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THE STUDY OF FUNCTIONAL AND METABOLIC CONTINUUM BY METABOLISM PARAMETERS IN BLOOD PLASMA OF HEALTHY PEOPLE AS COMPARED WITH PATIENTS WITH TYPE 2 DIABETES AND HYPERTENSION AGAINST THE BACKGROUND OF TYPE 2 DIABETES

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Abstract

It is known that existing systems of regulation of energy homeostasis provide adequate needs of the body, depending on both the receipt and use of energy. Moreover, the organization of energy supply has its own characteristics in insulin-dependent and insulin-independent tissues. The main thing in the organization of energy supply is the achievement of the principle of compliance with the functional needs of the body, that is, the maintenance of the functional and metabolic continuum (FMC)

We studied the metabolic parameters of FMC in healthy people and patients with type 2 DM and patients with hypertension against the background of type 2 DM according to the study of some indicators of blood plasma.

The identified features, in our opinion, are one of the first manifestations of FMC disorder due to insulin resistance

With the advent of insulin deficiency, there are increasing disturbances of energy metabolism, which are mainly caused by endothelial dysfunction and neuro-hormonal regulatory shifts of a stressful nature.

The consequences or manifestations of these processes can probably be found in all environments of the body: blood, saliva, condensed air, that is, they have a systemic character.

Key words: insulin resistance; energy supply; metabolism; diabetes mellitus; hypertension

Until the twentieth century, traumas and infectious diseases were among the leading causes of death. The average life expectancy in the 18th century was 35-40 years. Even in the presence of chronic diseases of the internal organs, people often die not of these diseases as such, but of intestinal infections, tuberculosis, various complications in childbirth, from gangrene and sepsis – the companions of severe injuries and combat wounds. In the 19th-20th centuries, life in the countries of Europe and North America has drastically changed as a result of scientific and technological progress. There was no need for continuous physical labor to subsist, and more free time appeared, which in turn contributed to further scientific and technological progress. The development of epidemiology and microbiology, aseptics and antiseptics, promotion of hygiene, and finally, the discovery of antibiotics have dramatically reduced the morbidity and mortality due to infectious diseases. However, the human body, formed in the natural environment, was not ready for the test of "benefits of civilization", which in some cases had a negative impact on human health, especially in the 21st century [1].

Hence, the obvious role of hypodynamia is in the appearance of overweight and the development of obesity with all its complications, including atherosclerosis and diabetes mellitus (DM). Reduced load on the cardiovascular system in a sedentary lifestyle leads to weakening and weight loss of the heart muscle, deterioration of the coronary vessels and impaired metabolism in cardiomyocytes. According to statistics, mortality due to coronary heart disease is by 30% higher for patients with a sedentary lifestyle than for those who regularly exercise [1].

"Diseases of civilization" are widespread in the population of developed countries and associated with specific factors characteristic of large cities: pollution, overeating, emotional stress, vibration, noise, electromagnetic radiation, etc. In hypodynamia, the vascular tone weakens, the blood pressure decreases, the supply of tissues with oxygen and the intensity of metabolic processes in the body deteriorate. Low tone and vascular wall trophic disorders contribute to the development of venous insufficiency, atherosclerosis, arterial hypertension

(AH), endothelial dysfunction, etc. [1]. It has been established that the pathogenetic mechanisms that cause the development of hypertension, insulin resistance (IR) and type 2 diabetes mellitus (type 2 DM), largely overlap and lead to the progression of diseases with the development of complications. Thus, concomitant obesity in patients with hypertension and diabetes is a factor in the progression of metabolic disorders, IR, activation of markers of immune inflammation and atherogenesis [2].

Thus, in the modern conditions, a set of evolutionarily new causal factors is formed, which can cause the development of new pathological conditions, which are implemented with the participation of evolutionarily entrenched typical pathological processes, albeit with some specificity. This group of factors includes a decrease in physical activity, an increase in the calorie intake of food, a change in the spectrum of infectious agents, etc. Accordingly, each of these factors (individually and collectively) influences the body, interacting with the cells and tissues of the body, causes the development of insulin resistance, lipotoxicity, obesity, immune inflammation, etc. [3, 4, 5, 6, 7, 8].

It is known that existing systems of regulation of energy homeostasis provide adequate needs of the body, depending on both the receipt and use of energy. Moreover, the organization of energy supply has its own characteristics in insulin-dependent and insulin-independent tissues. The main thing in the organization of energy supply is the achievement of the principle of compliance with the functional needs of the body, that is, the maintenance of the functional and metabolic continuum (FMC) [9, 10, 7].

According to our hypothesis, one of the mechanisms that initiate the development and progression of cardiovascular disease may be changes in metabolism that are not adequate for functional adaptation reactions, accompanied by impaired functional and metabolic continuum (FMC) [2, 11, 12].

The aim of the research

The aim of this research was to study the metabolic parameters of FMC in healthy people and patients with type 2 DM and patients with hypertension against the background of type 2 DM (subjects aged 35-45 years, duration of the disease: 3-5 years, treatment – metformin) according to the study of some indicators of blood plasma.

Materials and methods

The study was conducted in 30 healthy individuals (20 women and 10 men) and 60 patients with type 2 diabetes mellitus, of whom 28 (19 women and 9 men) were diagnosed with type 2 diabetes and 32 (18 women and 14 men) were diagnosed with type 2 diabetes, complicated by hypertension.

The object of study was blood plasma. Blood plasma was obtained by centrifugation of heparinized blood (for 10 minutes at 2000 rpm) taken in the morning on an empty stomach from the cubital vein.

The concentration of ADMA was determined using LC 5000 liquid chromatograph (INGOS Czech Republic), the wavelength of 340 nm, in isocratic mode. Abselut Nexus cartridges (Varian) were used for solid phase extraction (purification and concentration) [13].

The activity of lipid peroxidation processes was assessed by the concentration of TBA-active products [14].

Determining SOD activity is based on the establishment of a percentage blockage of quercetin oxidation reaction in the presence of serum or plasma [15].

The activity of catalase was determined by spectrophotometric method (according to Chevari S. et al.) [16].

The content of calcium, total lipids, triglycerides, cholesterol, urea was determined by spectrophotometric methods using reagent kits of "Phyllis - Diagnostics" (Ukraine, Dnipro).

Zinc and copper content were determined by spectrophotometric methods using reagent kits from DAC-SpectroMedS.R.L (Moldova).

Lactate concentration was determined by the enzymatic colorimetric method using a set of reagents from LACTAT VITAL (St. Petersburg).

The differences between the two groups of independent indicators were assessed by Student's test.

Results and discussion

The data from our studies, which are shown in Table 1, indicate that the development of the disease in patients with type 2 DM, even in the presence of moderate hyperglycemia, is accompanied by simultaneous changes in lipid metabolism: in the blood plasma, lipid levels and cholesterol are significantly increased. Along with this, the levels of urea, uric acid and lactate increase. That is, under conditions of relative glucose deficiency in insulin-dependent cells of the body, there is a change in the structure of energy supply with the involvement of lipids and possibly proteins. However, in non-insulin-dependent tissues, glucose uptake is increased. Such changes in energy exchange occur at the expense of the neurohumoral regulatory systems, as indicated by the data in Table 2: the level of both adrenaline and cortisol increases in blood plasma. However, they cause smaller changes to more permanent homeostatic indicators, such as calcium.

Table 1

Metabolism in healthy people, patients with type 2 DM, and patients with hypertension against the background of type 2 DM according to blood plasma studies.

Indicators	Healthy subjects, n=30	Patients with type 2 diabetes mellitus, n=28	Patients with type 2 diabetes mellitus and hypertension, n= 32
Protein g / l	68.22 ±3.19	69.47 ± 4.31 P > 0.05	67.11 ± 5.63 P > 0.05
Lipids g / l	4.57 ± 0.24	5.93 ± 3.22 P < 0.02	7.12 ± 4.05 P < 0.01
Cholesterol mm / l	4.62 ± 0.37	6.04 ± 0.51 P < 0.01	7.59 ± 0.55 P < 0.01
Urea mmol / l	6.48 ± 0.31	8.42 ± 0.63 P < 0.02	9.65 ± 0.77 P < 0.01
Uric acid mmol / l	0.35 ± 0.02	0.41 ± 0.05 P > 0.05	0.64 ± 0.04 P < 0.01
Glucose mmol / l	5.15 ± 0.28	6.48 ± 0.52 P < 0.02	7.35 ± 0.54 P < 0.01
Lactate mmol / l	1 .87 ± 0.13	2.55 ± 0.91 P < 0.05	3.26 ± 0.24 P < 0.02

Note: p-significant differences in metric values.

Table 2

The ionic composition and content of some hormones in healthy people, patients with type 2 DM and patients with hypertension against the background of type 2 DM according to blood plasma studies

Indicators	Healthy subjects, n=30	Patients with type 2 diabetes mellitus, n=28	Patients with type 2 diabetes mellitus and hypertension, n= 32
Cortisol, nm / l	435.22 ± 16.11	502.21 ± 27.43 P < 0.02	573.41 ± 34.17 P < 0.01
Adrenaline, nm / l	3.93 ± 0.05	4.26 ± 0.35 P < 0.05	4.72 ± 0.29 P < 0.05
Calcium, mm / l	2.33 ± 0.12	2.43 ± 0.19 P > 0.05	2.29 ± 0.19 P > 0.05

Note: p - significant differences in the value of indicator

The increase in lactate levels found in patients with type 2 diabetes mellitus indicates an increased role of anaerobic glycolysis in the energy supply of tissues, which is probably due to hypoxia. The cause of hypoxia is probably endothelial dysfunction, which develops as a result of toxic action of glucose. This is confirmed by the increased content of ADMA

(Table 3). Hypoxia, endothelial dysfunction lead to the development of oxidative stress (a significant increase in the concentration of the Schiff bases with insufficient response from the antioxidant system), more pronounced in patients with type 2 diabetes mellitus and hypertension, as shown by the obtained results (Table 3).

Table 3

The activity of antioxidant system enzymes in healthy people, patients with type 2 DM and patients with hypertension against the background of type 2 DM according to blood plasma studies

Indicators	Healthy subjects, n=30	Patients with type 2 diabetes mellitus, n=28	Patients with type 2 diabetes mellitus and hypertension, n= 32
ADMA µmol / l	0.146± 0.008	0.191 ± 0.008 P< 0.01	0.231 ± 0.018 P < 0.001
Catalase, µcal / l	3.24 ± 0.17	4.55 ± 0.32 p< 0.01	3.97 ± 0.19 P < 0.05
SOD, µg / ml	32.17 ± 2.03	49.56 ± 3.14 p< 0.001	40.37 ± 2.08 p< 0.01
Schiff bases, µmol / l	38.47 ± 2.46	49.26± 4.15 P < 0.05	58.43 ± 4.66 P < 0.02

Note: p-significant differences in metric values.

In the group of patients with type 2 diabetes mellitus complicated by hypertension the severity of the disease increased, and its marker is even more significant, in comparison with patients with type 2 DM without complications, increased glucose level (Table 1), indicators of lipid metabolism, lactate, urea and uric acid. That is, an increase in IR, judging by hyperglycemia, is accompanied by enhanced changes in lipid and protein metabolism, which confirms our hypothesis of switching energy supply. This is also due to the subsequent neurohumoral activation (Table 2), without changes in calcium concentration. This restructuring of the metabolism also leads to further activation of LPO (Table 3), and although the antioxidant mechanisms (SOD, catalase) are increased, they are behind the increase in the concentration of the Schiff bases.

Thus, the main differences were that oxidative stress (OS) was observed in patients with type 2 DM. This is evidenced by a significant increase of ADMA and Schiff bases concentrations in blood plasma. Moreover, their concentrations increased with a simultaneous activation of OS. One of the possible mechanisms for this may be glucocorticoids and catecholamines, whose increased concentration of which confirms the body's stress [17, 18,

19]. An additional confirmation is the increased concentration of urea and uric acid in the blood, which can be considered as evidence of the catabolic effects of glucocorticoids. The identified features, in our opinion, are one of the first manifestations of FMC disorder due to insulin resistance.

Conclusions

1) With the advent of insulin deficiency, there are increasing disturbances of energy metabolism, which are mainly caused by endothelial dysfunction and neuro-hormonal regulatory shifts of a stressful nature.

2) The consequences or manifestations of these processes can probably be found in all environments of the body: blood, saliva, condensed air, that is, they have a systemic character.

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