Kuchynska Mariia
Kyiv National University of Technologies and Design (Kyiv, Ukraine)
Language and scientific supervisor – Denysenko V., senior lecturer

HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) CYTOREDUCTIVE SURGERY

This topic is about hyperthermic intraperitoneal chemotherapy (HIPEC) cytoreductive surgery, a multimodal therapy concept that is increasingly being used to treat peritoneal carcinoma. There are various therapeutic options for patients with peritoneal carcinoma, but this topic will be about the use of HIPEC. This activity describes and explains the role of the interprofessional team in improving the care of patients who have undergone HIPEC [1].

While primary peritoneal mesothelioma is rare, peritoneal carcinomatosis: PC (tumorous infiltration of the peritoneum) is most commonly seen in abdominopelvic malignancies. This is a common manifestation of gastrointestinal and gynecological malignancies during tumorigenesis, as some gastrointestinal and gynecological malignancies can progress to the abdominal cavity [2].

Worldwide, 240,000 women are diagnosed with ovarian cancer each year, and epithelial carcinomas account for about 90% of all cases. Ovarian cancer is often classified as a peritoneal surface malignancy due to its clinical presentation and, unfortunately, in late stages [3].

Treatment should be multimodal and include preoperative systemic chemotherapy, complete cytoreductive surgery, and intra-abdominal hyperthermia combined with intraoperative chemotherapy.

First described by Spratt in 1980 in animal experiments and known as the infiltration heat transfusion system, hyperthermic intraperitoneal chemotherapy is a multimodal therapy concept that has been increasingly used in the treatment of peritoneal carcinoma and in subsequent decades, is now an integral part of treatment. primary and secondary tumors of the peritoneum. This involves the

introduction of cytotoxic agents into the abdominal cavity at a high temperature (41–43 degrees C) to facilitate their absorption by neoplastic nodules [4].

Currently, surgical cytoreduction combined with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) has radically changed the approach to patients with malignant peritoneal tumors, which has improved the prognosis of appendicular, colorectal, ovarian, and peritoneal mesothelioma.

After the administration of cytostatics into the abdominal cavity, there is a difference in the concentration of the cytostatic between the peritoneal cavity and the plasma, which is associated with a relatively slow movement of the drug from the abdominal cavity into the plasma (peritoneal clearance) and is explained by the existence of the peritoneal-plasma barrier (Sugarbaker 1996).

Interestingly, surgical removal of the affected peritoneum does not affect the pharmacokinetics of intraperitoneal chemotherapy.

The outflow of blood from the surface of the peritoneum occurs through the portal vein to the liver, ensuring an increased effect of cytotoxic drugs on potential micrometastases in the liver.

Higher drug concentrations are observed in lymph than in plasma because the lymphatics transport some drugs to the systemic circulation, a second beneficial effect of intraperitoneal chemotherapy.

Some authors (Van der Speeten K et al.) refer to the three-compartment model, which includes the peritoneum containing the tumor as a third compartment where the drug enters the tissue.

The hyperthermia association is justified by the fact that malignant cells are selectively destroyed by hyperthermia in the range of 41 to 43 degrees Celsius. In addition, the microcirculation in most malignant tumors shows complete vascular stasis in response to hyperthermia. The combination of heat and cytotoxic drugs leads to increased cytotoxicity, which leads to increased absorption of the drug by malignant cells due to increased membrane permeability. Thus, the most important effect of hyperthermia is a synergistic effect with some cytostatics. A synergistic effect was described for doxorubicin,

cytostatics containing platinum, mitomycin C, melphalan, docetaxel, irinotecan, and gemcitabine (Sugarbaker PH, etc.).

Before starting the procedure, a preoperative assessment is required according to WHO recommendations. This evaluation should include medical and surgical history, evaluation of tumor generalization, history of preoperative or neoadjuvant chemotherapy, and analysis of cardiopulmonary examinations. Current treatment should also be noted, including the consumption of anticoagulants to minimize the risk of bleeding during surgical cytoreduction, as this is a major operation that will precede the act of HIPEC.

The patient must understand the advantages and disadvantages of the operation, as well as the benefit-risk ratio of HIPEC, as the procedure should be able to improve the survival of the cancer patient. A detailed description of the procedure is necessary to obtain informed consent from the patient.

The role of the anesthesiologist is important during cytoreduction and HIPEC. Special training is preferred.

Finally, this procedure must be performed in a qualified university center that specializes in medical-surgical oncology and is equipped with an appropriate medical surveillance infrastructure.

Before starting this procedure, the hospital must have a chemotherapy approval infrastructure equipped with a surgical infrastructure linked to a medical-surgical intensive care unit for patient monitoring.

HIPEC can be performed on an open or closed abdomen. In both perfusion models, the abdominal cavity is continuously perfused with a cytostatic solution heated to 41–43 degrees C through a drainage system consisting of inlet and outlet catheters.

Thus, this procedure requires the following equipment:

A heat exchanger connected to a thermostat to maintain a stable temperature of 42 degrees in extracorporeal circulation;

Output and inflow catheters to ensure infusion and absorption of cytostatic in the abdominal cavity;

Temperature probes that measure the temperature in the circuit and peritoneum;

Roller pump to support extracorporeal circulation of cytostatics; Reservoir of cytostatics;

A computer system that controls the heat exchanger and drainage pumps according to the thermoprobes;

A timer that measures the time of infusion;

Cytotoxic drugs used for intra-abdominal chemotherapy include mitomycin C, platinum, doxorubicin, paclitaxel, and irinotecan.

The chemical preparation is used with a carrier solution (mainly 0.9% NaCl or 5% glucose). The volume of the carrier solution is calculated based on the surface area of the body. Infusion volumes from 1.5 to 2 liters/m^2 of body surface are usually used.

Technique or treatment

In general, two methods of HIPEC have been described: the open abdomen technique and the closed abdomen technique.

Open Abdominal Technique: As described by Sugarbaker, at the end of surgical cytoreduction, a Tenckhoff catheter and four closed suction drains are sutured to the skin and inserted through the abdominal wall. Temperature probes are attached to the edge of the skin for intraperitoneal temperature monitoring. The skin edges at the level of the abdominal incisions are suspended to a self-retaining Thompson retractor with a monofilament to maintain free space in the abdominal cavity. To prevent leakage of the chemotherapeutic solution, a polyethylene sheet is inserted into this seam.

The surgeon's continuous perfusion manipulations make it possible to evenly affect all anatomical structures with heat and chemotherapy during the procedure. A pump system injects chemotherapy into the abdomen through a Tenckhoff catheter and draws it through constant-flow drains. The heat exchanger maintains the temperature of the intraperitoneal fluid at the level of 41 to 43 degrees, then the drug is introduced into the circuit and the timer for

perfusion is started. Duration varies from 30 minutes to 1 hour depending on the type of cancer.

The disadvantage of the open method is the dissipation of heat, which complicates the presence of a hyperthermic state.

Closed-abdominal technique: Thermal catheters and probes are placed in the same manner, but the laparotomy skin edges are tightly sutured to ensure closed-loop perfusion. To evenly distribute the heat, the surgeon shakes the abdominal wall manually during the infusion. In this technique, the perfusate volume is larger for contouring, and a higher abdominal pressure is achieved during perfusion, which facilitates drug penetration into the tissues. After the infusion, the abdominal cavity is opened again to remove the perfusate and prepare the anastomosis. This technique allows you to maintain the rapid achievement of hyperthermia, since heat loss is minimal.

REFERENCES

1. Marz L, Piso P. (2015)Treatment of peritoneal metastases from colorectal cancer. Gastroenterol Rep (Oxf). Vol. 3, no. 4. P.298-302.

2. Segelman J, Granath F. (2012) Incidence, prevalence and risk factors for peritoneal carcinomatosis from colorectal cancer. Br J Surg. . Vol.99, no. 5. P. 699-705.

3. Webb PM, Jordan SJ. (2017) Epidemiology of epithelial ovarian cancer. Best Pract Res Clin Obstet Gynaecol. Vol. 41. P.3-14.

4. Jacquet P, Sugarbaker Ph. (1996) Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Cancer Treat Res. Vol. 82, no.3 P.59-74.