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Experience of Magnesium and L-Carnitine Combine Use for Correction of Structural and Functional Heart Changes in Type 2 Diabetic Patients with End-Stage Kidney Disease

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Abstract

Introduction and purpose: It is important today to develop new pathogenetic strategies to reduce cardiovascular risk in type 2 diabetic patients with end-stage kidney disease (ESKD). The purpose of the study was to evaluate the efficacy of combine use of magnesium aspartate and L-Carnitine on character of heart changes in dynamics of complex treatment of the patients with diabetic kidney disease (DKD) undergoing hemodialysis (HD).

Material and methods: 42 type 2 diabetic ESKD patients were included in this prospective cohort study (male/female, 26/16; age, 59.5±0.7 years; HD duration, 31.2±4.6 months; diabetes mellitus duration, 174,6±7,8 months). The patients were divided into two groups: the 1st (main) group (n=22) was treated by combination of magnesium aspartate (0.5 g/day orally) by three 2-months' courses/year and L-carnitine (1 g/day parenterally after each HD session) throughout the year; the 2nd (comparison) group (n=20) was only on the basic therapy. The observation time was 12 months. A complete echocardiography and ultrasound scanning of

common carotid arteries (CCA) were performed. **Results:** During follow up period we found the reduction of the left atrium ($p=0.008$) and left ventricle (LV) diameters ($p=0.004$), decrease of LV mass index for 17,1% ($p=0.005$) and prevalence of pseudonormal and restrictive types of LV diastolic dysfunction for 53.3% ($p=0.026$), increase of the LV ejection fraction for 5.4% ($p=0.004$), and decrease the mean pulmonary artery pressure for 13% ($p=0.009$) in the main group. The annual incidence of both mitral and aortic valve calcification in the 2nd group was 10%, in the 1st group – 0%. After 12 months of treatment, increase of the CCA intima-media thickness ($p=0.23$) was recorded in the comparison group only. **Conclusions:** The combine use of magnesium and L-carnitine as part of a 12-month complex therapy provides an effective reduction of LV hypertrophy, improves its systolic and diastolic function, reduces pulmonary hypertension, and prevents the progression of cardiac valve calcification and atherosclerotic damage.

Key words: hemodialysis; diabetic kidney disease; heart remodeling; calcification of mitral and aortic valve; carotid intima-media thickness; progression; magnesium aspartate; L-carnitine

Introduction

Despite progressive scientific evidence, the survival of patients with end-stage kidney disease (ESKD), especially in diabetic kidney disease (DKD), remains quite low [1,2]. The main cause of very high incidence and mortality of such patients are cardiovascular complications – heart rhythm disorders, congestive heart failure (HF), coronary and cerebrovascular accidents [3, 4]. Ways of formation of maladaptive myocardial remodelling in patients with type 2 diabetes mellitus (DM) undergoing HD are complex and insufficiently studied, which complicates their adequate correction [5-7]. There are few reports on the therapeutic effect on the dynamics of structural and functional changes of the heart in ESKD patients with DKD [8, 9], mostly related to the pre-dialysis stage of chronic kidney disease (CKD) [10, 11] or the general HD population [12-14].

In recent years, it has been studied the role of disorders of magnesium homeostasis in the development and progression of cardiovascular disease in CKD [9, 11], as well as the possibility of its correction [15]. It has been established that hypomagnesemia is associated with increased atherosclerosis [16, 17], insulin resistance [18], dyslipidemia [19] and interferes (through the mechanisms of chronic inflammation, oxidative stress (OS), endothelial dysfunction (ED)) in the processes of pathological myocardial remodelling [17,

20, 21], vascular calcification, is a predictor of cardiovascular mortality in patients with type 2 DM who receive HD [22].

In the pathogenesis of structural and functional changes of the heart in ESKD patients with DKD an important role is given to disorders of energy metabolism of both myocardial and endothelial cells [10, 23, 24]. In terms of HD treatment, the effectiveness of L-carnitine as a powerful antioxidant and cytoprotector has been demonstrated in many observational studies [25-28], but separated from the cohort of patients with DM.

Given the presence of magnesium and L-carnitine deficiency in ESKD patients, the multifactorial mechanism of cardiovascular pathology at DKD, justified today is the search for new pathogenetic strategies for the treatment and prevention of hypertrophied myocardium, cardiac valve calcification (CVC), improvement of heart function, regression of pulmonary hypertension (PH), slowing the progression of atherosclerotic damage.

Purpose

The purpose of the study is to evaluate the effect of the combined use of magnesium aspartate and L-carnitine on the character of structural and functional changes in the heart in the dynamics of complex 12-month treatment of patients with type 2 DM undergoing HD.

Materials and methods

An open parallel longitudinal (prospective) study included 42 HD patients with DKD who have been treated in the Hemodialysis Department of Ternopil University Hospital (Ukraine). There have been 26 men and 16 women. The mean age of patients – 59.5 ± 0.7 years, the duration of HD has been 31.2 ± 4.6 months, and the duration of type 2 diabetes mellitus has been $174,6 \pm 7,8$ months.

The study has complied with patient safety rules, preserved their rights and canons of human dignity, as well as moral and ethical norms that comply with the basic provisions of the GSP (1996), the Council of Europe Convention on Human Rights and Biomedicine (1997), Helsinki Declaration of the World Medical Association on the ethical principles of conducting scientific medical research with human participation (1964-2008). All patients have given informed consent to participate in the study. The study protocol has been approved by the Commission on Bioethics of I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine. Criteria for inclusion in the study have included: the presence of type 2 DM, age 18-74 years, duration of HD ≥ 6 months, dose of HD $eKt/V \geq 1.4$, presence of informed consent of the patient, the ability to adequately cooperate in the study, lack of known hypersensitivity to components that are part of the drugs. Exclusion criteria: the presence of type 1 DM, age < 18 years, duration of HD < 6 months, $eKt/V < 1.4$,

decompensation of carbohydrate metabolism (glycosylated hemoglobin level $\geq 10\%$), acute and delayed (up to 6 months) myocardial infarction or stroke, hemoglobin level less than 80 g/L, cardiac decompensation (heart failure IIB-III stage), the presence of critical (severe) aortic stenosis or severe mitral or aortic insufficiency that required surgical treatment, cardiac arrhythmias and conduction that required constant antiarrhythmic treatment or pacemaker implantation, vascular thrombosis, obstructive pulmonary disease, severe liver disease, cancer, mental disorders, smoking, use of other metabolic drugs, aggravated allergy history, absence of consent to participate in the study.

When conducting clinical-diagnostic and treatment activities, we have relied on diagnostic and treatment protocols approved by the order of the Ministry of Health of Ukraine dated February 11, 2016 No. 89, on the recommendations of KDOQI and KDIGO on the diagnosis and treatment of CKD. HD has been performed to the patients according to the standard program (3 times a week for 4–4.5 h) using synthetic dialyzers and bicarbonate buffer. The provided dose of HD (coefficient Kt/V) has been calculated by the formula of natural logarithm.

According to the study design, depending on the method of treatment, all patients have been divided into two groups; the criterion by which the distribution took place has been the inclusion of the studied drugs in the complex treatment. Patients in both groups have been studied according to demographic, gender criteria, duration of DM, CKD, HD, dose of HD, rates of carbohydrate metabolism, blood pressure (BP), drug therapy, clinical and echocardiographic parameters. Basic therapy has consisted of hypoglycemic therapy, antihypertensive therapy (enalapril at a dose of 2.5-20 mg/d and amlodipine at a dose of 5-10 mg/d or bisoprolol at a dose of 5-10 mg/d); according to the indications – correction of anemia, hyperparathyroidism, hyperphosphatemia. The first (main) group (n=22) on the background of basic therapy has received a combination of magnesium aspartate (0.5 g/d (1 tablet 1 time per day) orally) and L-carnitine (1.0 g/d (5 ml of 20% solution for injection 3 times a week after a session of HD) parenterally). Administration of L-carnitine has been carried out continuously throughout the study period, magnesium aspartate – two-month courses three times a year. The second (comparison) group (n=20) has been only on basic therapy. The duration of observation in both groups – 12 months. In-depth clinical-laboratory and instrumental monitoring of patients has been performed three times: before treatment, after 6 months of treatment, after 12 months of treatment. The study period is sufficient to assess the effectiveness.

Morphometric and functional parameters of the heart, calcification of the mitral (MV) and aortic (AV) valves, the presence of valve dysfunction have been studied by performing echocardiography and Doppler echocardiography on an ultrasound system “Philips HD 11 XE” (USA) using a sensor with a frequency of 3.5 MHz according to the recommendations [29]. It has been used 2D-mode, M-mode with standard accesses, Doppler echocardiography (color Doppler echocardiography, pulse-wave and constant-wave Doppler echocardiography). The following parameters have been examined: diameter of the aortic root (Ao), the maximum size of the cavities of the left atrium (LA) and right ventricle (RV), the thickness of the interventricular septum (IVS) and the left ventricle posterior wall (LVPW) in diastole, left ventricle end diastolic size (LVED), diameter and mean pressure (PAP) in the pulmonary artery (PA). Left ventricle myocardial mass index (LVMI) has been calculated as the ratio of LV mass to body surface area []. Determined by the LV ejection fraction (EF) according to Simpson. Diastolic function of LV has been assessed by the ratio of transmitral flows in early (E) and late (A) diastole (E/A), time of slowing of early diastolic discharge of the left ventricle (DT), time of isovolumic relaxation time (IVRT) of the left ventricle. Interpretation of types of LV diastolic dysfunction has been performed according to standard methods [30]. The structure of MV and AV has been evaluated on a parasternal image along the short and long axes and characterized as norm, compaction and calcification [31]. The intima-media thickness of the common carotid artery (CCA IMT) as an indicator of the severity of atherosclerosis has been measured in the area contralateral to permanent vascular access and free of discrete plaques by ultrasound [32].

STATISTIC® Version 10.0 software package from “StatSoft, Inc.” (USA) has been used for statistical data analysis. Used methods of nonparametric statistics – Friedman’s method for comparison of dependent indices in three groups, Wilcoxon test – in two ones, Mann-Whitney U-test for comparison of independent indices in two groups, Pearson’s χ^2 -test for comparison of frequency values. When describing quantitative features, there have been given means and their standard errors ($M \pm m$), qualitative – percentages (%). Differences at $p < 0.05$ have been considered statistically significant.

Results

The results of evaluating the effectiveness of different treatment regimens on the dynamics of structural and functional indices of the heart in groups of patients with DKD undergoing HD are shown in tables 1 and 2.

Table 1. Echocardiography and Doppler echocardiography indices in HD patients with DKD on the background of modified therapy (M±m)

Index	Observation period			Friedman ANOVA χ^2/p
	before treatment (n=22)	after 6 months (n=22)	after 12 months (n=22)	
Ao diameter [cm]	3,79±0,03	3,76±0,03	3,74±0,03	3,84/0,146
LA diameter [cm]	4,38±0,12	4,26±0,11**	4,09±0,10***#	15,80/<0,001
LVED [cm]	5,55±0,10	5,40±0,11*	5,23±0,09***#	14,75/<0,001
IVS [cm]	1,24±0,02	1,20±0,03	1,17±0,02**	12,29/0,002
LVPW [cm]	1,19±0,02	1,13±0,02*	1,11±0,03*	10,22/0,006
LVMI [g/m ²]	184,6±9,9	167,7±7,7*	153,0±6,3***#	13,71/0,001
EF [%]	52,5±1,5	54,0±1,0*	55,5±1,1***#	10,26/0,006
E/A	1,31±0,11	1,11±0,09*	1,03±0,10*#	11,39/0,003
IVRT [ms]	90,6±5,8	103,0±7,1*	111,9±7,2***#	17,52/<0,001
DT [ms]	180,6±7,2	199,4±8,2*	209,9±9,1***#	17,37/<0,001
RV diameter [cm]	2,79±0,13	2,75±0,12	2,68±0,10*	8,13/0,017
PA diameter [cm]	2,88±0,12	2,83±0,11*	2,77±0,12***#	9,50/0,009
PAP [mmHg]	28,4±1,7	26,9±1,4*	24,6±1,1***#	13,29/0,001

Notes: Here and in table 2.

- * p <0,05, ** p <0,01 – in comparison with indices before treatment;
- # p <0,05, ## p <0,01 - in comparison with the data of the previous observation period.

Table 2. Echocardiography and Doppler echocardiography indices in HD patients with DKD on the background of basic therapy (M±m)

Index	Observation period			Friedman ANOVA χ^2/p
	before treatment (n=20)	after 6 months (n=20)	after 12 months (n=20)	
Ao diameter [cm]	3,88±0,05	3,87±0,05	3,89±0,06	1,68/0,433
LA diameter [cm]	4,56±0,13	4,51±0,11	4,43±0,09	3,46/0,177
LVED [cm]	5,76±0,17	5,72±0,15	5,73±0,15	3,29/0,193
IVS [cm]	1,23±0,03	1,21±0,03	1,20±0,03	2,67/0,264
LVPW [cm]	1,16±0,02	1,14±0,02	1,11±0,03*	5,39/0,068
LVMI [g/m ²]	182,6±12,7	176,3±11,0	173,5±10,7	4,28/0,118
EF [%]	52,0±1,4	52,7±1,0	53,0±1,0	2,05/0,358
E/A	1,31±0,13	1,27±0,12	1,23±0,11	5,55/0,062
IVRT [ms]	94,0±7,2	98,9±6,6	102,2±7,0*	9,15/0,010
DT [ms]	183,5±8,9	189,9±8,8	192,7±8,9*	7,09/0,029
RV diameter [cm]	2,88±0,14	2,85±0,13	2,83±0,13	1,71/0,424
PA diameter [cm]	2,84±0,14	2,83±0,14	2,81±0,14	2,91/0,233
PAP [mmHg]	31,8±2,0	30,5±1,7	29,6±1,5	4,26/0,119

For the first time we have found significant differences in almost all echocardiography and Doppler echocardiography indices in patients of the main group, while the dynamics of

these indices (except for LVPW, IVRT, DT) in the comparison group has been insignificant or absent, as confirmed by the Friedman test. Thus, after 12 months of therapy in patients whose basic treatment included a combination of magnesium aspartate and L-carnitine, it has been noted a decrease in LA diameter by 6.1% ($Z=2.66$, $p=0.008$), LVED – by 5.8% ($Z=2.86$, $p=0.004$), thickness of IVS – by 5.6% ($Z=2.74$, $p=0.006$) and LVPW – by 6.7% ($Z=2.03$, $p=0.043$), decrease in LVMI by 17.1% ($Z=2.80$, $p=0.005$), increase in EF by 5.4% ($Z=2.91$, $p=0.004$), IVRT – by 23.5% ($Z=2.84$, $p=0.005$), DT – by 16.2% ($Z=2.65$, $p=0.008$), decrease in E/A by 21.4% ($Z=2.17$, $p=0.030$), and in patients who has been on basic therapy, only a decrease in the thickness of LVPW – by 4.3% ($Z=2.10$, $p=0.036$), an increase in IVRT – by 8.7% ($Z=2.11$, $p=0.035$), DT – by 5% ($Z=2.07$, $p=0.038$). Moreover, by the end of the observation period in patients of the main group, in contrast to the comparison group, the prevalence of adverse (pseudonormal and restrictive) types of LV diastolic dysfunction has been significant (31.8 vs. 68.2%; $\chi^2=4.96$, $p=0.026$) less than before treatment, and the number of patients with normal function – more (18.2 vs. 0%; $\chi^2=4.40$, $p=0.036$). The index of Ao diameter in patients of the first and second groups during treatment has not changed significantly.

Changes in echocardiographic parameters regarding the characteristics of RV and PA in patients with type 2 DM, who have been on different treatment programs, are similar to the dynamics of the left parts of myocardium (see tables 1 and 2). One year after the start of treatment, patients in the main group showed a decrease in RV diameter by 3.9% ($Z=2.34$, $p=0.019$), LA diameter – by 3.8% ($Z=2.95$, $p=0.003$), PAP reduction – by 13.4% ($Z=2.61$, $p=0.009$), which has not occurred in the comparison group.

It should be noted that we registered positive significant changes in the structural and functional state of the heart in patients receiving modified treatment with magnesium aspartate and L-carnitine after 6 months of observation: LA diameter ($Z=2.58$, $p=0.010$), LVED ($Z=2.55$, $p=0.011$), LVPW ($Z=2.01$, $p=0.044$), LVMI ($Z=2.31$, $p=0.021$), EF ($Z=2.07$, $p=0.039$), E/A ($Z=2.00$, $p=0.046$), IVRT ($Z=2.03$, $p=0.042$), DT ($Z=2.16$, $p=0.031$), PA diameter ($Z=2.19$, $p=0.028$) and PAP ($Z=2.27$, $p=0.023$) (see table 1).

Characteristically, the degree of reduction of LV hypertrophy by LVMI index for a year in patients of the main group relative to patients of the comparison group has been significant (-31.6 ± 8.9 vs. 9.1 ± 7.1 g/m²; $Z=2.07$, $p=0.039$). In the third observation period, indices of Ao diameter ($Z=2.23$, $p=0.026$) LA diameter ($Z=2.42$, $p=0.015$), LVED ($Z=2.69$, $p=0.007$), EF ($Z=2.01$, $p=0.044$), DT ($Z=1.85$, $p=0.064$), PAP ($Z=2.55$, $p=0.011$) of the first and second groups differed.

According to the data presented in tables 3 and 4, the incidence of new cases of both calcification of MV and AV in patients with type 2 DM on basic treatment has been 10% per year, while the prevalence of CVC in patients, who obtained combination of magnesium aspartate and L-carnitine in the complex treatment, has not changed after 12 months of observation.

Table 3. State of MV in HD patients with DKD on the background of different therapy programs

MV	Main group (n=22)		Comparison group (n=20)	
	before treatment	after treatment	before treatment	after treatment
Norm [n/%]	4/18.2	3/13.6	6/30	3/15
Thickening [n/%]	6/27.3	7/31.8	3/15	4/20
Calcification [n/%]	12/54.5	12/54.5	11/55	13/65

Table 3. State of AV in HD patients with DKD on the background of different therapy programs

AV	Main group (n=22)		Comparison group (n=20)	
	before treatment	after treatment	before treatment	after treatment
Norm [n/%]	2/9.1	2/9.1	3/15	2/10
Thickening [n/%]	10/45.5	10/45.5	8/40	7/35
Calcification [n/%]	10/45.5	10/45.5	9/45	11/55

Of particular interest, in our opinion, are the results of a comparative assessment of the effect of different treatment programs on the dynamics of CCA IMT in patients with DKD undergoing HD (fig.1). Thus, in patients of the comparison group by the end of follow up there has been a significant increase in the average value of IMT by 9.1% (0.98 ± 0.04 vs. 1.07 ± 0.04 mm; $Z=2.27$, $p=0.023$), which did not occur in patients of the main group (0.88 ± 0.05 vs. 0.88 ± 0.05 ; $Z=0.09$, $p=0.925$). In addition, in the third period of the study, the first and second groups have differed in terms of CCA IMT ($Z=2.75$, $p=0.006$).

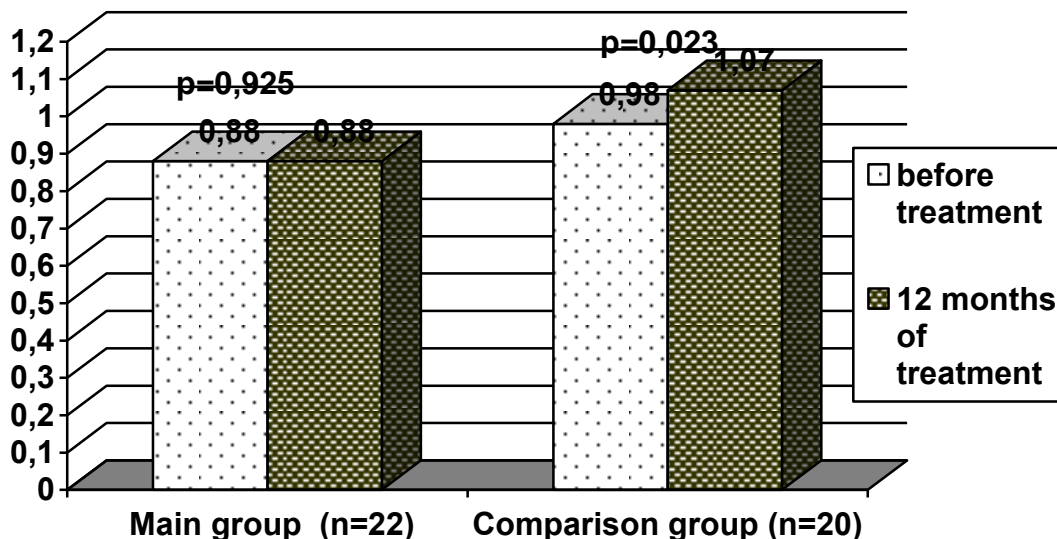


Fig. 1. Dynamics of changes of CCA IMT (mm) in HD patients with DKD on the background of different treatment programs.

Discussion

The results of this prospective observational study have proved for the first time the effectiveness of the combination of magnesium aspartate and L-carnitine in terms of positive dynamics of heart remodelling, prevention of progression of CVC and atherosclerotic damage in patients with type 2 DM. Modified pathogenetic therapy has provided a positive effect on the structural and functional state of the left and right heart – reduced the wall thickness of the LV, LVMI, cavity of LA, LV, RV, reduced mean PAP, improved LV systolic and diastolic function. At the same time, basic treatment has prevented the progression of left ventricular hypertrophy, its functional disorders, has suspended pathological remodelling of RV and PA, but has not prevented the progression of calcification of MV and AV, CCA TIM.

Data on the efficiency of angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers (CCBs) or β -blockers on processes of LV myocardial hypertrophy, its functions in ESKD are contradictory [33, 34], refer to the general cohort of HD patients, and there are no available reports on the influence of these antihypertensive drugs on the dynamics of echocardiography indices of RV, PH in DKD in the literature are not present at all. The positive but insufficient effect of basic treatment on the character of structural and functional disturbances of the myocardium and carotid vessels in patients with type 2 DM undergoing HD, is apparently due to the properties of ACE inhibitors, dihydropyridine CCBs and β -blockers to show hemodynamic, antiatherosclerotic, antifibrotic, endothelioprotective and other effects [35].

Based on KDIGO guidelines [36] for the development of new ways (endothelioprotective, anti-inflammatory, regenerative therapy) for the treatment and prevention of cardiovascular remodelling, CVC, etc. in ESKD, we have developed a new method of treating HD patients with DKD. The inclusion of magnesium aspartate and L-carnitine in our study is pathogenetically justified, based on significant experience in the use of these means for the prevention and treatment of pathology of the cardiovascular system [8, 13, 14, 17, 21, 25].

Carnitine (betaine- γ -amino- β -hydroxybutyric acid, nitrogen-containing hydroxy acid) is a low molecular weight substance with a mass of 162 daltons, partially (about 25%) synthesized by the kidneys and easily dialyzed during HD. The physiological form is the left-rotating isomer – L-carnitine [37]. As early as 1978, a decrease in serum carnitine concentration due to HD has been proved, which has been later confirmed by numerous studies [26, 38]. A clear decrease in carnitine after a session of HD is corrected by its movement from tissue depots, including from the myocardium, into the vascular bed, accompanied by a decrease in the concentration of carnitine in the heart muscle [26]. The content of total carnitine depends on the exogenous intake with food. However, HD patients with DKD often have MIA (malnutrition-inflammation-atherosclerosis) syndrome [39], which deepens energy metabolism, the intensity of OS, in particular in the myocardium. As far as fatty acid (FA) oxidation is the main source of energy, maintaining normal metabolism in the myocardium depends significantly on adequate carnitine levels. Depletion of L-carnitine reserves is currently considered as an additional pathogenetic mechanism for the development of cardiovascular complications [12-14, 26].

It has been experimentally proved [12, 26] that in the conditions of CKD, the catabolism of free FA in the myocardium decreases, the number of their underoxidized metabolites increases, including acyl-coenzyme A (acyl-CoA), which is formed under conditions of hypoxia of cardiomyocytes and vascular endothelium. L-carnitine, by lowering acyl-CoA levels, reduces the production of pro-inflammatory and prooxidant lipid metabolites that induce ED, myocardial hypertrophy and cardiomyocyte apoptosis [14, 40, 41]. It is believed [27, 41] that dyslipidemia significantly affects cardiovascular morbidity in patients with type 2 DM who receive HD. Thus, a number of studies have shown that the administration of L-carnitine increases the content of albumin, improves the lipid profile, reduces the content of C-reactive protein, reduces the manifestations of atherogenesis, OS and ED [25, 42, 43]. The results of many prospective studies have convincingly proven the anti-ischemic, anti-atherosclerotic, metabolic effects of L-carnitine, which helps to increase

tolerance to exercise and improve the quality of life of patients with ESKD [44]. Significant reduction in LVMI, improvement in myocardial remodelling, heart function in HD patients under the influence of myocardial cytoprotector L-carnitine has been demonstrated in several studies [35, 45]. In particular, Sakurabayashi et al. [14] have determined the direct effect of correction of impaired carnitine metabolism in the regression mechanisms of hypertrophied myocardium in ESKD. In the research of Fukami et al. [40] it is shown that oral L-carnitine supplementation leads to a decrease in advanced glycation end products, which is especially important for the reduction of ED in terms of HD and DKD [24].

In the current study, L-carnitine treatment has been combined with magnesium aspartate. Hemodynamic and non-hemodynamic effects of magnesium [8, 9, 11], most likely due to mechanisms of endothelial function and vascular-platelet hemostasis improvement, decreased chronic inflammation, lipid peroxidation, contribute to the positive dynamics of structural and functional indices of the heart in patients with type 2 DM. In addition, magnesium might augment the response to antihypertensive drugs [46]. It is possible that the direct inhibitory effect of magnesium on the active mechanisms of calcification and serum calcification propensity [46, 47, 49] prevented the progression of calcification of MV and AV and atherosclerosis in patients with DKD. In HD patients the annual incidence of valve calcification, especially of AV, reaches up to 8% [49]. Recently, Talari et al. [8] has shown that magnesium supplementation for 6 months leads to a decrease in CCA IMT in diabetic HD patients. Moreover, recently we have found a significant correlation of hypomagnesemia with impaired lipid profile, the number of desquamated endothelial cells, carotid artery lesions, CVC, as well as LV hypertrophy and dysfunction [50, 51].

Importantly, complex therapy with magnesium aspartate and L-carnitine in patients with type 2 DM who receive HD apparently helps to reduce postload on the myocardium by reducing peripheral vascular resistance, improving their elasticity, and thus – regression of hypertrophied myocardium. The search for new effective treatments should be aimed not only at eliminating diastolic dysfunction, but also at improving myocardial contractility.

Thus, magnesium and L-carnitine combine use in HD patients with DKD can determine the character of structural and functional transformations of the heart, its valve apparatus, atherosclerotic damage, which will ultimately contribute to the quality and life expectancy of this category of patients.

Conclusions

1. Inclusion in a complex 12-month therapy of a combination of magnesium aspartate and L-carnitine in patients with type 2 DM undergoing HD provides a positive effect

on the structural and functional state of the left and right heart – reduces the wall thickness of LV, LVMI, cavity of LA, LV, RV, reduces PH, improves systolic and diastolic function. Basic treatment prevents the progression of LV hypertrophy, its functional disorders and suspends pathological remodelling of RV.

2. Modified treatment, in contrast to standard therapy, prevents the progression of calcification of MV and AV, as well as the severity of atherosclerosis (CCA IMT) in HD patients with DKD.

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Information about the contribution of each participant:

O. Susla: concept and design of the study, formulation of conclusions, approval of the final version of the article.

Z. Litovkina: selection of patients for the study, analysis of the received data, preparation of the text of work.

I. Yakubyshyna: analysis of the sources of literature, preparation of the article for publication.

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