TREATMENT OF PERITONEAL CARCINOMATOSIS

LIJEČENJE KARCINOZE POTRBUŠNICE

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Abstract: *Cytoreductive surgery (CS) and hyperthermic intraoperative chemotherapy (HIPEC) is novel approach for treatment of patients with peritoneal carcinomatosis. Ninety four patients with intraperitoneal malignancy undergone cytoreductive surgery (CS) and hyperthermic intraoperative chemotherapy (HIPEC) in UHC Zagreb. Significant improvement in survival of patients was obsereved.*

Key words: *cytoreductive surgery, hyperthermic intraperitoneal chemotherapy*

Sažetak: *Citoreduktivna kirurgija i hipertermijska intraperitonealna kemoterapija (HIPEC) je novi pristup u liječenju bolesnika s peritonealnom karcinomatozom. Devedeset i četiri bolesnika s interperitonelanom karcinozom povrgnuto je navedenom zahvatu u KBC Zagreb. Ovom tehnikom ostvaren je značajan napredak u preživljenju bolesnika.*

Ključne riječi: *citoreduktivna kirurgija, hipertermijska intraperitonealna kemoterapija*

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1. Introduction

Performing surgery for peritoneal carcinomatosis (PC) was always considered only as palliative method. Since 2007, cytoreductive surgery (CS) and hyperthermic intraperitoneal chemotherapy (HIPEC) was introduced at our institution. Survival of patients with PC for nongynecological cancer was less than 6 months [1]. Colorectal cancer patients with PC and palliative treament had considerable less mean survival time, 5-7 months [2, 3], compared to patients treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy resulting in 5-year survival rate 20-53% [4]. Reported median survival for patients with malignant peritoneal mesothelioma in high volume tertiary institution treated without CS and HIPEC was 15 months [5] compared to 75% disease free survival at five years with CS and HIPEC [6]. Even better results are obtained for pseudomyxoma peritonei, resulting in 91% overall survival in 5 years [7]. Metastatic ovarian cancer median survival range from 12-25 months [8], and even in these cases better results are reported [9]. Possibility to perform CS in patients with peritoneal spread has a potential to remove macroscopic malignant diseases present in the abdomen, and combined with HIPEC even microscopic malignancy up to 2.5mm can be annihilated [10].

2. Methodology

94 patients with intraperitoneal malignancy undergone cytoreductive surgery (CS) and hyperthermic intraoperative chemotherapy (HIPEC) in UHC Zagreb for PC between January of 2007 and March 2014. Diagnosis by origin of the primary tumor were: colorectal adenocarcinoma in 17 patients, adenocarcinoma of the appendix in 7 patients, ovarian cancer in 46 patients, pseudomyxoma peritonei in 20 patients, mesothelioma in 2 patients, stomach cancer in 1 patient, and one patient was operated for the PC of the unknown origin. Inclusion criteria were diagnosis of PC based on intraoperative assessment during first operative procedure for intraabdominal malignancy or follow-up diagnostic imaging proof. Excluded were patients with known malignant proliferation outside abdomen and ASA score 4 and higher. All patients underwent cytoreductive surgery, based on principles introduced by Sugarbaker [11], with no macroscopic residual disease left whenever possible, including intestinal resection and lymph node dissection. Removal of the omentum and involved peritoneum was carried on in all patients, this mostly involved both paracolic spaces, pelvis, abdominal wall and both subdiaphragmatic and subhepatic areas. In some patients gastrectomy was necessary due tumor involvement, and colon resections with or without ileostomas. Usually gallbladder, removal of the liver Glisson capsule and splenectomy was peformed. Closed technique hyperthermic intraoperative chemotherapy through 4 abdominal tube drains (2 for inflow, and 2 for outflow) using cisplatin and doxorubicin of perfusate (carrier solution was normal saline in all cases) during 90 min with target temperature of 42.5°C (3 thermocouples in abdomen were used) followed in patients with ovarian cancer, gastric cancer, and mesothelioma cancer. Patients with colorectal cancer, pseudomyxoma peritonei and appendical adenocarcinoma recived mitomycin C or oxaliplatin or combination of

mitomycin C and doxorubicin. Usually after HIPEC bilateral thoracic tubes were inserted in all patients as fluid accumulation in the chest is expected as a result of peritonectomy and HIPEC. Peritoneal carcinomatosis index (PCI) [12] and completeness of cytoreduction scores (CC) were calculated for all patients following procedure. Two of the 94 patients undergone CRS and HIPEC again as a second line treatment in periods two years after the first CRS and HIPEC operations. They recived melphalan as intraperitoneal agent.

3. Results

In evaluated period we operated upon 94 patients, 76 (80,9%) female and 18 (19,1%) male. Range of the operating time was between 225 and 515 minutes. We were not able to achieve complete macroscopic cytoreduction in all patients. Early hospital mortality, defined as death in the first month after operation, was 0,1% (1 patient died 14th postoperative day). Early after operation, one more petient died, 42nd postoperative day, because of development of the thrombocytopenia and anaemia leading to disseminated intravascular coagulopathy in the end. During follow up, 9 patients who undergone CRS with HIPEC at our institution died.

4. Discussion

Combined treatment of local heated chemotherapy, which allows exposure to high drug concentration capable to penetrate tumor nodules up to 2.5mm thickness, and surgical removal of larger tumor deposits results in significantly improved survival in once untreatable patients. Obvious benefits of HIPEC are: higher intraabdominal concentration which helps to overcome chemoresistance, decreased systemic concentrations resulting in decreased side effects [13] in the management of ovarian cancer. As described by Sugarbaker et al. [14] peritoneal spread occurs first in subdiaphragmatic areas, pelvis and greater and lesser omentum, latter in subhepatic, retrohepatic and paracolic space and Treitz ligament, with finally spread to liver, gallbladder, stomach, colon and small bowel with adjunct mesentery at last. Peristalsis, gravity and reabsorption considered main factors for abdominal spread of low grade mucinous tumors. As seen in many studies, great risks are present in special patient subgroups. Inability to determine those patients becomes obvious when one summary the results of developing team as ours. Lower morbidity and better overall survival could be achieved with patient selection using preoperative PCI index. PCI index is described well as prognostic factor in patients with primary colon cancer with PC [12] predicting 48 months mean survival and a 50% survival rate in 5 years for group of patients with score 10 or bellow, in the other to subgroups with score 11-20 and 20 or above, survivals are 24 months median with 20% in 5 years and 12 months median with 0% in 5 years. Question is how to improve preoperative PCI assessment mostly based on helical CT imaging to avoid patients with poor prognosis. Male sex had been described as significant factor for morbidity [15], conclusion we are not able to investigate yet on our data. There is no consensus

considering timing for bowel anastomosis, either to do it before or after HIPEC [16]. We did bowel anastomosis before HIPEC, finding this less time consuming and safe. Optimal range of temperature for solution is considered 41-43°C.

5. Conclusions

CRS with HIPEC significantly improves survival of patients with PC and pseudomyxoma peritonei. Improvement in survival of ovarian cancer patients and colorectal origin adenocarcinoma patients exist, although not so encouraging as in pseudomyxoma group. During introduction period higher morbidity and mortality could be expected, as our institution also encountered 2 deaths in short postoperative period in first 5 cases.

6. References

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