Particularities of anesthesia and postoperative intensive care related to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

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Introduction

Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy improves the prognosis of selected patients, in particular those with appendiceal and colon carcinoma (1). At least one third of all patients is still alive after treatment. Main prognostic factors are completeness of cytoreduction and the tumor volume expressed by the Peritoneal Cancer Index (should be lower than 20 for colorectal malignancies)(2). This is a combined numerical score of lesion size (LS-0 to LS-3) and tumor localization (region 0-12)(3). Gastric cancer is different, mainly because of the aggressive tumor biology. The natural history is limited to few months and even with most modern, best available systemic treatment chemotherapies, the median survival is limited (4). Other indications are: gastric cancer with peritoneal carcinomatosis, recurrent ovarian cancer with peritoneal carcinomatosis and malignant peritoneal mesothelioma.

Cytoreductive surgery consists in these patients of so-called parietal and visceral peritonectomy procedures (5). Affected areas of the peritoneal surface have to be removed, often by multivisceral resections. Surgery may include parietal and visceral peritonectomy, greater omentectomy, splenec-

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tomy, cholecystectomy, resection of liver capsula, small bowel resection, colonic and rectal resection, (subtotal) gastrectomy, lesser omentectomy, pancreatic resection, hysterectomy, ovariectomy and urine bladder resection. In patients with mucinous tumors and infiltration of the umbilicus, an omphalectomy is necessary. The aim of CRS is to obtain complete macroscopic cytoreduction (CCR-0/1) as a precondition for the application of HIPEC.

For the microscopic disease, a hyperthermic intraperitoneal chemotherapy is performed using a special pump which re-circulates the perfusate into all quadrants at a temperature of 41-42 degrees Centigrade (Figure 1). This can be performed at open or closed abdominal cavity. Heat increases the cytotoxicity of the cytostatic agent which can be given intraperitoneal in higher dosage than intravenously, however, with limited systemic absorbiton.

This procedure has a long learning curve and a relative high morbidity, however, can be performed today in centers with a low mortality (7).

In the literature morbidity and mortality rates after CRS and HIPEC range from 25 % to 41 % and from 0 % to 8 %, respectively. Morbidity can be divided in surgery-related and chemotherapy-related complications. Common surgery-related complications are for example postoperative ileus, anastomotic leackage, wound infection, bleeding, thrombosys and lung embolism. The different cytostatic agents used for HIPEC can lead to leucopenia, anemia, thrombopenia, heart, liver or renal toxicity and other side effects (8).

Major surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) are challenging not only the surgical oncologist but also his partner anesthesiologist. Therefore, a close information exchange and interaction between surgeon and anesthetist is of most importance. Moreover, the team has to be aware of possible changes that may occur in the cardiovascular status, oxygen consumption, hyperthermia, pain management and coagulation status and consider them during the perioperative management.

Pathophysiological changes during CRS and HIPEC

Due to the aggressive treatment strategy, several pathophysiological changes of the patients vital functions and parameters occur during this procedure which sometimes last several hours. At the beginning, these changes are secondary to extended surgery, at the end, due to hyperthermia and increased intraabdominal pressure. These changes are described as follows:

Temperature

During the cytoreductive phase, due to the substantial fluid losses hypothermia may occur (9). During HIPEC, due to the hyperthermic intraperitoneal solution, body temperature rises with values up to 40.5 °C (mean 37.7 °C)

(10,11,12). The increased body temperature results in corresponding effects on metabolic rate. Patients develop an increased systemic oxygen demand redounding to a steady increase in heart rate and end tidal CO_2 levels with concomitant metabolic acidosis and elevated arterial lactate values reaching their maximum at the end of the HIPEC phase (11,12,13).

Volemia

During the cytoreductive phase, a substantial fluid losses due to drainage of ascites can be noticed (9). The abdomen is filled up with perfusate during closed HIPEC. This causes an increase in intra-abdominal pressure with cranial shift of the diaphragm resulting in a reduction of the functional residual capacity and an increase of airway pressure. These changes lead to a decrease in oxygenation ratio and an abrupt rise in the central venous pressure (10) which affects the cardiac output (14,15). It is also associated with a reduction of the abdominal blood volume and an increase in splanchnic vascular resistance (16,17).

Cardiac function

Due to the hyperthermic intraperitoneal solution used during HIPEC and the resulting hyperdynamic metabolic rate, an increased cardiac output (CO) and heart rate can be measured (9,13). The initial responses to heat stress is dilatation of the peripheral vasculature, which increases heat loss from the core to the environment. Heart rate increases in order to maintain cardiac output in the face of decreasing peripheral vascular resistance (3,10). This can be shown by the routinely use of extended invasive hemodynamic monitoring such as Swan-Ganz-catheters, transesophageal echocardiography or single transpulmonary thermodilution measurement using the PiCCO® device (Pulsion Medical Systems, Munich, Germany). CVP is a poor indicator of cardiac preload and patients' volume state due to the increased intra-abdominal pressure during HIPEC (11).

Blood loss

Major surgery is often associated with significant blood loss. Transfusion of PRBCs and FFPs is necessary in our experience in half of all patients intraoperatively and in about one third postoperatively. Impairment of coagulation due to the large volume shift and protein loss with high fluid turnover is possible. Laboratory analysis revealed disturbance of coagulation with decreased INR, AT III and fibrinogen values as well as prolonged aPTT and a reduced number of thrombocytes (12).

Intra and postoperative management

Being aware of all these pathophysiological changes during surgery and hyperthermic chemotherapy, the anesthetist can adequatly react during the procedure to compensate the different organ systems. If in advanced performed, some of the treatment options can prevent major changes at the end of the procedure with extreme perturbation of the cardiovascular system, temperature or coagulation. Main management principles are described in Table 1.

Postoperative management

Postoperatively, most patients should be transferred to the ICU, as postoperative fluid loss during the first 72 h following surgery is still very high due to the significant wound surface. Therefore, it is again of critical importance to maintain an adequate effective circulating volume by giving liberal intravenous fluids such as crystalline, colloid solutions or blood solutes. Average time on the ICU of the patients lies between 1-2 days, as the comorbidity of patients with cytoreductive surgery and HIPEC is rather low according to the selections criteria for this procedure (12).

Pain management

Supplementary epidural analgesia is an adequate tool for sufficient pain management of patients undergoing cytoreductive surgery and HIPEC resulting in a reduction of intraoperative need of opioids and of postoperative ventilation compared to patients without epidural anesthesia. Complications like bowel atonia (18,19) can be markedly reduced in ICU-patients treated with epidural anesthesia.

Table 1 Treatment particularities during peritonectomy procedures and HIPEC including both intraoperative and postoperative phase

Intraoperative Management	Postoperative Management
During CRS	**Substitution of the high fluid loss**
Balanced infusion strategy to maintain normovolemia (crystalline/colloids) 6-8-12 ml/kg/h	Up to 4 L/day fluid loss need to be compensate, if necessary with fresh frozen plasma
Forced air warming, warmed infusions	**Pain management**
Fresh frozen plasma for clinical evident bleeding	Epidural analgesia (T4-L2) e.g Ropivacaine 0.75%, Sufentanil
Restrictive regime for albumin substitution	**Enteral nutrition**

During HIPEC	Physiotherapy
Hyperventilation, cooled infusions	**CT scan**
Maintain normovolemia with normal blood volume and adequate urinary output (furosemide and low dose dopamine)	Clinical examination limited, in doubt, a CT scan should be performed to exclude major complications
Monitoring of the cardiac output by PiCCO	

Conclusion

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy has become standard treatment for selected patients with certain peritoneal surface malignancies. Extended surgery over several hours may be associated with relevant fluid, blood, protein and temperature losses. On the other hand, during closed hyperthermic intraperitoneal chemotherapy, increased intra-abdominal pressure and body temperature lead to an increased metabolic rate. Therefore, the main issue is to maintain or restore an adequate circulating volume by adequate substitution of intravenous fluids. Measurement of arterial blood pressure, central venous pressure and urinary output evaluate the volume status of the patient. Noninvasive hemodynamic monitoring might help the anesthesiologist to pick up information about the fluid status of the patient. Coagulation parameters have to be monitored closely and substituted if clinical relevant bleeding tendency occurs. Postoperative, thoracic epidural analgesia can be recommended to guarantee adequate pain therapy and to reduce the rate and duration of postoperative ventilation as well as postoperative intravenous opioid administration. Due to improved surgical technique and intra/postoperative management , this aggressive procedure can be performed with a low mortality in experienced centers providing a strong interaction between the surgeon and his partner anesthetist is warranted.

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