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PECULIARITIES OF TREATMENT OF CORONARY ARTERY DISEASE WITH CONCOMITANT TYPE 2 DIABETES MELLITUS WITH ANGIOTENSIN RECEPTOR BLOCKERS

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Summary

Introduction: the relevance of determining peculiarities of treatment of coronary artery disease with concomitant type 2 diabetes mellitus is high, as it solves several important medical, social and economic problems of society.
The aim: of research was to evaluate state of heart function (development of heart failure) and changes in glucose metabolism in patients with CAD with concomitant type II DM depending on diabetes stage and treatments with telmisartan and valsartan.
Materials and methods: Study included 106 patients with coronary artery diseases and type II DM with mean age 68.8±8.9 years; mean age of males (46.2%) was 65.2±9.0 years and females (53.8%) – 71.6±7.8 years. All patients were treated in cardiology department of CME «City clinical hospital № 27» of Kharkiv city government, which is clinical base of Departments of internal medicine № 2, clinical immunology and allergology of L. T. Malaya of Kharkiv National Medical University. All patients were divided into 4 groups depending on stage of diabetes. First group included patients with CAD and with no concomitant DM (n=36; mean age = 66.4±10.1 years); second – CAD and mild course of DM (n=21; mean age = 71.9±9.4 years); third group included patients with CAD and moderate DM (n=28; mean age = 69.7±8.0 years); and fourth group – patients with CAD and severe DM (n=21; mean age = 67.9±6.5 years).
Results: After treatment with valsartan and telmisartan no difference was observed in SBP, DBP and HR in both valsartan and telmisartan patients. However, it is obvious that levels of described variables mostly normalized, which suggests on high effectiveness of performed treatment.
Comparison of initial and post-treatment data showed significant changes observed both in heart function and glucose metabolism. It was found that valsartan users showed significant decrease in SBP, DBP and HR in patients with CAD only and CAD with moderate T2DM.
In all patients suggest that valsartan users will show decrease of HbA1c independently on DM stage, while telmisartan provides normalization of HbA1c only in moderate to severe DM patients. This suggests that telmisartan acts as protective and repairing medication in patients with concomitant CAD and T2DM, predominantly in moderate to severe stages of DM; valsartan increases cardiac function mostly in CAD only patients and in mild to severe DM, but influence on systolic and diastolic function was not found.
Conclusions: Our study demonstrates strong connection between glucose metabolism and heart function. It was shown that stage of T2DM significantly influence indices of morphological state of heart with effects on development of systolic and, predominantly, diastolic dysfunction, which further leads to development of heart failure. Moreover, it was shown, that treatments of patients with CAD with concomitant T2DM of different stages with ARBs (valsartan and telmisartan) provides protective effects on heart muscle and glucose metabolism. Study found significant correlations between levels of blood pressure, systolic and diastolic function and levels of glucose and HbA_{1c} in patients with different stages of T2DM.

Key words: **coronary artery disease, type 2 diabetes mellitus, valsartan, telmisartanglucose, correlations.**

INTRODUCTION

Course of coronary artery disease (CAD) is accompanied with chronic mismatch of oxygen usage and supply to myocardium [1]. Causes of ischemia include myocardial infarction in anamnesis and proven presence of atherosclerotic plague in coronary arteries [1]. Braun et al. [1] report of significant number of USA population aged 60-79 years with CAD. Authors also note that significant part of cardiovascular mortality is caused by CAD and in 2013 accounted up to 31% [1]. If speaking of treatment of CAD, it usually includes primary change of lifestyle, modification of risk factors, and usage of antiplatelet and antianginal medications [1].

Widely are discussed among medical scientists and practitioners risk factors, which significantly contribute to the development of course or exacerbations of CAD include increased blood pressure (BP), violated cholesterol and glucose levels [1, 2]. Reduction of CAD-associated mortality commonly includes treatment of comorbid hypertension and diabetes, accompanied with smoking and alcohol cessation [1]. Braun et al. [1] state that increasing of physical activity reduces cardiovascular mortality in patients with CAD (risk ratio: 0,74 [95% confidence interval 0,64-0,86]).

Initial treatment of hypertension in patients with diabetes [5] includes usage of angiotensin-converting enzyme inhibitors (ACEi), calcium channel blockers (CCB), diuretics and/or angiotensin receptor blockers (ARB) [1]. More attention is paid to CCB due to their impact on patients with CAD and heart rhythm violations [1].

Data suggest that diabetes mellitus (DM) and metabolic syndrome affects both men and women in same manner [3]. However, presence of type II DM impacts women more and influences survival rates [3]. It is also important to reach adequate glucose levels management, because diabetes is considered one of the most important risk factors for CAD [1, 2, 3], significantly affecting cardiovascular morbidity and mortality. However, data show that significant reduction of A1C less than 6% increases cardiovascular mortality in such patients compared to normal A1C levels up to 3.5 times [1].

According to literature [4], valsartan reduces incidence of new-onset DM in 14% in patients with cardiovascular diseases. Novel data also show that CCB reduce number of angina pectoris episodes up to 18%, but does not affect all-cause mortality and frequency of cardiovascular events [1]. Noteworthy, Liou et al. [2] show that CCB are independently associated with development of new-onset of diabetes in patients with hypertension (odd ratio: 1.10 [95% CI 1.02-1.08]) compared with non-users. Yang et al. [4] show that CCB compared to angiotensin receptor blockers increase incidence of DM (OR: 1.33 [95% CI 1.00-1.75]).

Moreover, Liou et al. [2] report that ARB decrease possible development of DM in patients with cardiovascular diseases: OR: 0.92 [95% CI 9.82-0.99], p=0.0028. Similar data are shown in research of Yang et al. [4]. Angiotensin receptor blockers have significantly lower odds of development of new-onset DM compared with other types of antihypertensive drugs [4]. Compared to ACEi, OR of DM development in ARB user is 0.98 [95% CI 0,76-1,30]; diuretics – 0,56 [95% CI 0,41-0,77]; β-blockers – 0,71 [95% CI 0,53-0,96]. Authors suggest that ARB significantly reduce risk of DM development and can act as preventive treatment for such patients [4].

The aim: of research was to evaluate state of heart function (development of heart failure) and changes in glucose metabolism in patients with CAD with concomitant type II DM depending on diabetes stage and treatments with telmisartan and valsartan.

Materials and methods. Study included 106 patients with coronary artery diseases and type II DM with mean age 68.8±8.9 years; mean age of males (46.2%) was 65.2±9.0 years and females (53.8%) – 71.6±7.8 years. All patients were treated in cardiology department of CME «City clinical hospital № 27» of Kharkiv city government, which is clinical base of Departments of internal medicine № 2, clinical immunology and allergology of L. T. Malaya of Kharkiv National Medical University.

All patients were divided into 4 groups depending on stage of diabetes. First group included patients with CAD and with no concomitant DM (n=36; mean age = 66.4±10.1 years); second – CAD and mild course of DM (n=21; mean age = 71.9±9.4 years); third group included patients with CAD and moderate DM (n=28; mean age = 69.7±8.0 years); and fourth group – patients with CAD and severe DM (n=21; mean age = 67.9±6.5 years).

Exclusion criteria included presence of oncology, concomitant acute or chronic diseases of digestive, respiratory and urinary system and rheumatological diseases. Diagnosis was based on local protocols of Ministry of Health of Ukraine.

Levels of glycated hemoglobin HbA_{1c} and glucose were evaluated in all patients by standard methods. Evaluation of heart failure based on examination of heart function using echocardiography (Ultrasound imaging Ultima PRO 30, Ukraine). Further parameters were observed: end-diastolic volume of left ventricle (EDV_{LV}), end-systolic volume of left ventricle (ESV_{LV}); left ventricle output volume (OV_{LV}) and ejection fraction (EF).

Statistical analysis was performed using IBM SPSS 25.0. Data are shown in means and standard deviation of continuous variables and in percent for categorical variables. Mann-Whitney U-test was used to assess statistical difference for two and Kruskal-Wallis test for several independent groups, and Wilcoxon matched pairs test for 2 dependent samples of continuous variables. Pearson's correlation coefficient was used to assess presence and power of linear dependence between continuous variables. Critical level of significance was $p<0.05$.

Results and discussion. Mean age, height, weight, SBP, DBP and HR of valsartan-users did not differ depending on DM stage. However, the highest numbers of SBP were observed in patients of 3 group, suggesting possible decompensation of heart function, which may have its manifestation in patients with moderate diabetes. The highest levels of DBP found in 4 group of patients treated with valsartan suggest on possible development of decompensation of cardiac relaxation and significant increase of arterial wall stiffness. Moreover, patients with severe DM had highest numbers of HR, which may reflect diastolic dysfunction (table 1).

In patients who were treated with telmisartan, data showed other tendencies. Mean age did not differ between DM groups (p=0.84). Height and weight was found to be significantly different (p<0.01 and p=0,04): patients with CAD only had the highest mean numbers of respective variables. Significant difference was also found in SBP (p=0.02): the highest value was in 2 group of patients with mild DM course, suggesting early development of hypertension. No significant difference was found in DBP and HR among DM groups of Telmisartan treated patients (table 1).

Comparison between valsartan and telmisartan showed significant difference between weight of patients with CAD and mild T2DM (77.3±10.3 kg and 69.1±7.8 kg, p=0,03) (table 1).

Table 1

Data on initial physical examination of treated patients

Valsartan					
	1 group (n=28)	**2 group (n=14)**	**3 group (n=14)**	**4 group (n=9)**	**p**
Age, years	66.4±9.6	71.9±9.9	70.1±6.3	67.7±8.2	0.27
Height, cm	170.4±7.6	166.6±5.5	169.7±6.0 ‡	169.2±7.4	0.48
Weight, kg	81.4±9.5	77.3±10.3	85.7±16.8	82.8±17.0	0.37
SBP, mm Hg	134.8±40.6	144.0±40.2	156.0±33.9	137.2±21.0	0.21
DBP, mm Hg	87.5±11.5	87.6±14.0	92.0±13.7	93.8±22.0	0.60
HR, bpm	76.0±11.9	73.4±10.0	79.7±15.2	81.3±17.4	0.64
Telmisartan					
	1 group (n=8)	**2 group (n=7)**	**3 group (n=14)**	**4 group (n=12)**	**p**
Age, years	66.2±12.2	71.8±8.8	69.4±9.8	67.9±4.9	0.84
Height, cm	173.8±8.3	161.3±6.7 §	173.7±8.0 ‡	169.0±5.7	<0.01
Weight, kg	83.2±10.0	69.1±7.8 *, §	81.4±10.8 ‡‡	80.6±11.3	0.04
SBP, mm Hg	110.7±42.7	164.2±15.1 §	154.3±15.5 §	140.2±50.5	0.02
DBP, mm Hg	80.7±18.4	91.3±8.9	86.8±8.2	98.3±23.6	0.26
HR, bpm	75.7±6.8	72.0±8.6	76.6±9.4	76.2±8.8	0.51

SBP=systolic blood pressure; DBP=diastolic blood pressure; HR=heart rate;
* = significance between telmisartan and valsartan groups, p<0.05;
§ = significance, compared to 1 group, p<0.01;
‡ = significance between 2 and 3 groups, p<0.01;
‡‡ = significance between 2 and 3 groups, p<0.05.

Table 2 presents data of initial echocardiography test of treated patients. We observed no significant difference in EDV of both valsartan and telmisartan groups. However, the highest values were in patients with CAD and severe T2DM, which suggest on increased cardiac preload and violations of diastolic function. No significant difference was found in ESV of both groups, but the highest numbers were also found in patients of 4 group, which suggests systolic dysfunction. Thus, data show that patients with severe T2DM may have systolic-diastolic violations of heart function. Ejection fraction and cardiac output did not differ between patients.

Table 2

Data of initial echocardiography of treated patients

Valsartan					
	1 group (n=28)	**2 group (n=14)**	**3 group (n=14)**	**4 group (n=9)**	**p**
EDV, ml	106.4±38.0	103.9±34.3	123.9±50.2	141.5±51.0	0.13
ESV, ml	49.4±20.7	46.9±17.9	60.7±39.8	71.3±41.6	0.38
EF,%	55.2±5.9	54.6±7.4	52.5±7.2	53.2±12.1	0.67
CO, ml	95.5±11.8	92.0±11.0	93.2±12.9	97.2±11.7	0.71
Telmisartan					
	1 group (n=8)	**2 group (n=7)**	**3 group (n=14)**	**4 group (n=12)**	**p**
EDV, ml	110.0±39.7	85.7±15.9	110.7±37.6	113.2±32.5	0.25
ESV, ml	51.0±29.4	36.8±8.3	50.2±20.7	52.1±17.7	0.34
EF,%	55.5±9.0	56.7±4.1	54.7±7.9	56.3±5.97	0.99
CO, ml	92.6±14.2	89.8±6.1	92.3±13.2	91.2±12.7	0.96

Table 3 summarizes data of glucose metabolism in treated patients. There was significant (p<0.001) difference in HbA_{1c} levels in both valsartan and telmisartan groups with highest values in patients with CAD and severe T2DM. Similar tendencies were observed in glucose levels with highest values in patients of 4 group. However, comparison between valsartan and telmisartan users showed significant difference only in 2 group in glucose levels (respectively 6.4±1.4 mmol/l and 4.9±1.5 mmol/l, p=0.04).

Next step was to examine patients after treatment with valsartan and telmisartan to evaluate changes and to compare two medications. Table 4 summarizes data of physical examination after treatment. No difference was observed in SBP, DBP and HR in both valsartan and telmisartan patients. However, it is obvious that levels of described variables mostly normalized, which suggests on high effectiveness of performed treatment.

Values of EDV in valsartan patients with different stages of T2DM showed tendency to significance (p=0.09). In severe T2DM patients the maximum values of EDV, ESV remained such compared to other DM stages. In telmisartan-users patients with mild T2DM had the lowest values of EDV and ESV, which suggests on improving of heart function after treatment (table 5).

Table 3

Data of initial assessment of glucose metabolism of treated patients

Valsartan					
	1 group (n=28)	**2 group (n=14)**	**3 group (n=14)**	**4 group (n=9)**	**p**
HbA_{1c},%	5.0±0.2	6.3±0.5 §	6.9±0.9 §,‡	8.6±1.1 §,⁂	<0.001
Glucose, mmol/l	4.3±0.8	6.4±1.4 *	6.9±2.2 §	9.4±2.2 §,⁋	<0.001
Telmisartan					
	1 group (n=8)	**2 group (n=7)**	**3 group (n=14)**	**4 group (n=12)**	**p**
HbA_{1c},%	4.6±0.3	6.2±0.4 §	7.3±1.0 §,‡	8.1±1.4 §	<0.001
Glucose, mmol/l	3.8±0.6	4.9±1.5*	7.7±2.7 §,‡	8.4±2.9 §	<0.001

§ = significance compared to 1 group, p<0.001;
‡ = significance between 2 and 3 group, p<0.05;
⁂ = significance between 3 and 4 groups, p=0.001;
⁋ = significance between 3 and 4 groups, p<0.05.

Table 4

Data on post-treatment physical examination of treated patients

Valsartan					
	1 group (n=28)	**2 group (n=14)**	**3 group (n=14)**	**4 group (n=9)**	**p**
SBP, mm Hg	115.6±10.9 ‡	121.8±7.2	119.8±6.8 ‡‡	122.2±8.7	0.13
DBP, mm Hg	75.3±8.2 ‡‡	73.5±4.5 ‡‡	70.3±15.2 ‡‡	75.5±5.2 ‡	0.77
HR, bpm	67.2±3.6 ‡‡	67.7±3.8	68.6±5.0 ‡‡	70.2±5.4	0.79
Telmisartan					
	1 group (n=8)	**2 group (n=7)**	**3 group (n=14)**	**4 group (n=12)**	**p**
SBP, mm Hg	115.0±5.9	117.8±3.9 ‡	123.2±18.5 ‡‡	120.0±6.0	0.26
DBP, mm Hg	76.2±5.1	75.7±5.3 ‡	75.0±4.8 ‡‡	72.5±3.9 ‡‡	0.30
HR, bpm	65.7±3.7 ‡	67.0±2.6	68.0±7.7 ‡	68.8±3.0 ‡	0.26

SBP=systolic blood pressure; DBP=diastolic blood pressure; HR=heart rate;
*=significance between telmisartan and valsartan groups;
‡=significance compared to initial data (p<0.05);
‡‡=significance compared to initial data (p<0,01).

Table 5

Data of post-treatment echocardiography of treated patients

Valsartan					
	1 group (n=28)	**2 group (n=14)**	**3 group (n=14)**	**4 group (n=9)**	**p**
EDV, ml	104.0±36.3 ‡‡	103.0±32.0	122.4±46.8	139.5±48.7 §	0.09
ESV, ml	48.6±19.5 ‡	46.4±17.1	59.8±38.7	69.8±40.1	0.38
EF,%	58.1±4.3 ‡‡	56.5±4.7 ‡	53.0±15.3 ‡	56.1±8.2	0.72
CO, ml	93.8±11.5 ‡‡	90.7±11.7	89.9±12.0 ‡‡	56.1±8.2 ‡	0.70
Telmisartan					
	1 group (n=8)	**2 group (n=7)**	**3 group (n=14)**	**4 group (n=12)**	**p**
EDV, ml	114.7±40.8	86.4±14.9	108.8±34.0 ‡	109±29.4 ‡	0.29
ESV, ml	50.1±28.3	36.2±8.8	49.2±19.4	51.0±16.9	0.32
EF,%	57.8±7.1	59.5±2.8 ‡	56.9±5.8 ‡‡	58.4±4.2 ‡	0.87
CO, ml	91.3±14.9	86.7±6.5 ‡	90.2±12.1 ‡	87.5±13.3 ‡‡	0.72

‡=significance compared to initial data (p<0.05);
‡‡=significance compared to initial data (p<0.01);
§ = significance compared to 1 group, p<0.05;

Analysis of glucose metabolism showed significant differences in levels of both HbA_{1c} in telmisartan and valsartan users (table 6). However, no differences was observed then comparing both treatment regiments.

Table 6

Data of post-treatment assessment of glucose metabolism of treated patients

Valsartan					
	1 group (n=28)	**2 group (n=14)**	**3 group (n=14)**	**4 group (n=9)**	**p**
HbA_{1c},%	4.9±0.3 ‡	6.2±0.7 ‡, §	6.7±0.9 ‡, §	8.1±0.7 ‡‡, χ	<0.001
Glucose, mmol/l	4.4±0.6	6.3±0.5 §	6.7±1.3 §	8.1±0.9 χ	<0.001
Telmisartan					
	1 group (n=8)	**2 group (n=7)**	**3 group (n=14)**	**4 group (n=12)**	**p**
HbA_{1c},%	4.99±0.1	6.1±0.4 §	7.1±0.9 ‡‡, §, ⁂	7.7±1.0 ‡‡, §	<0.001
Glucose, mmol/l	4.0±0.5	5.5±1.1 ⁋	7.3±1.7 §, ×	7.6±1.6 ‡, §	<0.001

*=significance between telmisartan and valsartan groups;
‡=significance compared to initial data (p<0.05);
‡‡=significance compared to initial data (p<0.01);
§ = significance compared to 1 group, p<0.001;
⁋ = significance compared to 1 group, p<0.05;
⁂ = significance between 2 and 3 group, p<0.05;
× = significance between 2 and 3 group, p<0.01;
χ = significance between 3 and 4 group, p<0.05.

Comparison of initial and post-treatment data showed significant changes observed both in heart function and glucose metabolism. It was found that valsartan users showed significant decrease in SBP, DBP and HR in patients with CAD only and CAD with moderate T2DM. In patients with mild and severe T2DM significant decrease was observed in DBP. On the other hand, patients treated with telmisartan showed significant decrease in SBP and DBP only in 2 and 3 group, while in 1 group both values decrease was nonsignificant and in 4 group – significant change was observed in DBP. Noteworthy that normalization of HR was found in all telmisartan users, but significant decrease – only in patients with CAD, CAD and moderate and severe T2DM (table 4).

It is remarkable, that valsartan users with CAD only showed significant changes in indices of heart function compared to pretreatment. Only in CAD and moderate DM significant increase of EF and decrease in CO was observed. In patients with severe DM significant change was observed only in CO values Analysis of telmisartan users showed significant changes in EF and CO in patients with concomitant mild DM, in patients with both moderate and severe DM significant decrease of EDV and CO with significant increase of EF was found. This suggests that telmisartan acts as protective and repairing medication in patients with concomitant CAD and T2DM, predominantly in moderate to severe stages of DM; valsartan increases cardiac function mostly in CAD only patients and in mild to severe DM, but influence on systolic and diastolic function was not found (table 5).

In all patients who used valsartan levels of HbA_{1c} significantly decreased compared to pretreatment values. However, no significance was found in glucose levels of those patients. On the other hand, it was showed that levels of glycated hemoglobin significantly changed only in patients with moderate to severe concomitant DM and only in patients with severe DM significant change of glucose levels was found. Data suggest that valsartan users will show decrease of HbA_{1c} independently on DM stage, while telmisartan provides normalization of HbA_{1c} only in moderate to severe DM patients (table 6).

Last step of current study included correlation analysis between studied indices. As it present in table 7, no significant correlations were found in 1, 2 and 3 group of patients treated with valsartan. In patients with CAD and severe T2DM SBP showed tendency to significant correlation with glucose levels (r=0.61, p=0.07); HbA_{1c} – with EDV (r=0.61, 0.08) (table. 7).

Significant indirect correlation was found between SBP and glucose levels in CAD only patients (r= –0.73, p=0.03); tendencies were found between SBP and HbA_{1c} of 2 and 3 group. In CAD only group DBP significantly correlated with glucose levels (r= –0.77, p=0.02). Indices of EDV in patients with severe diabetes showed indirect significant correlation with glucose levels (r= –0.63, p=0.02) (table 8).

Analysis of posttreatment correlations showed significant direct correlation between SBP and HbA_{1c} in CAD only patients (r=0.42, p=0.02). In second group, SBP tented to directly correlate with glucose levels (r=0.47, p=0.08); direct significant correlation was found between EDV, ESV and HbA_{1c} levels (respectively r=0.54, p=0.04, r=0.51, p=0.05), which proves significant influence of glucose metabolism violations on systolic and diastolic dysfunction (table 9).

On the other hand, in telmisartan users analysis revealed higher number of correlations. In CAD only patients, levels of HbA_{1c} significantly directly correlated with SBP, DBP and CO (respectively r=0.77, p=0.02;

r=0.90, p<0.01 and r=0.71, p=0.04); indirect – with HR r= –0.90, p<0.01. However, in patients with mild T2DM HR tended to direct correlation with glucose levels (r=0.72, p=0.06). In patients with moderate T2DM levels of glucose tended to correlate with DBP (r=0.45, p=0.09) (table 10).

Table 7

Matrix of correlation of initial indices of heart function and glucose metabolism of valsartan treated patients (n=65, r_{crit}≈0.240)

HbA_{1c}.%		1 group (n=28, r_{crit}=0.361)		2 group (n=14, r_{crit}=0,497)		3 group (n=14, r_{crit}=0,497)		4 group (n=9, r_{crit}=0,602)	
		Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	
SBP, mm Hg	r	0.05	-0.01	-0.06	0.02	0.45	0.10	0.44	0.61
	p	0.80	0.98	0.81	0.92	0.10	0.71	0.23	0.07
DBP, mm Hg	r	0.19	0.01	-0.13	0.03	0.26	0.07	-0.01	-0.35
	p	0.32	0.95	0.65	0.89	0.36	0.80	0.97	0.34
HR, bpm	r	-0.15	-0.21	-0.40	0.01	-0.45	-0.20	0.23	-0.19
	p	0.42	0.28	0.15	0.99	0.10	0.48	0.53	0.60
EDV, ml	r	-0.10	0.20	0.18	-0.25	-0.18	0.02	0.61	0.21
	p	0.58	0.30	0.51	0.39	0.52	0.93	0.08	0.57
ESV, ml	r	0.04	0.23	0.25	-0.16	-0.12	-0.01	0.49	0.08
	p	0.80	0.23	0.38	0.57	0.66	0.96	0.17	0.83
EF,%	r	-0.02	-0.05	-0.21	-0.03	-0.15	-0.09	-0.28	0.15
	p	0.89	0.78	0.46	0.91	0.59	0.74	0.45	0.69
CO, ml	r	0.18	0.08	0.27	0.27	0.21	0.05	0.26	-0.09
	p	0.34	0.68	0.34	0.33	0.45	0.86	0.49	0.80

Table 8

Matrix of correlation of initial indices of heart function and glucose metabolism of telmisartan treated patients (n=41, r_{crit}=0,304)

HbA_{1c}.%		1 group (n=8, r_{crit}=0,632)		2 group (n=7, r_{crit}=0,707)		3 group (n=14, r_{crit}=0,497)		4 group (n=12, r_{crit}=0,532)	
		Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	
SBP, mm Hg	r	-0.29	-0.73	0.71	0.10	0.50	0.49	0.07	0.01
	p	0.47	0.03	0.06	0.82	0.06	0.07	0.81	0.98
DBP, mm Hg	r	-0.22	-0.77	0.34	-0.24	-0.18	0.02	0.14	-0.33
	p	0.58	0.02	0.45	0.60	0.53	0.94	0.65	0.29
HR, bpm	r	0.24	0.64	-0.12	0.14	-0.01	-0.08	-0.16	-0.32
	p	0.56	0.08	0.79	0.75	0.96	0.76	0.61	0.30
EDV, ml	r	0.41	0.31	0.57	-0.01	-0.32	-0.14	-0.38	-0.63
	p	0.30	0.44	0.17	0.98	0.25	0.61	0.21	0.02
ESV, ml	r	0.58	0.44	0.41	0.04	-0.43	<0.01	-0.17	-0.37
	p	0.12	0.26	0.35	0.92	0.11	0.97	0.57	0.22
EF,%	r	-0.67	-0.56	0.19	0.01	0.46	-0.20	-0.14	-0.08
	p	0.06	0.14	0.67	0.98	0.09	0.49	0.64	0.79
CO, ml	r	0.62	-0.06	0.59	0.13	-0.28	-0.04	-0.36	-0.31
	p	0.09	0.87	0.16	0.76	0.32	0.88	0.24	0.32

Table 9

Matrix of correlation of posttreatment indices of heart function and glucose metabolism of valsartan treated patients (n=65, r_{crit}≈0.240)

HbA_{1c}.%		1 group (n=28, r_{crit}=0.361)		2 group (n=14, r_{crit}=0,497)		3 group (n=14, r_{crit}=0,497)		4 group (n=9, r_{crit}=0,602)	
		Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	
SBP. mm Hg	r	0.42	-0.01	-0.28	0.47	-0.03	0.16	-0.15	0.01
	p	0.02	0.99	0.32	0.08	0.91	0.57	0.68	0.97
DBP. mm Hg	r	-0.17	-0.02	-0.28	0.40	-0.23	0.20	0.22	0.27
	p	0.37	0.89	0.32	0.14	0.42	0.49	0.55	0.46
HR. bpm	r	-0.20	0.01	-0.08	0.02	-0.22	0.21	0.48	0.44
	p	0.28	0.94	0.76	0.94	0.43	0.46	0.18	0.23
EDV. ml	r	-0.01	0.28	0.54	-0.13	-0.19	-0.03	0.44	0.41
	p	0.94	0.14	0.04	0.65	0.49	0.91	0.22	0.26
ESV. ml	r	0.05	0.29	0.51	-0.08	-0.12	-0.04	0.37	0.32
	p	0.79	0.12	0.05	0.76	0.67	0.88	0.31	0.39
EF.%	r	0.07	-0.04	-0.11	0.05	0.11	-0.18	-0.14	-0.09
	p	0.72	0.80	0.70	0.86	0.69	0.51	0.70	0.80
CO. ml	r	0.05	0.15	0.46	0.35	0.38	0.11	0.14	0.16
	p	0.80	0.42	0.09	0.21	0.17	0.69	0.71	0.67

Table 10

Matrix of correlation of posttreatment indices of heart function and glucose metabolism of telmisartan treated patients(n=41, r_{crit}≈0,304)

HbA_{1c}.%		1 group (n=8, r_{crit}=0,632)		2 group (n=7, r_{crit}=0,707)		3 group (n=14, r_{crit}=0,497)		4 group (n=12, r_{crit}=0,532)	
		Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	HbA_{1c}.%	Glucose. mmol/l	
SBP. mm Hg	r	0.77	0.04	-0.62	-0.19	0.28	0.21	-0.36	-0.17
	p	0.02	0.91	0.13	0.67	0.32	0.46	0.24	0.58
DBP. mm Hg	r	0.90	-0.12	-0.14	-0.54	0.43	0.45	-0.47	-0.36
	p	<0.01	0.76	0.75	0.20	0.11	0.09	0.11	0.24
HR. bpm	r	-0.90	-0.31	-0.23	0.72	-0.22	-0.35	0.17	-0.16
	p	<0.01	0.44	0.60	0.06	0.43	0.20	0.59	0.59
EDV. ml	r	0.40	-0.19	0.61	-0.36	-0.28	-0.01	-0.32	-0.51
	p	0.31	0.64	0.14	0.42	0.32	0.98	0.29	0.08
ESV. ml	r	0.52	0.01	0.45	-0.09	-0.39	0.19	-0.07	-0.31
	p	0.18	0.97	0.30	0.83	0.15	0.49	0.81	0.31
EF.%	r	-0.62	-0.02	-0.29	-0.28	0.41	-0.32	-0.13	0.14
	p	0.09	0.95	0.52	0.53	0.14	0.26	0.66	0.65
CO. ml	r	0.71	-0.66	0.61	0.07	-0.21	0.19	-0.32	-0.25
	p	0.04	0.07	0.13	0.86	0.45	0.50	0.30	0.42

CONCLUSIONS

Our study demonstrates strong connection between glucose metabolism and heart function. It was shown that stage of T2DM significantly influence indices of morphological state of heart with effects on development of systolic and, predominantly, diastolic dysfunction, which further leads to development of heart failure. Moreover,

it was shown, that treatments of patients with CAD with concomitant T2DM of different stages with ARBs (valsartan and telmisartan) provides protective effects on heart muscle and glucose metabolism. Study found significant correlations between levels of blood pressure, systolic and diastolic function and levels of glucose and HbA_{1c} in patients with different stages of T2DM.

LIMITATIONS AND PERSPECTIVES

Limitations of study include relatively small sample of patients with different stages of T2DM and treatment regiments included comparison only between valsartan and telmisartan. Possible perspectives include comparison with other antihypertensive medications in order to find the best combination for treatment of patients with CAD and T2DM of different stages; increasing number of patients to find other peculiarities of concomitant course of CAD and T2DM; analysis of exacerbations and complication of comorbid diseases depending on different treatment regiments.

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COMPLIANCE WITH ETHICS REQUIREMENTS

The ethical approval was obtained from Bioethics Committee of the Kharkiv National Medical University. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law. Informed consent was obtained from all the patients included in the study.

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Резюме

ОСОБЛИВОСТІ ЛІКУВАННЯ ІШЕМІЧНОЇ ХВОРОБИ СЕРЦЯ ІЗ КОМОРБІДНИМ ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ БЛОКАТОРАМИ РЕЦЕПТОРІВ АНГІОТЕНЗИНУ

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Вступ: актуальність визначення особливостей лікування ІХС із супутнім цукровим діабетом 2 типу є високою, оскільки вирішує ряд важливих медико-соціальних та економічних проблем суспільства.
Мета дослідження: оцінити стан функції серця (розвиток серцевої недостатності) та зміни метаболізму глюкози у хворих на ІХС із супутнім ЦД ІІ типу залежно від стадії ЦД та лікування телмісартаном і валсартаном.
Матеріали і методи. Обстежено 106 хворих на ІХС та ЦД ІІ типу середній вік яких склав 68,8±8,9 років; середній вік чоловіків (46,2%) становив 65,2±9,0 років, жінок (53,8%) – 71,6±7,8 років. Усі пацієнти проходили лікування в кардіологічному відділенні КНП «Міська клінічна лікарня № 27» Харківської міської ради, яке є клінічною базою кафедр внутрішньої медицини № 2, клінічної імунології та алергології Л. Т. Малої ХНМУ. Усі пацієнти були розподілені на 4 групи залежно від стадії цукрового діабету. Першу групу склали пацієнти з ІХС без супутнього ЦД (n=36; середній вік = 66,4±10,1 років); другу – із ІХС та ЦД легкого ступеня тяжкості (n=21; середній вік = 71,9±9,4 років); третю – пацієнти з ІХС та ЦД середнього ступеня тяжкості (n=28; середній вік = 69,7±8,0 років); четверту – хворі на ІХС із тяжким ЦД (n=21; середній вік = 67,9±6,5 років).
Отримані результати: після лікування валсартаном і телмісартаном не спостерігалося різниці в САТ, ДАТ і ЧСС як у пацієнтів, які приймали валсартан, так і телмісартан. Проте очевидно, що їх рівні здебільшого нормалізувалися, що свідчить про високу ефективність проведеного лікування.
Порівняння початкових даних і даних після лікування показало значні зміни, що спостерігалися як у функції серця, так і в метаболізмі глюкози. Було виявлено, що ті, хто приймав валсартан визначили значне зниження САТ, ДАТ і ЧСС у пацієнтів лише з ІХС та ІХС із помірним ЦД 2 типу.
У всіх пацієнтів, що вживали валсартан, відбулося зниження HbA_{1c} незалежно від стадії ЦД, тоді як телмісартан забезпечува нормалізацію HbA_{1c} лише у пацієнтів із помірним та важким ЦД.
Отримані дані свідчать про те, що телмісартан діє як захисний та відновлюючий препарат у пацієнтів із супутньою ІХС та ЦД 2 типу, переважно при помірних та важких стадіях ЦД; валсартан же посилює серцеву функцію переважно у пацієнтів із ізольованою ІХС та при легкому та тяжкому ЦД, загалом не впливаючи на систолічну та діастолічну функції.
Висновки: наше дослідження демонструє тісний зв'язок між метаболізмом глюкози та функцією серця. Показано, що стадія ЦД 2 суттєво впливає на показники морфологічного стану серця, впливаючи на розвиток систолічної та, переважно, діастолічної дисфункції, що в подальшому призводить до розвитку серцевої недостатності. Крім того, показано, що лікування хворих на ІХС із супутнім ЦД 2 різних стадій БРА (валсартаном і телмісартаном) забезпечує протективну дію на серцевий м'яз і метаболізм глюкози. Дослідження виявило значні кореляції між рівнями артеріального тиску, систолічною та діастолічною функціями та рівнями глюкози та HbA_{1c} у пацієнтів із різними стадіями ЦД 2 типу.

Ключові слова: **ішемічна хвороба серця, цукровий діабет 2 типу, валсартан, телмісартанглюкоза, кореляції.**