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Violation of the Immune System and Their Immunorehabilitation in Patients Chronic Pancreatitis

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Abstract: Immune system studied in 36 patients with chronic pancreatitis (CP) and 36 healthy individuals. In patients with CP showed a deficit of T-lymphocytes and its subpopulations voltage humoral immunity and cytokine profile. Using thymoptinum (dose 0.8-1.0 mg per course) in combined with conventional trea-tment in patients with CP led to an increase in cellular immunity and stabilization of cytokine levels.

Keywords: chronic pancreatitis, immunity, thymoptinum, immunotherapy, cytokines.

Changes in the environment, food industry technologies, lifestyle and the spread of "Western nutrition" are the cause of the increase in pancreatic pathologies. Over the past 30 years, a global trend has emerged towards an increase in the incidence of chronic pancreatitis (CP) by more than 2 times [1, 8, 11].

In terms of prevalence, increased incidence, temporary disability and disability, CP is an important socio-economic problem of modern medicine. In the structure of morbidity of the gastrointestinal tract, this pathology ranges from 5.1 to 9%, and in general clinical practice - from 0.2 to 0.6% [1, 8].

Inflammatory processes in the pancreas can develop as a result of immune disorders, which are based on allergic reactions, as well as a response to a bacterial factor [4–7, 9, 10].

However, to date, immune disorders and their correction in patients with CP remain poorly studied.

The purpose of the work is to study immune changes and carry out immunocorrective treatment in patients with CP.

Materials and methods

36 patients (33-65 years old) diagnosed with CP were examined. The diagnosis was made on the basis of complaints, medical history, objective and laboratory examination, instrumental data: Ultrasound examination, Fibrogastroduodenoscopy.

The control group of donors consisted of 32 practically healthy individuals (25-55 years old).

The concentration of serum immunoglobulins (SI) classes A, M and G was determined by radial immunodiffusion according to Mancini et al. (1965). The parameters of cellular immunity (T-lymphocytes and its subsets, B-lymphocytes) were identified using monoclonal antibodies (Sorbent-Service LLC, Russia) [3].

Quantitative assessment of the levels of TNFα, IL-6, IL-4 in blood serum was carried out using a set of ProCon reagents (Protein Contour LLC, St. Petersburg) by enzyme-linked immunosorbent assay [2].

Immunocorrective therapy was carried out in 15 patients with the drug thymoptinum (Uzbekistan) 0.8 -1.0 mg per course of treatment (dose 100 mcg/day for 8 - 10 days). Immunity indicators were studied twice: before and after 1 month. after treatment).

Results and discussion

In patients with CP, immunodeficiency of the cellular level was revealed: 0.7-fold suppression of the total pool of lymphocytes - T(CD3) - 35.3 ± 2.6% compared to the control group - 52.4 ± 1.8% ($p<0.001$); 0.8-fold decrease in the absolute number of T(CD3) cells ($p<0.05$).

They also revealed a noticeable inhibition of subsets of T lymphocytes with a helper-suppressor function - Th (CD4) - 29.5 ± 1.1% ($p<0.001$) and 341.8 ± 32.1 cells/1 μl of blood ($p <0.001$) (in control 36.5 ± 0.7% and 616.4 ± 44.3 cells/1 μl of blood, respectively), Ts(CD8) content - 13.8 ± 1.4% ($p <0.05$) and 127.3 ± 9.8 cells/1 μl of blood ($p<0.01$).

On the part of the B(CD19)-cell link, on the contrary, a tendency was observed to increase as a relative parameter - 20.6 ± 2.3% ($p <0.05$), which was 1.4 times higher than those values in the control group , and absolute - 1.7-fold increase - 385.8 ± 33.4 cells/1 μl of blood (in the control - 230.1 ± 26.7 cells/1 μl of blood). Noticeable activation of the B-cell component of immunity against the background of T-cell suppression in CP was reflected on the SI spectrum.

Noteworthy was the increase in IgA production to 3.97 ± 0.41 g/l ($p <0.05$), which is likely a reflection of the immunological restructuring of the body of patients with CP in response to enzyme intoxication of the body. A significantly high IgG content was found - 22.42 ± 0.75 g/l ($p < 0.001$) (in the control 15.9 ± 0.94 g/l).

The IgM concentration was within the normal range of 1.7 ± 0.2 g/l ($p>0.05$).

Under the influence of conservative treatment, there was no restoration of T(CD3) cells and its subpopulation profile. At the same time, there was a trend towards a decrease in the SI of the Ig A and Ig G classes.

Analysis of the spectrum of cytokines showed that in patients with CP during the period of exacerbation, the values of pro-inflammatory cytokines significantly increased: TNF-α to 202.6 ± 22.3 pg/ml (normal - 24.5 ± 5.1 pg/ml; $p<0.001$), and IL-6 was increased 6 times (317.4 ± 53.5 pg/ml and 47.8 ± 11.2 pg/ml, respectively, $p< 0.001$).

The level of the anti-inflammatory cytokine IL-4 increased 4.3 times compared to normal, which was statistically confirmed (157.5 ± 36.7 pg/ml and 32.6 ± 14.3 pg/ml, respectively; $p< 0.001$).

In patients with CP, secondary immunodeficiency was discovered, to eliminate which we used timoptin, used in combination with therapy (anti-enzyme agents, antispasmodics, antibacterial drugs, etc.).

Immunocorrective therapy led to an increase in both relative - 54.7 ± 3.2% - and absolute values of T(CD3)–lymphocytes - 992.3 ± 64.8 cells/1 μl. In parallel, an increase and stabilization of Th(CD4) and Ts(CD8) was observed. At the same time, the immunoregulatory index was 2.2. IgA concentrations decreased moderately during treatment.

A trend was observed in increasing IgM to 2.23 ± 0.2 g/l and IgG to 23.7 ± 1.62 g/l 1 month after treatment, however, it should be noted that in remission period, the IgG level was high, which was probably due to the severity and duration of the pathological process.

During traditional treatment in patients with CP, there was a moderate decrease in the levels of TNFα, IL-6 ($p>0.05$; compared with data before treatment) and a slight increase in IL-4 to 172.3 ± 41.1 pkg/ml.

Under the influence of immunocorrective therapy carried out against the background of traditional treatment, a noticeable decrease in pro-inflammatory cytokines was revealed in patients with CP: TNFα to 118.4 ± 29.1 pg/ml, IL-6 to 133.6 ± 51.8 pg/ml . In addition, a

decrease in the production of the anti-inflammatory cytokine IL-4 (95.2 ± 27.4 pg/ml) was observed.

Conclusions:

1. Deep suppression of T(CD3)–lymphocytes and its subpopulations and tension of humoral immunity were observed in patients with CP. In patients with CP, a trend was revealed in increasing levels of pro- and anti-inflammatory cytokines, which to a certain extent characterizes the pathological process occurring in the pancreas.

2. The combination of traditional treatment and thymoptinum was effective in patients with CP, as it contributed to the restoration and stabilization of most parameters of the immune system.

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