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LEVELS OF GLUCOSE AND ITS METABOLITES, PANCREATIC HORMONES, AND ADIPONECTIN IN THE ARCTIC POPULATION

The search for the causes underlying changes in carbohydrate metabolism remains relevant due to the lifestyle of the Arctic population and its changes in the indigenous population, which leads to a change in the "northern" hormonal and metabolic profile and the development of metabolically related diseases, including diabetes mellitus. The aim of the study was to identify the characteristics of carbohydrate metabolism, pancreatic hormones, and adiponectin in an almost healthy Arctic population, depending on their ethnicity and lifestyle. Materials and methods. A cross-sectional study of the population of the local Caucasian population and the aborigines of the Arctic (Nenets) aged 18 to 74 years was conducted. The levels of proinsulin, insulin, and adiponectin in blood serum were studied by enzyme immunoassay, and glucose, lactate, and pyruvate were studied by spectrophotometric analysis. The HOMA, Caro, lactate/pyruvate, and Proinsulin/Insulin indices were calculated. Results and discussion. The analysis of glucose levels showed that a statistically significantly high glucose content was found in the local Caucasian population relative to nomadic and sedentary aborigines. At the same time, 21.9% of nomadic aborigines, 17.8% of settled Aborigines and 28.9% of the local Caucasian population had excess glucose levels and 7.1%, 8.8% and 10.0% had prediabetic blood levels. Lactate levels, lactate/pyruvate values, and insulin in the groups were highest in sedentary Aborigines ($p=0.001$, $p<0.001$, $p=0.046$), while in nomadic aborigines and the local Caucasian population, insulin levels were minimal ($p=0.046$), and proinsulin levels and proinsulin/insulin values ($p<0.001$), on the contrary, is higher in the absence of significant differences in the level of pyruvate. A significantly low content of adiponectin was observed in sedentary aborigines, both relatively nomadic and the local Caucasian population ($p<0.001$). Conclusion. The lowest levels of glucose and insulin found in nomads against the background of increased proinsulin and adiponectin may indicate a decrease in the secretory activity of pancreatic beta cells and an improvement in insulin resistance; in sedentary aborigines, the predominance of anaerobic processes over aerobic ones is associated with a restriction of proinsulin production and is associated with an increase in insulin resistance with low levels of adiponectin, while in the local Caucasian population, insulin levels increase slightly while maintaining a higher level, which leads to an increased load on beta cells of the pancreas, causing an increase in adiponectin synthesis.

Key words: glucose, lactate, pyruvate, insulin, proinsulin, insulin resistance, adiponectin, Arctic population.

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Introduction. Trends in the spread of diabetes mellitus 2 (DM 2) persist among the indigenous population of the Arctic (about 20% of cases) [3]. In this regard, it is of interest to evaluate the metabolic mechanisms underlying its development in the practically healthy population of the Arctic. At the same time, such rearrangements occur in different directions for each indicator and lead to the formation of a specific "northern" hormonal

and metabolic profile of the body, characterized by minimizing the carbohydrate component of metabolism against the background of intensification of lipid (L.E. concept Panina, 1978), resulting in a completely different structure of metabolic relationships [6]. Perhaps one of the reasons for the decrease in glycemia among the indigenous inhabitants of the Arctic of the last century may be the type, intake regime and amount of

carbohydrates that gradually entered the diet, and thus a more pronounced competition between glucose and fatty acids for the oxidation of tissues sensitive to increased insulin [8]. In general, there is no consensus among the Arctic population about the features of the functional activity of the pancreatic insulin apparatus, and the available data still remain very contradictory. It is pointed out that the aborigines of the North, with the condition of preserving the traditional protein-lipid type of nutrition, were characterized by a special, "economical" type of metabolism with a decrease in blood insulin [4]. In addition, residents of the North are characterized by an increase in proinsulin levels against a background of a decrease in insulin and an increase in the proinsulin/insulin ratio. At the same time, other studies show that there are many points of interaction between insulin and adipose tissue [1, 5]. Currently, adipose tissue is considered as a hormonally active system that produces biologically active adiponectin, which is involved in the development of insulin resistance [7]. There is little data in the literature on the effect

of adiponectin on the level of glycemia in the inhabitants of the North. It has been found that its blood levels vary depending on ethnicity. Thus, the Caucasian population is characterized by a higher content of adiponectin in comparison with African Americans or Asians [14]. Other studies relate to the experimental study in mice of the role of the adiponectin pathway in reducing insulin resistance [10, 14], which, in turn, is a key factor in the development of metabolically related diseases, including diabetes mellitus (DM) [5, 9, 11]. In this regard, the search for the causes underlying the changes in carbohydrate metabolism remains relevant.

The aim of the study was to identify the characteristics of carbohydrate metabolism, pancreatic hormones, and adiponectin in an almost healthy Arctic population, depending on their ethnicity and lifestyle.

Materials and methods. In the course of a single-center observational cross-sectional study, residents of the village of Nelminsky in the North Caucasus Federal District (67°58' s.w.), the municipalities of Sokolskoye (65°17' s.w.),

Soyanskoye (65°46' s.w.), and in the village of Dolgoshchelye in the Mezen district of the Arkhangelsk region (66°05' s.s.) – 457 people, as well as the villages of Seyakha (70°10's.s.), Tazovsky (67°21's.s.), Gyda (70°54's.s.), Nyda (66°37's.s.), Nori (66°09' n), Antipayuta (69°06'n) – 660 people. The total sample size was 1,117 people (794 women and 323 men), the age of the subjects was 18-74 years. The study examined populations of the local Caucasoid population (ME) of 447 people and the indigenous inhabitants of the Far North (Nenets), who were divided into two groups according to their lifestyle - nomadic (KA, 143 people) and sedentary (OA, 527 people) aborigines. The study was conducted in compliance with the ethical standards set out in the Helsinki Declaration of the World Medical Association of 1964, as amended and supplemented in 2013, and was approved by the Commission on Biomedical Ethics at the Institute of Physiology of Natural Adaptations of the Federal State Budgetary Educational Institution FITSKIA Ural Branch of the Russian Academy of Sciences (protocols

The content (Me – 25%; 75%) of carbohydrate metabolism parameters, pancreatic hormones, and adiponectin in the practically healthy aboriginal and local Caucasian population of the Arctic

Indicators	Nomadic Aborigines (AS) (1)	Settled Aborigines (SA) (2)	The local Caucasian population (LCP) (3)	H - test	The Kraskel-Wallis criterion (H-test) with the Bonferoni correction
Glucose (Glu)	4.70(4.24;5.32)	4.74(4.21;5.35)	5.01(4.49;5.60)	H = 23.812 p < 0.001	1-2 = 2.698 1-3 = 0.007 2-3 < 0.001
Lactate (Lac)	2.88(2.36;3.41)	3.07(2.47;3.73)	2.80(2.22;3.52)	H = 15.817 p = 0.001	1-2 = 0.319 1-3 = 0.860 2-3 < 0.001
Pyruvate (Pyr)	0.035 (0.03;0.04)	0.033(0.02;0.04)	0.034(0.02;0.04)	H = 5.258 p = 0.217	1-2 = 0.087 1-3 = 0.097 2-3 = 2.973
Lac/Pyr	89.28(73.2;110.7)	99.58(77.9;125.7)	90.75(68.9;115.3)	H = 19.006 p < 0.001	1-2 = 0.011 1-3 = 2.686 2-3 < 0.001
Insulin (Ins)	6.36(3.70;13.23)	8.41(4.54;13.75)	6.86(4.42;12.20)	H = 8.373 p = 0.046	1-2 = 0.050 1-3 = 0.901 2-3 = 0.074
Proinsulin (ProIns)	2.70(1.55;4.80)	1.76(0.54;2.82)	2.50(1.79;4.05)	H = 53.851 p < 0.001	1-2 < 0.001 1-3 = 2.918 2-3 < 0.001
ProIns/Ins	0.06(0.02;0.15)	0.02(0.01;0.07)	0.06(0.03;0.10)	H = 56.552 p < 0.001	1-2 < 0.001 1-3 = 0.881 2-3 < 0.001
HOMA	1.40(0.72;3.00)	1.82(0.90;2.97)	1.46(0.90;2.67)	H = 4.787 p = 0.274	1-2 = 0.134 1-3 = 0.808 2-3 = 0.507
Caro	0.72(0.37;1.18)	0.57(0.35;0.93)	0.70(0.43;1.07)	H = 13.052 p = 0.004	1-2 = 0.048 1-3 = 2.116 2-3 = 0.003
Adiponectin (Adn)	19.08(13.7; 29.0)	12.44 (8.2; 15.5)	22.40 (11.9; 34.9)	H = 42.797 p < 0.001	1-2 < 0.001 1-3 = 1.786 2-3 < 0.001

Note. Statistically significant differences are highlighted in bold ($p \leq 0.05$), while trending differences are highlighted in italics ($0.05 < p \leq 0.1$).

dated 2.02.2009, 4.02.2013, 9.11.2016 and 15.02.2022). Exclusion criteria were applied in the survey: people working in shifts), the presence of diabetes, CVD, thyroid diseases, acute pathological conditions and exacerbations of chronic diseases in the subjects.

Venous blood sampling from the examined individuals was carried out in the morning from 8.00 a.m. to 10.00 a.m. on an empty stomach in the Beckton Dickinson BP vacutainers, at the same time questionnaires were conducted with questions regarding chronic diseases and ethnicity. The glucose level (Glu, reference value 3.9–6.1 mmol/L) was determined by the spectrophotometric method using Chronolab AG kits. The content of adiponectin (Adh, norm 10–30 ng/ml), proinsulin (ProIns, norm 0.7–4.3) was determined in blood serum using the enzyme immunoassay kits "DRG Instruments GmbH" on a tablet analyzer for enzyme immunoassay (ELISA, ELISYS Uno, Human GmbH, Germany) and a StatFax 303 photometer (USA). pmol/l and insulin (Ins, the norm is 2.1–22 µed/ml). The indices of the ratio of ProIns to Ins (ProIns/Ins) were calculated. The values specified in the instructions for the kits used were taken as normative. The indices characterizing the presence of insulin resistance (IR) were also calculated: NOME according to the formula $NOMA = (Glu \text{ (mmol/l)} \times Ins \text{ (µme/ml)}) / 22.5$ and Sago according to the formula $Sago = Glu \text{ (mmol/L)} / Ins \text{ (mcME/ml)}$.

Statistical data processing was carried out using the IBM SPSS Statistics 22.0 application software package. The samples obtained were checked for the normality of the distribution based on the results of calculating the Shapiro-Wilk criterion. The median (Me) values were calculated, and the scattering measures included the values of the 25th and 75th percentiles. The statistically significant differences between the independent groups were evaluated using the Kraskel-Wallis test (H-test) with the Bonfferoni correction (to keep the error of the first kind within 5%) [2].

Results and discussion. The indicators of carbohydrate metabolism, pancreatic hormones and adiponectin are presented in Table 1. Thus, the analysis of the level of Glu showed that there are significant differences between the groups under consideration ($H=23.812$, $p<0.001$). At the same time, a statistically significantly high content of Glu and ME was detected relative to OA and KA. There were no significant differences in the level of Pir depending on the lifestyle of the surveyed. The Lac

level ($H=15.817$, $p=0.001$) and the Lac/Pir value ($H=19.006$, $p<0.001$) were the highest in the OA population, while the CA and ME were the lowest. In addition, it was shown that in OA, the values of Ins were maximum ($H=8.373$, $p=0.046$), in the KA and ME groups they were minimum ($H=8.373$, $p=0.046$), and the level of Ins ($H=53.851$, $p<0.001$) and the value of Ins/Ins ($H=56.552$, $p<0.001$), the opposite is true between the groups under consideration. At the same time, based on the data of Glu and Ins on an empty stomach, the value of the NOME index was calculated, it is informative in detecting IR in people with intolerance to Glu, i.e. those with violations of its level, and the Sago index, which is more sensitive in the absence of changes in the content of Glu. No statistically significant changes were found for the NOME index ($H=4.787$, $p=0.274$). Statistically significant changes between the groups were noted for the Sago index ($H=13.052$, $p=0.004$). Our comparative assessment of the blood pressure level showed that there were statistically significant differences between the compared groups ($N=42.797$, $p<0.001$). Its significantly low content was observed in OA, both relative to KA and ME ($p<0.001$).

The socio-economic transformations carried out in recent decades, the influx of migrants and the growth of urbanization have changed the traditional way of life and diet of indigenous peoples, which led to the disruption of adaptive processes with increased intensification of carbohydrate metabolism, which serves as an amendment to Panin's concept [6]. At the same time, the most favorable changes, in our opinion, are represented by nomads who have preserved the traditional way of life with a dietary diet, compared with the settled contingent. At the same time, the lowest level of Glu against the background of a decrease in the level of Ins and an increase in ProIns may indicate a reduced load on the β-cells of the pancreas, and an increase in the level of Adn may improve the IR index, although the risk of developing latent metabolic disorders remains. In turn, sedentary people have multidirectional adaptive mechanisms for regulating glucose homeostasis. Thus, in OA, the predominance of anaerobic processes over aerobic ones is probably due to an increase in the proportion of carbohydrates while maintaining the proportion of lipids in the actual diet, which increases the risk of developing previously unusual somatic diseases, including diabetes. In addition, in OA, a change in the traditional way of life, fixed for centuries, leads to

a loss of sensitivity to Ins, which in turn may be a consequence of a decrease in blood pressure [5]. In ME, an increase in the level of glycemia compared with the native population should be accompanied by an increase in the production of Ins for glucose uptake by tissues in order to utilize it, however, we have shown that IU increases the level of Ins more slowly while maintaining a higher level of ProIns and the value of ProIns/Ins compared to OA, which may indicate the entry of immature ProIns into the blood. This, apparently, leads to an increased load on the β-cells of the pancreas and the need for differentiation of adipose tissue, which leads to an increase in Adp synthesis. This may lead to greater oxidation of fats (with a low content of Ann and a high content of Glu). Thus, experiments on mice have shown that an increased level of Adh is a protective property that preserves the function of pancreatic beta cells while limiting the metabolic flow of Glu from beta cells [10, 13], and a decrease in its concentration leads to IR in patients receiving a high-fat diet [12].

Thus, in our opinion, the multidirectional nature of the changes in the studied indicators is related to the peculiarities of nutrition (diet, amount of carbohydrates consumed primarily) and lifestyle among the aboriginal and local Caucasian populations of the North, which themselves vary significantly. Probably, there is competition between Glu and fatty acids at the tissue level to maintain an optimal level of energy exchange in the harsh climate of the North. This issue will be investigated by us in the future.

Conclusion. The results of our study showed that nomads have the lowest Glu levels against the background of a decrease in the level of Ins and an increase in ProIns may indicate a reduced load on the β-cells of the pancreas, and an increase in the level of Adn may improve the IR index. In OA, the predominance of anaerobic processes over aerobic ones against the background of an increase in blood pressure at a lower level of blood pressure may be associated with an increase in the proportion of carbohydrates while maintaining the proportion of lipids in the actual diet due to lifestyle changes, which increases the risk of developing previously uncommon somatic diseases. In MEN, the level of Ins increases slightly while maintaining a higher value of ProIns/Ins, which, apparently, leads, on the one hand, to an increase in the load on the β-cells of the pancreas, and on the other, to the need for differentiation of adipose tissue, which causes an increase in Adp synthesis.

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THE EFFECT OF ELEVATED AND PHYSIOLOGICAL CONCENTRATIONS OF CATECHOLAMINES ON THE FORMATION OF IMMUNOGLOBULINS IN HEALTHY INDIVIDUALS IN THE NORTHERN TERRITORIES OF THE RUSSIAN FEDERATION

An immunological assessment of the health status of 75 Arkhangelsk residents who had no history of acute or chronic diseases at the time of the study was carried out. The aim of the study was to study the effect of elevated and physiological concentrations of catecholamines on the formation of immune responses in residents of the northern territories of the Russian Federation. During a comprehensive immunological examination, a morphological analysis of the blood was performed, including a study of its cellular composition (hemogram). Thus, it has been established for the first time that practically healthy residents of the European North of the Russian Federation experience changes in the content of catecholamines and immunological parameters. An increase in the average dopamine content and a slight increase in the average IdM content was found, which amounted to 33.7 ± 3.56 and 1.83 ± 0.04 , respectively. Studies have shown that patients have a tendency to increase the content of IgE immunoglobulin (74.3 ± 8.16). In addition, abnormally high concentrations of IdM ($36.84 \pm 3.18\%$) and elevated concentrations of IgG ($25.0 \pm 2.49\%$) were detected. There was also a slight increase in the concentrations of cells capable of proliferation (CD10+), which amounted to $1.7 \pm 0.22\%$. Elevated concentrations of catecholamines in practically healthy people have not been established. Concentrations of dopamine were $7.81 \pm 0.43\%$, norepinephrine $4.76 \pm 0.08\%$ and adrenaline $3.08 \pm 0.27\%$. The remaining immunological parameters did not exceed the values considered physiologically normal. These changes correlate with the impact of negative climatic factors. Such factors include violation of the light regime and low temperatures, which provoke a chronic state of stress in the body and, as a result, increased stress on the immune system. This phenomenon leads to a malfunction of the immune system and accelerated physiological wear of the body, which can become a predisposing factor for the development of various diseases.

Keywords: catecholamines, dopamine, norepinephrine, adrenaline, immune reactions, northern territories of the Russian Federation, lymphocytes. CD10+, CD95+, immunoglobulins.

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