THE INFLUENCE OF THE COMPOSITION OF INTESTINAL MICROBIOTA ON BIOCHEMICAL PARAMETERS IN PATIENTS WITH TYPE 2 DIABETES

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Annotatsiya

Ushbu tezis 2-turi qandli diabet (T2DM) bilan og‘rigan bemorlarda ichak mikrobiotasi tarkibining biokimyoviy ko‘rsatkichlarga ta’sirini o‘rganishga bag‘ishlangan. Tadqiqotda ichak mikrobiotasining disbiozi (muvozanat buzilishi), xususan, Firmicutes va Bacteroidetes nisbati o‘zgarishi, butirat ishlab chiqaruvchi bakteriyalar (Akkermansia muciniphila, Faecalibacterium prausnitzii, Roseburia va boshqalar) kamayishi, shuningdek, opportunistik patogenlar (Escherichia coli, Lactobacillus ayrim turlari, Bacteroides vulgatus) ko‘payishi T2DM patogenezida muhim rol o‘ynashi ko‘rsatilgan..Natijalar kasallikni oldini olish va davolashda mikrobiotani modulyatsiya qilishning ahamiyatini ta’kidlaydi.

Аннотация

Данная тезис посвящена изучению влияния состава кишечной микробиоты на биохимические показатели у пациентов с сахарным диабетом 2 типа (СД2). В работе рассматривается дисбиоз микробиоты кишечника, в частности, изменение соотношения Firmicutes/Bacteroidetes, снижение бутират-продуцирующих бактерий (Akkermansia muciniphila, Faecalibacterium prausnitzii, Roseburia), увеличение условно-патогенных бактерий (Escherichia coli, Lactobacillus spp., Bacteroides vulgatusРезультаты подчеркивают важность модуляции микробиоты для профилактики и лечения .

Abstract

This thesis examines the impact of intestinal microbiota composition on biochemical indicators in patients with type 2 diabetes mellitus (T2DM). It explores gut microbiota dysbiosis, including shifts in the Firmicutes/Bacteroidetes ratio, reduced abundance of butyrate-producing bacteria (e.g., Akkermansia muciniphila, Faecalibacterium prausnitzii, Roseburia), and increased opportunistic pathogens (Escherichia coli, certain Lactobacillus species)Findings highlight the role of microbiota modulation in T2DM prevention and management.

Introduction

Type 2 diabetes mellitus (T2DM) is one of the most common metabolic diseases worldwide, reducing the quality of life and life expectancy of millions of people. The prevalence of this disease is also increasing rapidly in Uzbekistan, which is associated with dietary habits, lack of physical activity, obesity and genetic factors. Recent studies have shown that the intestinal microbiota - the collection of trillions of microorganisms in the human body - plays an important role in the pathogenesis of T2DM. Changes in the composition of the intestinal microbiota (dysbiosis) directly affect biochemical parameters, increasing insulin resistance, impaired glucose metabolism, inflammation and oxidative stress.

The intestinal microbiota is a complex ecosystem, dominated by the phyla Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria. In healthy individuals, the microbiota is highly diverse and maintains homeostasis by regulating digestion, immune function, and the production of metabolites (short-chain fatty acids — SCFA: acetate, propionate, butyrate). In patients with T2DM, the composition of the microbiota is significantly altered: the number of butyrate-producing bacteria (Faecalibacterium prausnitzii, Roseburia, Akkermansia muciniphila, Bifidobacterium, Bacteroides) decreases, while opportunistic pathogens (Escherichia coli,

Clostridium hathawayi, Bacteroides vulgatus, Veillonella, some Lactobacillus species) increase. The Firmicutes/Bacteroidetes ratio is often reduced or disrupted, which increases energy intake and contributes to obesity and insulin resistance.

Mechanisms:

SCFA deficiency: Butyrate maintains the integrity of the intestinal epithelium, reduces inflammation, stimulates the hormones GLP-1 and PYY, and regulates appetite and glucose levels. In T2DM, decreased SCFA increases intestinal permeability, LPS (lipopolysaccharide) enters the bloodstream, causing systemic inflammation (metabolic endotoxemia). This increases markers such as TNF-α, IL-6, hs-CRP, and impairs insulin signaling.

Other important metabolites

Imidazole propionate — impairs insulin signaling via p38γ–p62–mTORC1, may reduce the effect of metformin.

Indole metabolites (Indole-3-propionic acid — IPA) — are good, reduce inflammation and maintain insulin secretion.

p-Cresyl sulfate and other phenolic compounds — increase insulin resistance.

Inflammation and immune response: Gram-negative bacteria increase LPS, which activates the NF-κB pathway via TLR4 receptors. As a result, chronic low-grade inflammation develops, which disrupts insulin receptor phosphorylation.

BCAA and other metabolites: Some bacteria (certain strains of Prevotella copri) increase the production of branched-chain amino acids (BCAA), which activate the mTOR pathway and increase insulin resistance. Metabolites such as imidazole propionate, trimethylamine N-oxide (TMAO) also have a negative effect.

Biotin and other vitamin metabolism: Microbiota synthesizes B vitamins; disruption of this process in T2DM exacerbates metabolic disorders.

Relationship with biochemical parameters:

Glucose and HbA1c: Positive correlation with increased Lactobacillus, decreased Clostridium; Akkermansia shows a negative correlation.

Lipids: Increased triglycerides and LDL, decreased HDL are associated with microbiota dysbiosis.

Inflammatory markers: elevated hs-CRP, IL-1β, TNF-α, IL-6.

Insulin and HOMA-IR: Microbiota composition can predict insulin sensitivity.

Diagnostic and therapeutic options:

Microbiota analysis (fecal microbiota profiling) can be used as a biomarker. Prebiotics (fiber), probiotics (Ackermansia, Bifidobacterium), synbiotics and fecal microbiota transplantation (FMT) are effective in therapy. Diet (high-fiber diet) and physical activity help restore the microbiota.

Conclusion:

Alterations in the composition of the intestinal microbiota in type 2 diabetes significantly disrupt biochemical parameters and are one of the main factors in the progression of the disease. Modulation of the microbiota opens up new therapeutic strategies. Future studies require more in-depth analyses taking into account ethnic groups, age and treatment conditions. This approach could be an important step in the effective management of T2DM**.**

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