

ORIGINAL ARTICLE

FEATURES OF SOME ANTHROPOMETRIC INDICES AND INDICES OF INSULIN RESISTANCE IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS ON THE BACKGROUND OF OBESITY AND OSTEOARTHRITIS

DOI: 10.36740/WLek202004123

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ABSTRACT

The aim: To estimate the diagnostic and predictive value of anthropometric indices indicating obesity and glycemic parameters in the progression of NASH due to comorbidity with OA and OB.

Materials and methods: 90 patients were examined and distributed into three groups: group 1 included patients suffering from OA, grade II-III according to Kellgren and Lawrence classification, with normal body mass, group 2 - patients with NASH and obesity without OA, group 3 - patients with OA, NASH and obesity. The control group consisted of 30 healthy individuals of the corresponding age.

Results: There was a correlation between lipid and carbohydrate metabolism. This fact was confirmed by the evidence that under the influence of IR there was an increase in the level of lipoproteins enriched in triglycerides, the concentration of cholesterol of low density lipoprotein and reduction in level cholesterol of high density lipoprotein, which led to the progression of the clinical course of NASH.

It was established that anthropometric indices of patients with comorbid flow of NASH, OA and OB were significantly ($p < 0.05$) higher than in experimental groups. A positive correlation was found between some anthropometric indices and the following glycemic parameters: fasting blood glucose, HOMA-IR suggested that insulin resistance contributed to the growth of glycated compounds leading not only to the progression of NASH and affect the dysfunction of chondrocytes, but also influencing destruction of subchondral bone in osteoarthritis.

Conclusions: The outcomes of the study result in the necessity of studying the metabolic status in patients with a comorbid progression of NASH, OB and OA for timely correction of the revealed disorders, which will reduce the run of NAFLD.

KEY WORDS: non-alcoholic steatohepatitis, osteoarthritis, obesity, insulin resistance, anthropometry

Wiad Lek. 2020;73(4):746-750

INTRODUCTION

Currently, non-alcoholic fatty liver disease (NAFLD) is one of the most common diseases in hepatology, which leads to a deterioration in the quality of life, a decrease in life expectancy. It arises primarily due to the high risk of progression of non-alcoholic steatohepatitis (NASH) with the development of liver failure and hepatocellular carcinoma. The maximum risk factors of NAFLD was observed in the group of individuals with obesity, hypertriglyceridemia [1-3]. The etiology of NAFLD is diverse, although its close association with insulin resistance (IR) is noted. The liver is the main target for damage in conditions characterized by IR, which is a risk factor for the progression of liver steatosis in NASH with its inherent risk of progression to cirrhosis [4].

IR is more pronounced in patients with abdominal type of obesity. These differences are due to genetically unequal expression of adipocyte genes in abdominal and subcutaneous fatty tissue [5]. Hyperglycemia and hyperinsulin-

emia have an important prognostic value in patients with NAFLD. It is proved that the carbohydrate intolerance and type 2 diabetes mellitus stimulates lipogenesis [6]. Today, the increasing number of people with overweight and obesity (OB) is one of the most urgent health problems in all countries related to the great number of diseases associated with high body weight [7].

Anthropometric measurements with the use of discriminant analysis in patients with type 2 diabetes, obesity, have allowed to determining the number of criteria on the basis of which diseases can be predicted [8]. It was established that subcutaneous fat is fairly labile and responsive to a variety of stressful situations, which in turn helps to increase or decrease it. A number of studies have shown that waist circumference is the best indicator of the amount of visceral and subcutaneous adipose tissue among white and black men and women than the body mass index (BMI) [9].

It was also proved that the increase in the degree of abdominal obesity leads to an increased degree of liver ste-

atosis [10]. The weight of the visceral adipose tissue (VAT) is increased in patients with NAFLD and independently associated with an increased risk for developing NASH with significant fibrosis [11]. This condition may have resulted from the fact that the liver receives venous blood from the portal system, which contains free fatty acids and cytokines secreted by VAT [10].

It is well known that NAFLD is common in the context of metabolic syndrome (MS). The prevalence of MS in patients with NAFLD rises with the increase of BMI [12-14]. Particular attention is paid to the combination of MS and osteoarthritis (OA). To date, there are many studies suggesting a combination of these diseases. Each component of the MS negatively affects the course of OA. The so-called metabolic variant of OA developed in patients with obesity, atherosclerosis, other metabolic disorders and, in most cases, is a reflection of systemic metabolic disorders, realized through proinflammatory mediators in the tissues of joints [15-17].

THE AIM

To estimate the diagnostic and predictive value of anthropometric indices indicating obesity and glycemic parameters in the progression of NASH with OA and OB comorbidity.

MATERIALS AND METHODS

The study was carried out on the basis of the Higher State Educational Institution of Ukraine "Bukovinian State Medical University" and is a fragment of research work of the Department of Internal Medicine, Clinical Pharmacology and Occupational Diseases "Features of the Comorbidity of Diseases of Internal Organs: Risk Factors, Mechanisms of Development and Interaction, Pharmacotherapy" (State registration number: 0114U002475).

90 patients were examined and distributed into three groups: group 1 ($n = 30$) included patients suffering from OA, grade II-III according to Kellgren and Lawrence classification, with normal body mass ($BMI = 21-25 \text{ kg / m}^2$), group 2 ($n = 30$) - patients with NASH and obesity without OA ($BMI > 30 \text{ kg / m}^2$), group 3 ($n = 30$) - patients with OA with NASH and obesity (BMI more than 30 kg / m^2). The control group consisted of 30 healthy individuals of the corresponding age. The average age of patients was ($62,3 \pm 5,7$) years.

The diagnosis of NASH was established on the ground of anamnestic, clinical, laboratory data, determination of serological markers for hepatitis B and C viruses, the results of USG according to the unified clinical protocol, approved by the Order of the Ministry of Health of Ukraine № 826 from 06.11.2014, in the presence of criteria for the exclusion of chronic diffuse liver disease of the viral, hereditary, autoimmune or medicinal genesis as causes of cholestatic or cytolytic syndromes, taking into account the 10th revision of ICE. The OA diagnosis was made on the basis of the EULAR recommendations (2010) and the Order of the Ministry of

Health of Ukraine № 676 dated October 12, 2006, "Clinical Protocol for the Provision of Medical Aid to Patients with Osteoarthritis" in accordance with section 13 "Rheumatology" and the Protocol of the Ministry of Health of Ukraine № 263 from section "Rheumatology" April 11, 2014. The presence of abdominal obesity in patients was established on the basis of the Order of the Ministry of Health of Ukraine № 16 dated January 14, 2013 "Methodical Recommendations for General Practitioners – Family Medicine on Counseling Patients on the Basic Principles of Healthy Eating".

The anthropometric examination included the following steps: measurements of height, waist circumference (WC), hip circumference (HC), and body weight in all patients. To define the nature of body fat distribution, the ratio of WC / HC was used. Obesity was considered abdominal, with $WC > 94 \text{ cm}$ for men and $> 80 \text{ cm}$ for women, the value of WC / HC in women $> 0,88$, in men $> 0,9^5$. WC was measured between the margin of the lower rib and the sacral part of the iliac bone; HC – lower large femoral heads. Body mass index (BMI) was calculated by the Ketley formula: $BMI = BW / \text{height}^2$, where BMI is the body mass index, kg / m^2 ; BW – body weight, kg; patient height, m.

The degree of compensation of carbohydrate metabolism and IR was determined by fasting glycemia level and two hours after glucose application (glucose tolerance test (GTT)), fasting insulin level (by immunogenic assay (IFA) (DRGSystem)), the index HOMA-IR (Matthews et al.), an index of peripheral tissue insulin sensitivity calculated using the HOMA Calculator Version 2.2 Diabetes Trials Unit of the University of Oxford (UK).

The protocol for the examination of patients was approved at the meeting on biomedical ethics at HSEI of Ukraine „Bukovinian State Medical University“. The document has been compiled in accordance with the requirements regulated by the 6th chapter of the manual CH GPC (1996) and created on the basis of its national guide "Guidelines for Clinical Research. Medicines. Approved Clinical Practice "; approved by the Order of the MOH of Ukraine No. 373 dated July 22, 2005. In drawing up the protocol they adhered to the basic principles of the Helsinki Declaration on Biomedical Research (1974), adapted to the 41st International Assembly in Hong Kong (September 1989), in which a person acts as their object, as well as "Ethical Principles for Medical Research Involving of Human Subjects", adopted by the 52nd Assembly of the World Medical Association (2000). The Committee on Biomedical Ethics of the HSEI of Ukraine „Bukovinian State Medical University“ has not revealed any violations of moral and legal standards during the scientific research.

The statistical processing of the research outcomes was carried out on a personal computer with the help of the standard applications Microsoft Excellence and SPSS Statistics 20 Multilingual. The mean values (M), the arithmetic mean (t), and the validity of the differences p according to Student's t -distribution were evaluated. The difference in indices for various periods of the study was considered probable at $p < 0.05$. To determine the relationship between the indices, Kendall's tau-b correlation coefficient was used.

Table I. Anthropometric indices of patients with non-alcoholic steatohepatitis depending on comorbid obesity and osteoarthritis (M ± m)

	Practically healthy persons (n=30)	OA with normal body weight (n = 30) 1 group	NASH + OB (n = 30) 2 group	NASH + OB+ OA (n = 30) 3 group
WC, cm	72,13±1,18	74,98±1,19	100,40±1,22* ^o	110,74±1,21* ^o *
HC, cm	93,00±1,15	94,53±1,10	101,21±1,18* ^o	105,72±1,23* ^o
WC / HC	0,78±0,01	0,80±0,01	0,99±0,02* ^o	1,05±0,01* ^o
BMI, kg / m ²	20,17±1,20	21,64±1,25	34,39±1,38* ^o	36,98±1,55* ^o

Notes: * - the difference in rates is probable ($p < 0.05$) with a group of practically healthy individuals.^o - the difference of the indicators is probable ($p < 0.05$) between group 1 and groups 2 and 3,*- the difference in rates is probable ($p < 0.05$) between groups 2 and 3.

Table II. Characteristics of biochemical parameters of carbohydrate metabolism of patients with NASH, OB and OA (M ± m)

	Practically healthy persons (n=30)	OA with normal body weight (n = 30) 1 group	NASH + OB (n = 30) 2 group	NASH + OB+ OA (n = 30) 3 group
Fasting glycemia, mmol / l	4,06±0,04	4,28±0,05*	5,48±0,05* ^o	6,08±0,08* ^o *
Glucose in 2 hours, mmol / l	7,48±0,12	7,66±0,13	8,69±0,13* ^o	10,35±0,12* ^o *
Insulin, μD / ml	9,57±0,04	9,79±0,05*	25,09±0,21* ^o	26,89±0,17* ^o *
HOMA-IR	1,17±0,01	1,21±0,01	3,23±0,03* ^o	3,53±0,02* ^o *

Notes: * - the difference in rates is probable ($p < 0.05$) with a group of practically healthy individuals.^o - the difference of the indicators is probable ($p < 0.05$) between group 1 and groups 2 and 3,*- the difference in rates is probable ($p < 0.05$) between groups 2 and 3.

RESULTS AND DISCUSSION

The average values and changes in body mass index, WC, HC, as well as marker of abdominal adipose tissue distribution – WC/HC and BMI in patients of all experimental groups, were analyzed, their comparison with each other and with a group of practically healthy persons (PHP) (Table I). It was established that the anthropometric indices of patients in all groups statistically significantly differed from the corresponding indices of healthy people with the presence of intergroup difference ($p < 0.05$). In particular, in patients of group 1 WC did not change (increase by 3.95%, $p > 0.05$), in group 2 – exceeded data in PHP by 39.19%, in patients of group 3 – by 53.53% ($p < 0.05$). As for the HC, the data for patients in groups 2 and 3 exceeded the index in the PHP by 8.82 and 13.68% ($p < 0.05$) respectively in the comparison groups, while in group 1 they did not differ from the reference values ($p > 0.05$).

The WC/HC ratio was the maximal value in patients of group 3 and exceeded the control data by 34.62%, in group 2 the index exceeded the control values by 26.92% and in group 1 the changes were statistically unreliable ($p < 0.05$). The body mass index exceeded the PHP group's indices patients in group 2 in 1.7 times ($p < 0.05$), and in group 3 – in 1.8 times ($p < 0.05$).

The results of glycemic indices, insulinemia and IR indices in patients with OA with normal BMI, NASH with obesity and NASH with comorbid obesity and osteoarthritis are presented in Table II.

The analysis of the conducted studies showed that in patients of the 2nd group, the probable increase in fasting glycemia level was found 1.3 times ($p < 0.05$) in comparison with the PHP, while in patients with the 3rd group glycemic parameters were maximally increased by 1.5 times (see

Table II). Analysis of indices of postprandial glycemia, obtained during glucose tolerance test (GTT), in patients of group 3 also showed a maximum increase in fasting glucose after 120 minutes in 1.4 times ($p < 0.05$) compared with the indices in the PHP group, in patients of 2nd group – an increase was in 1.2 times ($p < 0.05$), whereas in the 1st group changes were unlikely ($p > 0.05$). The insulin content in fasting blood glucose test detected a probable hyperinsulinaemia, which in patients of the 2nd group exceeded the norm in 2.7 times ($p < 0.05$), and in patients of the 3rd group in 2.8 times ($p < 0.05$) (see Table II).

The presence of insulin resistance in peripheral tissues in patients with NASH and obesity and associated with OA indicates a possible increase in the HOMA-IR index (2.8 and 3.0 times, respectively ($p < 0.05$), respectively) ($p < 0.05$), with the probable difference between these groups ($p < 0.05$).

It was determined that the level of fasting glycemia correlated with BMI ($r = 0.75$; $p < 0.05$), WC ($r = 0.76$; $p < 0.05$), the ratio of WC / HC ($r = 0.64$; $p < 0.05$). Correlation analysis also detected significant positive correlations between the HOMA-IR and BMI indices ($r = 0.76$; $p < 0.05$), WC ($r = 0.75$; $p < 0.05$), WC / HC ratio ($r = 0.62$; $p < 0.05$). The IR promotes the production of glycosylated compounds, leads to increased formation of oxygen radicals that not only contribute to the progression of NASH, but also affect the chondrocyte dysfunction, as well as the destruction of subchondral bone in osteoarthritis.

Close relationship was observed between WC and increase in concentration of TC ($r = 0.59$; $p < 0.05$), LDL cholesterol ($r = 0.48$; $p < 0.05$), and TG ($r = 0.54$; $p < 0.05$). There was a correlation between lipid and carbohydrate metabolism, namely, between TC and fasting blood glucose

($r = 0.58$; $p < 0.05$), HOMA-IR index ($r = 0.57$; $p < 0.05$); TG and fasting blood glucose ($r = 0.53$; $p < 0.05$), HOMA-IR index ($r = 0.53$; $p < 0.05$); LDL cholesterol and fasting blood glucose ($r = 0.46$; $p < 0.05$), HOMA-IR index ($r = 0.44$; $p < 0.05$). This is confirmed by the data that under the influence of IR there is a change in the activity of lipoprotein lipase and hepatic tricyclic glycerolipase, which leads to an increase in the synthesis and secretion of VLDL cholesterol, the violation of their elimination, an increase in the level of lipoproteins enriched with TG, the concentration of LDL cholesterol and lowering of HDL cholesterol, an increase in the synthesis and secretion of apolipoprotein – B.

CONCLUSIONS

In patients with NASH, on the background of obesity and osteoarthritis, the maximum manifested IR syndrome has been established, which is probably the primary (hereditary predisposition), and may be secondary to liver damage on the background of NASH.

The most considerable metabolic prerequisites for the development of NASH on the background of obesity and OA are likely postprandial hyperglycemia, hyperinsulinemia, peripheral tissue IR.

REFERENCES

- Popescu M., Popescu I.A., Stanciu M., et al. Non-alcoholic fatty liver disease – clinical and histopathological aspects. "Romanian Journal of Morphology and Embryology" 2016;57(4):1295–1302.
- Filippova A.Yu. Clinical characteristics of patients with hepatic steatosis and non-alcoholic steatohepatitis combined with obesity and disorders of the biliary tract, depending on the body mass index]. "Medical Perspectives" 2016;21(1):70–79.
- Hardy D.S., Stallings D.T., Garvin J.T., et al. Best anthropometric discriminators of incident type 2 diabetes among white and black adults: A longitudinal ARIC study. "PLoS One" 2017;12(1):e0168282.
- Rinella M.E. Nonalcoholic fatty liver disease: a systematic review. "JAMA" 2015;313(22):2263–2273.
- Hadizadeh F., Faghihmani E., Adibi P. Nonalcoholic fatty liver disease: Diagnostic biomarkers. "World Journal of Gastrointestinal Pathophysiology" 2017;8(2):11–26.
- Global Health Observatory (GHO) data: Obesity. Geneva: World Health Organisation; 2018. http://www.who.int/gho/ncd/risk_factors/obesity_text/en/ (Accessed on March 11, 2019).
- Motamed N., Rabiee B., Hemasi G.R., et al. Body Roundness Index and Waist-to-Height Ratio are Strongly Associated With Non-Alcoholic Fatty Liver Disease: A Population-Based Study. "Hepatitis Montlily" 2016;16(9):e39575.
- Khukhlina O.S., Lyakhovich O.D., Voyevodka O.S., et al. Features of markers of liver damage and lipid profile in patients with non-alcoholic steatohepatitis, osteoarthritis and obesity. "Ukrainian Therapeutical Journal" 2018;3-4:20-26.
- Kim D., Chung G.E., Kwak M.S., et al. Body fat distribution and risk of incident and regressed nonalcoholic fatty liver disease. "Clinical Gastroenterology and Hepatology" 2016;14(1):132-138.
- Park S.K., Ryoo J.H., Choi J.M., et al. The Risk of Abdominal Obesity according to the Degree of Non-Alcoholic Fatty Liver Disease in Korean Men. "Journal of Korean Medical Science" 2016;31(3):410–416.
- Kuhle S., Maguire B., Ata N., et al. Percentile Curves for Anthropometric Measures for Canadian Children and Youth. "PLoS One" 2015;10(7):e0132891.
- Macaluso F.S., Maida M., Petta S. Genetic background in nonalcoholic fatty liver disease: A comprehensive review. "World Journal of Gastroenterology" 2015;21(39):11088–11111.
- Sayiner M., Koenig A., Henry L., et al. Epidemiology of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis in the United States and the Rest of the World. "Clinics in Liver Disease" 2016;20(2):205–214.
- Than N.N., Newsome P.N. Non-alcoholic fatty liver disease: when to intervene and with what. "Clinical Medicine" 2015;15(2):186–190.
- Wang X., Hunter D., Xu J., et al. Metabolic triggered inflammation in osteoarthritis. "Osteoarthritis and Cartilage" 2015;23(1):22-30.
- Yu S.J., Kim W., Kim D., et al. Visceral obesity predicts significant fibrosis in patients with nonalcoholic fatty liver disease. "Medicine (Baltimore)" 2015;94(48):e2159.
- Zelber-Sagi S., Shoham D., Zvibel I., et al. Predictors for advanced fibrosis in morbidly obese non-alcoholic fatty liver patients. "World Journal of Hepatology" 2017;9(2):91–98.

LIST OF ABBREVIATIONS

NAFLD = non-alcoholic fatty liver disease

NASH = non-alcoholic steatohepatitis

IR = insulin resistance

VAT = visceral adipose tissue

MS = metabolic syndrome

OA = osteoarthritis

OB = obesity

BMI = body mass index

WC = waist circumference

HC = hip circumference

W/H = waist/hip ratio

PHP = practically healthy persons

GTT = glucose tolerance test

TC = total cholesterol

TG = triglycerides

LDL cholesterol = cholesterol of low density lipoprotein

HDL cholesterol = cholesterol of high density lipoprotein

FBG = fasting blood glucose

HOMA-IR = Homeostasis Model Assessment of Insulin Resistance

The study was carried out in the Higher State Educational Institution of Ukraine "Bukovinian State Medical University", Ukraine, and is a fragment of the research of the Department of Internal Medicine, Clinical Pharmacology and Occupational Diseases «Features of the Comorbidity of Diseases of Internal Organs: Risk Factors, Mechanisms of Development and Interaction, Pharmacotherapy»; (State registration number: 0114U002475).

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Conflicts of interest:

Authors declare no conflict of interest.

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Received: 21.06.2019

Accepted: 14.02.2020

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis,
D – Writing the article, **E** – Critical review, **F** – Final approval of the article