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THE ASSOCIATION OF INSULIN RESISTANCE AND VISCERAL ADIPOSE TISSUE DYSFUNCTION WITH COMPONENTS OF METABOLIC SYNDROME IN MEN OF WESTERN-YAKUT INDUSTRIAL REGION

ABSTRACT

We have compared the association of parameters of insulin resistance and visceral fat dysfunction with the main and additional components of metabolic syndrome in men who permanently reside in West Yakutia industrial region and work in mining company. There was a close connection between insulin resistance and analyzed main and additional components of metabolic syndrome. However, we have found no association between the dysfunction of visceral fat tissue and disorders of carbohydrate metabolism, which is the principal component of metabolic syndrome. Cardiometabolic risk assessment using the criteria of visceral fat dysfunction can therefore result in underestimated contribution of carbohydrate metabolism disorder to cardiometabolic risk. Thus, insulin resistance criteria are more informative in population studies of metabolic syndrome epidemiology and pathogenesis than the criterion of visceral fat tissue dysfunction.

Keywords: West Yakutia industrial region, men, metabolic syndrome, insulin resistance index, visceral adiposity index.

In spite of the consensus on metabolic syndrome (MS) definition achieved by professionals from different fields of medicine and international organizations, there are still many controversial issues of metabolic syndrome pathogenesis. MS is currently considered a cluster of factors of increased cardiovascular risk including the following five pathological conditions, which are the main components of MS: abdominal obesity (AO), arterial hypertension (AH), carbohydrate metabolism disorders (CMDs), hypertriglyceridemia (HTG), and decreased level of high density lipoprotein cholesterol also known as hypoalphacholesterolemia (HACL) [7].

The majority of researchers believe that insulin resistance (IR) is a key element of MS pathogenesis. HOMA-IR index of insulin resistance is used to

evaluate the insulin sensitivity. This index is calculated on the basis of carbohydrate metabolism regulation parameters (glucose and insulin blood levels) [8]. It has been also demonstrated that insulin resistance is associated with other diseases and hormonal and metabolic disorders such as excess body weight (EBW), hypercholesterolemia (HCL), purine metabolism disorders (PMDs), proinflammatory and prothrombotic changes in blood system, testosterone deficiency, etc. [2, 3, 6, 9]. These pathologic states are classified as additional components of MS.

There is also an alternative viewpoint on MS pathogenesis. According to this viewpoint, pivotal role in MS pathogenesis is played by AO and visceral fat dysfunction (VFD) based on the disbalance secretion of adipokines (leptin, resistin, adiponectin, etc.) and the hyperproduction of proinflammatory cytokines, free fatty acids, etc. [5, 11]. A special model of fat distribution is therefore proposed to measure the level of individual cardiometabolic risk. This model calculates the visceral adiposity index (VAI) using the anthropometric characteristics of obesity (Ketle index and waist circumference) and biochemical markers of fat dysfunction (blood levels of triglycerides and high density lipoprotein cholesterol) [10].

There is a direct correlation between HOMA-IR and VAI indices and between these indices and MS [10]. However, it is not quite clear if these indices are equally associated with various components of MS. We need to know this to determine how exactly these indices should be used in epidemiological and pathogenetic studies of MS, especially in certain cohorts of examined people.

We have shown earlier that from 1991 to 2007 the frequency of MS in workers of West Yakutia industrial region increased more than three times [1]. In 2007 the following three components of metabolic syndrome dominated: AH, AO and HACL [4].

The aim of this study was to perform the compare the relationships between IR and VFD and the main and additional components of MS in men who permanently reside in West Yakutia industrial region and work in mining company.

MATERIAL AND METHODS

The study involved 242 non-indigenous men aged from 21 to 61 years who constantly lived in Mirny Republic of Sakha (Yakutia) and worked at the mine "International". Body length (BL, m), body weight (BW, kg), waist circumference (WC, cm), systolic and diastolic blood pressure (SBP and DBP, mm Hg) was measured, and the concentration of glucose (mmol/L), triglycerides (TG, mmol/L), total cholesterol (TCL, mmol/L), high density lipoprotein cholesterol (HDL, mmol/L), uric acid (UA, μmol/L) and immunoreactive insulin (IRI, reference values 4-16 MU/ml) were determined in the blood serum. The presence of AO, AH, CMDs, HTG and HACL was diagnosed according to criteria NCEP ATP III [7]. The presence of excess body weight was recorded at value of Ketle index (IK), calculated as the ratio of BW (kg) / BL (m^2), equal to or more 25.0. The presence of HCL was diagnosed at the concentration of TCL in the blood higher 5.2 mM; PMDs was defined at the concentration UA higher 400 mmol/L. The presence of MS was verified in two ways: the patient had at least three main components (according the recommendations of experts NCEP ATP III), or there are three or more any components (main and additional). HOMA–IR index was counted for determination of sensitivity to insulin according to the formula: glucose (mmol/L) •IRI (MU/ml)) / 22.5; IR was registered for values of the index more than 2.77 conventional units (CU) [8]. Visceral adiposity index was calculated by the formula: VAI = (WC / (39.68 ± 1.88 •IK)) • (TG / 1.03) • (1.31 / HDL); the index value more than 1.00 CU demonstrated the presents of VFD [10].

The results are presented as mean indicator values and the standard deviation (M±SD) or the frequency of a sign (%). Average values of HOMA-IR and VAI indexes were compared using the Mann-Whitney U-test. The $\chi 2$ test with Yates correction was used to compare the frequency of IR and VFD. Distinctions were recognized significant at $p<0.05$.

RESULTS AND DISCUSSION

Average values of VAI and HOMA-IR indices in total sample of men were 1.68±1.55 and 3.70±2.64 CU, respectively. The frequencies of VFD and IR were 63.6% and 55.4%, respectively. The analysis of these parameters in relation to MS and its components are shown in table.

The table shows that VAI and VFD frequency depended on the presence of MS (irrespective of the method of its identification), its four main and three studied additional components. However, VAI and VFD were not connected with CMDs, the principal component of MS. HOMA-IR index depended on the presence of MS when each of two verification techniques was used. HOMA-IR index also depended on all main and additional MS components. Similar relationships were identified between IR and MS and its components except for HCL, which had no influence on IR frequency. These findings suggest that VFD parameters in studied man sample were less connected with MS than insulin resistance parameters.

Total index of ratios (TIR) was calculated to range MS components by the level of their connection with VFD and IR. TIR for VFD is the sum of the ratio of average VAI values in groups with presence or absence of certain MS component and the ratio of VFD frequencies in the same groups. For instance, TIR for HTG was calculated as follows: average VAI values in groups with presence or absence of HTG were 3.63 and 1.12, respectively (table); the ratio of these average VAI values was 3.24; VFD frequencies in groups of men with HTG or without HTG were 98.1% and 53.7%, respectively, and their ratio was 1.83. TIR for HTG is therefore 5.07 (3.24+1.83)**.** TIR for other components were calculated in the same way. In case of VFD, studied components of MS in descending order of TIR values were the following: HTG (5.07); HACL (4.75); EBW (4.61); AO (3.27); AH (3.18); PMDs (3.03); HCL (2.8); CMDs (2.41).

In case of IR, TIR values for MS components were calculated in the same way as TIR values in case of VFD: ratio of average HOMA-IR values in groups with presence or absence of certain MS component was summed up with the ratio of IR frequencies in the same groups. In case of IR, studied components of MS in descending order of TIR values were the following: EBW (3.54); CMDs (3.43); AO (3.31); HTG (3.15); HACL (3.04); PMDs (2.93); AH (2.8); HCL (2.44).

Remarkably, there were significant differences between TIR-based scales demonstrating the association between VFD and MS components and association between IR and MS components. Two types of dyslipidemia (HTG and HACL) and two components characterizing obesity and fat distribution (EBW and AO) were on 4 top positions, while the same two components related to the total amount of fat in body and fat topography as well as CMDs and HTG (the type of dyslipidemia) were at the upper part of IR scale. Taking into account the revealed features of the scales and the last place of CMDs in the scale for VFD, we can conclude that CMDs contribution to cardiometabolic

Table

Indexes of visceral obesity and insulin resistance, the frequency of visceral fat dysfunction and insulin resistance depending on the presence of metabolic syndrome and its components in the men

Metabolic syndrome and its components	Index of visceral obesity (CU)	The frequency of VFD (%)	HOMA-IR (CU)	The frequency IR (%)
The presence of MS by the main components (n=59)	3,26±2,25	98,3	5,69±4,00	84,7
The absence of MS by the main components (n=183)	1,18±0,70	52,5	3,06±1,56	45,9
P	<0,0001	<0,0001	<0,0001	<0,0001
The presence of MS by the all components (n=141)	2,25±1,80	85,1	4,42±3,12	68,8
The absence of MS by the all components (n=101)	0,89±0,42	33,7	2,71±1,19	36,6
P	<0,0001	<0,0001	<0,0001	<0,0001
The presence of abdominal obesity by criterion WC (n=61)	2,36±1,44	90,2	5,01±3,31	82,0
The absence of abdominal obesity by criterion WC (n=181)	1,46±1,52	54,7	3,26±2,20	46,4
P	<0,0001	<0,0001	<0,0001	<0,0001
The presence of arterial hypertension (n=146)	1,89±1,61	77,4	4,09±2,74	63,7
The absence of arterial hypertension (n=96)	1,38±1,41	42,7	3,12±2,36	42,7
P	<0,0001	<0,0001	<0,0001	0,0021
The presence of carbohydrate metabolism disorders (n=65)	1,97±1,70	70,8	5,41±3,89	78,5
The absence of carbohydrate metabolism disorders (n=177)	1,58±1,48	61,0	3,08±1,59	46,9
P	0,0552	0,2124	<0,0001	<0,0001
The presence of hypertriglyceridemia (n=54)	3,63±2,20	98,1	5,28±4,04	75,9
The absence of hypertriglyceridemia (n=188)	1,12±0,55	53,7	3,25±1,85	49,5
P	<0,0001	<0,0001	<0,0001	0,0010
The presence of low level high density lipoprotein cholesterol (n=77)	2,97±2,11	97,4	4,72±3,56	74,0
The absence of low level high density lipoprotein cholesterol (n=165)	1,09±0,57	47,9	3,23±1,90	46,7
P	<0,0001	<0,0001	<0,0001	0,0001
The presence of overweight (n=166)	2,02±1,71	78,3	4,16±2,97	65,7
The absence of overweight (n=76)	0,95±0,67	31,6	2,71±1,23	32,9
P	<0,0001	<0,0001	<0,0001	<0,0001
The presence of hypercholesterolemia (n=110)	2,03±1,83	73,6	4,19±3,15	60,0
The absence of hypercholesterolemia (n=132)	1,39±1,19	55,3	3,30±2,04	51,5
P	<0,0001	0,0048	0,0246	0,2332
The presence of purine metabolism disorders (n=78)	2,33±2,14	76,9	4,73±3,60	70,5
The absence of purine metabolism disorders (n=164)	1,38±1,04	57,3	3,22±1,85	48,2
P	<0,0001	0,0048	<0,0001	0,0018

risk is underestimated when VFD is studied. Insulin resistance criteria with established diversified relationships with both lipid and carbohydrate disorders give more objective evidence in epidemiological or group studies on MS.

CONCLUSION

In sample of men working in West Yakutia industrial region the association of IR parameters with MS and its components proved to be closer and more diversified then that of fat distribution model parameters. Thus, insulin resistance criteria are more informative in population studies of metabolic syndrome epidemiology and pathogenesis than the criterion of visceral fat tissue dysfunction.

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HORMONAL STATUS AND LIPID SPECTRUM IN THE POPULATION OF SAMBURG VILLAGE, THE YAMAL - NENETS AUTONOMOUS REGION

ABSTRACT

We estimated main indices of lipid metabolism and hormonal status in blood serum obtained from indigenous inhabitants (tundra Nenetses) of Samburg village and non-indigenous population (mostly Russians) who arrived from other regions. The study revealed an increased concentration of insulin in all groups and a lower level of cortisol and thyroxin (women) in non-indigenous population. Hypertriglyceridemia and hypercholesterolemia as well as a high atherogenic index were found in the representatives of non-indigenous male population. A high level of insulin, an increased content of atherogenic fractions of lipoproteins, and a decrease in HDL content at a low activity of the thyroid gland and adrenal cortex are likely to result in the development of metabolic syndrome, especially in the representatives of non-indigenous population.

Keywords: hormones, lipid spectrum, tundra Nenets, non-indigenous population, Samburg village the Yamal-Nenets Autonomous Okrug.

INTRODUCTION

Human adaptation in the Far North is accompanied by essential alteration of all physiological systems. The so-called "polar stress syndrome" emerges in non-indigenous population and deteriorates functional parameters of many systems of the body. The formation of a "northern type of metabolism" is characterized by rearrangement of the exchange of proteins, lipids and carbohydrates [2].

The study aimed to compare the level of hormonal metabolism and lipid status in non-indigenous and indigenous population of Samburg village, the Yamal-Nenets Autonomous Okrug.

MATERIALS AND METHODS

The study was carried out under the agreement on scientific cooperation with the Institute of Cytology and Genetics SB RAS (ICG SB RAS). Material for the study was collected during the expeditions to the Yamal-Nenets Autonomous Region (YNAR) in 2014 by researchers from the Laboratory of population ethnogenetics at ICG SB RAS under the supervision of the Laboratory Head Ph.D. (biol.) Osipova L.P.

The study was approved by the bioethics Commission Institute of Cytology and genetics. Blood donations were taken in compliance with international rules using the informed consent from volunteers who were practically healthy at the time of the study. The study involved indigenous persons and non-indigenous population of Samburg village (latitude 67°0' north, longitude 78° 25′ east), Purovsky district. Overall, 80 inhabitants (40 men and 40 women) 21 – 65 years of age were examined. Among them were representatives of indigenous nation (tundra Nenetses) and non-indigenous population (mostly Russians) who came from other regions.

Blood was taken from the ulnar vein after 10-12 hours of night fasting. The concentrations of thyroxin (T4), triiodothyronine (T3), thyrotrophic hormone (TTH), cortisol, dehydroepiandrosterone sulfate (DHEAS) and testosterone in blood serum were measured with ELISA test kits (St. Petersburg), estradiol with HEMA ELISA kits (Germany), insulin with Monobind Inc kit (USA), and ACTH with Biomerica