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THE ROLE OF PROBIOTICS IN CORRECTING THE METABOLISM OF INTESTINAL MICROFLORA

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Abstract
Cardiovascular diseases are the leading causes of death in people of different age categories. The cause of many cardiovascular diseases is atherosclerosis - a chronic disease of the arteries of the elastic and muscular type, accompanied by the deposition of cholesterol and lipoproteins in the intima of the vessels and the occlusion of the lumen of the vessel. With a pronounced narrowing of the lumen of the coronary arteries by an atherosclerotic plaque, coronary heart disease (CHD) can occur. Currently, despite the use of a complex of drugs for the treatment of CHD, mortality from this disease remains significant. In view of this, scientists pay much attention to the study of the complex processes of the occurrence and progression of atherosclerosis, along with other processes leading to atherothrombosis, such as accelerated platelet aggregation. With the development of new methods of laboratory diagnostics, it became possible to study the composition of the intestinal microbiome and its metabolic activity in various diseases.

INTRODUCTION

In an analysis of the metabolic profile of patients with cardiovascular diseases, Tang et al, a compound was found - trimethylamine-N-oxide (TMAO), a product of phosphatidylcholine and L-carnitine metabolism, the concentration of which was higher in people with a higher cardiovascular risk. Experiments on mouse models do not allow to fully confirm or refute the hypothesis regarding the atherogenic and thrombogenic potential of TMAO. In studies involving humans, conflicting data were also obtained regarding the effect of this substance on the cardiovascular system. Scientists agree on the important influence of microflora in the processes of formation and utilization of TMAO, in connection with which in many studies the microbiome is mentioned as a potential target for the treatment of atherosclerosis and related diseases. It is known that TMAO is produced by the microflora of the distal small intestine and throughout the colon. However, normally the total number of bacteria in the small intestine is significantly less than in the colon. In many gastrointestinal diseases accompanied by intestinal motility disorders, the proliferation of bacteria in the small intestine and their metabolic activity leads to the development of bacterial overgrowth syndrome (SIBO). Few studies have demonstrated the relationship between SIBO and the development of cardiovascular diseases. However, changes in methylamine metabolism in patients with SIBO and their relationship in patients with coronary heart disease have not been studied to date. Probiotics and antibiotics have been proposed as means of influencing the composition and metabolism of microflora. The use of antibiotics is the standard treatment for SIBO. Studies involving healthy volunteers have demonstrated a marked decrease in the concentration of TMAO in the blood against the background of taking broad-spectrum

antibiotics (fluoroquinolones) with its subsequent restoration. Regarding probiotics, only individual studies with a small sample have been carried out, which do not allow us to draw a conclusion about the rationality of their use to influence the concentration of TMAO.

The aim of the work. Correction of cardiovascular risk indicators by changing the composition and metabolic activity in patients with coronary heart disease.

Objectives of the study. To analyze the differences in the structure of fecal microflora between patients with coronary heart disease and relatively healthy individuals of the same age and gender. To assess changes in TMAO concentrations in patients with coronary heart disease compared to relatively healthy individuals of the same age and gender. To determine the contribution of concomitant factors (age, gender, adverse family history of cardiovascular disease, body mass index, smoking, diet, presence or absence of small intestinal bacterial overgrowth syndrome) to TMAO production in patients with coronary heart disease.

Methodology and methods of the study. The methodological basis of the study was a combination of clinical, laboratory, instrumental and statistical methods. Microbiota is a fundamental factor determining human health. Currently, the entire scientific world is showing increased interest in the study of human microbiota and its impact on health. Microflora, or microbiota, is a collection of microorganisms that colonize human organs and tissues, such as the skin, oral cavity, vagina, and milk ducts. The highest concentration of microorganisms in the human body is found in the large intestine (about 100 trillion, consisting of more than 1000 species). Microorganisms inhabiting the human body mostly belong to the domain " Bacteria " - prokaryotes , represented by eubacteria , slightly fewer among them are prokaryotes from the domain " Archaea ", represented by archaebacteria . Each domain, according to the accepted classification, includes kingdoms, types, classes, orders, families, genera, species. One of the main taxonomic categories is the species - a set of individuals united by similar properties, but differing from other representatives of the genus. The relationship between the human body and the microflora inhabiting it has long been considered commensal , in which only one participant, namely the microorganism, benefits from the interaction . Currently, with the expansion of knowledge about the functions of microflora, this hypothesis has been revised in favor of symbiotic relationships built for mutual benefit for all participants in the process. The colonization of the intestines with microorganisms begins already during the passage of the child through the birth canal of the mother. Thus, the first bacteria for a person are from the vagina, normally represented mainly by lacto- and bifidobacteria, and the intestinal flora of the mother from the nearby anus, then the diversity of species increases due to anaerobic microorganisms coming from the ducts of the mammary gland along with colostrum, and also located on the skin of the nipple. Significant changes in the composition of the intestinal microbiota occur further when breastfeeding is discontinued, as well as when the child's teeth erupt. At the same time, intensive secretion of hydrochloric acid begins at the age of about three months, and only after a few years its concentration will reach the level of an adult, which contributes to intensive bacterial colonization of the gastrointestinal tract in the first years of human life. The structure and function of the human microbiome: from the depths of history to evidence-based medicine. The history of studying the interaction of man with his microbiome goes back several centuries. In 2011, A. Leeuwenhoek discovered microorganisms in human feces and put forward a hypothesis about the coexistence of various types of bacteria in the gastrointestinal tract. One of the founders of the theory of symbiotic microflora and its influence on the human body was the great Russian scientist, Nobel Prize laureate I.I. Mechnikov. Back in 2018, he suggested that the cause of many diseases is the combined effect on the cells and tissues of the macroorganism of various toxins and other metabolites produced by bacteria that inhabit the digestive tract in abundance. In his works "Etudes in Optimism" and "Etudes in the Nature of Man", I.I. Mechnikov wrote that numerous associations of microbes inhabiting the human intestine largely determine its spiritual and physical health. The scientist put forward an assumption about the connection between a number of somatic diseases and the activity of microorganisms. He wrote that "with time, it will probably be possible to discover parasites not only in diseases of a typically infectious nature, but also in diseases of a completely different kind." The study of intestinal microflora received a "second wind" already in the 70s, largely due to the work of A.M. Ugolev , who substantiated the concept of a violation of the qualitative and quantitative composition of microflora and its connection with human health.

The emergence of new diagnostic methods has allowed us to take a completely new look at the intestinal microbiota. In 2019, a sequencing method (determination of the nucleotide sequence) of the 16S RNA gene was introduced. This gene exists in the bacterial genome, but is absent in eukaryotes and viruses, which allows it to be used for species identification of bacteria. Many projects today are devoted to studying the composition of the normal microbiome and its changes in various diseases. The largest of them, " Human Microbiome " (Human Microbiome Project), was initiated in 2008 in the United States. The study involved 200 scientists from nearly 80 US research institutes. The results were published in June 2012 in the journals Nature and Public Library of Science . The researchers collected tissue samples from the oral cavity, nose and nasopharynx, larynx, various places on the skin, gastrointestinal tract, and vagina. Using sequencing, bacterial DNA was separated from human DNA, which made it possible to establish the composition of normal flora. According to the results of genetic analysis of the collected material, it was revealed that more than 10 thousand species of various microbes live in the human body. The number of bacterial genes in a person is 360 times greater than the number of his own.

Conclusions

In patients with coronary heart disease, there are changes in the composition of fecal microflora towards an increase in the number of bacteria producing trimethylamine (Verrucomicrobiaceae, Enterobacteriaceae). Metabolic activity of the intestinal microbiome in relation to TMAO production is higher in patients with coronary heart disease compared to healthy volunteers. Patients with coronary heart disease consume more products associated with an increase in TMAO levels (beef, pork, milk) compared to healthy volunteers, which may serve as one of the mechanisms for increasing cardiovascular risk. Protective function - prevention of excessive colonization by opportunistic and pathogenic microorganisms. Metabolic function - participation in the metabolism of carbohydrates, lipids, proteins and other substances of the macroorganism with the formation of metabolites that perform a certain role, including energy supply to the epithelium. Detoxification function - the ability to neutralize and utilize exogenous and endogenous toxic substances, regulation of cytochromes P450 in the liver and production of P450-like cytochromes. Synthetic function - synthesis of vitamins B, K, nicotinic acid.

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