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Insights into the role of the gut microbiome in metabolic syndrome

Abstract: Metabolic syndrome is a worldwide epidemic which is a combination of various metabolic disorders of organism. Nowadays biodiversity in gut microbiome and its impact on health is being studied very intensively. Gut microbiome has a main role as a reservoir of human genetics. Therefore its study is very topical. There are a lot of factual materials which indicate that gut undeniable influence on the immune system and intestinal barrier function, digestion, metabolism and systemic inflammation. It can be rightfully claimed that microbes «in dialogue» with the whole body by way of sending us signals, which have to be researched and identified in the future.

Key words: metabolic syndrome, metagenome, gut, microbiome, bacteria.

Introduction

Nowadays one of the most prevalent public health problems in the world is metabolic syndrome. Metabolic syndrome is a combination of various metabolic disorders of organism and it is considered as worldwide epidemic. This syndrome contains group of risk interconnected factors that increases the risk for heart disease, atherosclerosis and other health problems, such as diabetes and stroke [1]. There are different definitions of the metabolic syndrome. Historically, professor Reaven was the first who used the term «syndrome X» on his investigations on different factors of organism which lead to diseases. Then the term was renamed into metabolic syndrome [2]. Worldwide Health Organization (WHO) proposed the following definition: Metabolic syndrome is multiplex risk factors which constitute of basic components of abdominal obesity, high triglyceride level of blood, less HDL cholesterol, great fasting glucose, arterial pressure, dyslipidemia, high or low density of lipoproteins, and high level of BP.

Table 1: The new International Diabetes Federation (IDF) definition

According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have:

Central obesity (defined as waist circumference* with ethnicity specific values)

plus any two of the following four factors:

Raised triglycerides	≥ 150 mg/dL (1.7 mmol/L) **or specific treatment for this lipid abnormality**
Reduced HDL cholesterol	< 40 mg/dL (1.03 mmol/L) in males < 50 mg/dL (1.29 mmol/L) in females **or specific treatment for this lipid abnormality**
Raised blood pressure	systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg **or treatment of previously diagnosed hypertension**
Raised fasting plasma glucose	(FPG) ≥ 100 mg/dL (5.6 mmol/L), **or previously diagnosed type 2 diabetes** If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

** If BMI is >30kg/m², central obesity can be assumed and waist circumference does not need to be measured.*

[3].

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If three or more of the measurements attend, this means that metabolic syndrome occurs [4]. Having just one of these conditions doesn't mean metabolic syndrome. However, any of these conditions increase risk of serious disease. If more than one of these conditions occurs in combination, risk is even greater [3, 4]. However pathogenic mechanism and criteria for diagnosis of metabolic syndrome have not been fully investigated.

Epidemiology of metabolic syndrome

It was thought that metabolic syndrome is mostly related to middle-aged and old people for a long time; especially it is disseminated between men. But recent studies have shown that young people tend to metabolic syndrome too.

According to the data of Worldwide Health Organization about 30% of populations in the world are overweight, 16.8% of them – women and 14.9% are men. The number of people with obesity increases progressively every 10 years by 10%. Likelihood of arterial hypertension is high for 50% between people with obesity than those with normal weight. According to the Framingham study, systolic blood pressure increases by 4.4 in men and 4.2 among women for every extra 4.5 kg weight. Several conducted investigations elucidate that body weight is direct proportional to total mortality. Obesity increases the risk of 2 type diabetes [5].

Over the past 15 years more than 20 epidemiological studies carried out on the prevalence of the metabolic syndrome. Large-scale meta-analysis has shown that in an adult population by 10% in China and 24% in the US are diagnosed with metabolic syndrome. Most studies have identified common patterns that play an important role in the development of metabolic syndrome, such as age, women's postmenopausal status, behavioral factors – sedentary lifestyles and the prevalence of carbohydrate diet, socioeconomic status. Research recently conducted in Russian on a random sample of the adult population have shown the data of 20.6% of persons aged 30-69 have metabolic syndrome; it occurs 2.4 times more frequently in females than between man; the more the age, the higher the number of patients with metabolic syndrome [6].

According to the data of Kuopio Ischemic Heart Disease Risk Factors Study the risk for coronary heart disease is higher for 2,9-4,2 times and death rate from ischemic heart disease for 2.6-3.0 times in patients with metabolic syndrome. In another prospective study ARIC (Atherosclerosis Risk in Communities) we can notice the results have elucidated that patients with metabolic syndrome can tend to stroke 2 times more than the control group: the risk was 1.9 for men; for women – 1.52 [7].

Metabolic syndrome is a cluster of risk factors associated with prothrombotic, proinflammatory conditions, non-alcoholic fatty liver disease, and dysfunction of the reproductive system. The prevalence of metabolic syndrome depends on gender, age, ethnicity, as well as the use of diagnostic criteria, and varies over a wide range between male populations from 8% in India to 25% in the US, among women from 7% in France to 46% Iran. The study INTERHEART showed that metabolic syndrome related to 26% of adult population in the world.

In South Asia the prevalence of metabolic syndrome is 2.5 times higher than in Europe. Its frequency is very high among obese patients: metabolic syndrome is revealed in 49% of them. According to the opinion of some researchers, the metabolic syndrome is a consequence of urbanization, the increasing prevalence of obesity and sedentary lifestyles [8].

Metabolic syndrome is widespread in Asia. According to statistics, 17 million people die from stroke in China every year. 60% of patients with diabetes in Asia are Chinese citizens. In China If the index of weight is 30 kg/m3 and higher, it means that people tend to obesity. According to this 64 million people suffer from metabolic syndrome. Children in China also prone to metabolic syndrome and 15% of children tend to obesity [9]. The studies conducted in Taiwan have determined that 9 boys from 100000 and 15 girls from 100000 have a diagnose of diabetes [10].

314 million people with metabolic syndrome are estimated in the world in 2001, as well as 400 million – in 2006. It's predicted that number of patients will increase up to a 500 million in 2025. Epidemiological studies conducted in different countries have shown that of metabolic syndrome occurs on average 10-40% of individuals depending on the population [11]. According to studies high prevalence of this syndrome is marked in Greece, the Netherlands and Finland. For example, in Greece, the figure is 41.8% (63.0% among men, 37% – women) by NCEP criteria and 43.4% according to the criteria IDF. Pilot studies conducted in Russia showed that 20.6% of persons aged 30-69 suffer from metabolic syndrome. According to the Federal State Institution «Endocrinology Research Center» syndrome was diagnosed in 66% of patients with obesity [12].

There are only a few studies on the prevalence and ethnic characteristics of the metabolic syndrome

in Kazakhstan. Shalharova carried out the epidemiological research in South Kazakhstan, and the results corresponded with European results [13].

The role of the gut microbiome on development of metabolic syndrome

Nowadays biodiversity in gut microbiome and its impact on health is being studied very intensively. Gut microbiome has a main role as a reservoir of human genetics. Therefore its study is very topical. The human gut microbiome contained 1.5 kg of microorganisms, about 1000. The microflora performs a number of very important functions: differentiation of the intestinal epithelium, protection against pathogens and metabolic – involved in the processes of deposit in the liver and adipose tissue formed as a result of fermentation of energy substrates, which makes up 10% of the energy homeostasis. MetaHIT project's purpose is to create the «microbiome» – gene bank of microflora. «Microbiome» contains 3.3 million of coding sequences of nucleotides – it is 150 times larger than the human genome, and has been called 'our other genome».

The development of the metabolic syndrome is associated with systemic inflammation of lower grades. The role of the microflora in the origin of obesity can be explained by two aspects: 1. Additional extraction of energy from the indigestible part of food; 2. the maintenance of systemic inflammatory response due to the increased lipopolysaccharide of bacteria, in other word – endotoxemia. In addition, certain bacteria can inhibit the expression of the protein induced by starvation in the intestinal contents, which exhibits the properties of an inhibitor of lipoprotein lipase.

Active studies the role of gut microbiome on pathogenesis of the metabolic syndrome started with experiments on mice which demonstrate that obesity is associated with an increased content of microbial groups *Firmicutes* and reduced levels of *Bacteroides* [14]. Many studies indicate that people with obesity and 2 type diabetes are characterized by changes in the composition of intestinal microflora, in particular the reduction of species that are actively produce the butyrate – *Roseburia intestinalis* and *Faecalibacterium prausnitzii.* Apparently butyrate has an antidiabetic effect. Low variability in the composition of microflora is considered as a possible predictor of obesity treatment absence by diet [15].

Behaviors of the microbiota on inflammatory bowel disease, allergic diseases are being studied extensively. Fecal microflora transplantation from healthy donors is one of the newest and effective methods. This method has proven itself particularly in the treatment of recurrent infection of *Clostridium difficile*. The latest recommendations of the American College of Gastroenterology allow the transplantation of fecal microflora after the third recurrence of *Clostridium difficile* in case of failure of vancomycin [16].

There is a widespread interest in transplantation of microflora in other diseases too. It is believed that in some situations, this arrangement will avoid prescribing. Patients with metabolic syndrome showed increased sensitivity of peripheral tissues to insulin and an increase in species diversity of the microbiota, when fecal transplants from healthy donors [17, 18].

The limitations of the method of transplantation above are explained by insufficiently established procedures for screening donors and insufficient study of the method. There are a lot of factual materials which indicate that gut undeniable influence on the immune system and intestinal barrier function, digestion, metabolism and systemic inflammation. It can be rightfully claimed that microbes «in dialogue» with the whole body, and send us signals, which have to be researched and identified.

Conclusion

There is a widespread interest in researching metabolic syndrome because it is a worldwide epidemic which is a combination of various metabolic disorders of organism. Interaction between gut microbiome and metabolic syndrome is very topical studies. There are a lot of factual materials which indicate that gut undeniable influence on the immune system and intestinal barrier function, digestion, metabolism and systemic inflammation. It can be rightfully claimed that microbes «in dialogue» with the whole body by way of sending us signals, which have to be researched and identified in the future. Studying Kazakhstani population with metabolic syndrome, researching their gut behavior will help scientists to identify new methods of treating the dangerous diseases such as an obesity, diabetes, atherosclerosis, coronary heart disease and so on.

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