTHMIAS AND CARDIOHEMODYNAMIC DISORDERS IN PATIENTS VIRAL CIRRHOSIS OF THE LIVER //Scientific progress. – 2021. – Т. 2. – №. 2. – С. 196-202.

10. Yarmukhamedova S. et al. Features of diastolic dysfunction of the right ventricle in patients with hypertonic disease //Journal of Advanced Medical and Dental Sciences Research. – 2020. – Т. 8. – №. 9. – С. 74-77.
11. Yarmukhamedova S. et al. Study of indicators of intracardial hemodynamics and structural state of the myocardium in monotherapy of patients with arterial hypertension with moxonidin //Journal of Advanced Medical and Dental Sciences Research. – 2020. – Т. 8. – №. 9. – С. 78-81.
12. Normatov M.B. EFFICACY OF AMLODIPINE IN ARTERIAL HYPERTENSION COMBINED WITH TYPE 2 DIABETES MELLITUS //Журнал кардиореспираторных исследований. – 2022. – Т. 3. – №. 1.