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The Nature of Changes in Fatty Tissue Hormones and Free Fatty Acids in Patients with Chronic Generalized Periodontitis Associated Metabolic Syndrome

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Abstract: The purpose of this study was to study the characteristics of the indicator of hormones of adipose tissue and free fatty acid in the blood of patients with chronic hepatitis C associated metabolic syndrome. 72 patients with moderate CGP were examined. Of these, 24 patients without concomitant diseases; 48 patients with CGP in combination with MS. Patients with chronic hepatitis C combined MS at the age of 40-65 years were mainly contingents suffering from metabolic disorders, in particular the syndrome of insulin resistance and were outpatient observation. It was revealed that metabolic parameters in the examined patients are characterized by insulin resistance, dyslipidemia, impaired secretory activity of adipose tissue and a complex of independent factors, hyperleptinemia, hypoadiponectinemia. Hypoadiponectinemia is considered an unfavorable prognostic sign, since adiponectin has an angioprotective effect, anti-inflammatory and angiotrombogenic properties, and can also be one of the causes of impairment in the hemocoagulation system.

Keywords: chronic generalized periodontitis; metabolic syndrome; hepatitis C; fatty acids; adipose tissue hormones.

INTRODUCTION

According to the conclusion of WHO experts, the rapid increase in the frequency of MS, the "pandemia of the 21st century", is continuing. The main characteristics of MS are an increase in the mass of visceral fat, insulin resistance, hyperinsulinemia (1.3). The last decades this problem is paid great attention by doctors of almost all specialties. Given the current trends, the number of persons suffering from MS by the middle of this century will exceed half a billion people. However, with timely diagnosis and treatment, metabolic disorders can be reversible, or correction of the manifestations of MS (2.6) is possible.

In the formation of MS in patients with chronic diseases of periodontal tissues, the hyperactivity of the hypothalamic-pituitary-adrenal system and sympathoadrenal reactions plays a role, increasing insulin resistance and reducing adiponectin production. The peculiarities of polymorphism of dopamine and leptin receptor genes associated with MS with hyperactivity of the sympathetic nervous system (Pasechnik, A.V. et al., 2002; Smetnik, V.P. 2007) are noted.

An important link in the pathogenesis of the metabolic syndrome in accordance with lipocentric theory is abdominal-visceral adipose tissue. One of the main factors in MS in patients with chronic hepatitis C can be considered android obesity. According to S.A.Boutrova *et al.*, (2004), in the android type of obesity, insulin resistance was found in 88% of patients, in the case of the ginoid type of obesity, only in 32% of patients.

Numerous studies have shown that hyperinsulinemia leads to the depletion of the insular apparatus of the pancreas (their mass decreases, the conversion of proinsulin to insulin is disturbed). As a result, insulin secretion decreases, and reduced glucose tolerance and diabetes mellitus (Frystyk, J. *et al.*, 2007; Koerner, A. *et al.*, 2005) are gradually being formed. Based on the foregoing, the purpose of this study was to study the characteristics of the indicator of hormones of adipose tissue and free fatty acid in the blood of patients with CGP associated metabolic syndrome.

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MATERIAL AND RESEARCH METHODS

A comparative analysis of the biochemical parameters of blood and oral fluid was carried out in the clinical diagnostic laboratory of the clinic TGSI and in the laboratory of RNPCSM. To achieve this goal, under our supervision there were 72 patients with moderate CGP. Of these, 24 patients without concomitant diseases; 48 patients with CGP in combination with MS. Patients were on outpatient treatment in the clinic TSGI. Patients with chronic hepatitis C combined MS at the age of 40-65 years were mainly contingents suffering from metabolic disorders, in particular the syndrome of insulin resistance and were outpatient observation. In 86.8% of patients, concomitant arterial hypertension and obesity were noted. In working with the examined, ethical principles were observed, which were reflected in the Helsinki Declaration of the World Medical Association (1964). For an objective assessment of the condition of periodontal tissues, patients with CGP combined with MS were examined according to the following parameters: determination of papillary-marginal-alveolar index by C. Parma (1960), determination of bleeding gums when probing according to Barer, Lemetskaya (1996), test of capillary functional resistance according to Kulazhenko V.I. (1960), determination of the index of peripheral blood circulation in periodontal tissues by Dedova L.N. (1981), determination of the degree of tooth mobility, according to A.I. Evdokimov (1953), determination of the depth of periodontal pockets according to WHO (1990), determination of the periodontal index according to Russel A. (1956), determination of the hygienic index according to Green J.C., Vermilion J.R. (1960). The content of insulin was determined by the ELISA method (set of the company "DRG-Diagnostika" Germany). To assess the hormonal activity of adipose tissue, the level of adiponectin,

leptin and resistin was studied on a Cobas 311 analyzer from Roche (Switzerland) using BioHimMac (Russia) kits. In addition, the study of fatty acids by the enzymatic method, using sets of the same company. As an independent predictor of impaired glucose tolerance, IR and diabetes. Statistical data processing was performed on an individual computer using the Microsoft Excel spreadsheet.

RESEARCH RESULTS AND DISCUSSION

It is known that intensive lipolysis in visceral adipocytes leads to the release of a large number of FFA, mainly in the portal circulation and the liver. In the liver, FFAs inhibit the binding of insulin to hepatocytes, causing the development of insulin resistance, a decrease in insulin extraction by the liver, and the development of systemic hyperinsulinemia. Getting into the systemic circulation, FFAs contribute to impaired absorption of glucose and its utilization in muscle tissue and, thus, increased peripheral insulin resistance. Excess blood FFA is a source of accumulation of TG and non-oxidative metabolism of FFA in skeletal and cardiac muscles and causes a violation of insulin-dependent glucose utilization in these tissues. Numerous studies in recent years have shown that FFAs have a direct toxic effect on β -cells of the pancreas (lipotoxicity effect).

This condition is combined with hyperglycemia, which gives an additional amount of substrate for the synthesis of triglyceride. The relationship of glucose-insulin homeostasis and free fatty acids dictates the need to study them in the examined individuals with MS, in whom the level of free fatty acids is 2.5 times higher than in healthy individuals.

Indicator	Comparison group, n = 14	Patients with CGP associated MS n=48	Patients with chronic hepatitis C without MS n = 24
Free fatty acids, mmol/l	0,33±0,02	0,81±0,07*	0,48±0,03*

Table 1. The content of free fatty acids in the blood of patients with CGP combined with MS

Note: * - differences relative to the comparison group are significant P <0.05

The increase in free fatty acid levels caused by hyperinsulinemia, insulin resistance and arterial hypertension in patients with chronic hepatitis C associated with MS is associated with a change in metabolism in mitochondria, whose consumption as an energy substrate of glucose is reduced due to insensitivity of cells to insulin. Free fatty acids, dissociating oxidative phosphorylation, are one of the reasons for the accumulation of reactive oxygen species and cell death. This process also affects the morphological structure of the periodontium. Consequently, MS in patients with chronic hepatitis C affect adipose tissue, enhancing the lipolytic effect of insulin - which leads to the accumulation of FFA and glycerol. In this situation, FFA enters the liver, where it becomes the main source of the formation of atherogenic lipoproteins of very low density (VLDL) and triglycerides (TG).

The next stage of our research was the study of the level of adipose tissue hormones in the blood of the examined persons.

Indicator	Comparison group, n = 14	Patients with CGD associated MS n=48	Patients with chronic hepatitis C without MS n = 24
Leptin, ng / ml	$5,84\pm0,46$	34,88±3,03*	12,01±1,03*
Adiponectin, mg / ml	10,34±0,82	5,33±0,24*	8,73±0,54*
Resistin, ng / ml	8,14±0,63	15,89±0,96*	9,69±0,68*

Table 2 Hormones of	adipose	tissue in	patients with	CGP	combined with MS
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Note: * - differences relative to the comparison group are significant P < 0.05

Abdominal obesity, which usually develops after 30 years, apparently, is a consequence of the agerelated increase in the activity of the hypothalamus, in particular cortisol. Cortisol stimulates cortic-dependent lipoprotein lipase on the capillaries of the fat cells of the upper half of the body, abdominal wall and visceral fat (cortisol-dependent adipose tissue). As a result, fat deposition increases, fatty cell hypertrophy and abdominal obesity develop. It is proved that in patients with MS, the level of $11-\beta$ -hydroxysteroid dehydrogenase increases.

As can be seen from the presented research results, the level of leptin in patients with CGP associated MS is higher than that of healthy individuals by an average of 6 times, whereas in patients with CGP without MS, it exceeded the initial level only 2 times, which indicates their leptin resistance (Table 2).

Currently, the world is developing drugs of leptin and its analogues with a lower molecular weight and greater solubility, which will allow them to penetrate the blood-brain barrier, to define new approaches to the treatment of obesity and its complications.

The adiponectin concentration was different. In patients with CGP combined with MS, the level of adiponectin in the blood averaged $5.33 \pm 0.44 \ \mu g / ml$, which is 51% lower than the reference values of the comparison group (P <0.05). The dynamics of resistin was similar to that of leptin. Its plasma concentration in patients with CGP combined with MS exceeded the value of the comparison group by 2 times (P <0.05).

Thus, in patients with CGP associated MS, the content of adipose tissue hormones was significantly different from that of the comparison group and patients with CGP without MS. An increase in the concentration of free fatty acids, a decrease in the level of adiponectin, an increase in the concentration of leptin and resistin indicate an imbalance of the adipose tissue hormones in the examined individuals with MS.

The need for laboratory monitoring of patients with chronic hepatitis C associated with MS is dictated

by the fact that the reasons why obesity in some cases does not respond to treatment are not clear enough.

Metabolic indices in the examined patients are characterized by insulin resistance, dyslipidemia, impaired secretory activity of adipose tissue and a complex of independent factors, hyperleptinemia, hypoadiponectinemia. Hypoadiponectinemia is considered an unfavorable prognostic sign, since adiponectin has an angioprotective effect, antiinflammatory and angiotrombogenic properties, and can also be one of the causes of impairment in the hemocoagulation system.

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