

SYMBIOTIC RELATIONS OF THE INTESTINAL MICROFLORA IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Rheumatoid arthritis (RA), a chronic autoimmune process, directly or indirectly affects the patient, affecting all organs and systems. Complications and concomitant diseases in RA lead to severe disability, social dysfunction and premature death. A number of studies support the view that RA may be due to asymptomatic urinary tract infections caused by bacteria *Proteus*. Despite the results of studies showing the primary role of *Proteus mirabilis* in the etiopathogenesis of RA, this hypothesis is still controversial, therefore further study of the role of the microbial factor in rheumatic diseases is required. The main reservoir of opportunistic microorganisms in humans is the intestine. Microorganisms living in the intestine are in certain symbiotic relationships between themselves and the host's organism, affecting many aspects of the metabolism, physiology and immunity of the host. To assess the microbiota, it is important to consider not an aggregate of individual species, but an interdependent network of microbes. The change in the symbiotic relationship of microorganisms can be accompanied by a violation of the positive functions of the microflora up to its participation in the etiopathogenesis of various pathological conditions. Better understanding of the human intestinal ecosystem is necessary to understand the role of microbiota in the development of chronic autoimmune diseases.

Objective: To study the symbiotic relationship of the main representatives of the intestinal microbiocenosis in patients with rheumatoid arthritis.

Materials and methods. Bacteriological method was used to study the microflora of the large intestine in 130 patients with rheumatoid arthritis and 40 persons in the comparison group. Among the RA patients examined, women predominated (ratio 1: 7,7). The mean age of patients was $59,89 \pm 12,06$ years. The average age at onset of the disease was $43,89 \pm 7,15$ years. The average duration of the disease: $12,14 \pm 11,22$ years. The average activity index of DAS 28 was $4,17 \pm 0,83$ points. Patients with a moderate (56,15%) degree of RA activity prevailed among the patients examined. The number of individual representatives of the intestinal microflora in CFU/g of feces and the frequency of isolation of individual microorganisms were determined. The typology of the dominants of microbiocenosis was determined on the basis of the indicator of occurrence of species. The selected species are divided into permanent, additional and transient.

Results and discussion. The analysis of the symbiotic relationship of the intestinal microflora of RA patients on the basis of the study of the index of the constancy of microorganisms showed a significant change in the nature of the biocenosis of this biotope. In the dominant species, not only *Bifidumbacterium spp.* (100% of patients), *Lactobacillus spp.* (100%), *Bacteroides spp.* (100%), lactose-positive *Escherichiae coli* (100%), but opportunistic representatives of the family *Eenterobacteriaceae* (54%), *Enterococcus spp.* (76%), *Clostridium spp.* (56%), *Staphylococcus spp.* (60%), *Escherichiae coli* with decreased enzymatic activity (59%). Opportunistic representatives of the family *Enterobacteriaceae* were isolated in 54% of patients, while in the comparison group they were not detected ($p < 0,01$). Opportunistic representatives of the family *Enterobacteriaceae* due to the isolation of endotoxin can reduce the activity of TLR4 and the barrier function of the intestinal mucosa. Increased permeability of the intestinal mucosa is accompanied by an increase in the level of LPS in plasma and leads to the development of metabolic endotoxemia. The group of additional species included *Staphylococcus aureus*, lactose-negative *Escherichiae coli* and fungi of the genus *Candida*. In the comparison group *Staphylococcus aureus* was not detected in the large intestine ($p < 0.01$). Colonization of the organism of patients with *Staphylococcus aureus* is one of the factors of increased risk of development of infectious complications. Inclusion of opportunistic microorganisms having pathogen-associated molecular patterns interacting with specific receptors (TLRs NOD, NALP, CRP) in symbiosis may be accompanied by a change in the immune response of the patient's organism and influence the development of rheumatoid arthritis.

Conclusion. The change in the symbiotic relations of the microflora of the large intestine and the inclusion of opportunistic microorganisms into the associative symbiosis were detected in rheumatoid arthritis.