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THE FEATURES OF LIPID METABOLISM IN PATIENTS WITH CHRONIC PANCREATITIS WITH CONCOMITANT ARTERIAL HYPERTENSION

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The aim of this study was to determine the features of lipid metabolism in patients with chronic pancreatitis with concomitant arterial hypertension. 54 patients aged 45–65 years (median age – 50.7 [45.4; 58.0] years) with chronic pancreatitis in combination with arterial hypertension were examined. Patients were divided into 2 groups: 1st (n=30) – patients with a combined course of chronic pancreatitis and hypertension; 2nd (n=24) – patients with chronic pancreatitis without concomitant hypertension. The content of total cholesterol, triglycerides, high-density cholesterol in serum was determined by standard enzyme-linked immunosorbent assay. Elevated levels of triglycerides, low density cholesterol and total cholesterol were observed in 43 (80 %), 48 (89 %) and 51 (94 %) patients, respectively. Patients of the 1st group had significantly higher levels of triglycerides on 36 %, low density cholesterol cholesterol on 15 %, total cholesterol on 24 %, atherogenic ratio on 18 % and significantly lower high-density cholesterol on 17 %. The duration of chronic pancreatitis was positively correlated with the level of triglycerides, low-density cholesterol – r=0.40; p=0.0013; r=0.39; p=0.0034, respectively. Men had a significantly higher level of cholesterol, high-density cholesterol, triglycerides, atherogenic ratio compared to women – by 17.2 %, 15.1 %, 32.8 % and 24.8 %, respectively. Patients with a comorbid course of chronic pancreatitis with arterial hypertension had statistically more significant changes lipid metabolism disturbance. The presence of arterial hypertension may predict decreasing of high-density cholesterol in patients with chronic pancreatitis.

Key words: *blood lipid profile, high density lipoproteins, chronic pancreatitis, arterial hypertension*

Relationship of the publication with planned research works. The present work is part of the research topic of the Department of Internal Medicine 2 and Phthisiology of the Dnipro State Medical University «Cardiovascular risk, vascular pattern, markers of fibrosis and metabolism of adipose tissue in patients with cardiovascular diseases in conditions of comorbidity: optimization of treatment, prognosis and prevention of complications», state registration №№ 0118U 006632.

Introduction. Despite the growth of medical scientific knowledge and novel therapeutic options, chronic pancreatitis (CP) remains a actual public health problem [1]. Given the problems of population aging, the incidence of CP tends to increase in recent years; dyslipidemia also contributes to the development of cardiovascular morbidity in those middle-aged and elderly people [2]. The relationship between CP and dyslipidemia requires attention.

As known, lipid metabolism disorders play prominent role in the formation of atherosclerotic plaques [3]. In clinical practice, the routine determination of blood lipids is of great importance [4, 5]. A clinical study by Zhang et al showed that compared with healthy people, patients with CP showed decrease in the level of low density lipoproteins (LDL), very low density lipoproteins [6]. However, there was no significant difference in high density lipoproteins (HDL) levels between healthy controls and the CP group. The authors concluded that total cholesterol may be a risk factor for the development of CP; and HDL may be a protective factor in terms of the development of CP [7].

According to the UK BioBank cohort study, in patients with CP, the incidence of comorbid diseases is higher than in people without CP, including essential hypertension [8]. Arterial hypertension (AH) has its own characteristics of lipid profile disorders. An important role in the development of AH can be played by a group of genes encoding proteins involved in lipid metabolism. Polymorphisms of lipid metabolism genes modify systolic blood pressure and lipid levels and may have a general influence on the development of AH and dyslipidemia [9]. Patients with hypertension are more likely than patients with normal blood pressure to experience dyslipidemia, including elevated levels of total cholesterol (TC), LDL, triglycerides (TG), and reduced HDL cholesterol [10, 11]. However, information about changes in lipid metabolism in the conditions of the combined course of CP and AH is limited.

The aim of the present study was to determine the features of lipid metabolism in patients with chronic pancreatitis with concomitant arterial hypertension.

Object and methods of research. The study was conducted with approval from the Local ethics committee according to principles outlined in the Helsinki declaration. All participants of presented study have been informed, written consent. 54 patients (26 men, 28 women) aged 45–65 years (median age – 50.7 [45.4; 58.0] years) with CP in combination with AH were examined.

Diagnosis of CP was based on history, clinical manifestations and results of laboratory and instrumental studies, taking into account the recommendations of the United European Gastroenterology for the

diagnosis and treatment of chronic pancreatitis, based on evidence [2]. The diagnosis of AH was established according to the clinical recommendations of the European Society of Hypertension and the European Society of Cardiology [11]. Inclusion criteria were the presence of a verified diagnosis of stage II, grade 1 and 2 hypertension; presence of a diagnosis of CP, consistently selected therapy for CP (at least 6 months) and constant antihypertensive therapy for 1 month, age 45–65 years, voluntary informed consent to participate in the study. Exclusion criteria: established and verified diagnosis of coronary heart disease, acute pancreatitis, stage III and III hypertension, prior therapy with hypolipidemic drugs, chronic heart failure III–IV functional class (FC), diabetes mellitus, hypothyroidism, glomerular filtration rate < 60 min./1.73 m^2, obesity 3–4 degrees.

All patients with CP received standard therapy with the inclusion of pancreatin drugs in the form of minimicrospheres and mini-tablets. At the same time, all included patients with hypertension received stably selected, unchanged (for the last three months) antihypertensive therapy (combination of perindopril with amlodipine).

Patients were divided into 2 groups: 1st (n=30) – patients with a combined course of CP and hypertension; 2nd (n=24) – patients with CP without concomitant hypertension. At baseline, patients in groups 1 and 2 were comparable in age, gender structure, BMI, and duration of CP and its course, received therapy **(table 1)**. Normal body weight was determined in 32 (29 %) examined patients, overweight – in 35 (31 %) patients, first-degree obesity – in 26 (23 %) patients, second-degree – in 17 (15 %) patients.

Table 1 – Baseline characteristics of the study population

Characteristic	1st group (n=30)	2nd group (n=24)	p
Median of age, years	66 [57.5; 74.4]	64 [54.4; 72.8]	0.35
BMI, kg/m^2	26 [24.4; 35.2]	30 [25.3; 36.8]	0.39
duration of CP, years	3[2.4; 5.0]	3.3[2.6; 5.5]	0.44
Systolic blood pressure, mm Hg	138.5 [125.8; 144.6]	128.4 [114.2; 138.5]	0.03
Diastolic blood pressure, mm Hg	75.6 [71.4; 78.3]	71.1 [68.2; 73.7]	0.15

Notes: p – between study and control groups (the Mann-Whitney U-test).

All patients were measured for height and weight, waist circumference, and BMI according to a standard formula. The content of TC, TG, HDL in serum was determined by standard enzyme-linked immunosorbent assay.

Data processing and analysis were performed using Libre Office and licensed program STATISTICS (license № AGAR 909E 415822FA). More than 50 % of the data had a different than normal type of distribution according to the Shapiro-Wilk test, so the analysis used non-parametric statistics, the data were described as the median and 25 and 75 quartiles. Comparing quantitative indicators, the Mann – Whitney test was used; Pearson's Chi-square test ($\chi 2$) was used to compare qualitative indicators. Correlation analysis was performed using the non-parametric Spearman correlation coefficient (ρ). The trend lines on the charts correspond to the linear regression lines. The significant level of p for statistical hypotheses is taken <0.05 [12].

Research results and their discussion. The majority of examined patients with CP had established dyslipidemia. Thus elevated levels of TG, LDL cholesterol and TC were observed in 43 (80 %), 48 (89 %) and 51 (94 %) patients, respectively. Decreased levels of HDL cholesterol were found in 19 (35 %) patients. It was established that patients of the 1st group had significantly higher levels of TG on 36 %, LDL cholesterol on 15 %, TC on 24 %, atherogenic ratio on 18 % and significantly lower HDL on 17 %), the medians of the indicators are given in **table 2**. The correlations between age and the level of atherogenic ratio, LDL were estimated – r=0.38; p=0.0045; r=0.42; p=0.0087, respectively. The duration of CP was positively correlated with the level of TG, LDL – r=0.40; p=0.0013; r=0.39; p=0.0034, respectively.

Table 2 – The indicators of lipid spectrum in examined patients

Indicator	All patients (n=54)	CP+AH (n=30)	CP (n=24)	p
TC, mmol/l	6.8 [6.0;7.6]	7.4 [7.0;7.9]	5.8 [5.2;6.2]	<0.01
HDL, mmol/l	1.0 [0.9;1.4]	1.1 [0.8;1.2]	1.3 [1.1;1.5]	<0.01
LDL, mmol/l	3.5 [3.1;4.2]	3.8 [3.3;4.2]	3.3 [2.7;3.7]	<0.01
VLDL, mmol/l	0.9 [0.7;1.0]	0.9 [0.7;1.1]	0.8 [0.6;1.0]	>0.01
TG, mmol/l	3.8 [3.2;4.2]	4.2 [3.8;4.7]	2.7 [2.2;3.4]	<0.01
Atherogenic ratio	4.2 [3.6;4.6]	4.5 [4.0;4.8]	3.6 [3.4;4.0]	<0.01

Notes: TC – total cholesterol; TG – triglycerides; HDL – high-density cholesterol; LDL – low-density cholesterol; VLDL – very low-density cholesterol.

In the analysis of lipid spectrum in patients with combined CP with hypertension depending on gender structure, it was found that men had a significantly higher level of cholesterol, LDL, TG, atherogenic ratio compared to women – by 17 %, 15 %, 33 % and 25 %, respectively **(table 3)**.

Table 3 – Indicators of the lipid spectrum in patients with a combined course of CP and hypertension depending on gender structure

Indicator	Men CP+AH (n=25)	Women CP+AH (n=45)	p
TC, mmol/l	7.9 [6.4;8.6]	6.6 [5.8;7.4]	<0.01
HDL, mmol/l	1.18 [1.0;1.18]	1.1 [0.7;1.4]	>0.01
LDL, mmol/l	4.11 [3.6;4.8]	3.6 [3.2;3.5]	<0.01
VLDL, mmol/l	0.9 [0.8;1.3]	0.7 [0.5;1.1]	>0.01
TG, mmol/l	4.7 [3.9;4.82]	3.17 [2.78;3.87]	<0.01
Atherogenic ratio	4.8 [4.3;5.4]	3.6 [3.2;4.1]	<0.01

Notes: TC – total cholesterol; TG – triglycerides; HDL – high-density cholesterol; LDL – low-density cholesterol; VLDL – very low-density cholesterol.

The obtained results indicate that patients with a comorbid course of CP with AH had statistically more significant changes lipid metabolism disturbance.

It should be emphasized that the majority of enrolled patients with CP and AH were overweight, so there is an accumulation of a number of phenotypic prerequisites for the formation of high cardiovascular risk. Significantly higher levels of proatherogenic lipid fractions in men might associate with low treatment compliance, non-compliance with dietary habits.

Thus, the presence of concomitant AH had a negative impact on lipid metabolism in patients with CP, which requires early detection and active drug exposure.

Conclusions. Our results suggest that presence of AH may predict certain disturbances in lipoprotein metabolism with decreasing of HDL in patients with CP. This association should be taken into account to develop future strategies in management of this patients.

Prospects for further research. Further study of lipid metabolism, namely ApoA-I, ApoB, and genetic examination of patients with combined course of CP and hypertension is promising. The question of the effectiveness of drug therapy in these patients is also relevant and needs further research.

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ОСОБЛИВОСТІ ЛІПІДНОГО ОБМІНУ У ПАЦІЄНТІВ З ХРОНІЧНИМ ПАНКРЕАТИТОМ ІЗ СУПУТНЬОЮ АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

Філіппова О.Ю., Кривошей В.В.

Резюме. У пацієнтів з хронічним панкреатитом висока частота супутніх захворювань, особливо артеріальної гіпертензії. Проблема порушення ліпідів у хворих на хронічний панкреатит та супутню артеріальну гіпертензію залишається актуальною.

Метою даного дослідження було визначення особливостей ліпідного обміну у хворих на хронічний панкреатит із супутньою артеріальною гіпертензією.

Об'єкт і методи дослідження. Обстежено 54 пацієнти віком 45–65 років (медіана – 50,7 [45,4; 58,0] років) з хронічним панкреатитом у поєднанні з артеріальною гіпертензією. Пацієнти були розділені на 2 групи: 1-ша (n=30) – хворі з комбінованим перебігом хронічного панкреатиту та АГ; 2-й (n=24) – хворі на хронічний панкреатит без супутньої АГ. Вміст загального холестерину, тригліцеридів, холестерину високої щільності в сироватці крові визначали стандартним імуноферментним методом.

Результати. Підвищені рівні тригліцеридів, холестерину низької щільності та загального холестерину спостерігалися у 43 (80 %), 48 (89 %) та 51 (94 %) пацієнтів відповідно. Пацієнти 1 групи мали достовірно вищий рівень тригліцеридів на 36 %, холестерину низької щільності на 15 %, загального холестерину на 24 %, коефіцієнта атерогенності на 18 % і достовірно нижчого холестерину високої щільності на 17 %. Тривалість хронічного панкреатиту позитивно корелювала з рівнем тригліцеридів, холестерину низької щільності – r=0,40; p=0,0013; r=0,39;

p=0,0034 відповідно. У чоловіків значно вищий рівень холестерину, холестерину високої щільності, тригліцеридів, коефіцієнт атерогенності порівняно з жінками – відповідно на 17,2 %, 15,1 %, 32,8 % та 24,8 %.

Висновки. У пацієнтів з коморбідним перебігом хронічного панкреатиту з артеріальною гіпертензією спостерігалися статистично більш значущі зміни порушення ліпідного обміну. Наявність артеріальної гіпертензії може бути предиктором зниження рівня холестерину високої щільності у хворих на хронічний панкреатит.

Ключові слова: ліпідний профіль крові, ліпопротеїни високої щільності, хронічний панкреатит, артеріальна гіпертензія.

THE FEATURES OF LIPID METABOLISM IN PATIENTS WITH CHRONIC PANCREATITIS WITH CONCOMITANT ARTERIAL HYPERTENSION

Filippova A. Yu., Kryvoshei V.V.

Abstract. Patients with chronic pancreatitis have high frequency of comorbidity, especial with arterial hypertension. The problematic of lipid disorders in patients with chronic pancreatitis and concomitant arterial hypertension is still actual.

The aim of this study was to determine the features of lipid metabolism in patients with chronic pancreatitis with concomitant arterial hypertension.

Materials and methods. 54 patients aged 45–65 years (median age – 50.7 [45.4; 58.0] years) with chronic pancreatitis in combination with arterial hypertension were examined. Patients were divided into 2 groups: 1st (n=30) – patients with a combined course of chronic pancreatitis and hypertension; 2nd (n=24) – patients with chronic pancreatitis without concomitant hypertension. The content of total cholesterol, triglycerides, high-density cholesterol in serum was determined by standard enzyme-linked immunosorbent assay.

Results. Elevated levels of triglycerides, low density cholesterol and total cholesterol were observed in 43 (80 %), 48 (89 %) and 51 (94 %) patients, respectively. Patients of the 1st group had significantly higher levels of triglycerides on 36 %, low density cholesterol cholesterol on 15 %, total cholesterol on 24 %, atherogenic ratio on 18 % and significantly lower high-density cholesterol on 17 %. The duration of chronic pancreatitis was positively correlated with the level of triglycerides, low-density cholesterol – r=0.40; p=0.0013; r=0.39; =0.0034, respectively. Men had a significantly higher level of cholesterol, high-density cholesterol, triglycerides, atherogenic ratio compared to women – by 17.2 %, 15.1 %, 32.8 % and 24.8 %, respectively.

Conclusions. Patients with a comorbid course of chronic pancreatitis with arterial hypertension had statistically more significant changes lipid metabolism disturbance. The presence of arterial hypertension may predict decreasing of high-density cholesterol in patients with chronic pancreatitis.

Key words: blood lipid profile, high density lipoproteins, chronic pancreatitis, arterial hypertension.

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Conflict of interest:
The Authors declare no conflict of interest.

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