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EFFECT OF PROBIOTICS ON ZONULIN LEVELS AND INTESTINAL MICROBIOTA COMPOSITION IN FUNCTIONAL GASTROINTESTINAL DISORDERS

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Abstract. Functional gastrointestinal disorders (FGIDs) are among the most prevalent chronic conditions in gastroenterological practice and are characterized by persistent gastrointestinal symptoms in the absence of identifiable structural pathology. Increasing evidence indicates that impaired intestinal barrier function and alterations in gut microbiota composition play a central role in the pathogenesis of FGIDs. Zonulin, a key regulator of intestinal tight junctions, serves as a biomarker of increased intestinal permeability and is frequently elevated in patients with FGIDs.

This study was conducted at the Khorezm regional multidisciplinary medical center and aimed to evaluate the effect of probiotic therapy on serum zonulin levels and intestinal microbiota composition in patients with functional gastrointestinal disorders. Patients were stratified into study groups based on treatment modality. The results demonstrate that probiotic supplementation significantly reduces zonulin levels, improves gut microbiota balance, and alleviates clinical symptoms, confirming the role of probiotics as an effective adjunct in FGID management.

Key words: functional gastrointestinal disorders, zonulin, intestinal permeability, gut microbiota, probiotics

Introduction. Functional gastrointestinal disorders represent a heterogeneous group of chronic diseases characterized by abdominal pain, bloating, altered bowel habits, and dyspeptic symptoms without detectable organic abnormalities. According to epidemiological data, FGIDs affect up to 40% of the adult population worldwide, with a higher prevalence among women and individuals of working age [1,2]. These disorders significantly impair quality of life and are associated with substantial healthcare utilization.

Recent advances in gastroenterology have shifted the understanding of FGIDs from purely functional conditions to disorders of gut–brain interaction, involving immune activation, visceral hypersensitivity, dysregulation of intestinal permeability, and gut microbiota imbalance [3,4]. The integrity of the intestinal epithelial barrier plays a crucial role in maintaining gastrointestinal homeostasis by preventing the translocation of luminal antigens and microorganisms into the systemic circulation.

Zonulin is a physiological modulator of intercellular tight junctions and regulates paracellular permeability of the intestinal epithelium. Elevated serum zonulin levels indicate increased intestinal permeability, commonly referred to as "leaky gut," which has been implicated in the pathogenesis of FGIDs, irritable bowel syndrome, and other chronic inflammatory conditions [5,6]. Several studies have demonstrated higher zonulin concentrations in patients with functional gastrointestinal disorders compared to healthy controls [7].

Alterations in gut microbiota composition are closely linked to intestinal barrier dysfunction. Dysbiosis, characterized by a reduction in beneficial bacterial species such as Lactobacillus and

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Bifidobacterium and an overgrowth of opportunistic microorganisms, contributes to low-grade inflammation, abnormal fermentation, and symptom persistence in FGIDs [8,9].

Probiotics have gained increasing attention as a therapeutic approach aimed at restoring microbial balance, enhancing epithelial barrier function, and modulating immune responses. Experimental and clinical studies suggest that probiotics may reduce intestinal permeability by regulating tight junction proteins and decreasing zonulin expression [10,11]. However, data regarding their effects on zonulin levels and microbiota composition in patients with FGIDs remain limited and require further investigation, particularly in regional clinical settings.

Aim of the study. The aim of this study was to assess the impact of probiotic therapy on serum zonulin levels, intestinal microbiota composition, and clinical manifestations in patients with functional gastrointestinal disorders.

Materials and methods. A prospective observational study was conducted between 2023 and 2024 at the Khorezm Regional Multidisciplinary Medical Center. A total of 85 patients aged 18–55 years diagnosed with functional gastrointestinal disorders according to the Rome IV criteria were enrolled. Patients were divided into three groups. The first group consisted of 35 patients with FGIDs receiving standard symptomatic therapy and the third one 30 patients with FGIDs receiving standard therapy combined with probiotic supplementation.

The third group constituted 20 patients apparently healthy individuals without gastrointestinal complaints. Inclusion criteria included confirmed diagnosis of FGIDs, absence of organic gastrointestinal disease, and informed consent. Exclusion criteria were inflammatory bowel disease, celiac disease, severe systemic illnesses, recent antibiotic use, and pregnancy. All participants underwent clinical evaluation, assessment of gastrointestinal symptoms using validated questionnaires, laboratory measurement of serum zonulin levels by enzyme-linked immunosorbent assay (ELISA), and stool analysis for qualitative and quantitative assessment of intestinal microbiota. Patients in Group II received a multi-strain probiotic containing Lactobacillus and Bifidobacterium species for 8 weeks. Follow-up assessments were performed after completion of therapy.

Results. Baseline serum zonulin levels were significantly elevated in patients with FGIDs compared to the control group ($p < 0.01$), indicating increased intestinal permeability. Patients receiving probiotic therapy demonstrated a significant reduction in zonulin levels after 8 weeks compared to baseline and to Group I ($p < 0.05$).

Microbiota analysis revealed pronounced dysbiosis in FGID patients, characterized by reduced levels of beneficial bacteria and increased counts of opportunistic microorganisms. Probiotic supplementation resulted in normalization of gut microbiota composition, with a significant increase in Lactobacillus and Bifidobacterium populations. Clinically, patients in the probiotic group reported a marked reduction in abdominal pain, bloating, and stool irregularities, whereas symptom improvement in the standard therapy group was less pronounced.

Discussion. The findings of this study confirm the important role of intestinal permeability and gut microbiota alterations in the pathogenesis of functional gastrointestinal disorders. Elevated zonulin levels reflect compromised epithelial barrier function, which contributes to symptom persistence and chronicity. Probiotic therapy demonstrated a significant beneficial effect by reducing zonulin levels, restoring microbial balance, and improving clinical outcomes. These effects may be attributed to the ability of probiotics to enhance tight junction integrity, suppress pathogenic

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microorganisms, and modulate local immune responses. Early identification of intestinal barrier dysfunction and dysbiosis at regional multidisciplinary medical centers allows timely initiation of targeted therapy and prevention of disease progression.

Conclusions. Functional gastrointestinal disorders are associated with increased intestinal permeability and gut microbiota imbalance. Probiotic therapy effectively reduces serum zonulin levels, improves intestinal microbiota composition, and alleviates clinical symptoms. Incorporation of probiotics into the comprehensive management of FGIDs may enhance treatment outcomes and improve patients' quality of life.

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