



Influence of the Drug on the Immune Status of Patients with Tumors of the Gastrointestinal Tract

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Abstract: It has been established that in patients with gastric cancer disturbances occur in the immune status, expressed in the suppression of some (T- and B-lymphocytes, T-helpers, IgG, IgA, IgM) and an increase (T-suppressors, NK-cells) other indicators. Under the influence of LactoFlor, cellular and humoral parameters of immunity are restored in patients with gastric cancer.

Keywords: gastric cancer, LactoFlor, immune status.

Background. Gastric cancer (GC) is one of the deadliest malignancies, with an estimated 769,000 deaths worldwide in 2020 [1]. In recent years, increasing data have suggested that obesity is involved in cancer (such as breast cancer [2], esophageal cancer [3], and GC [4]), diabetes [5], fatty liver [6], and inflammation [7]. Obesity, as a modifiable lifestyle factor, has become a worldwide epidemic, currently affecting > 2 billion people [8]. Hence, much attention has been given to the impact of obesity on cancer incidence, progression, and therapeutic outcomes [9–11]. Of note, complementary therapies based on lipid-lowering agents or anti-obesity pharmacotherapy for cancer have been proposed, given the function of these drugs in reducing inflammation and oxidative stress [12–14]. In GC, the lymph node is the leading metastatic site, and its involvement is deemed an important prognostic factor and can guide crucial clinical decisions of GC patients [15]. However, the association between obesity and LNM remains unclear. Cancer cells experience lipid metabolic changes to fulfill the growing demand for lipids during metastasis [7]. These lipids can be acquired from endogenous synthesis or exogenous sources (for example, adjacent adipocytes and circulating lipids) [10]. Hence, several studies have proposed that obesity can promote tumor progression by reprogramming lipid metabolism in cancer cells [9, 13]. The lymph node is a lipid-rich microenvironment, resulting in a preference for tumor cells to utilize fatty acids as an energy source in metastatic lymph nodes [11]. Meanwhile, cellular and animal models have also shown that primary tumor cells increase fatty acid utilization to promote lymph node metastasis.

It is known that in oncological diseases, violations of immunological homeostasis occur, expressed in the suppression of some and activation of other parameters of the immune system. Various natural and synthetic agents are used to correct immunological changes in the body in oncological diseases [4–5]. A good therapeutic effect in the clinic and experiment was obtained using soy proteins [1–2], antibodies [6], or modified polysaccharides [3].

The aim of the study was to study the effect of the biological preparation Lacto Flor, obtained from cow colostrum, on immunological parameters in patients with gastric cancer (GC).

Material and methods. The object of the study were 30 patients aged 20–50 years with gastric cancer, who were hospitalized. Of these, 18 men and 12 women. The diagnosis of gastric cancer was made on the basis of a comprehensive clinical and instrumental study. 20 practically healthy donors served as controls.

Immunological studies were carried out twice: on admission and before discharge. Lacto Flor was administered as an intramuscular injection of 1 ml for 10 days. In peripheral blood, the number of leukocytes, lymphocytes, relative and absolute values of T-lymphocytes, T-helpers, T-suppressors, B-lymphocytes, NK cells, immunoglobulins of classes G, A, M were determined. Populations and subpopulations of lymphocytes were detected using monoclonal antibodies in the reaction of indirect rosette formation. The results of immunological analyzes are presented in the table.

Statistical analysis. Comparisons of baseline characteristics were conducted using the Pearson chi-squared test or unpaired Student's t test. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using the logistic regression model. Before variables entered the model, we detected linear relationships between the continuous independent variables and the logit transformation value of the dependent variable using the Box-Tidwell method. Restricted cubic spline (RCS) analysis was applied to explore the nonlinear association between continuous BMI and lymph node status, with knots at equally spaced percentiles. P for interaction in subgroup analysis was obtained after the incorporation of two-factor interaction terms. SPSS version 22.0 and R version 4.1.3 were used to conduct all statistical analyses

Results. At admission in patients with gastric cancer, the number of leukocytes and the relative index of lymphocytes increase by 1.2 times. The absolute number of lymphocytes increases by 1.4 times compared with the control. At the same time, there is a significant decrease in the relative (by 1.6 times) and absolute (by 1.3 times) index of T-lymphocytes, and the number of T-helpers decreases by 1.5 times. Against this background, the relative index of T-suppressors increases by 1.4 times. In gastric cancer, there is a sharp increase in the population of NK-cells. The relative and absolute values of these cells increased by 2.3 and 3.2 times, respectively. Significant changes in B-lymphocytes in patients with gastric ulcer do not occur (table 1).

TABLE 1. *Influence of Lactoflor on the immune status of patients with gastric cancer*

Indicators	control (n=20)	before treatment (n=30)	aftertreatment (n=30)
1.Leukocytes	5926±150,7	7162±147,2 ^a	6510,9±133,9 ^{ab}
2.Lymphocytes (%)	28,4±0,7	33,7±0,7 ^a	32,7±0,7 ^a
3.Lymphocytes (aḃc.)	1675,3±47,3	2412,6±64,6 ^a	2109±61,0 ^{ab}
4.T-lymphocytes (%)	51,3±1,7	31,6±0,8 ^a	44,1±1,1 ^{ab}
5.T-lymphocytes (abs.)	853,6±25,8	758,3±24,2 ^a	914,1±31,3 ^b
6.T-helpers (%)	33,0±1,6	23,9±0,9 ^a	28,6±1,1 ^{ab}
7.T-helpers (abs.)	282,4±19,4	183,2±10,3 ^a	262,4±13,8 ^{ab}
8.T-suppressors (%)	15,0±1,0	20,4±1,0 ^a	15,7±0,8 ^b
9.T-suppressors (abs.)	127,5±9,7	156,7±10,5	142,6±8,1
10.NK cells (%)	8,7±0,8	19,6±1,3 ^a	12,4±0,8 ^{ab}
11.NK cells (abs.)	146,7±14,4	475,0±36,1 ^a	263,0±19,7 ^{ab}
12. B-lymphocytes (%)	12,0±1,0	10,4±0,6	11,4±0,6
13.B-lymphocytes (abs.)	201,0±18,0	247,2±13,7	240,8±15,0
14.IgG, mg/%	1396±53,8	823,6±24,5 ^a	1152,9±34,3 ^{ab}
15.IgA, mg/%	246,0±12,3	138,9±5,3 ^a	208,6±8,0 ^{ab}
16.IgM, mg/%	144,2±6,2	101,2±3,3 ^a	131,6±4,3 ^b

Note: ^a - significant to the control, ^b - significant to the group before treatment

In the process of development of the tumor process, inhibition of humoral factors of immunity is observed. Thus, the level of IgG, IgA and IgM decreases by 1.7, 1.8 and 1.4 times, respectively.

The results obtained indicate the development of an imbalance in the immune status in stomach ulcers. Against the background of an increase in the number of T-suppressors and NK-cells, all other cellular and humoral indicators of immunity are suppressed.

After assessing the immune status, the patients were prescribed LactoFlor for 10 days, and the immune status of the patients was again assessed before discharge. After stopping the immunomodulator and before the patient was discharged, an average of 10-20 days passed. During this period, there was a slight decrease in leukocytes, but their level was still significantly higher than the control.

The increased number of lymphocytes decreased after immunocorrection. Positive changes were found in the T-lymphocyte population. Their relative index, in comparison with the data before treatment, increased by 1.4 times, and the absolute index reached the control values. Similar changes occurred in the T-helper population.

The increased number of T-suppressors (%) decreased to the control background. As mentioned, with stomach cancer, there is a sharp increase in the number of NK-cells. After immunocorrection, the relative and absolute values decreased by 1.6 and 1.8 times, respectively, but in both cases remained above the control. There were no changes in B-lymphocytes.

The appointment of LactoFlor contributed to an increase in the concentration of IgG and IgA, and the level of IgM reached the control level.

Conclusion. Thus, it can be concluded that the biopreparation LactoFlor, to a certain extent, normalizes disorders in the immune status in patients with gastric cancer. Its inclusion in traditional treatment can help improve clinical and immunological parameters in patients with oncopathology.

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