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ACCOMPANYING IMMUNOPHARMACOTHERAPY IN PATIENTS WITH OVARIAN CANCER USING CYCLOFERON AND TACTIVIN

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SUMMARY

An imbalance in the cytokine: IFN-γ / IL-6 ratios was studied. In norm IFN-γ / IL-6 - 1,2. In the group of patients with OC before treatment: IFN-γ / IL-6 - 0.5; in the group of patients after PCT without the use of immunotherapy - IFN-γ / IL-6 - 0.24; in the group of patients with EIPHT + cycloferon - 1.1, and in the group of patients with EIPHT + tactvin - IFN-γ / IL-6 - 0.9. Thus, in groups of patients with EIPHT and immunotropic drugs, there is a positive trend in the state of the immune system, which is reflected in the immunomodulating effect of IFN-γ and a decrease in IL-6. Apparently the use of immunotherapy in a combination of chemotherapy in our opinion is a justified and effective method that leads to the normalization of immunological parameters of the immune system, improves the immediate results of treatment, leads to a decrease in the intoxication of the disease, leads to a decrease in clinical manifestations of the disease.

KEYWORDS: Cytokines, ovarian cancer, immunopharmacotherapy, polychemotherapy, interferon inducers, thymic preparations.

INTRODUCTION

As is known, mortality from ovarian cancer (OC) is greater than that from cervical cancer and the body of the uterus combined, despite the progress made in diagnosis and treatment. Thus, ovarian cancer occupies a stable third place in the structure of oncogenital pathology.[2,5,6,9,13,18] It is proved that the course of the tumor process in OC is accompanied by the formation of endotoxicosis and secondary immunological failure. At the same time, endotoxicosis is a complex, multicomponent process, which is caused by the accumulation in the tissues and biological fluids of endotoxic substances under conditions of a decrease in the physiological processes of detoxification. Chemotherapy conducted on this background, and even more so, polychemotherapy promotes further growth of endogenous intoxication, inhibition of the body's immunological parameters, which complicates the course of the main oncological disease, and sometimes, with the development of organ and systemic disorders, limits the ability to conduct an adequate course of antitumor treatment.[12,14,17,22] It should be noted that against the background of polychemotherapy not only cellular parameters are inhibited, but also humoral factors down to cytokines, which are important in the implementation of antitumor immunity. Moreover, it is known that few immunological preparations are used to stimulate immunity in oncology, which have a wide range of immunotropic effects. However, until now, as in the CIS countries, as well as in our Republic, there are no immunotherapy protocols in oncology that could help overcome oncologic endotoxicosis and secondary immunological failure. In this regard, approaches to the use of immunotropic drugs of different origin and direction of action to achieve the goal are being actively developed. And the goal in this situation is to reduce endotoxemia, increase antitumor and anti-infective immunity, and clinically, to improve the condition, increase the effectiveness of chemotherapy and achieve full-fledged antitumor therapy. In connection with the foregoing, the purpose of this work was to study the effect of drugs cycloferon and taktivin on the results of the use of accompanying immunotherapy in patients with ovarian cancer.

MATERIALS AND RESEARCH METHODS

Women were examined for ovarian cancer $T_{2-3}N_{0-1}M_0$ stages, which were treated in the gynecological and chemotherapy departments. Accompanying immunotherapy was performed with cycloferon and tactivin. In this regard, women were divided into the following groups: group 1 - 29 women with OC to PCT; Group 2 - 32 women with OC after PCT without immunotherapy; Group 3 - 26 women with OC after PCT in combination with EIPHT cycloferon; Group 4 - 28 patients with OC after PCT in combination with EIPHT with tactivin. Immunotherapy was carried out in 2 sessions at admission and before discharge from the

hospital. Patients with OC were given combination therapy in an adjuvant or neoadjuvant regimen, including polychemotherapy according to the cisplatin 75 mg / m2 + cyclophosphane 1000 mg / m2 scheme for 1 day for 4-6 courses 1 time per 3 weeks and surgical treatment in the amount of radical surgery. EIPHT using immunomodulators was performed during the period of radiotherapy and chemotherapy in the hospital. The method of extracorporal immunopharmacotherapy (EIPHT) was carried out with the aim of reducing toxic manifestations after polychemotherapy and improving the immunoresistance of the organism. EIPHT was carried out by exfusion of 500-1000 ml of autologous blood into sterile containers "Gemakon" or "Terumo" and centrifuged at 3000 rpm for 30 minutes. 50-80 ml of blood plasma supernatant were removed. Then, the obtained leukotrombossa and erythrocyte mass were incubated with an immunotropic preparation in a total dose of 30 mg at 37 ° C for 60-100 minutes, followed by the return of the conjugate to the circulatory system of patients. Groups of patients by age, stages of cancer, concomitant somatic pathology were comparable. Immunological studies included serum evaluation of the main cytokines of the immune system. Serum levels of cytokines (IL-6, IFN-γ) were determined by ELISA using test systems from the company Human (Germany) in the course of complex treatment. When conducting a statistical analysis of the data presented in the work, the results of the study were entered into databases prepared in Microsoft Excel XP. Numerical (continuous) values were presented as arithmetic means and mean error (M ± m). Comparison of quantitative traits was carried out using student's criterion, for continuous variables - paired student's criterion. A $p < 0.05$ was taken as the boundary comparative criterion of statistical significance of reliability.

THE RESULTS OF THE STUDY AND THEIR DISCUSSION

The use of immunotherapy is aimed at the induction of both innate and adaptive immunity of the organism for the implementation of antitumor activity. The study of IL-6 allowed us to identify a statistically significant increase in IL-6 in groups of patients with OC, before treatment, after PCT without the use of immunotherapy, as well as a slight increase in IL-6 in the group of patients using EIPHT with tactivin. The analysis showed that the level of IL-6 was statistically elevated in these groups listed above. Thus, the level of IL-6 when comparing between groups revealed that the greatest value of IL-6 was detected in the group of patients with OC before treatment and after treatment, except for the group where immunotherapy was used in the form of EIPHT with tactivin, where there was a significant decrease in the level of IL-6. Moreover, when comparing the values of the groups using cycloferon and tactivin, a decrease in IL-6 is observed in the group of patients with OC. Where they used immunotherapy with tactivin. From the data obtained it is clear that taktivin more influenced the decrease in IL-6 compared with the action of cycloferon. So, IL-6 in the 2nd group of patients with OC after treatment increased when compared with the value before treatment without immunotherapy by 2.5 times, in the 3rd group after PCT using EIPHT with cycloferon, a decrease in IL-6 in 1.4 times, in the case of immunotherapy with tactivin, a decrease in IL-6 is observed in comparison with those before treatment - by 2 times. Consequently, the highest level of IL-6 was detected in the group of patients with ryumenia before and after treatment without the use of immunotherapy. From the literature it is known that IL-6 is an important diagnostic indicator of the malignancy of the oncological process.[18,21] On this basis, it should be said that immunotherapy has a beneficial effect on the course of the pathological process. Moreover, it is known that a high level of IL-6 can interfere with effective immunotherapy.[4,6,8,11,14] Therefore, its measurement is necessary for carrying out polychemotherapy and immunotherapy. IL-6 is also referred to as intermediate cytokines, which in turn indicates the dominance of TX2-type cytokine production.[3,13,17,20] Thus, carrying out EIPHT with immunotropic drugs in the PCT complex in patients with OC with the presence of tumor intoxication causes positive dynamics of the main parameters of the immune system, as well as a decrease in the level of an important serum cytokine, like IL-6, which has pronounced proliferating properties.[4,7] Thus, the evaluation of the functional state of the interferon system is the study of the content of the interferons themselves.[1,6,19] The study of the state of mediators of the immune system during malignant processes undergoes certain difficulties, which are expressed in the instability of the oncological process, in the presence of various forms and morphological variants of the disease. In this regard, the study of cytokines in patients with OC is not only scientific, but also of practical importance for assessing the state of the immune system and predicting the disease. As is known, the interferon system is an integral part of the immune system, which provides for the coordination of the proliferation, differentiation and activation of the effector cells of the immune system. As it is known, the inclusion of EIPHT with the use of immunotropic drugs in the complex of accompanying treatment is one of the ways to reduce endogenous intoxication during antitumor drug therapy. IFN-γ is a cytokine produced by TX1 - type, and has antiviral and tumororic activity, activates monocytes and macrophages, natural killers (cytotoxicity), proliferation and differentiation of T-lymphocytes, inhibits tumor growth, proliferation, proliferation of B-lymphocytes.[2,9,10,16] The study of IFN-γ revealed a slight decrease in its groups of patients with ryumenia before and after treatment without the use of immunotherapy. The analysis showed that in the groups of patients with OC, to whom EIPHT was performed with cycloferon and taktivin, a significant increase in its serum level was observed. The analysis showed that IFN-γ in the group of patients with OC using cycloferon and tactivin, when compared with the group before treatment and after treatment without using immunotherapy, was increased

3.2 times and 1.8 times, respectively. The highest content of IFN-γ in the serum of peripheral blood was detected in the group of patients after PCT in the complex EIPHT with cycloferon. Obviously, this approach to immunotherapy has a positive effect on the immune system, which is reflected in the immunomodulating effect of IFN-γ, which is an immune or lymphocytic cytokine. The data obtained by us are consistent with the literature data, where the positive effect of carrying out EIPHT is presented, and the use of both drugs, which have immunomodulatory properties, and effectively affect cellular adaptive immunity, was important. As shown above, PCT contributes to an increase in the blood content of pro-inflammatory cytokines, for example, IL-6. Next, the imbalance in the ratio of cytokines: IFN-γ / IL-6. In norm IFN-γ / IL-6 - 1,2. In the group of patients with OC before treatment: IFN-γ / IL-6 - 0.5; in the group of patients after PCT without the use of immunotherapy - IFN-γ / IL-6 - 0.24; in the group of patients with EIPHT + cycloferon - 1.1, and in the group of patients with EIPHT + tactvin - IFN-γ / IL-6 - 0.9. Thus, in groups of patients with EIPHT and immunotropic drugs, there is a positive trend in the state of the immune system, which is reflected in the immunomodulating effect of IFN-γ and a decrease in IL-6. It is obvious that the use of immunotherapy in combination of chemotherapy in our opinion is a justified and effective method that leads to the normalization of immunological parameters of the immune system, improves the immediate results of treatment, leads to a decrease in the intoxication of the disease, leads to a decrease in the clinical manifestations of the disease.

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