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THE ROLE OF ASPROSIN IN LIPID METABOLISM IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND CHRONIC PANCREATITIS*

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Type 2 Diabetes Mellitus (T2DM) is a highly prevalent metabolic disorder affecting millions globally [1]. Major complications, such as cardiovascular diseases, nephropathy, and neuropathy, significantly impair patients' quality of life and increase mortality [2]. A crucial aspect requiring detailed investigation is the relationship between T2DM and chronic pancreatitis (CP), as both conditions substantially impact the body's metabolic processes, particularly lipid metabolism [3].

Asprosin, a recently discovered hormone, is key in regulating glucose homeostasis and appetite [4]. It is primarily synthesized in adipose tissue and released in response to fasting, stimulating the liver to release glucose into the bloodstream [5]. Studies have demonstrated that elevated asprosin levels are associated with obesity, insulin resistance, and T2DM, making it a potential biomarker for the diagnosis and monitoring of metabolic disorders [6].

Studying the impact of asprosin on lipid metabolism is essential. Lipid metabolism entails the intricate processes of synthesizing, transporting, and utilizing fats within the body [7]. Disruptions in this process are commonly observed in patients with T2DM and CP, leading to dyslipidemia and an increased risk of cardiovascular diseases [8]. Understanding the relationships between asprosin and lipid metabolism markers can provide new insights into the pathophysiological mechanisms of these diseases and open new avenues for their diagnosis and treatment.

The relevance of studying the correlations between asprosin levels and lipid metabolism increases significantly in the context of the combination of T2DM and CP [9]. Patients with T2DM face an increased risk of developing CP due to the damage to pancreatic islets and insulin resistance caused by chronic inflammation [10].

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Examining the connections between asprosin levels and lipid metabolism indicators in individuals with T2DM and CP not only enhances the comprehension of their reciprocal effects but also identifies potential biomarkers that could enable more precise diagnosis and effective therapeutic interventions. Specifically, this research can contribute to the development of new therapeutic approaches aimed at normalizing asprosin levels and improving the lipid profile, which can significantly enhance the prognosis and quality of life of patients.

MATERIALS AND METHODS

The study included 100 patients treated at the Kharkiv Regional Clinical Hospital between 2020 and 2022. The participants were divided into two groups - the first group included 70 patients with T2DM and comorbid chronic pancreatitis (men — 64%, women — 36%), mean age — 62.3 ± 6.7 years, while the second group comprised 30 patients with T2DM (men — 63%, women — 37%), mean age — 64.4 ± 6.6 years. Average duration of T2DM in the first group is 12.6 ± 5.4 years, while in the second group — 11.2 ± 6.8 years. The control group comprised 20 relatively healthy men and women of the appropriate age.

All patients provided informed consent to participate in the study. The studies were conducted in compliance with the principles of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, and the current legislation of Ukraine. The study protocol was approved by the Ethics and Bioethics Commission of Kharkiv National Medical University.

The diagnoses of chronic pancreatitis and T2DM were established based on the regulations set by the Ministry of Health of Ukraine.

Inclusion criteria were: the presence of voluntary consent to participate in the study, the presence of chronic pancreatitis, T2DM.

Exclusion criteria included: patient age under 18 years, HbA1c level > 9%, patients with type 1 diabetes mellitus, patients with acute pancreatitis, patients with chronic kidney disease, patients with stage III hypertension, patients with stage IIB-III heart failure, acute inflammatory processes, oncological diseases, history of alcohol and substance abuse, and presence of HIV/AIDS.

Blood asprosin levels were determined by indirect non-competitive heterogeneous enzyme immunoassay on a «Labline-90» analyzer (Austria) using commercial test systems manufactured by «Elabscience» (China).

Lipid profile indicators were planned to be determined by standard biochemical methods, including total cholesterol, triglycerides, high-density lipoprotein cholesterol (enzymatic-photometric method with cholesterol oxidase/peroxidase using the «DAC-Spectro Med» kit), low-density lipoprotein cholesterol (mathematical calculation using the Friedewald formula), and very low-density lipoprotein cholesterol.

The obtained data were statistically processed using the Prism 9.0 statistical data processing software package (GraphPad Software, USA). The relationship between the obtained characteristics was assessed using Pearson's linear correlation coefficient. Correlations were considered inverse if the r-value ranged from 0 to – 1.0, and direct if the r-value ranged from 0 to 1.0. An r-value from 0 to 0.3 indicated a weak correlation, 0.4 to 0.7 indicated a moderate correlation, and 0.7 to 1.0 indicated a strong correlation. The results were presented as the r-value and the corresponding p-value.

RESULTS AND THEIR DISCUSSION

The following lipid metabolism indicators were studied: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C). The levels of lipid metabolism indicators in the studied groups are presented in Table 1.

The levels of all studied lipid metabolism indicators exhibit statistically significant differences between the control group and both the first and second groups. The levels of total cholesterol ($p = 0.089$), LDL-C ($p = 0.423$), and VLDL-C ($p = 0.7053$) in the blood serum did not show statistically significant differences between the studied groups of patients. The

Table 1

Indicators of lipid metabolism in patients with type 2 diabetes mellitus and chronic pancreatitis (M ± m)

Indicator	Group 1 (T2DM + chronic pancreatitis) (n = 70)	Group 2 (T2DM) (n = 30)	Control group (n = 20)	p-value
Total cholesterol, mmol/L	5.01 ± 0.78	5.35 ± 1.15	4.25 ± 1.08	$p_{1,2} = 0.089$ $p_{1,c} < 0.001$ $p_{2,c} < 0.05$
Triglycerides, mmol/L	1.91 ± 0.64	2.29 ± 0.84	1.01 ± 0.25	$p_{1,2} < 0.05$ $p_{1,c} < 0.001$ $p_{2,c} < 0.001$
HDL-C, mmol/L	1.03 ± 0.14	1.19 ± 0.19	1.31 ± 0.22	$p_{1,2} < 0.05$ $p_{1,c} < 0.05$ $p_{2,c} < 0.001$
LDL-C, mmol/L	3.32 ± 1.1	3.5 ± 0.8	2.35 ± 0.55	$p_{1,2} = 0.423$ $p_{1,c} < 0.001$ $p_{2,c} < 0.001$
VLDL-C, mmol/L	0.92 ± 0.47	0.96 ± 0.51	0.65 ± 0.21	$p_{1,2} = 0.7053$ $p_{1,c} < 0.05$ $p_{2,c} < 0.05$

Notes:
$p_{1,2}$ — statistical significance of differences between the 1st and 2nd groups;
$p_{1,c}$ — statistical significance of differences between the 1st and control groups;
$p_{2,c}$ — statistical significance of differences between the 2nd and control groups;
T2DM — type 2 diabetes mellitus.

Table 2

Correlation relationships between asprosin and lipid metabolism indicators in patients with type 2 diabetes mellitus and chronic pancreatitis (n = 70)

Indicator	Asprosin	Total cholesterol	Triglycerides	HDL-C	LDL-C	VLDL-C
Asprosin	1.0	0.35*	0.24	– 0.15	0.45**	0.25
Total cholesterol	0.35*	1.0	0.4*	– 0.22	0.4*	0.2
Triglycerides	0.24	0.4*	1.0	– 0.31*	0.38*	0.42**
HDL-C	– 0.15	– 0.22	– 0.31*	1.0	– 0.48**	– 0.36*
LDL-C	0.45**	0.4*	0.38*	– 0.48**	1.0	0.22
VLDL-C	0.25	0.2	0.42**	– 0.36*	0.22	1.0

Notes:
* $p < 0.05$,
** $p < 0.01$.

similar lipid metabolism indicators observed in patients with isolated T2DM and those with comorbid T2DM and chronic pancreatitis may be attributed to the general disturbances in lipid metabolism that characterize T2DM, regardless of the presence of concomitant chronic pancreatitis.

However, the triglyceride levels were significantly higher in the group of patients with T2DM compared to the group with combined T2DM and chronic pancreatitis ($p < 0.05$). Furthermore, the study revealed significant differences in HDL-C levels between the patient groups. Specifically, HDL-C concentrations were notably lower in individuals with T2DM and chronic pancreatitis, which may be linked to impaired lipid metabolism and inflammation in this patient population.

Table 3

Correlation relationships between asprosin and lipid metabolism indicators in patients with type 2 diabetes mellitus (n = 30)

Indicator	Asprosin	Total cholesterol	Triglycerides	HDL-C	LDL-C	VLDL-C
Asprosin	1.0	0.37**	0.17	-0.42**	0.47**	0.21
Total cholesterol	0.37**	1.0	0.41**	– 0.22	0.31*	0.22
Triglycerides	0.17	0.41**	1.0	– 0.27	0.32*	0.4**
HDL-C	– 0.42**	– 0.22	– 0.27	1.0	– 0.42**	– 0.17
LDL-C	0.47**	0.31*	0.32*	– 0.42**	1.0	0.3*
VLDL-C	0.21	0.22	0.4**	– 0.17	0.3*	1.0

Notes:
* $p < 0.05$,
** $p < 0.01$.

Asprosin concentrations were significantly elevated in the group with combined T2DM and chronic pancreatitis (10.06 ± 3.56 ng/mL), as well as in the group with T2DM alone (7.34 ± 2.08 ng/mL), in comparison to the control group (2.81 ± 1.34 ng/mL, $p < 0.05$).

The study also examined the relationship between asprosin levels and lipid metabolism markers in the studied groups.

When analyzing the relationships between asprosin and lipid metabolism indicators, moderate correlations were found predominantly with HDL-C, LDL-C, and TG. The results are presented in Tables 2 and 3.

In patients with T2DM and CP, statistically significant moderate direct correlations were found between asprosin and total cholesterol (TC), and LDL-C levels (see Table 2). A distinct inverse correlation with HDL-C levels was also observed. There were no strong or moderate correlations between asprosin and triglycerides, or between asprosin and VLDL-C.

It was found that in patients with T2DM without chronic pancreatitis, there were statistically significant moderate direct correlations between asprosin levels and total cholesterol, and LDL-C (Table 3). Similar to the first group, no strong or moderate correlations were found between asprosin and triglycerides or VLDL-C.

The results obtained in this study are consistent with existing research demonstrating the relationship between T2DM, lipid metabolism parameters, and asprosin levels [11, 12].

The regulatory functions of adipose tissue as an endocrine organ in metabolism and energy homeostasis have been confirmed previously [13]. It has been shown that secreted components of adipose tissue can influence insulin function and lipid metabolism. Excess adipose tissue can cause insulin resistance, which is a major cause of T2DM; therefore, obesity is associated with several metabolic disorders, including T2DM and metabolic syndrome [14].

Asprosin, a recently discovered adipokine, is secreted by white adipose tissue and plays an important role in regulating blood glucose and lipid levels. Experimental studies on animals have shown that reducing asprosin concentrations by administering antibodies against it leads to improved insulin sensitivity and reduced lipid disorders [5]. However, due to the diversity of populations and sample types, the exact association of asprosin with various metabolic disorders has not been well established.

According to previous research, asprosin levels are significantly elevated in patients with insulin resistance and lipid disorders [15, 16]. In our study, significant correlations were also demonstrated between asprosin and atherosclerosis-related lipid metabolism indicators. Asprosin may serve as an independent marker of metabolic disorders in patients with T2DM and CP.

CONCLUSIONS

1. The highest asprosin level was noted in the patients with type 2 diabetes mellitus and chronic pancreatitis.
2. In the patients with type 2 diabetes alone significant moderate correlations between asprosin and total cholesterol, and LDL-C (direct) and HDL-C (reverse) levels were established.
3. In the group of patients with type 2 diabetes mellitus and chronic pancreatitis, significant moderate direct correlations between asprosin and total cholesterol, and LDL-C levels were also established.

Therefore, asprosin is a new important adipokine associated with lipid metabolism disorders, that making it a potential target for therapeutic intervention in type 2 diabetes mellitus and its complications. Further research is needed to better understand the role of asprosin in the pathogenesis of these diseases and to develop new approaches to their treatment.

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THE ROLE OF ASPROSIN IN LIPID METABOLISM IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND CHRONIC PANCREATITIS

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Background. Type 2 Diabetes Mellitus (T2DM) is a highly prevalent metabolic disease that significantly affects patients' quality of life and increases mortality due to complications. Understanding the relationships between T2DM and chronic pancreatitis (CP) is very important, as both conditions significantly impact metabolic processes in the body, particularly lipid metabolism. Asprosin, a recently discovered adipokine, plays a key role in regulating glucose homeostasis and appetite. Its elevated levels are associated with obesity, insulin resistance, and T2DM, making it a potential biomarker for diagnosing and monitoring metabolic disorders.

Objective. The objective of this study was to investigate the relationships between asprosin levels and lipid metabolism indicators in patients with T2DM and CP.

Materials and Methods. The study included 100 patients treated at the Kharkiv Regional Clinical Hospital from 2020 to 2022, divided into two groups: the first group included 70 patients with T2DM and CP, and the second group consisted of 30 patients with T2DM.

The control group consisted of 20 relatively healthy men and women of appropriate age. Asprosin levels were determined by indirect non-competitive heterogeneous enzyme immunoassay. Lipid profile indicators were determined by standard biochemical methods. Correlations were assessed using Pearson's linear correlation coefficient.

Results. In the group of patients with T2DM and CP, the level of total cholesterol (TC) was 5.01 ± 0.78 mmol/L, triglycerides (TG) — 2.29 ± 0.84 mmol/L, high-density lipoprotein cholesterol (HDL-C) — 1.19 ± 0.19 mmol/L, low-density lipoprotein cholesterol (LDL-C) — 3.32 ± 1.1 mmol/L, and very low-density lipoprotein cholesterol (VLDL-C) — 0.92 ± 0.47 mmol/L. In the T2DM group, the levels of TC, TG, HDL-C, LDL-C, and VLDL-C were 5.35 ± 1.15, 1.91 ± 0.64, 1.03 ± 0.14, 3.5 ± 0.8, and 0.96 ± 0.51 mmol/L, respectively. In the control group, these indicators were 4.25 ± 1.08, 1.01 ± 0.25, 1.31 ± 0.22, 2.35 ± 0.55, and 0.65 ± 0.21 mmol/L, respectively.

The levels of all studied lipid metabolism indicators exhibited statistically significant differences between the control group and both the first and second groups. The highest asprosin level (10.06 ± 3.56 ng/mL) was noted in the group with T2DM and comorbid chronic pancreatitis. In the patients with isolated T2DM significant moderate correlations between asprosin and total cholesterol, and LDL-C (direct) and HDL-C (reverse) levels were established. In the group of patients with T2DM and chronic pancreatitis, significant moderate direct correlations between asprosin and total cholesterol, and LDL-C levels were also established.

Conclusions. Asprosin is a new adipokine associated with lipid metabolism disorders, that making it a potential target for therapeutic intervention in type 2 diabetes mellitus and its complications. Further research is needed to better understand the role of asprosin in the pathogenesis of these diseases and to develop new approaches to their treatment.

Keywords: type 2 diabetes, chronic pancreatitis, insulin resistance, lipid metabolism, asprosin.

РОЛЬ АСПРОСИНУ В ЛІПІДНОМУ ОБМІНІ У ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ 2 ТИПУ ТА ХРОНІЧНИЙ ПАНКРЕАТИТ

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Актуальність. Цукровий діабет (ЦД) 2 типу — надзвичайно поширене метаболічне захворювання, яке значно впливає на якість життя пацієнтів та підвищує смертність через ускладнення. Розуміння взаємозв'язків між ЦД 2 типу та хронічним панкреатитом є дуже важливим, оскільки обидва стани значно впливають на метаболічні процеси в організмі, зокрема на ліпідний обмін. Аспросин, нещодавно відкритий адипокін, відіграє ключову роль у регулюванні гомеостазу глюкози та апетиту. Його підвищені рівні асоціюються з ожирінням, інсулінорезистентністю та ЦД 2 типу, що робить його потенційним біомаркером для діагностики та моніторингу метаболічних розладів.

Метою цього дослідження було вивчення взаємозв'язків між рівнями аспросину та показниками ліпідного обміну у пацієнтів з цукровим діабетом 2 типу та хронічним панкреатитом.

Матеріали та методи. Дослідження включало 100 пацієнтів, які знаходилися на лікуванні у Харківській обласній клінічній лікарні з 2020 по 2022 роки та були розділені на 2 групи: перша група включала 70 пацієнтів з ЦД 2 типу та хронічним панкреатитом, друга група складалася з 30 пацієнтів з ЦД 2 типу без хронічного панкреатиту. Контрольна група складалася з 20 відносно здорових чоловіків і жінок відповідного віку. Рівні аспросину визначали за допомогою непрямого неконкурентного гетерогенного імуноферментного аналізу. Показники ліпідного профілю визначали за допомогою стандартних біохімічних методів. Кореляцію оцінювали за допомогою лінійного кореляційного коефіцієнта Пірсона.

Результати. Рівні показників ліпідного обміну вивчалися у трьох групах пацієнтів. У групі пацієнтів з ЦД 2 типу та хронічним панкреатитом рівень загального холестерину (ЗХ) становив 5,01 ± 0,78 ммоль/л, тригліцеридів (ТГ) — 2,29 ± 0,84 ммоль/л, холестерину ліпопротеїнів високої щільності (ХС ЛПВЩ) — 1,19 ± 0,19 ммоль/л, холестерину ліпопротеїнів низької щільності (ХС ЛПНЩ) — 3,32 ± 1,1 ммоль/л, холестерину ліпопротеїнів дуже низької щільності (ХС ЛПДНЩ) — 0,92 ± 0,47 ммоль/л. У групі з ЦД 2 типу рівні ЗХ, ТГ, ХС ЛПВЩ, ХС ЛПНЩ та ХС ЛПДНЩ складали відповідно 5,35 ± 1,15, 1,91 ± 0,64, 1,03 ± 0,14, 3,5 ± 0,8 та 0,96 ± 0,51 ммоль/л. У контрольній групі ці показники складали 4,25 ± 1,08, 1,01 ± 0,25, 1,31 ± 0,22, 2,35 ± 0,55 та 0,65 ± 0,21 ммоль/л відповідно.

Рівні всіх досліджуваних показників ліпідного обміну виявили статистично значущі відмінності між контрольною групою та обома досліджуваними групами. Найвищий рівень аспросину (10,06 ± 3,56 нг/мл) відзначений у групі з ЦД 2 типу та хронічним панкреатитом. У хворих на ізольований цукровий діабет 2 типу встановлено достовірні помірні кореляційні зв'язки між аспросином і рівнем загального холестерину, ХС ЛПНЩ (прямі) і ХС ЛПВЩ (зворотний). У групі хворих на ЦД 2 типу та хронічний панкреатит також встановлено достовірні помірні прямі кореляційні зв'язки між аспросином та рівнями загального холестерину та ХС ЛПНЩ.

Висновки. Аспросин є новим адипокіном, асоційованим з порушеннями ліпідного обміну, що робить його потенційною ціллю для терапевтичного втручання при цукровому діабеті 2 типу та його ускладненнях. Подальші дослідження необхідні для кращого розуміння ролі аспросину у патогенезі цих захворювань та розробки нових підходів до їх лікування.

Ключові слова: цукровий діабет 2 типу, хронічний панкреатит, інсулінорезистентність, ліпідний обмін, аспросин.