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Clinical and Immunological Characteristics and Immunocorrection of Ulcerative Colitis

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Abstract. The pathology of digestive system at present takes a view of chronic inflammatory diseases of gastrointestinal tract. In the overall structure one of the top places are occupied by inflammatory diseases of the colon (including non-specific ulcerous colitis). They are serious from the perspective of diseases courses and prognosis, whose worldwide incidence continues to rise steadily in the last decades. The disease is prevalent with a chronic course, a seasonal tendency to exacerbations, a high rate of severe complications, high disability, and conveys majorly to individuals of young and mature pro working age. So far, no predominant etiological factor triggering the genesis of NUC has been identified. There is a growing opinion in recent years that the state of the immune system plays a pivotal role in NUC pathogenesis, hence largely determining the choice of immunocorrection and, ultimately, the disease outcome. Self-perpetuating pathophysiological processes, local and generalized autoimmune inflammation, which develop on the background of a genetic predisposition to an insufficient immune response from the immune system of the organism as a whole and the local immune system of the gastrointestinal tract, are responsible for the emergence of the extremely complex and complex diseases. In this connection, a lot of interest is formed to the study of the functional characteristics of T and B lymphocytes and cytokines — inflammatory mediators. Changes in the pathogenesis of NUC have now been materialized recently in a study, which validates the significance of alterations in specific components of the immune system: decrease in the overall count of cells in immune system. T-cell heterogeneity of its subpopulations, B-cell and natural killer disorders are being examined. The study of features of changes in the immune system in accordance with the severity and form of the disease, activity of the pathological process in the colon, clinical and immunological diagnostic criteria, prediction of the disease outcome and development of principles of immunocorrective therapy are topical questions of today.

Keywords: Large Intestine, Ulcerative Colitis, Immunology, Inflammation

Research Objective

To form a clinical and immunological characteristics and principles of immunocorrective treatment of non-specific ulcerative colitis, depending on the severity and form of the disease.

Related to this objective, the following steps were determined:

features of changes in cellular and humoral immunity in patients with NUC of different degrees of severity depending on the form of the disease.

to investigate the functional status of natural killer cells (NKC) in patients of varying severity of disease course and modes;

Design of clinical trials: 1) with NUC before treatment; 2) determine the effectiveness of NUC treatment in combination with immunocorrecting agents.

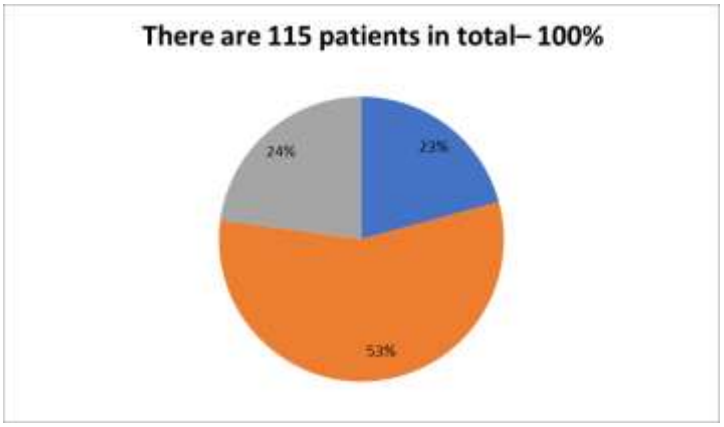
Materials and Methods

Among 115 patients diagnosed with the disease "Non-specific ulcerative colitis in the acute phase" who were under the supervision of the gastroenterology department of MHC No. 1 in Samarkand. Patients ranged in age from 15 to 67 years (42 men and 73 women). All patients were evaluated based on the following criteria: biochemical, radiological, endoscopic (rectoromanofibroccopy, colonofibroscopy), immunological, bacteriological and histological examinations of intravital colon biopsies. A total of 30 practically healthy individuals aged 17-56 years were included in the control group.

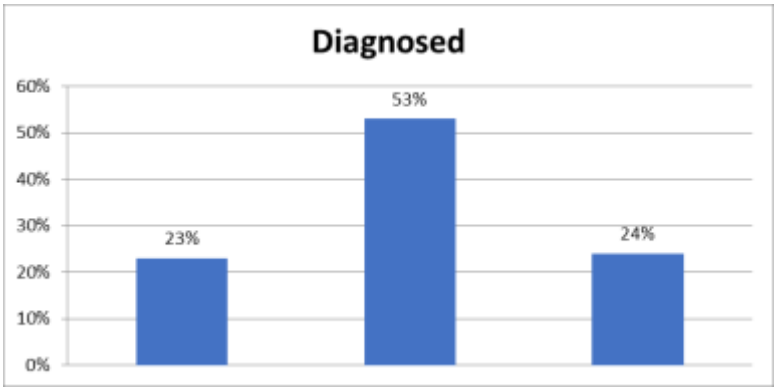
The distribution of patients according to the severity of the course, clinical forms of the disease and localization of the process is given in accordance with the classification of NUC and is provided in the Table 1.

Course of the disease		Clinical form			Localization of the process			Total	
		Chronic continuous	Chronic recurrent	Sharp	Total	Left - sided	Distal	ABS.	%
Light		7	20	-	-	12	15	27	23
Medium - heavy		21	33	6	8	35	17	60	53
Heavy		14	10	4	19	3	6	28	24
Total	abs.	42	63	10	27	50	38	115	
	%	37	55	8	24	43	33		100

In our studies, 55% were patients with chronic recurrent NUC, 37% with chronic continuous NUC, and 8% with acute NUC.



A mild course of the disease was diagnosed in chronic recurrent I - in 23% of patients. Moderate course was observed in 53%, severe course-in 24% of patients.



Immune status assessment was done according to the recognised diagnosis standards. Total and relative number of T-lymphocytes, populations of theophylline-resistant and theophylline-sensitive cells were also determined. We also assessed the B-link of immunity by determining the concentration of immunoglobulins of classes A, M, G, number and functional activity of natural killer cytotoxic cells (NKC). The data obtained were statistically processed.

Research Results

Patients' demographic, clinical and immunological characteristics of mild NUC

Twenty-seven patients (range, 17-65 years) with NUC were studied. Among them, 8 men, 19 women. In addition to these diseases, chronic hepatitis, chronic cholecystitis and acute appendicitis were also diagnosed in 13 patients. A careful history and physical examination in these patients showed signs of ulcerative colitis. In 14 patients, the disease was not related to anything. A decree on the basis of the anamnesis in all patients chronic recurrent form of a disease was established. The range of time the disease lasts is 1-14 years. Immunological study of patients of this group demonstrated a 21 reduction in the relative count of lymphocytes. 8+0.88% (in healthy 25.76+1.0%), and some redistribution of their populations: the relative number of T-lymphocytes decrease − 54.9+2,6%; 0,76+0,06x109/l (in healthy 59.7+1,0%; 0,8+0. Vasopressin excess was associated with a lower percentage and number of T-lymphocytes – 49.91+3,1%; 0,75+0,09x109/l (healthy 54.53+1,4 %; 1,07+0,04); P<0.01 and higher percentage (H = 254,4, P<.0001) (OR = 151.86, P=0.003) and number (OR = 399, P=0.01) of B-lymphocytes – 24.08+1,5%; 0,33+0.03x109/l (healthy 20.5+1,0%; 0,26+0.02), P<0.01. T-lymphocyte subpopulation (TPRC and TPSC) remained unchanged in such patients. The argon-plasma therapy induced a statistically significant rise in concentration IgE and IgA (P<0.01), and level of IgMin compared with levels in control group — by 2.5 times. Functional activity of the NKC tended to lower only.

Therefore, the immune system changes in mild NUC patients are represented only by a reduction of T-lymphocytes and a rise in lymphocytes and immunoglobulins of class A and M, with the changes in the former and latter being potential diagnostic criteria for diagnosis of mild recurrent NUC.

Clinical and Immunological Features of Patients with Moderate NUC

Among 60 patients with NUC aged 15-67 years, the diagnosis was moderate course in 35% (chronic continuous UC). Almost two-thirds (65 percent) have a form of the disease that is chronic recurrent.

From the study of the immune system status of patients, it is shown that the number of T-lymphocytes decreased ‰ 48.3 + 1,2%; 0,72 + 0,06x109/l (in the control group 59.7 + 1,0%; 0,8 + 0. 04x109/l) P<0. 6+1,3%; 0,36+0. 003x109/l (healthy 37.7+1,7%; 0,5+0. Results: In the suppressor population differences were found in the levels of the activated T-cells and T-suppressors - 14.4 + 1,31%; 0,19 + 0,02 x 109/ l (healthy 19.4 + 1,3%; 0,25 + 0,02 x 109/ l), P < 0.01, as well as in the quantity of the unstable E-rosette-forming cells. In the setting of T-immune system insufficiency, there was a rise in B-lymphocytes (EAC-(EAC-rosette forming cells -26,3+1,2%; 2,33+0. 07x109/l healthy people - 20,5+1,0% [0,26+0,02x109/l] M-rosette-forming lymphocytes - 13,2+0,8% [0,20+. 04x109/l; in healthy individuals — 95+0,48%; 12+0,02x109/ l). P<0.001. Examination of humoral immunity markers demonstrated apparent elevation of serum IgA and IgM. Concentration IgM was 2.3-fold greater than in the control group, and this parameter increased 3-7-fold in individual patients. Level IgA was also inclined to rise 1.7 times.

Among patients with moderate NUC, 35% were found to have a chronic continuous form of the disease. We observed the lowmost indices of T-cell immunity with a prevailing reduction of T-suppressors in these patients, in some patients — by 4 times lower in comparison with the control group. IgA average indicators They did not differ from those in healthy people.

So, the data presented above show that moderate-to-mild NUC occurs — on the one hand — with a more evident clinical picture of the disease, and on the other hand, with an obvious deficiency in T — immune, their subpopulations as well as in natural killers, functional activity. While the absence of T-suppressors, an increase in B-lymphocytes associated with imbalance of subpopulations of the T-immune system is confirmed by the concentration increase of IgA and IgM.

Clinical and immunological traits of patients with severe NUC

NUC had a severe course in 28 patients (22–51 years) in our studies. Among them, there were 4 patients with acute, 14 with chronic continuous, and 10 with chronic recurrent types.

It was revealed against the background of normal values of the number of lymphocytes in peripheral blood — the decrease in the T-lymphocytes to 40.5% was estimated by compared with the appropriate control group. 970 x109/ l (антифосфолипидные антитела (+ 2,29%; 0,51+0,06x109/ l (у здоровых людей—59. 7+1,0%; 0,8+0. 08x109/l), P<0.001. Acute and chronic continual course of the mosque, the local and general complications, long-term receiving levomycetin, tetracycline, delayed diagnosis verification, anaemia, cachexia, hepatomegaly, myocardial dystrophy, and decrease of protein s20 34 (21–36% [14] Prov), (0.23–0.43 x 109 total protein in 41%) in a few patients with acute 36 or chronic 53 u}m.

Within patients with severe NUC with a T-lymphocyte deficiency, subpopulations of lymphocytes decreased (as T-helpers); · 52+2,49%; 0,37+0. 052x109/ l (in healthy people-37. 7+1,7%; 0,5+0. T-helpers - 60,28+1,36% 0,39+0,03 x 10^9/l, and T-suppressors - 12,23+1,26% 0,15+0,02 x 10^9/l (norm-19. 4+1,3%; 0,25+0,02x109P<0.001. Nevertheless, the extent of decrement was different, especially because of T-suppressors (TPSC). So, in the case of ratio between the number of immunoregulatory cells, the coefficient increased to 2.4 +0.2 (in the control 1.94+0,09). Minimums of T-suppressors were found in 68,2 % of patients with boundaries of its oscillation of 0,04–0,19 x 109/ l (both acute and chronic continuous forms of the disease). At the same time there was also a reduction in the T-helpers along with the T-suppressors get reduced. There were also decreases in E-rosette-forming cells of significance (P<0.001) in the extreme (4th) degree of the disease as compared with the 1st degree of the disease.

Patients were stratified into three severity groups (mild, moderate and severe) and clinical and immunological parameters were assessed in each group – NKC precursors were present at high concentrations, however their functional capacity was lower comparing to all NUC patients we have analysed.

Therefore, we can conclude that the changes of cellular and humoral immunity, the functional activity of NKC in patients with NUC are connected with the activity of the pathological process in the colon, the severity state and the form of the disease. Even when the chronic recurrent form is mild in relation to its severity, variations of the T and B immune systems can be detected in low organ infiltration. With an increase in the activity of the disease, the extent of the pathological process in the colon, the severity of clinical and endoscopic manifestations, the deficiency of the T — immune system deepens with a pronounced decrease in the subpopulation of both T — helpers and T — suppressors, and inhibition of the functional activity of the NKC. The distorted T - immune system causes autoimmune reactions, systemic lesions of all parts of the gastrointestinal tract, liver, heart and blood.

Such manifestations are especially characteristic of chronic continuous and acute forms of non-specific ulcerative colitis of moderate and severe degrees. It was observed that most probably the irrational unsystematic usage of antibiotics may aggravate the immune system defect, lead to process dissemination and an unfavourable disease course.

Since the pathogenesis of NUC involves an imbalance of the immune system with functional suppression of immunoregulatory T helper cells and T suppressors, such patients do not require so much suppression of the natural defenses of the body as their correction.

The aim of this study was to evaluate the efficacy of immunostimulating agents in the office treatment of NUC, the drug "Thymogen" and "T-activin" being prescribed to patients. Thymogen 100 mg given intramuscularly once a day with 5 to 10 injections, depending on the severity of the disease. Used "T-activin" by subcutaneous injections in the dosage of 100 mcg Once a day, 5–10 injections in addition to basic therapy. The complex application of Thymogen and T-activin drugs in the traditional therapy of these patients has been attended with clinical improvements: stool normalization, absence of blood clots, pus, mucus in the feces, increase of body weight and other favorable dynamics. In patients, there was an increase in both the total number of lymphocytes in the peripheral blood. On this background, there was an increased absolute and relative number of T-lymphocytes. This profile corresponds to certain peculiarities of immune response induced by the action of the drug T-activin om, revealed in the patients at the end of the course of its treatment. T-lymphocyte absolute and relative number were in a meaningful increased in both groups. A benefit of the proposed methods of immunotherapy is that complications and side effects are absent.

Conclusion

For diseases of the immune system (cellular and humoral immunity) of the form of the disease, the degree of severity of the course and the activity of the pathological process are directly responsible in patients with NUC. The low indices of functional activity of the NKC testify to an unfavorable course and an unfavorable prognosis of the disease, and serve as the diagnostic criteria for the severity of the disease. Thymogen or T-activin — of drugs used in the complex traditional therapy of NUC significantly increases the clinical efficiency of treatment, accelerates the eradication of basic clinical signs of the illness, leads to the conductive of ulcers healing, suppresses or diminishes recurrences and elevates duration of remissions. This gives a significant contribution to the immunocorrection of separate components of the immune system, improves the treatment efficiency, as well as the speedy relief of exacerbation of the disease, the performance of all necessary rehabilitation measures, and prolongs the remission period of the Clinic [1].

Therefore, the state of the immune system (cellular and humoral immunity) in NUC can be used as a criterion for determining the forms and severity of NUC. Functional activity of natural killer cells should be measured as a further immunological criterium for the diagnosis of ulcerative colitis. Decreased functional activity of the NKC indicates the severity of the pathological process and the form of the disease. Rates are lowest where the acute form shows most severe severity. In contemporary approaches to differentiated therapy of immunomodulatory drugs it is advisable to determine the sensitivity of peripheral blood T-lymphocytes of patients to immunomodulatory drugs.

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