INFLUENCE OF AMITOZYN PREPARATION ON ANTITUMOR RESISTANCE AND IMMUNE SYSTEM OF THE ORGANISM

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Introduction. One of the most urgent questions in the present-day oncology is a search of the effective remedies that have an antitumor action. Herbal drugs, possessing low toxicity, marked regulatory functions, and possibility of the long-term use, can be perspective in this regard. Amitozyn preparation is of interest as it has certain antitumor and immunomodulatory effects. In spite of the fact that "Amitozyn" antitumor effectiveness has been studied on the different strains of the experimental tumors (sarcoma-37, lymph sarcoma LIO-1, Gu-rin's carcinoma, Garding-Passi's melanoma), studies directed on elucidation of the antimetastatic preparation action are lacking.

At the same time, for clinical substantiation of the antitumor preparations use, not only evaluation of their direct effect on tumor is very important, but also their influence on the metastasis processes. As after surgical removal of the tumor in clinical practice, survival rate of the patients depends on the metastatic nodes formation and growth in different organs and tissues.

It is well known, the process of tumor growth is accompanied by immunodisfunction that plays determinant role in forming the antitumor organism resistance. Therefore, the use of preparations possessing, along with antitumor action, capacity to renew immune reactions activity of the tumor-bearing organism, can lead to improvement of the long-term results of antitumor treatment.

Consequently, a study of antitumor and antimetastatic action of Amitozyn preparation on metastasizing model of Luis' carcinoma (LC), evaluation of the preparation's influence on average lifetime and also on the certain immunologic indexes of these animals with the aim of substantiation of its use possibility in the patients' treatment schemes, are the purposes of given research.

Material and methods. The experimental researches were conducted on 100 mice of C57Bl/6 line, vivarium breeding of the Institute of Molecular Biology and Genetics of NAS of Ukraine, at the age of 2.0 – 2.5 months, mass – 18-25 g. For LC induction, the tumor cells in number 2.5 x 105/mouse were transplanted intramuscularly - 0.2 ml in the mice' thigh. The animals were divided into the next groups: control – the animals with LC and they obtained 0.2 ml of distilled water, and experimental group – the animals with tumors and they obtained Amitozyn preparation injections (100 mg/mouse, subcutaneously, in a day, total dose – 10 injections). The antitumor and antimetastatic action of the preparation was evaluated by comparing sizes of the primary tumor node, number and sizes of metastases. Along with antitumor action of the preparation, its influence on certain immunity system indexes has been studied. Endocrine thymus function, serum interferon level (IF), intensity of immune response on immunization, state of the natural organism resistance, adhesive macrophage properties of peritoneal exudate and hematologic indexes have been determined. The results were statistically worked out with ι-criterion use.

Investigation results. Influence of the investigated preparation on blastoma process development depends on its dosage schedule. Thus, "Amitozyn" preparation introduction (from 7^{th} day after subinoculation) had no essential effect on the tumor growth and on average lifetime of the tumor-bearing animals. But its introduction from the 13^{th} day – inhibited tumor growth, on the 15-19^{th} days after subinoculation on 36-39% and less on further observation stages achieving minimum value (17%) on the 44^{th} day of the observation. Average lifetime of these animals in the control group was 40.84±1.74 days and in the experimental group – 44.18±2.85 days. Introduction of the preparation from the 5^{th} day after tumor cells subinoculation had no essential influence on the primary tumor growth, but slightly decreased metastasis intensity of the animals in experimental group.

As results of our researches showed, tumor process development leads to significant thymus endocrine dysfunction that reveals in TSF level decreasing on all research stages in the control group of animals comparing to intact animals.

Under “Amitozyn” preparation influence, TSF level in the circulation significantly increases on the 25th day after tumor subinoculation. The animals of experimental group had high level of this hormone remained on the 33rd day of the tumor growth process, but it was observed certain decreasing of its level comparing to the previous research stage. TFS level in the experimental group (both on 25th day, and on 33rd days) was even higher comparing to intact animals.

At the observation of serum IF content in the control and experimental groups, it was determined that “Amitozyn” was the inducer of interferon. Thus, in 2 days after the last injection of the preparation (that corresponded with the 25th day of the tumor growth), sufficiently high IF level was registered in the blood serum of the animals in experimental group: IF titer at this stage was equal 1:32 - 1:64, whereas in the control group it was practically absent (<1:2). On 33rd day after subinoculation, although IF level decreased comparing to the previous research stage (up to 1:16), but was still higher then in control group.

The tumor process development leads to decreasing of the antibody-forming cells number in the spleen of animals with LC comparing to intact animals ($P<0.05$). “Amitozyn” preparation introduction facilitated certain increase of antibody-forming intensity in the spleen (1.3 times) on the 25th day after tumor subinoculation comparing to control group of animals, but the difference was not essential.

The animals with tumor had considerably decreased peritoneal macrophages’ adhesive characteristics comparing to intact animals both on 25th day, and on 33rd day after subinoculation. Introduction of Amitozyn preparation to the mice with LC had no essential influence on macrophages adhesion: this index in the experimental group of animals was the same as in control group, both on the 25th, and on 33rd days after subinoculation.

“Amitozyn” preparation introduction had no essential influence on the number of big granular lymphocytes and monocytes in peripheral blood of mice with Luis’ carcinoma, but prevented from decreasing of the lymphocytes number

in the tumor development process and preserved complete neutrophils number within its boarders of the intact animals.

Conclusion. Thus, in the following conditions of the experiment arrangement and using mentioned experimental tumor model, Amitozyn preparation does not reveal evident antitumor and antimetastatic action, but possesses certain activity in thymus endocrine function and interferon production increasing. This fact substantiates the appropriateness of continuation the experimental researches, directed on further studies of the Amitozyn preparation antitumor and antimetastatic action at the other conditions of the experiment arrangement, on the one hand, and on the other hand – the obtained data substantiate the appropriateness of its clinical use as recurrence and metastases prevention after conduction of the basic course of treatment.