

MANAGING THE BUSINESS ACTIVITY OF THE MEDICAL CENTER FOR CANCER TREATMENT

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ABSTRACT

***Aim of the Study:** The study included 200 women with stage IIB–IIIA MP RG (T2N1M0, T3N0M0, T1N2aM0, T2N2aM, T3N1M0, T3N2aM0). The patients were divided into 2 groups – the main group (n=103) and the control group (n=97). All patients underwent NPHT according to the standard FAC scheme, which includes cyclophosphamide, which is administered at the rate of 500 mg/m², 5-fluorouracil-500 mg/m² and doxorubicin-50 mg / m².*

***Methodology:** All patients were examined in full: standard clinical laboratory examinations, x-ray examinations-mammography in direct and lateral projections, axilography, complex ultrasound examination of the breast and breast cancer, computed tomography of the chest and abdominal cavity, pelvis.*

***Conclusion:** Patients of the control group were given 4 courses of npht according to the FAC scheme, after which control mammography was performed in order to assess the effect of the therapy and plan further treatment. When a positive effect was detected – a reduction in the size of the primary tumor and/or a reduction in the size of metastatic RLV or stabilization of the process, patients underwent radical surgery. When the primary tumor or metastatic RLV progressed, the patients changed the PCT scheme with subsequent individualization of the treatment plan.*

Keywords: Entrepreneurship, Innovation System, Risk Management, Stock, Component, Formation.

INTRODUCTION

One of the most significant types of treatment for all malignant diseases is chemotherapy. In RGS, the appointment of systemic antitumor therapy largely depends on the subtype of the tumor. There are more than 30 different schemes of PCTs, which are based on the organotropicity of drugs and individual sensitivity of tumors to treatment. If it is impossible to determine the individual sensitivity of the tumor, the PCT schemes include drugs that act on different phases of the cell cycle.

The effectiveness of chemotherapy has already been repeatedly proven, but there remains a significant portion of patients with RGS who are poorly or not at all sensitive to it. The main reason for the low effectiveness of treatment is considered to be the resistance of the tumor to cytostatic drugs. Increasing the effectiveness of PCTs is both to overcome drug resistance and to increase the sensitivity of tumor cells to chemotherapy drugs. When using PCTs, it is necessary to exclude the possibility of developing resistance, because such treatment is dangerous in terms

of the probability of stimulating the growth of resistant clones and the rapid development of distant metastases. So, the choice of adequate systemic antitumor treatment is now considered as one of the main ways to improve the effectiveness of treatment of RGS. One of the most common chemotherapy regimens for the treatment of RGS is FAC, which includes doxorubicin, cyclophosphamide, and 5-fluorouracil.

Doxorubicin (doxorubicin) refers to antitumor antibiotics, anthracyclines, and related compounds. The main pharmacotherapeutic effect is a high antitumor and anti-leukemic effect, the mechanism of which is based on the intercalation of doxorubicin into the cell deoxyribonucleic acid (DNA) molecule and the effect on the cell membrane, highly active relative to a large number of tumors of various localization and leukemia.

Side effects and complications when using doxorubicin are cardiotoxicity and myelosuppression; alopecia (usually reversible), possible hypersensitivity to the drug with allergic manifestations, vascular disorders in the form of phleboscrosis, loss of appetite, nausea, vomiting, redness around the vein with rapid administration; in the case of extravasation, necrosis of the surrounding tissues may occur. Contraindications to the use of doxorubicin are leukopenia, thrombocytopenia, anemia, myocarditis, acute myocardial infarction (severe heart rhythm disorders), acute hepatitis, tuberculosis, gastric ulcer, bilirubinemia, pregnancy, severe liver and kidney function disorders (Lam, 2017).

Cyclophosphamide-refers to alkylating compounds, antineoplastic agents. Farmacoterapeutica the main effect of cyclophosphamide is pronounced cytotoxic, antitumor, and immunosuppressive activity; antitumor activity is achieved by its biotransformation by phosphatases to the active metabolite, which leads to disruption of cell activity and blocks their mitotic division; the nuclei of the hyperplastic cells (tumor) tissues and lymphoid tissue have high sensitivity to the action of cyclophosphamide (Cardoso, 2005).

Side effects and complications when using cyclophosphamide may be leukopenia, anemia, thrombocytopenia; cardiotoxic effect; nausea, vomiting, diarrhea, stomach pain; menstrual cycle disorders, amenorrhea, azoospermia, hemorrhagic cystitis; alopecia, hyperpigmentation, internal hemorrhage, muscle and bone pain, chills, headache, vertigo; interferes with ovulation and spermatogenesis and may cause infertility in men and women; those who were treated with cyclophosphamide at prepubescent age may later have children.

Contraindications to use are anemia, leukopenia (white blood cell count $<3, 5 \times 10^9/l$), thrombocytopenia (platelet count $<120 \times 10^9/l$), cachexia, heart failure, severe liver and/or kidney disease, hypersensitivity to the drug (Van Den Broeke, 2013).

Fluorouracil-refers to antineoplastic agents, antimetabolites, structural analogues of pyrimidine. This is a cytostatic antitumor agent, a structural analog of pyrimidine; antitumor activity is due to the conversion in tissues to active metabolites, including 5-fluorodeoxyuridine and 5-fluorouridine; 5-fluorodeoxyuridine, which inhibits thymidylate synthetase and blocks the reaction of deoxyuridylic acid to thymidylic acid, which leads to a deficiency of thymidine and inhibition of DNA synthesis. 5-fluorouridine is embedded in ribonucleic acid (RNA) instead of uridine, which leads to a violation of RNA processing and protein synthesis; fluorouracil suppresses the growth of epithelial neoplasms, and to a lesser extent acts on tumors of glandular origin (Koshkin, 2018).

METHODOLOGY

Side effects and complications when using fluorouracil are anorexia, vomiting, diarrhea, stomatitis, esophagitis, leukopenia, thrombocytopenia, anemia, hemorrhages, less frequently observed dermatitis and alopecia, hyperpigmentation; the effect on hematopoiesis is manifested in some cases in the middle of the course, and 8-14 days after the end of the course of treatment; possible pain in the heart, accompanied by changes in the cardiogram for ischemic type, angina, thrombophlebitis; possible neurological disorders, dizziness, ataxia, tremor, optic neuritis, headache, nystagmus, visual impairment, euphoria, disorientation; amenorrhea, azoospermia; urticaria, bronchospasm.

Contraindications to the use of fluorouracil are hypersensitivity to the drug, inhibition of bone marrow function, especially after radiation therapy or treatment with other antitumor drugs, significant deviations in the number of shaped elements in the blood, bleeding, stomatitis, ulceration of the oral mucosa; severe diarrhea; severe liver and/or kidney function (plasma bilirubin level > 85 mmol/l); severe infectious diseases; severe exhaustion.

Recently, IN the treatment of RGS, npht has become relevant, which allows us to expand the indications for performing radical OZO and RVO and improve long-term treatment results. When using NPHT, you can achieve maximum devitalization of the tumor, which allows you to reduce the proliferative potential of cancer cells, increase the ablation of surgical interventions, and reduce the risk of relapses and metastasis.

Potential advantages of NPHT are: reduction of the biological activity of tumor cells both in the tumor focus and in its micro-and macro-metastases, creation of favorable conditions for surgery, and reduction of the probability of generalization of RGS. It is also important to determine the sensitivity of the tumor to a specific treatment regimen after NPHT, in order to individualize postoperative (adjuvant) therapy, to abandon ineffective regimens and prescribe more effective chemotherapy.

RESULTS AND DISCUSSION

NPHT is indicated primarily for patients with locally common, primary inoperable, edematous-infiltrative and inflammatory forms of RGS. But it is also used for operable RGS to "*Reduce the stage*" of the tumor process and create conditions for the implementation of OSO. The current standard of treatment for RGS is to use 2-6 courses of NPHT. Adjuvant systemic PCT (APCT) remains very relevant.

The use of APCT helps to reduce the risk of disease progression. The signs that indicate the need for the use of APCT include: low expression of hormone receptors ER and Pg, a high degree of malignancy or a high level of "*Proliferative*" markers, large tumor size and widespread peritumoral vascular invasion. PCT schemes that include the use of anthracyclines, as well as DNA-destructive drugs (CAF, CEF, AC schemes) remain appropriate, especially in the treatment of patients with "three times negative" tumors-ER (-), Pg (-), NR2/neu (-).

Optimization of cytotoxic therapy of RGS is one of the most promising ways to improve treatment results. Developments in this area make it possible to potentiate the effectiveness of PCTs by: first, creating new chemotherapy drugs; second, improving methods of drug transport to the tumor; third, using CT modifiers; and fourth, assigning individualized chemotherapeutic regimens.

Many chemical modifiers have now been studied. For example, the effectiveness of using hydrogen peroxide as a modifier of chemotherapy drugs in patients with RGS with resistance to first-line chemotherapy was revealed.

To increase the effectiveness of neoadjuvant antitumor therapy, it is important to overcome drug resistance. Therefore, increasing the effectiveness of antitumor therapy today is seen in increasing the sensitivity of tumor cells to cytostatic drugs, for which modifiers are used. In recent years, in order to modify chemotherapy, various physical factors are used – hyperthermia, pressure oxygenation, etc. The effect of which is associated with an increase in blood flow to the tumor and saturation of the latter with oxygen (Abramov, 2017). The modifying action in this case consists of the following points: increasing sensitivity to chemotherapy drugs; reducing the ability of cells to repair sublethal and potentially lethal damage; damage to cells that are in the resistant phase of the mitotic cycle (late S-phase).

Work was carried out to study the effectiveness of treatment of patients with MP RGS using neoadjuvant system-selective polychemotherapy in combination with a chemiomodifier (calcium gluconate). The data obtained from experimental studies using RGS cell cultures in vitro and the direct results of treatment proved the feasibility and safety of using calcium gluconate as an important component of the therapy scheme developed by the authors.

There are certain contraindications to medical treatment. One of the most important factors for the possibility of special treatment is the assessment of the General condition of the patient. To simplify this procedure, certain scales have been developed that serve to assess the quality of life and dynamics in the treatment process. Basically, the karnovsky scale is used, which determines the overall status as a percentage-from 100 % at full (normal) activity to 0 % (fatal) with gradations of 10 %, and the ECOG-who system in points - from 0 (normal activity) to 4 (the patient is unable to serve himself, is bedridden). It is considered the most correct to include in clinical trials patients with an activity index on the karnovsky scale of at least 70% and the ECOG-who scale – no more than two points.

Contraindications to special treatment of patients with RGS are:

1. State on the ECOG scale of 4 points;
2. Severe condition of the patient due to decompensated disorders of the liver, kidneys, endocrine glands;
3. Severe leukopenia, agranulocytosis, anemia.

One of the most powerful modifiers of chemotherapy is hyperthermia (GT). Its effectiveness has been proven by years of research. As early as about 500 BC, the Greek physician Parmenides said "*Give me the power to cause a fever, and I will cure all diseases*", which became the motto of doctors engaged in GT (Carlson, 2012).

The first mention of the effectiveness of GT in Oncology dates back to 1779, when de Kizowitz described the inhibition of tumor development by fever caused by malaria (France). In the XXI century, the study of the effects of hyperthermia was continued, and the work of the XX century caused significant changes in the consciousness of the world cancer community and the perception of hyperthermia as a method of treating cancer.

In 1866, Bush W. in Germany successfully treated cancer with fever caused by artificial infection; in 1898, Westermarck F. successfully studied the effect of a hyperthermic bath in cervical cancer. In the early twentieth century, in 1912, Muller C. (USA) successfully combined hyperthermia and radiotherapy in 100 cases; in 1927, Westermarck K. conducted experiments on rats using local hyperthermia, in the same year Wagner-Jauregg J. received the Nobel prize in

physiology or medicine for the discovery of the therapeutic effect of malaria infection in the treatment of progressive paralysis. In 1947 Moritz A. R. and Henriques F. C. in the United States published the work "*Study of heat damage*". In 1964, von Ardenne M. investigated the effectiveness of a two-chamber hyperthermic bath with head cooling. For the first time in 1965, Holland U., Freireich E. and Frei E. (USA) proposed the principle of combined chemotherapy, and von Ardenne M. the concept of thermometabolic cancer therapy.

The following year, von Ardenne M. developed a heat exchanger for General extracorporeal hyperthermia, and in 1968 he proved the thermosensitivity of tumor cells in acidification. In 1969, the Stehlin J. and R. Cavaliere (Italy) performed the first regional chemohyperthermic perfusion. In 1971, Westra A. and Dewey W.C. (USA) conducted experimental studies on hyperthermia in mammalian cells. In 1975, under the chairmanship of Robinson E. J., the first international Symposium on hyperthermia in Oncology was held in the United States. In 1975, von Ardenne M. he developed the first hyperthermic high – frequency device, the Seplectotherm, and in 1977 proved the reduction of tumor microcirculation in hyperthermia and hyperglycemia. In 1979, a prototype of the thermotron hyperthermic unit was created in Japan. In 1982, hyperthermia was first used in the United States for the treatment of prostate adenoma. In 1984, Japan released the device "*Thermotron*" (company Yamamoto Vinita Co), which was allowed to use. In 1984,

Overgaard K. in Denmark, published the book "*Hyperthermia in Oncology*", and in 1985 the international journal of hyperthermia was established in the UK. In 1985, von Ardenne M. in Germany developed the first hyperthermic system for General near-infrared hyperthermia-IRATHERM. In 1987, the European Union of hyperthermic Oncology (ESHO) was formed in the UK. In 1994, von Ardenne M. published the results of phase 1 clinical trials of SMT and "Principles and Concepts of SMT", and in 1997 he published the monograph "Systemic multi-stage cancer therapy". In 1998 OncoThermKft's ehy-2000 hyperthermic system has entered the market. In 1999, ESHO (the Netherlands) proved that hyperthermia increases the effectiveness of radiation and chemotherapy, and hyperthermia began to be used as the main type of treatment for cervical cancer. In 1999, BSD MedicalCorp (USA) launched the BSD – 2000 hyperthermia system.

In 1999, the European conference on hyperthermic Oncology was held in Rotterdam (the Netherlands), where the results of 10 studies on the effectiveness of combined hyperthermic and chemotherapeutic treatment of a number of tumors, including RGS, were presented. Studies have shown that the combination of chemotherapy and hyperthermia increases survival and improves the results of radiation treatment in combination with hyperthermia (Loprinzi, 2012).

In 2000, the LANCET in Germany published an article on the effectiveness of GT in rectal cancer, and published data on the success of hyperthermia in the treatment of cervical cancer.

In 2001, P. K. Sneed, at the annual NAHC conference, reported on the results of stage III randomized clinical trials of the use of radiation therapy and hyperthermia in combination. The rate of complete remission of melanoma after radiation therapy with hyperthermia was 46% vs. 28 % for isolated radiation therapy, 60% vs. 38 % for relapse of RGS, 83% vs. 57% for late – stage cervical cancer, and the 2-year survival rate for glioblastoma was 31% vs. 15% for isolated radiation therapy. In 2001, R. Issels from the University of Munich (Germany) published a paper "*Hyperthermia and hypoxia for the destruction of cancer cells*", which deals with a combination of hyperthermia and chemotherapy in 59 patients with soft tissue sarcomas, which increases the 5-year survival rate.

CONCLUSION

In 2002, Nakahata K. from the University of Nagasaki (Japan), received data on the "Mitotic Catastrophe" in malignant tumors after GT, and normal cells remained intact, on the basis of which it was concluded that GT damages the DNA structure of malignant cells, they lose the ability to divide. In 2003, M. Wesolowski, ESHO (Germany) proved that GT increases the survival rate of children with cancer. In 2004 Das Handelsblatt In Germany successfully combined hyperthermia and chemotherapy and concluded that cancer was winning in Germany.

In 2005, Amsterdam published a report on 90 % complete remission with a combination of hyperthermia, radiation and chemotherapy for cervical cancer. In 2006, the American Cancer Society (USA) reported that hyperthermia comes to the fore in the treatment of GP tumors. In the same year, ESTRO (Germany), the European Convention on radiation Oncology focuses on the use of targeted GT, Microsoft. Fitness Magazine (USA) publishes a paper on complete remission in breast cancer in 2/3 of patients after a combination of radiation therapy and hyperthermia. In 2006 The Society of Thermal Medicine (USA) recognizes hyperthermia as the most powerful known radiosensitizers. Boston Globe (USA) suggests that hyperthermia may be one of the most powerful remedies against cancer. At the same time, the Journal of Clinical Oncology (USA) published data on an almost three-fold increase in the effectiveness of treatment of primary and recurrent RGS in the combination of radiation therapy with GT compared to isolated radiation therapy (from 24 to 68) %. in 2007, the hyperthermic system Celsius TCS was launched in Germany. Since 2007 to this day, American standards for the treatment of cancer patients recommend GT for recurrent RGS.

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