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Anesthesia Management in Citoreductive Surgery and Hypertermic Intraperitoneal Chemotherapy Cases

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Abstract

Hyperthermic intraperitoneal chemotherapy (HIPEC) applied in conjunction with cytoreductive surgery (SRC) is an effective multimodal treatment option that has been applied in recent years, especially in selected cases of peritoneal malignancies such as peritoneal carcinomatosis, pseudomixoma peritonei and primary peritoneal tumors [1,2]. Cytoreductive Surgery involves the excision of macroscopic tumors and visceral and / or parietal peritonectomy in a single session or a series of operations, ranging from isolated omentectomy to removal of the gastrointestinal tract, pancreas, spleen, bladder, uterus, ovaries and liver. The purpose is to clean all tumor tissue up to 2.5 mm, and to ensure that the rest is affected with a cytotoxic agent. The success of cytoreductive surgery and the prediction of 5-year survival depend on the peritoneal cancer index [3] and abdominal eksplorasyon depends on the time it was made [4-7].

In hyperthermic intraperitoneal chemotherapy, the purpose is to eliminate the tumor tissue at microscopic level by applying chemotherapeutic perfusate prepared to all quadrants at 41-42 °C via a special pump.This major surgery and HIPEC application, which has high morbidity (25-41%) and mortality (0-8%), is not only for surgeons and oncologists, but also for anesthesiologists. Conditions of interest to an anesthesiologist are the purpose and objectives of the operation, the anticipated metabolic and physiological disturbances, and sthe possible chemotherapeutic toxicity [7]. For this reason, between surgeon and anesthesiologist's cooperation and information sharing is very important. The team must be alert to the cardiovascular status, oxygen consumption, hypo and, or hyperthermia, pain management, and coagulation status in these patients and must be able to make collective decisions in perioperative management.

Hyperthermic Intraperitoneal Chemotherapy

It is the maximum exposure of tissues exposed to chemotherapeutic agents at doses 20-1000 times higher than the targeted plasma levels during hyperthermic intraperitoneal chemotherapy procedure and minimum exposure of normal tissue. HIPEC drugs, they are high molecular weight hydrophilic agents that cannot cross the peritoneal fluid-plasma barrier and their peritoneal clearance is slow. It shows its effect by creating a direct cytotoxic effect and immune-mediated attack in tumor cells through hyperthermia, inhibition of DNA repair mechanisms, protein denaturation and activation of heat shock proteins. Hyperthermic intraperitoneal chemotherapy is more effective when applied immediately after SRC. When this procedure is applied before the gastrointestinal tract reconstruction, it prevents the maling cells from settling into the scar tissue, adhesion and anastomosis sites. HIPEC can be applied with a closed or open abdominal technique (the abdomen remains open during the procedure) Advantages of the closed technique: Reduced heat loss, Increased tissue penetration with the effect of increased intra-abdominal pressure and Reduced contamination risk [8,9].

In the intraoperative period in HIPEC application with the closed abdomen technique, following peritonectomy procedures, it is performed in the abdomen with one / two suprahepatic inflow and two / three pelvic outflow catheters. Perfusate circulates in the abdominal cavity using a Roller pump at 42-43 °C [10]. The temperature is monitored throughout the procedure with multiple probes placed in different areas within the peritoneal cavity. Heated cytotoxic agents are added to the perfusate and HIPEC application takes 30-90 minutes according to different

protocols. Following the perfusion of the chemotherapeutic agent, abdominal lavage, drainage and closure of the abdomen are performed. Compared to early postoperative intraperitoneal chemotherapy, it is more effective on survival time. The results are better than normotermic intraperitoneal chemotherapy, and compared to systemic chemotherapy, the average survival time is prolonged by 16-24 months and the 5-year survival rate is increased by 30-45% [11].

During this procedure, the toxic effects of chemotherapeutics, which type of carrier solution is used and how much is important for an anesthesiologist. Although isotonic solutions or dextrose-based peritoneal fluids are generally used, 5% dextrose-based water solutions are used, as chloride ions for Oxaliplatin alone will reduce Oxaliplatin to less cytotoxic metabolites. This can cause hyperglycemia, metabolic acidosis, and hyponatraemia [11,12]. There is also an increased risk of intraperitoneal bleeding and thrombocytopenia for hypertonic carrier solutions [12-14]. In addition, due to the use of Cisplatinium (half-life 20-30 minutes), as a result of renal loss of Mg, prolongation of QT (pre and intraoperative Mg levels are important) and deterioration in hemodynamic functions with direct cardiotoxic effect may occur [14,15].

Physiopathological Changes During Cytoreductive Surgery and Hipec

During this aggressive treatment, many physiopathological changes occur in vital function and parameters within hours. These initially develop secondary to major surgery, and eventually due to hyperthermia and increased intraabdominal pressure. Hypothermia due to excessive fluid loss in the cytoreductive phase. During hyperthermic intraperitoneal chemotherapy, intraperitoneal application of hot solutions increases body temperature up to 40.5°C (mean 37.5 °C). Increased body temperature increases the metabolic rate: increased heart rate, end tidal CO2 level, metabolic acidosis and arterial lactate levels increase in systemic oxygen demand, which reaches maximum levels at the end of the HIPEC period. In the cytoreductive phase, excessive fluid loss may occur due to acid drainage. Afterwards, filling the abdomen with perfusate during the closed HIPEC period causes an increase in intra-abdominal pressure. This causes the diaphragm to shift towards the cranial, leading to a decrease in functional residual capacity and an increase in airway pressure.

These changes cause a sudden increase in central venous pressure by affecting the decrease in oxygenation and cardiac output.

This is also associated with decreased abdominal blood volume and increased splenic vascular resistance. Cardiac output and heart rate can be measured as high due to the hyperthermic intraperitoneal solution used during hyperthermic intraperitoneal chemotherapy and the increased metabolic rate. The initial response to heat stress is peripheral vascular dilatation, which increases heat loss from the center to the periphery. Heart rate increases in order to maintain the increased cardiac output due to decreased peripheral resistance. Due to increased intraabdominal pressure, central venous pressure (CVP) is considered to be a poor indicator of reflecting the volume status. Cardiac output measurement may be required with a swan-Ganz catheter and thermodilution method, transesephageal echocardiography or Picco device. In half of the patients intraoperative, and one third of them postoperatively, there is blood loss that requires replacement. Large fluid shifts and protein loss due to excessive fluid turnover can cause coagulation disorders. Fibrinogen, INR and AT III levels decrease, prolongation of aAPTZ level and thrombocytopenia may be seen.

Preoperative Preparation

What is important in the preoperative anesthesia care of these patients is that the systemic absorption of peritoneal fluid caused by this type of operation, blood loss, aAcute kidney damage, aAcid presence / evacuation, eElectrolyte imbalances, hHypothermia and hHyperthermia, as well as surgery and anesthesia maintenance can be difficult. It is to be borne in mind that it can cause failure. Cardiac risk in this group of patients is the same as in other patient groups. What is important is whether these patients can compensate for the operation-specific physiological changes, such as tachycardia, increased cardiac index and increased oxygen consumption. In patients with advanced age or risk in cardiac tests, the American College of Cardiology / American Heart Association Noncardiac Surgery Quideline should be followed [15,16]. Preoperative mandatory laboratory examination consists of electrolytes, blood urea nitrogen and creatinine level, albumin, bilirubin, hemogram, coagulation levels and glucose levels.

Although the renal damage associated with HIPEC is reversible, the level of the preoperative calculated glomerular filtration rate in these cases is also accepted as a postoperative renal damage indicator. Also, the presence of preoperative renal dysfunction was found to be associated with perioperative cardiovascular events [16,17].

Conditions to be Considered In Intraoperative Anesthesia Management

In the cytoreductive phase, hypothermia develops due to excessive fluid loss. One of the most important issues in

the intraoperative anesthesia management of these patients is the risk of hyperthermia that may occur by bringing the carrier solution to 42-43 °C (mean 37.7 °C, sometimes 40.5 °C). Hyperthermia; Iit can cause coagulopathy, arrhythmia, liver / kidney damage, peripheral neuropathy and convulsions. Therefore, controlled hypothermia application before HIPEC may be preferred by methods such as reducing the operating room temperature, application of cooled intravenous fluid or not using a surface warmer. However, although the risk of hypothermia is more tolerable against hyperthermia, it should be kept in mind that hypothermia may lead to changes in anesthetic drug pharmacokinetics and increase in blood loss, the risk of surgical site infection and adverse cardiovascular effects [17-21].

With total body hyperthermia, heart rate, cardiac index and oxygen consumption increase, systemic vascular resistance decreases. Plasma norepinephrine levels increase in parallel with the increase in temperature. Therefore, radial artery catheter and invasive arterial monitoring should be added to the standard monitoring recommended by ASA in these patients. Central venous pressure monitoring due to increased intraabdominal pressure is considered a poor indicator in reflecting the volume status. Cardiac output measurement may be required with a swan-Ganz catheter and thermodilution method, transesephageal echocardiography or Picco device [19-23].

In the cytoreductive phase, excessive fluid loss may occur due to acid drainage. Afterwards, filling the abdomen with perfusate during the closed HIPEC period causes an increase in intra-abdominal pressure. This causes the diaphragm to shift cranially, resulting in a decrease in functional residual capacity and an increase in peak airway pressure. As a result, deterioration in oxygenation, sudden increase in central venous pressure, Vena cava inferior compression, decrease in abdominal blood volume, increase in splenic vascular resistance, decrease in preload and increase in gastric pCO2 and pH decrease (microcirculation effect) are observed. Intraabdonminmal pressure can reach up to 12-26 mmHg and this requires good muscle relaxation [24].

These changes cause a decrease in oxygenation and a sudden increase in central venous pressure by affecting cardiac output. This is also associated with decreased abdominal blood volume and increased splenic vascular resistance. In half of the patients intraoperative, and one third of them postoperatively, there is blood loss that requires replacement. Bleeding is not only associated with surgical reasons, but also with large fluid shifts, hyperthermic chemotherapy and protein loss due to excessive fluid turnover. There is a decrease in Fibrinogen and AT III level, prolongation in Fibrinogen, INR and aPTT, and a decrease in coagulation factors such as Thrombocytopenia and F XIII [25-27].

In these cases, blood volume plays a major role in the maintenance of systemic and regional perfusion in the intraoperative period. Decreased regional perfusion is a cause of acute renal failure. For the prevention of acute renal failure, administration of Ffurosemide (mean 25 mg), diuresis control and normovolemia are important. Acid drainage and excessive debulking can cause protein loss of up to 700 g / dayG. Therefore, in some centers, coagulopathy and accompanying albumin deficiency - if albumin <1.5-2 g - are also performed with fresh frozen plasma and albumin replacement [28-29].

Features of the Postoperative Period

In these cases, follow-up in the intensive care or recovery unit may be considered due to multiple organ failure that may develop due to disorders in the perioperative period or physiological changes. The important thing is to monitor the organ functions with constant close monitoring and to start continous positive airway pressure (CPAP) application in order to provide adequate oxygenation in these cases when necessary. In this period, management of intraoperative complications and, if any, coagulopathy and / or metabolic disorders should be corrected in the early period. In order to maintain pneumatic compression initiated in the operating room for deep vein thrombosis prophylaxis until mobilization and to prevent postoperative ileus, it is important to start oral intake early and to provide postoperative pain with epidural analgesia, if possible [30-32].

Expected risks specific to the postoperative period; Intestinal perforation, Anastomotic leak, Bile leak, Fistula, Pancreatitis, Postoperative bleeding, Deep vein thrombosis, Pulmonary embolism and wound opening. Also, Volume expanders and / or Norepinephrine or vasopressin may be used depending on the post-HIPEC vasodilation (SIRS). However, regardless of fluid response, aggressive fluid loading It may cause an increase in cardiac filling pressures and pulmonary edema [33].

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