INNOVATIVE METHOD OF CANCER TREATMENT - AEROSOL CHEMIOTHERAPY UNDER PRESSURE

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ABSTRACT

The incidence and death rate due to cancer is constantly increasing. Cancer affects not only the elderly, as one of the effects of an aging population, but also of young people, due to the increased rate of metabolism or genetic predisposition to malignancy of the cancer. The basic method of treatment of malignant tumor is chemotherapy, used in several ways, including intravenously, orally and intraperitoneally. The new method of delivering drugs directly to the abdominal cavity, producing a pressure gradient and spraying the chemotherapeutic directly into neoplastic changes is PIPAC (Pressurized Intraperitoneal Aerosol Chemotherapy), i.e. Intraperitoneal Vacuum Chemotherapy Aerosol. The method was developed by Professor Marc Reymond from the University Hospital in Tübingen. Its aim is to improve the quality and extend the lives of patients in a palliative state. Therapy is used in patients with stomach, ovarian and large intestine cancer, it also aims to induce regression of metastases to the peritoneum. The aim of the work is to present innovative PIPAC therapy in the context of application, course and assessment of the effectiveness of the method based on the available scientific literature.

BACKGROUND

Malignant neoplasms in Poland are the second most common cause of deaths - as a result of these diseases, about 96,000 Poles die annually, which accounts for 25% of all deaths. Colorectal cancer and stomach cancer are among the five most common malignancies in the world [17]. From a clinical point of view, their tendency is to easily spread and metastasize to the peritoneum. This condition is referred to as peritoneal cancer (PC). The average survival time for peritoneal carcinoma is 6-12 months [18]. The main reason for this is the poor penetration of chemotherapeutics used intravenously, which is related to the existence of the blood-peritoneal barrier. PIPAC or Pressure Intraperitoneal Chemotherapy in Aerosol is an innovative combination of laparoscopy techniques with a modern method of drug delivery in the form of properly dispersed drops of aerosol under pressure, inducing regression of tumor metastases to the peritoneum. It is a technique that supports treatment with both intravenous chemotherapeutics and may help support surgery. Peritoneal cancer is a significant clinical problem in contemporary oncology and oncological surgery. The term refers to the phenomenon of metastasis and uncontrolled, rapid tumor growth within the peritoneal cavity, most often cancer: ovary, stomach, large intestine, pancreas, gall bladder and several other tumor subtypes, including primary ones [5,13]. In colon cancer, metastases to the peritoneum can be observed in approximately 15% of cases [15]. Metastasis to the peritoneum is associated with poor prognosis. The pioneering treatment, for the first time in the world, was made in 2011 in Germany by a team led by Prof. Marc Reymond. This technique gives clinical hope for lengthening and increasing the comfort of life for patients who were still low to 30/30 years ago with no major therapeutic options. 800 treatments have been performed all over the world. Poland is in the group of 15 countries that are leaders in the dissemination of the PIPAC method. Currently, the procedure is performed in 20 countries, mainly Western Europe, and for the first time in this part of Europe and for the first time in Poland, it was performed on May 10 at the Oncology Center named after Prof. F. Łukaszczyka in Bydgoszcz at the Department of Cancer Surgery CM UMK a team of doctors composed of: Professor Wojciech Zegarski, PhD MD and Maciej Nowacki, PhD.

CANCER TREATMENT METHODS AND PIPAC

PIPAC treatment is used as a neoadjuvant therapy before CRS and HIPEC. Neoadjuvant treatment - treatment preceding radical surgery or radical radiotherapy. It aims to destroy the alleged metastases or to reduce the tumor mass. HIPEC is the procedure for intra-peritoneal perfusion chemotherapy in conditions of elevated temperature along with the surgical removal of the affected tissue, while the basic idea of CRS is the removal of all macroscopically visible tumor foci [6, 14]. Unfortunately, the CRS and HIPEC procedure as aggressive surgical methods, burdened with the possibility of a wide range of perioperative complications are not the methods of choice in all patients diagnosed with an advanced degree of neoplastic changes within the peritoneum, especially in the elderly, in a poor clinical condition not allowing for full surgical intervention [5, 7, 14]. In addition, both methods carry moderate improvement and often not the best prognosis. Although systemic chemotherapy has made tremendous improvements in the treatment of systemic metastases (especially of the liver and lungs), it appears to be much less effective in peritoneal dissemination, mainly due to pharmacokinetic limitations, probably due to poor peritoneal vasoconstriction that hinders normal drug distribution [6,7]. In a systematic review of literature on complications resulting from the use of both methods, it has been demonstrated that in large specialist centers, the prevalence is 12-52%, while the mortality rate is 0.9-5.8% [16]. In contrast, commonly known tumor markers are ineffective in diagnosing and evaluating response to treatment [3]. PIPAC can be used to improve the results of CRS and HIPEC, to select patients with chemosensitive tumors, to extend the indications of CRS and HIPEC and to reduce the scope of cytoreductive surgery [5]. Considering the pharmacokinetics of HIPEC restriction, PIPAC may be an alternative to patients who are not eligible for radical treatment with HIPEC [7, 9].

PREPARATION OF THE PATIENT

The patient who will be subjected to the PIPAC method of delivering the drug first of all goes through many consultations. Clinical oncologists with surgeons are qualified for this procedure. He comes to the clinic usually one two days before surgery. All basic research and supplementary examinations are performed. The patient is admitted to the surgery clinic. The feeding regime is maintained. Then it is anaesthetized as for a standard surgery. After the surgery, the patient can return home very quickly. Staying in the hospital after applying the procedure is about 3 days. The treatment can also go several times at intervals of six to two weeks, which is a plus of this method [10].

THE COURSE OF THE PROCEDURE

The procedure is performed under general anesthesia in standard operating room conditions. Initially, several biopsies are taken from cancer nodes for further histopathological examination. As a rule, two trocars are used, which, through appropriately made small cuts, with a diameter of 5-12 mm within the abdominal wall, allow to create conditions for insufflation and access to the camera and device spraying therapeutic substances so-called. "Nebulizer" (Figure 1). Then for 30 minutes in the abdominal cavity spray is sprayed under pressure in the process of so-called "Snow storm" in the CAWS system - a closed aerosol discharge system [5, 8, 11]. Spraying causes the drug to reach all corners of the abdomen and directly go to those tissues that are covered with cancer [5]. The pressure in the range of ~ 1500 kPa increases local penetration of tissues and allows to obtain high concentrations of gas molecules within the tumor. Currently recommended doses of aspirated chemotherapeutics are: oxaliplatin, 92 mg / m^2 of body surface area, in colorectal cancer and doxorubicin 1.5 mg

/ m^2, cisplatin 7.5 mg / m^2 in case of cancer with other ethiology [8, 12].

After completing the drug delivery process, the gas from the abdominal cavity is completely aspirated (removed) and the skin incisions for the trocars are closed using standard layered sutures. The entire procedure usually takes about 90 minutes. The PIPAC procedure is also possible to use it as a few-minute supply of medicine between treatments, i.e. supply in the diagram.

THE ADVANTAGES OF THE METHOD

In many scientific studies, a positive therapeutic response and a slowdown in the progression and growth of tumor cells has been demonstrated, which may have a significant impact on the improvement of survival and quality of life [11]. This method, due to its minimally invasive nature, is associated with a much smaller number of complications and therapeutic complications associated, for example, with infections, the possibility of a hernia or adhesions, and intraperitoneal supply reduces systemic toxicity. An important aspect of the interaction is better delivery of anti-cancer compounds and control of peritoneal cancer as part of fully personalized and targeted therapy. It is a technique that supports treatment with both intravenous chemotherapeutics and may allow supportive surgery [2, 4, 9].

POSSIBLE COMPLICATIONS AND SIDE EFFECTS

Most adverse events and perioperative complications do not differ from those associated with standard laparoscopic procedures in oncological surgery. The most common complications, about 50%, include: abdominal pain, vomiting and fever. For relatively rare (1%) intestinal injuries caused by attaching trocars, injuries associated with biopsy retrieval. In contrast, very rare complications (<1%) are: an undesirable skin reaction, metastases within the abdominal integuments, i.e. injection sites. It may also lead to a hernia, intestinal obstruction, hematomas, postoperative bleeding and inflammation of the bladder [8].

CONCLUSION

Although the PIPAC technique is an innovative solution, it should be emphasized that it is not an experimental treatment. PIPAC can have a significant advantage over existing chemotherapy techniques that are painful and debilitating and associated with long-term stay in the clinic and high risk of adverse events. Low-dose intraperitoneal chemotherapy in aerosol (PIPAC) with cisplatin and doxorubicin is a form of intra-abdominal chemotherapy that can be used repeatedly and potentially prevents systemic side effects of chemotherapy. A number of studies are currently underway that bring very positive results.

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ABBREVIATIONS

CRS – Cytoreductive Surgery
HIPEC – Hyperthermic Intraperitoneal Chemotherapy
PIPAC – Pressurized Intraperitoneal Aerosol Chemotherapy

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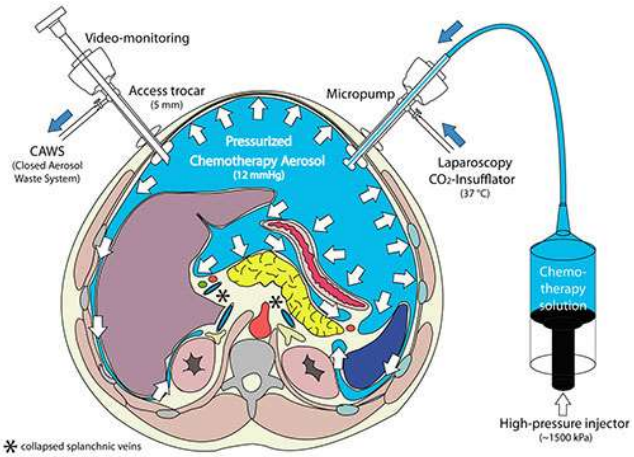
LIST OF FIGURES

FIG. 1. DIAGRAM OF DEVICES USED FOR THE PIPAC TECHNIQUE, TAKING INTO ACCOUNT THE INCISION SIZE, TEMPERATURE AND PRESSURE UNDER WHICH THE PROCEDURE IS PERFORMED [19].

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