



THE ADVANCEMENT OF NONSPECIFIC PROPHYLAXIS AND THERAPY PSEUDOTUBERCULOSIS AND INTESTINAL YERSINIOSIS

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Abstract

Recent years have witnessed the development and clinical implementation of the new approaches to prophylaxis and treatment of different nosological forms of diseases - combination of conventional therapy and immunocorrection. The review analyzes present-day state of nonspecific prophylaxis and treatment of pseudotuberculosis and intestinal yersiniosis. Information is presented on the effectiveness of immunomodulators, products of vital activity of plant cells and sea creatures, prebiotics, immunoglobuline complex (CIP) in prophylaxis and therapy of these diseases.

Keywords: pseudotuberculosis, intestinal yersiniosis, immunoglobulins, immunocorrection, prebiotics.

Microorganisms belonging to the genus *Yersinia* of the Enterobacteriaceae family are the cause of serious diseases affecting animals and humans and characterized by various clinical manifestations. There is reason to believe that diseases caused by pathogens of pseudotuberculosis and yersiniosis are much more common than diagnosed. This often leads to the fact that the infection becomes generalized with the involvement of various organs and systems in the pathological process, recurs and continues for several months.

It was revealed that frequent chronicity of the process in pseudotuberculosis can be caused by disorders in the immune status, as well as by the lack of adequate therapy that can normalize these disorders [1]. It was shown that the causative agents of pseudotuberculosis and intestinal yersiniosis not only induce apoptosis of macrophages and dendritic cells, but also suppress the induction of TNF- α , IL-12 and IL-10. In addition to the effect on the cells of innate immunity, *Yersinia* disrupt the formation of an adaptive immune response, changing the properties of T- and B-





lymphocytes (T- and B-Lf) [2]. The thermostable toxin of pseudotuberculosis bacteria suppresses the phagocytic activity of neutrophils and macrophages, as well as the humoral immune response, reducing the number of antibody-producing cells [3]. A number of clinical strains of *Yersinia* have drug resistance, which leads to the generalization of the process against the background of a decrease in the body's resistance, making the traditional treatment of these infections ineffective. All of the above indicates the need for the combined use of drugs and substances of various chemical nature for the treatment and prevention of pseudotuberculosis and yersiniosis.

New approaches to the prevention and treatment of various nosological forms of diseases are being developed and introduced into wide clinical practice - a combination of basic therapy with immunocorrection [4, 5]. One of the first Plotnikov K.P. [6] showed that the use of thymogen along with etiotropic therapy reduces the duration of clinical manifestations and relapses of pseudotuberculosis, which correlates with the normalization of the functional activity of Lf, immunoregulatory index, the number of T-activated Lf. The use of an immunomodulator is especially effective in patients with severe and moderate pseudotuberculosis.

The results obtained by O.A. Burgasova et al. [7] in experiments on animals, indicate the protective effect of the immunomodulator "Bestim", manifested in the limitation of dissemination of *Y. pseudotuberculosis* into organs and tissues in 80-90% of mice, a reduction in the development time (by 6 days) of the pathological process in them and preventing death.

The use of the drug "Cycloferon" in the treatment of pseudotuberculosis and intestinal yersiniosis in children, in contrast to traditional antibiotic therapy, leads to a more rapid relief of local and systemic symptoms. The positive effect of the drug on the anti-infectious resistance of the colon mucosa was expressed in the normalization of the microecology of its lumen and the elimination of pathogens and opportunistic microflora [8, 9].

When used in complex therapy of recurrent forms of pseudotuberculosis, the drug Roncoleukin, a recombinant human IL-2, has proven itself well. In patients who received this drug, the duration of the period of intoxication was significantly reduced, the rash, cardiopathy, etc. disappeared faster. Not a single patient who received Roncoleukin developed repeated relapses [10]. The maximum protective effect of another cytokine (recombinant IL-1v) in experiments on animals was established. There was a decrease in the number of dead mice by 30% compared to the control and by 1-4 orders of magnitude in the concentration of *Yersinia* in the internal organs of infected animals, which indicates its positive effect on the severity of experimental





pseudotuberculosis [11]. The inclusion of sodium nucleonate in the complex therapy of children with yersiniosis did not have a significant effect on the content of T- and B-lymphocytes, but significantly improved the phagocytic activity of blood neutrophils, smoothing the clinical manifestations of the disease [12].

Extensive studies of the immunomodulatory action of drugs of various chemical nature, including the waste products of plant cells and sea dwellers, are being carried out. Thus, a biopolymer of natural origin arabinogalactan (an intracellular polysaccharide of Dahurian and Siberian larch trees) increases the phagocytic activity of macrophages against pseudotuberculosis microbes and stimulates antitelogenesis [13]. It was also shown that glucans, glycoproteins and peptides of natural origin (mytilan, coral, translam, ponasan, etc.) isolated from marine organisms and representatives of the Far Eastern flora (mussels, corals, algae, etc.)

promote an increase in the functional activity of phagocytes, enhancing the absorption and digestion of *Y. pseudotuberculosis* [14]. Currently, research in this direction continues. Thus, scientists of the Pacific Oceanological Institute, together with colleagues from the Research Institute of Epidemiology and Microbiology of Vladivostok, showed that the drug "Pentakan" (extract from Far Eastern galaturias) had immunomodulatory activity, stimulating the functional activity of macrophages in pseudotuberculosis infection in mice [15].

Much attention of modern researchers is paid to studying the possibility of including preparations of normal intestinal microflora in the treatment regimen and non-specific prophylaxis of many infectious diseases. It has been proven that the constant presence of resident microorganisms adhered to its wall in the intestine prevents the reproduction of pathogens, creates an environment unfavorable for their development due to the formation of antimicrobial compounds, and also stimulates the restoration of immune cells in the submucosal layer [16]. The most important aspects of the interaction of probiotic strains with the intestinal microflora and the body are the formation of antibacterial substances, competition for nutrients and the site of adhesion, changes in microbial metabolism (increase or decrease in enzymatic activity), stimulation of the immune system, which indicates the promise of using probiotics for non-specific prevention of diseases.

The possibility of preventing the development of pseudotuberculosis and intestinal yersiniosis in conventional white mice with the prebiotic "Stimbifid" and low-molecular exometabolites of the supernatant of native cultures of probiotic bifidobacteria and lactobacilli was studied. It was found that these drugs arrest the development of the infectious process and its generalization both in the course of prophylactic and therapeutic courses [17-19].





There is an opinion that when choosing the means of "starting" therapy in the initial period of the disease in mild and moderate forms of infectious diseases (including intestinal), preference should be given not to antibiotics and chemotherapy, but to drugs that have a direct or indirect etiopathogenetic effect on pathogens [20].

The widely used immunoglobulin (Ig) drugs for passive immunotherapy are such drugs. Increasing the effectiveness of the treatment of infections with the use of antibodies consists in the immediate implementation of their direct effect not only on the microorganism (opsonization, phagocytosis and elimination), but also on the immune system of the macroorganism. By binding to the corresponding antigens, antibodies neutralize them, convert them into an insoluble form, as a result of which the mechanisms of phagocytosis, complement-dependent lysis and subsequent elimination of antigens from the body are triggered.

A complex immunoglobulin preparation (CIP) developed by employees of the Moscow Research Institute of Epidemiology and Microbiology. G.N. Gabrichevsky, contains a high concentration of antibodies to gram-negative enteropathogenic bacteria of the intestinal group (*Shigella*, *Salmonella*, *Escherichia*, etc.). Immunobiological properties of instrumentation are due to the content of immunoglobulins of three classes IgA (25%), IgM (25%) and IgG (50%). IgM, activating complement and causing bacterial lysis, has a bactericidal effect on pathogenic microorganisms, IgA makes it difficult for them to attach to the epithelium of the mucous membrane and ensures rapid removal from the intestine, IgG neutralizes microbial toxins and viruses, mediates the "adhesion" of bacteria to macrophages with their subsequent phagocytosis. Therefore, instrumentation, which is very important, can be used without antibiotic therapy [21]. In addition to removing pathogenic and opportunistic microorganisms from the body, CIP promotes the growth of normal intestinal microflora (*bifidobacteria*, *lactobacilli*, *enterococci* and non-pathogenic *E. coli*), increases the production of secretory IgA and normalizes altered indicators of systemic immunity. The drug is recommended for the prevention of infectious diseases in people with acquired immunodeficiency, as well as for immunocorrective therapy in people with reduced activity of humoral immunity factors (premature babies; infants who are artificially fed; people suffering from chronic diseases of the gastrointestinal tract; elderly people age, etc.) [22].

Employees of the Rostov-on-Don Anti-Plague Institute [23-24] studied the influence of instrumentation on the development and outcome of experimental pseudotuberculosis and intestinal yersiniosis and the formation of a cellular and humoral immune response to the causative agents of these diseases.





It was revealed that this drug, acting on the initial stages of initiation of the infectious process upon oral intake of pathogens into the body, prevents their adhesion to epithelial cells of the intestinal mucosa of animals, colonization, further invasion, and, consequently, dissemination of pathogens in parenchymal organs, preventing the development of pathological processes and the death of mice. It was found that the use of the drug enhances the absorptive, digesting ability of phagocytes, the expression of receptors on their membranes, the bactericidal activity of these cells, providing complete phagocytosis of *Yersinia*. In addition, KIP has a positive effect on antibody production and the process of utilization of circulating immune complexes. The results obtained indicate that the use of instrumentation is promising for the prevention and treatment (including in conjunction with etiotropic therapy) of experimental pseudotuberculosis and yersiniosis.

Thus, the results of experimental and clinical studies indicate that the combined use of drugs of various chemical nature, as well as prebiotics, opens up new approaches to the prevention and treatment of pseudotuberculosis and intestinal yersiniosis.

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