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EFFECT OF MEDICINE USE ON THE IMMUNOLOGICAL STATUS OF PATIENTS WITH GASTROINTESTINAL TRACT TUMORS

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Abstract: Studies have shown that patients suffering from gastric cancer have disturbances in their immune status, which are manifested by a decrease in the level of certain elements, such as T- and B-lymphocytes, T-helper cells, IgG, IgA and IgM antibodies, and an increase in other components, including suppressor T cells and NK-cells. The use of the drug «LactoFlor» leads to the restoration of both cellular and humoral parameters of immunity in patients suffering from gastric cancer.

Key words: *gastric cancer, «LactoFlor», immune status.*

Introduction: Gastric cancer (GC) remains one of the deadliest cancers, with an estimated 769,000 deaths worldwide in 2020 [1]. Recent studies indicate an association between obesity and various diseases such as breast cancer, esophageal cancer and liver cancer, as well as diabetes and inflammatory diseases [2, 7]. The global obesity epidemic, affecting more than 2 billion people, raises important questions about the impact of obesity on treatment practices, progression, and outcomes [8, 11]. Research has also looked at cancer treatments, including lipid-lowering drugs and obesity pharmacotherapy, which may reduce health and oxidative stress [12, 14].

Lymph nodes play a crucial role in metastasis in GC and are considered a critical prognostic factor influencing health decisions [15]. However, the relationship between obesity and lymph node metastasis remains poorly understood. Cancer cells rearrange their lipid energy to increase lipid demand during metastasis [7]. These lipids can be obtained either through self-synthesis or from external sources, including surrounding adipocytes and circulating lipids [10]. Therefore, it has been suggested that obesity may promote the progression of tumor formation by reprogramming the lipid metabolism of cancer cells [9, 13]. Lymph nodes provide a lipid-enriched microenvironment

that converts fatty acids into energy for metastatic cells [11]. Experiments in cell and animal models also suggest that primary tumor cells utilize fatty acids to promote lymph node metastasis.

It is known that in the presence of cancer, the balance in the immune system is disturbed, manifesting itself as the suppression of certain components and the activation of others. To correct these changes in the immune system in cancer, a variety of natural and synthetic drugs are used [4, 5]. In clinical practice and experimental studies, significant therapeutic effects have been achieved using soy proteins, antibodies or modified polysaccharides [1, 3, 6].

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

Material and methods. The study included 30 patients aged 20 to 50 years suffering from gastric cancer and undergoing hospital treatment. Among them are 18 men and 12 women. The diagnosis of stomach cancer was established on the basis of comprehensive clinical and instrumental studies. The control group consisted of 20 practically healthy donors.

Immunological tests were performed twice: upon admission of patients and before their discharge. The drug «LactoFlor» was administered to patients intramuscularly, 1 ml daily for 10 days. In the peripheral blood, the number of leukocytes, lymphocytes, relative and absolute numbers of T-lymphocytes, T-helpers, T-suppressors, B-lymphocytes, NK-cells, as well as the level of immunoglobulins of classes G, A and M were studied. Populations and subpopulations of lymphocytes were determined with using monoclonal antibodies in the indirect rosette reaction. The results of immunological analyzes are presented in the table.

Statistical analysis. Comparisons of initial characteristics were made using either the Pearson chi-square test or the unpaired Student t test. We calculated odds ratios (OR) and their 95% confidence intervals (CI) using a logistic regression model. Before including variables in the model, we tested for linear relationships between continuous independent variables and the logit transformation of the dependent variable using the Box–Tidwell method. We used restricted cubic spline (RCS) analysis to examine nonlinear associations between BMI and lymph node status at equidistant percentiles. Interactions in subgroup analyzes were identified after inclusion of two-way interaction terms. We used SPSS version 22.0 and R version 4.1.3 software to perform all statistical analyses.

Results. When treating patients with gastric cancer, there is an increase in the number of leukocytes and the relative content of lymphocytes by 1.2 times. The absolute number of lymphocytes increases 1.4 times compared to patients in the control group. At the same time, there is a significant decrease in the relative content of T-lymphocytes by 1.6 times and the absolute number of T-lymphocytes by 1.3 times. The number of T-helpers decreases by 1.5 times, and the relative content of T-suppressors increases by 1.4 times. In the case of gastric cancer, there is a marked increase in the NK-cell population, where their relative and absolute values increase by 2.3 and 3.2 times, respectively. In patients with gastric ulcer, no significant changes in the content of B-lymphocytes are observed (Table 1)

Table 1

Influence of «LactoFlor» on the immune status of patients with gastric cancer

Indicators	**control (n=20)**	**before treatment (n=30)**	**after treatment (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 (абс.)	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±0,8b
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

During the development of the tumor process, a decrease in humoral immunity factors is observed. Therefore, the levels of IgG, IgA and IgM are 1.7-, 1.8- and 1.4-fold permeable, respectively. These results indicate an imbalance of the immune system in gastric ulcer disease. With an increase in the number of suppressor T cells and NK-cells, other cellular and humoral parameters of immunity are suppressed.

After assessing the immune effects, patients were prescribed a course of «LactoFlor» for 10 days, and before discharge, the immune status of the patients was re-evaluated. After completion of treatment with the immunomodulator and before discharge, an average of 10-20 days passed. During this period, there was a slight decrease in the level of leukocytes, but their number remained significantly higher than in patients in the control group.

The level of lymphocytes, which was present, decreased after immunocorrection. Positive changes were noticed in the structure of T-lymphocytes, where their relative number increased by 1.4 times compared to previous data, which absolutely reached the control level. Changes are also taking place in the T-helper cell industry. 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. As a result of the study of stomach cancer, significant changes in the immune status of patients were revealed. The oncological process is accompanied by inhibition of humoral immune factors, which is manifested by a decrease in the levels of IgG, IgA and IgM. There is also an increase in the NK cell population and a decrease in other cellular and humoral indicators of immunity, including T lymphocytes and T helper cells.

However, immunocorrection using the drug «LactoFlor» led to positive changes in the immune status of patients. After treatment, an increase in the relative and absolute number of T-lymphocytes was observed, as well as a decrease in the level of lymphocytes, bringing them closer to control values.

These results highlight the importance of immunomodulators, such as «LactoFlor», in correcting the immune status of patients with gastric cancer. Further research and clinical trials may

further our understanding of the mechanisms by which such therapeutic modalities influence the immune system and their potential role in the treatment of gastric cancer.

References:

1. Gianni L, Pienkowski T, Im YH, Roman L, Tseng LM, Liu MC, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet Oncol. 2012;13(1):25–32. doi: 10.1016/S1470-2045(11)70336-9.

2. Granai M, Mundo L, Akarca AU, Siciliano MC, Rizvi H, Mancini V, et al. Immune landscape in Burkitt lymphoma reveals M2-macrophage polarization and correlation between PD-L1 expression and non-canonical EBV latency program. Infect Agent Cancer. 2020;15:28.

3. Hecht JR, Bang YJ, Qin SK, Chung HC, Xu JM, Park JO, et al. Lapatinib in combination with Capecitabine plus Oxaliplatin in human epidermal growth factor receptor 2-positive advanced or metastatic Gastric, esophageal, or gastroesophageal adenocarcinoma: TRIO-013/LOGiC--A randomized phase III trial. J Clin Oncol. 2016;34(5):443–451. doi: 10.1200/JCO.2015.62.6598.

4. Jang J, Wang T, Cai H, et al. The U-shaped association between body mass index and gastric cancer risk in the Helicobacter pylori Biomarker Cohort Consortium: a nested case-control study from eight East Asian cohort studies. Int J Cancer. 2020;147(3):777–84. https://doi.org/10.1002/ijc.32790

5. Khabibullaev B.B. Chitosanning metal tutgan complexlari erdamida experimental usma kasalligida ikkilamchi immuno tankisliging correction //Pathology. 2005. - No. 1. - S. 70 - 72.

6. Lee CK, Jeong SH, Jang C, et al. Tumor metastasis to lymph nodes requires YAP-dependent metabolic adaptation. Science. 2019;363(6427):644–9. https://doi.org/10.1126/science.aav0173.

7. Nemtsova E.R., Sergeeva T.V., Andreeva K.L. et al. Prevention of malignant neoplasms in the experiment using natural products / Russian journal of oncology. –2000. - Number 3. - S. 30-34.

8. Sun J.-M., Shen L., Shah M.A., Enzinger P., Adenis A., Doi T., et al. / Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. Lancet. 2021; 398: 759-771 https://doi.org/10.1016/S0140-6736(21)01234-4

9. Sung H, Ferlay J, Siegel RL. Global cancer statistics 2020 GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021. https://doi.org/10.3322/caac.21660

10. Tajima Y, Murakami M, Yamazaki K, et al. Risk factors for lymph node metastasis from gastric cancers with submucosal invasion. Ann Surg Oncol. 2010;17(6):1597–604. https://doi.org/10.1245/s10434-010-0930-6

11. Thangaraj S J Jl, Vo T H, Chu , Phan K H, Lee , Ahn Sy, Kim G Y, Song , Ahn Js, Yang , Kim D, Cho J J, Lee / Expanded natural killer cells potentiate the antimyeloma activity of daratumumab, lenalidomide, and dexamethasone in a myeloma xenograft model Cancer Immunol Immunother Posted: 2022

12. Thuss-Patience P.C., Högner A., Goekkurt E., Stahl M., Kretzschmar A., Schädlich B., et al. / Ramucirumab, avelumab, and paclitaxel (RAP) as second-line treatment in gastro-esophageal adenocarcinoma, a phase II trial of the Arbeitsgemeinschaft Internistische Onkologie (AIO). J Clin Orthod. 2022; 40, 4051–4051. https://doi.org/10.1200/JCO.2022.40.16_suppl.4051

13. Wagner A.D., Oertelt-Prigione S., Adjei A., Buclin T., Cristina V., Csajka C., et al. / Gender medicine and oncology: report and consensus of an ESMO workshop. Ann Oncol. 2019; 30: 1914-1924

14. Wagner AD, Kang YK, Van Dieren J, Mauer M, Grabsch H, Caballero C, et al. 64. EORTC-1203: integration of trastuzumab, with or without pertuzumab, into perioperative chemotherapy of HER-2 positive stomach cancer: INNOVATION EudraCT number 2014-000722-38; NCT02205047. Eur J Surg Oncol. 2016;42(9):S91–SS2. doi: 10.1016/j.ejso.2016.06.070.

15. Yamao T, Shirao K, Ono H, et al. Risk factors for lymph node metastasis from intramucosal gastric carcinoma. Cancer. 1996;77(4):602–606. https://doi.org/10.1002/(sici)1097-0142(19960215)77:4%3c602::aid-cncr3%3