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Assessment of lipid metabolism in patients with coronary artery disease and generalized periodontitis

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ABSTRACT

Introduction. It has been assumed that generalized periodontitis (GP) adversely affects the qualitative and quantitative composition of plasma lipids and lipoproteins. On the other hand, periodontal treatment and reduction of general periodontal pocket infection in patients with GP are associated with a decrease in total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C) and triglycerides (TG). The aim of the study was to conduct a comparative assessment of the state of lipid metabolism in patients with coronary artery disease (CAD) depending on the GP severity.

Methods. The study included 101 patients (mean±SD age - 58.2 ± 8.3 years) with CAD and GP, 58 men (57.4%) and 43 women (42.6%). According to the severity of GP, study participants were divided into 3 groups: group I - patients with CAD and GP stage I (initial periodontitis), group II - patients with CAD and GP stage II (moderate periodontitis) and group III - patients with CAD and GP stage III and IV (severe periodontitis). The control group included 9 patients with CAD and clinical gingival health on an intact periodontium (mean±SD age - 56.3 ± 6.1 years), 5 men (55.6%) and 4 women (44.4%). The diagnosis of CAD and the results of lipid metabolism were obtained by analyzing the inpatient medical records.

Results. It was revealed that the values of TC, LDL-C, very low-density lipoprotein-cholesterol (VLDL-C), TG and atherogenic coefficient (AC) were lower in the group of patients with CAD and clinical gingival health compared to the level of the corresponding indicators in the groups of patients with CAD and GP ($p<0.05$). In the analysis of lipid profile in patients with CAD and GP of varying severity, it was found that the average levels of TC, LDL-C, and AC in the subjects of group I were significantly lower compared to the corresponding indicators of groups II and III ($p<0.05$). There was no statistical difference in the values of lipid metabolism in groups II and III ($p>0.05$). No significant difference was found in high-density lipoprotein-cholesterol (HDL-C) levels between the comparison groups including the patients with CAD and clinical gingival health ($p>0.05$), as well as the gender characteristics of the analyzed indicators in the examined patients.

Conclusions. Average levels of TC, LDL-C, and AC in patients with CAD and GP increase with increasing destructive-inflammatory changes in periodontal tissues, therefore, with the severity of GP indicating the progression of atherogenesis along with the increased inflammatory process in the periodontium.

Keywords: periodontitis, coronary artery disease, lipid metabolism, lipoproteins.

Оцінка показників ліпідного обміну у пацієнтів з ішемічною хворобою серця та генералізованим пародонтитом

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РЕЗЮМЕ

Вступ. Існує припущення, що генералізований пародонтит (ГП) несприятливо впливає на якісний і кількісний склад ліпідів та ліпопротеїнів плазми крові. З іншого погляду, пародонтологічне лікування та зниження загального інфікування пародонтальних кишень при ГП асоційоване зі зниженням рівня загального холестерину (ЗХС), холестерину ліпопротеїнів низької щільності (ХС ЛПНЩ) і тригліцеридів. Мета дослідження – провести порівняльну оцінку стану ліпідного обміну у хворих на ішемічну хворобу серця (ІХС) залежно від стадії тяжкості ГП.

Методи дослідження. В дослідження було включено 101 пацієнт (середній вік – 58.2±8.3 роки), в яких діагностовано ІХС та ГП. З них 58 (57.4%) пацієнтів були чоловіки та 43 (42.6%) – жінки. Відповідно до стадії тяжкості ГП учасників дослідження було поділено на 3 групи: I група – пацієнти з ІХС та ГП стадія I (початковий пародонтит); II група – пацієнти з ІХС та ГП стадія II (помірний пародонтит); III група – пацієнти з ІХС та ГП стадія III та IV (важкий пародонтит). До групи контролю входили 9 пацієнтів з ІХС та клінічно здоровими яснами при інтактному пародонті (середній вік - 56.3±6.1 роки), з яких 5 (55.6%) пацієнтів були чоловіки та 4 (44.4%) – жінки. Діагноз ІХС та показники ліпідного обміну хворих отримували з карт стаціонарних хворих.

Результати. З'ясовано, що значення показників ЗХС, холестерину ХС ЛПНЩ, холестерину ліпопротеїнів дуже низької щільності (ХС ЛПДНЩ), тригліцеридів і коефіцієнта атерогенності (КА) були нижчими у групі хворих на ІХС із клінічно здоровими яснами порівняно з рівнем відповідних показників у групах хворих із ІХС та ГП ($p<0.05$). Під час аналізу ліпідограм у хворих на ІХС та ГП різної стадії тяжкості виявили, що середні рівні ЗХС, ХС ЛПНЩ плазми крові та КА в обстежених I групи були суттєво нижчими порівняно з відповідними показниками груп II та III ($p<0.05$). Не виявлено статистичної різниці значення показників ліпідного обміну у II та III групах ($p>0.05$). Не виявили значних відмінностей між показниками холестерину ліпопротеїнів високої щільності (ХС ЛПВЩ) між групами порівняння, у тім числі групи хворих із ІХС та клінічно здоровими яснами ($p>0.05$), а також гендерних особливостей проаналізованих показників у обстежених пацієнтів.

Висновки. Середні рівні ЗХС, ХС ЛПНЩ та КА у хворих на ІХС та ГП збільшуються з наростанням деструктивно-запальних змін у тканинах пародонта, відповідно, стадією тяжкості ГП, що свідчить про прогресування атерогенезу поряд із посиленням запальних явищ у пародонті.

Ключові слова: пародонтит, ішемічна хвороба серця, ліпідний обмін, ліпопротеїни.

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Introduction

Generalized periodontitis (GP) is one of the most common dental diseases, leading to premature tooth loss due to the destruction of the soft tissues of the periodontium and alveolar bone. The microflora of dental plaque and products of its vital activity, the state of local and general immunity, local and systemic factors that ensure periodontal homeostasis, bad habits, genetic predisposition, ecological and social living conditions, etc. play an important role in the development of pathological processes in the periodontium [4]. Thus, the multifactorial etiology, the tendency to rapid irreversible progression and the relationship of GP with the functioning of body systems make GP one of the most topical issues not only in modern dentistry but also in general medicine.

Literature data indicate the close relationship of GP with cardiovascular diseases including coronary artery disease (CAD) [2,12,14,16,17,18,19]. CAD is a disease that combines angina, myocardial infarction, cardiosclerosis etc., and occurs due to narrowing of the coronary vessel lumen, often with subsequent thrombosis, which leads to insufficient oxygen supply to the heart muscle [11].

It has been suggested that GP may contribute to dysfunction and damage of blood vessels, including coronary arteries [2]. From this perspective, GP can act as an independent risk factor for CAD, along with common factors such as hypertension, diabetes, dyslipidemia, obesity, smoking, and others [1,12,14, 23]. The pathogenesis of atherosclerosis due to GP is primarily associated with the presence of pathogenic anaerobic microorganisms in periodontal pockets, endotoxins which provoke the body's immune response with the subsequent development of systemic inflammation, production of C-reactive protein and proinflammatory cytokines (IL-6, TNF-a) [2,5,8]. These cytokines are involved in atherogenesis, activate the processes of functional and structural impairment of the endothelium in the arterial walls (endothelial dysfunction), which subsequently leads to the formation of atherosclerotic plaques [12,15]. On the other hand, irreversible dystrophic changes in the microcirculatory system of the periodontium occur along with the progression of systemic atherosclerosis, leading to hypoxia and profound metabolic disorders in periodontal tissues with the subsequent development of GP [4,12].

To date, dyslipidemia is one of the most aggressive stimuli of damage of vascular wall, which causes the manifestation of the atherosclerotic process whether alone or interacting with other risk factors [11,14,23]. Therefore, the integral direction of treatment and prevention of atherosclerosis-related diseases is the normalization of lipid metabolism, in particular, levels of total cholesterol (TC), high atherogenic low-density lipoprotein-cholesterol (LDL-C) and very low-density lipoprotein-cholesterol (VLDL-C) [14,23].

There is a hypothesis that the pathogenetic mechanisms of GP and their negative impact on biochemical processes in the body may initiate or exacerbate functional and compositional impairment of plasma lipoproteins [1,6,7,9,20]. On the other hand, periodontal treatment and reduction of the periodontal pocket infection due to GP may be associated with a decrease in the level of TC, LDL-C, and VLDL-C etc. [13,22].

Despite the above assumptions, there is insufficient literature evidence about the issue of impaired blood lipid metabolism in the case of GP. This leads to further study of the association between lipid metabolism and periodontal status of patients with GP and CAD.

Methods

The selection of clinical material was performed on the basis of Cardiology Department of Lviv Clinical Emergency Care Hospital during the period from January 2017 to December 2019. The study included 101 patients (mean±SD age - 58.2 ± 8.3 years) with CAD and GP, 58 men (57.4%) and 43 women (42.6%). All included patients had at least 10 teeth. Exclusion criteria were the following: other systemic diseases in the anamnesis, recently (up to six months) suffered from myocardial infarction, total secondary adentia. According to the severity of GP, study participants were divided into 3 groups: group I - patients with CAD and GP stage I (initial periodontitis), group II - patients with CAD and GP stage II (moderate periodontitis) and group III - patients with CAD and GP stage III and IV (severe peri-

odontitis) (table 1). The control group included 9 patients with CAD and clinical gingival health on an intact periodontium (mean±SD age - 56.3 ± 6.1 years), 5 men (55.6%) and 4 women (44.4%).

The diagnosis of CAD and indicators of lipid profiles of patients were obtained from the inpatient medical records. The diagnosis of CAD was established on basis of patient complaints, history taking, assessment of risk factors and the results of *electrocardiogram*, echocardiogram and coronary angiography. Reference values of lipid profile indicators for healthy individuals are the following: TC – <5.2 mmol/L, LDL-C – <2.6 mmol/L, VLDL-C– 0.3-0.6 mmol/L, high-density lipoprotein-cholesterol (HDL-C) – >0.9 mmol/L, triglycerides (TG) – <1.7 mmol/L, atherogenic coefficient (AC) male – 2.36-2.6, AC female – 1.74-2.14. All study participants were in the very high-risk group for cardiovascular events, the target level for LDL-C, in this case, was 1.4 mmol/L.

The research was conducted according to the requirements of the basic bioethical provisions of the European Convention on Human Rights and Biomedicine from 04.04.1997 and the Helsinki Declaration of the World Medical Association on ethical principles for medical research involving human subjects (1964-2008). All patients signed consent for examination and research (protocol No.3 from 25.03.2019, discussed and approved by the Committee on ethics of scientific research, experimental development and scientific works of Danylo Halytsky Lviv National Medical University).

Statistical analysis of the results was performed using "Microsoft Excel" and IBM SPSS Statistics 20. The samples presented in the article are checked for normality of distribution by the Shapiro-Wilk test. The samples corresponds the criteria of normal (Gaussian) distribution. The results of the study are presented as mean±standard errors (M±m). The mean values in the groups were compared using Student's t-test, and the difference was considered significant if $p<0.05$.

Results

The results of the analysis of the lipid metabolism indicator level in patients with CAD and GP showed that the values of TC, LDL-C, VLDL-C, TG were lower in group of patients with CAD and clinical gingival health compared with the groups of patients with CAD and GP ($p<0.05$) (table 2).

Comparing the lipid profiles of patients with CAD and GP of varying severity, it was found that the TC plasma level in patients with GP stage I was 5.11±0.16 mmol/L, which was significantly lower than in groups of patients with CAD and GP II and III-IV stages (6.30±0.20 mmol/L and 6.41±0.35 mmol/L, respectively), ($p<0.05$). Moreover, a similar tendency was observed for LDL-C and AC where values of lipid indicators were significantly lower in group I compared to study groups II and III, ($p<0.05$) (table 2). For instance, LDL-C was 2.98±0.17 mmol/L in group I, 3.97±0.18 mmol/L – in group II and 4.08±0.31 mmol/L – in group III, ($p<0.05$). It should be noted that the mean LDL-C value was higher than normal in patients with CAD and GP according to the level of the target LDL-C value for this category of patients with a high risk of cardiovascular events.

There was no significant difference between the value of TC, LDL-C, VLDL-C, TG and AC in groups II and III, ($p>0.05$).

Table 1

Distribution of study groups

		I group	II group	III group	IV group
		Patients with CAD and GP I stage	Patients with CAD and GP II stage	Patients with CAD and GP stage III-IV	Patients with CAD and clinical gingival health
Total	n	43	40	18	9
	%	42,6	39,6	17,8	100
Male	n	22	21	15	5
	%	51.2	52.5	83.3	55.6
Female	n	21	19	3	4
	%	48.8	47.5	16.7	44.4

No significant difference was found between HDL-C levels in the comparison groups, including the group of patients with CAD and clinical gingival health (p>0.05).

Analyzing the gender characteristics of the lipid metabolism values in patients with CAD and GP (table 3), no statistically significant difference was found among men and women, except for the level of HDL-C in group I, LDL-C in group II, TC and LDL-C in group III, (p<0.05).

Discussion

One of the main risk factor for the development of atherosclerosis and CAD is an increase in the level of cholesterol, especially LDL-C in blood plasma. In addition to these indicators, the detection of the level of VLDL-C, HDL-C, TG, and AC is an important component for assessing the risk of CAD and its complications. Epidemiological and clinical studies indicate a close relationship between CAD and destructive-inflammatory diseases of periodontal tissues, in particular GP [8, 12, 14, 17].

Several scientific studies have analyzed the relationship between plasma lipid levels and the GP severity, some periodontal indicators, including the probing depth, clinical attachment loss, bleeding etc. [1, 6, 7, 9]. According to literature sources, in particular, in the works of Tang et al. and Machado et al., there

Table 2

The average value of the indicators levels of lipid metabolism in patients with CAD and GP (M±m)

Indicators of lipid metabolism *(value)*	Patients with CAD and GP stage I **n=43**	Patients with CAD and GP stage II **n=40**	Patients with CAD and GP stage III-IV **n=18**	Patients with CAD and clinical gingival health **n=9**
Total cholesterol *(mmol/l)*	5.11±0.16*	6.30±0.20	6.41±0.35**	4.19±0.27#
HDL cholesterol *(mmol/l)*	1.26±0.04	1.24±0.05	1.20±0.08	1.29±0.11
LDL cholesterol *(mmol/l)*	2.98±0.17*	3.97±0.18	4.08±0.31**	2.21±0.32#
VLDL cholesterol *(mmol/l)*	0.86±0.06	1.01±0.08	1.09±0.14	0.59±0.06#
Triglycerides *(mmol/l)*	2.01±0.18	2.29±0.20	2.47±0.33	1.31±0.13#
Atherogenic coefficient	3.24±0.19*	4.34±0.27	4.53±0.36**	2.45±0.38#

Note:
* - difference between the indicators of GP stage I and GP stage II, p<0.05
** – difference between the indicators of GP stage I and GP stage III-IV, p<0.05
# - difference between the indicators of GP and clinical gingival health, p<0.05

Table 3

The average value of indicators of lipid metabolism in male and female patients with CAD and GP (M±m)

Indicators of lipid metabolism *(value)*	Patients with CAD and GP stage I **n=43**		Patients with CAD and GP stage II **n=40**		Patients with CAD and GP stage III-IV **n=18**		Patients with CAD and clinical gingival health **n=9**	
	male n=22	female n=21	male n=21	female n=19	male n=15	female n=3	male n=5	female n=4
Total cholesterol *(mmol/l)*	4.98 ±0.27	5.25 ±0.20	6.02 ±0.34	6.60 ±0.21	6.02 ±0.31*	8.36 ±0.83	4.21 ±0.45	4.18 ±0.39
HDL cholesterol *(mmol/l)*	1.17 ±0.06*	1.36 ±0.06	1.21 ±0.08	1.26 ±0.07	1.13 ±0.06	1.51 ±0.41	1.34 ±0.17	1.22 ±0.18
LDLcholesterol *(mmol/l)*	2.75 ±0.28	3.23 ±0.17	3.62 ±0.28*	4.34 ±0.22	3.68 ±0.26*	6.05 ±0.42	2.03 ±0.54	2.43 ±0.44
VLDL cholesterol *(mmol/l)*	0.96 ±0.10	0.75 ±0.07	1.12 ±0.13	0.87 ±0.07	1.15 ±0.17	0.81 ±0.13	0.63 ±0.07	0.55 ±0.12
Triglycerides *(mmol/l)*	2.30 ±0.31	1.71 ±0.17	2.64 ±0.35	1.89 ±0.16	2.60 ±0.39	1.78 ±0.30	1.39 ±0.16	1.20 ±0.25
Atherogenic coefficient	3.42 ±0.30	3.06 ±0.23	4.39 ±0.46	4.28 ±0.32	4.46 ±0.41	4.88 ±1.01	2.33 ±0.62	2.61 ±0.59

Note: *- significant difference between the indicators in male and female, p<0.05

was no statistically significant difference between plasma lipid levels in patients with diagnosed GP and patients with clinical gingival health [10, 21]. Moreover, Tang et al. showed the results that the levels of TC, LDL-C, TG were significantly higher in patients with GP and CAD comparing to patients with CAD and clinical gingival health, ($p<0.05$) [21]. Song et al. demonstrated the data that periodontitis may affect levels of blood lipids [20]. In particular, the presence of periodontitis in the examined patients was associated with a reduced level of HDL-C, the presence of tooth loss was associated with an increased changes in TG level. It was also established that improving daily oral hygiene can reduce the risk of dyslipidemia by increasing HDL-C level and decreasing the TG level [20]. Lee et al. studied the relationship between blood lipids levels in women and men and found that high levels of LDL-C and low levels of HDL-C were more common in women with periodontitis than in those who were not diagnosed with periodontitis. In return, there was no significant relationship between plasma lipid levels and periodontitis in men [7].

There are a number of studies that indicate improvement in plasma lipids and lipoproteins levels after conduction of the periodontal treatment. Tawfig et al. found that non-surgical periodontal therapy in patients with hyperlipidemia, along with improving of periodontal state contributed to a significant reduction of LDL-C and TG serum level after 3 months of treatment [22]. Pejcic et al. revealed positive changes in lipid metabolism indicators in patients with GP after periodontal treatment. Accordingly, a significant reduction in TC, LDL-C, and TG levels was observed after 12 months of local therapy of GP, along with improving the condition of periodontal tissues, reducing the periodontal pocket depth and bleeding [13].

In conclusions, the relationship between the plasma levels of proatherogenic indicators of lipid metabolism and the severity of GP in patients with CAD was established. The levels of TC, LDL-C and AC significantly rise with increasing destructive-inflammatory changes in periodontal tissues in GP stage II, III and IV, respectively, which indicates the progression of atherogenesis along with increased inflammatory processes in the periodontium. No clear gender features of the analyzed indicators of the lipid profile were revealed, except for HDL-C in group I, LDL-C in groups II and III, as well as TC in group III.

Thus, the association between the severity of proatherogenic dyslipidemia and the GP progression indicates that periodontal status should be taken into account in the treatment of patients with CAD and prevention of its complications.

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