



Anaesthesiology

ANESTHETIC MANAGEMENT OF CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY PROCEDURES

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ABSTRACT Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy procedure are done with increasing frequency to treat patients with diffused peritoneal mucinomatosis or carcinomatosis. These procedures have showed increased life expectancy in what was previously considered a "terminal condition". These patients face major and life threatening derangements of their hemodynamic, respiratory and metabolic physiologic balance during the surgery and in the immediate postoperative period. Despite the need of an advanced organ monitoring and support these perioperative derangements seem to be mild and short-lived when timely addressed, at least in the majority of patients. Intensive care physicians are involved in providing surveillance and organ support till the patient is effectively weaned after the operation. Moreover, the anesthesiologist as perioperative physician is involved in pain control, metabolic and nutritional support of this cohort of patients. This task can be challenging considering that major cohort of the patients are already on a long list of pain control medication after previous surgery or chemotherapy. A malnourished state is common and it is secondary to difficult feeding, wasting syndrome from the tumor and massive ascites. The last issue the anesthesiologists need to be aware of is the impact over the quality of life (QoL) of this procedure. The patient's underlying pathology is unlikely to be definitively cured so no treatment is an acceptable choice. The possibility to withhold the treatments must be part of the consultation process like the discussion about the QoL in the immediate, as well as in the long-term, after the operation. Careful monitoring and treatment of every aspect which can impact the QoL must be taken and the efforts to preserve the QoL must be doubled when compared with a patient scheduled for major abdominal surgery.

KEYWORDS :

DISCUSSION

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are extensive, life and quality of life (QoL) threatening procedure. All the available studies covered an extremely selected population of patients usually less than 70 years old, without relevant comorbidity [mainly American Standards Association (ASA) 1 or 2]. We will provide an overview of the challenges the anaesthesiologist has to face; for every issue we will provide preoperative, intraoperative and postoperative considerations, when appropriate.

RESPIRATORY STATUS

These patients could be pre-operatively hypoxic because of ascites, pleural effusion and atelectasis. As the abdominal cavity is filled-up with the chemotherapeutic agent there is elevation of the diaphragm and an increase in the intra-abdominal pressure. Increased PaCO₂ and a decrease in the A-a gradient and arterial pH is the hallmark of the gas exchanges deterioration. Preoperative consideration standard evaluation with Chest X-ray and careful medical history record is probably enough. Continuous Positive Airway Pressure (CPAP) periods should be considered in order to optimize pulmonary reserve before surgery.

Intraoperative considerations: intraoperatively due to increased airway pressure of low a lung protective strategy consisting of low tidal volume, positive end expiratory pressure and recurrent recruitment maneuvers should be considered

Postoperative considerations : The vast majority of patients can be extubated at the end of surgery. Anyway, beside patients still on mechanical ventilation at the end of the procedure all the patients should be monitored postoperatively for respiratory complications. Postoperative CPAP can be extremely useful to speed up the recovery and should be discussed pre-operatively with the patients and planned for the first postoperative period.

HEMODYNAMIC BALANCE: During the CRS an extreme surface exposure, often severe bleeding, massive ascites evacuation, as in the

case of ovarian tumors, and extensive tumor and peritoneal resection. Keeping normovolemia to maintain an adequate end-organ perfusion as detected by urinary output or appropriate advanced hemodynamic monitoring. Hemodynamic parameters during the HIPEC phase is: an increase in heart rate, central venous pressure (CVP), pulmonary artery pressure, wedge pressure, intrathoracic blood volume index and cardiac index; on the contrary mean arterial pressure and systemic vascular resistance showed a reduction over the baseline. An increase in end tidal CO₂ and an increase in oxygen extraction and consumption rate are the signs of the hypermetabolic state that is due to the hyperthermia. Several studies conducted during the procedures of whole-body hyperthermia showed how when the core temperature gets warmer the hyperdynamic state gets worst.

Preoperative considerations: Patients with uncontrolled cardiac disease were excluded as no patient with ASA higher than 3 was considered eligible. Beside this we refer every patients to a cardiologist if he/she had a possible cardiotoxicity from previous chemotherapy and/or he/she developed a fast malnourishment state. Indication for HIPEC should be questioned whenever an uncontrolled cardiac disease is detected and eventually the patients should be considered for palliative care only.

Intraoperative considerations : Major fluid shift anticipated and fluid administration guided by hemodynamic monitors, hourly urinary output, CVP and an invasive arterial line, trans-esophageal echocardiography can be extremely helpful in guiding transfusion and fluid turn-over therapy.

Postoperative considerations: Hemodynamic imbalances are usually short lived. Careful fluid turn-over substitution and timely weaning from vasopressor support advocate for an intensive, or at least intermediate, care to deliver adequate post-operative surveillance so to prevent renal dysfunction and decreased end-organ perfusion.

PAIN CONTROL: The elective pain control modality in the vast majority of the centers is thoracic epidural.

Preoperative considerations: Consultation with the palliative care/chronic pain physician can be useful in order to plan a follow-up of the patients when they're discharged from the hospital. Thoracic epidural is probably the best option to control pain perioperatively. It is associated with a shorter mechanical ventilation period and a better patient satisfaction. Coagulation imbalances are common: however risk benefit ratio is probably in favor of thoracic epidural considering the difficulty to control pain and wean from mechanical ventilation that these patients have.

Intraoperative considerations: There's an increasing amount of data that suggest how the use of epidural analgesia may improve patients survival rate by decreasing the incidence of tumor relapse or at least elongating the time to relapse. This possible positive effect can be secondary to the increased function of natural killer cells when the surgical stress response is reduced and high level of intravenous opioids is avoided.

Postoperative considerations: In case of the development of chronic pain the patients should be referred to a palliative care center or to a chronic pain clinic.

COAGULATION CONSIDERATIONS : Coagulation abnormality is, probably, multifactorial in its genesis. The two sides of the problems seem to be a dilutional dysfunction secondary to massive fluid shift and bleeding and an impairment of coagulation factors profiles due to massive ascites and malnourishment.

Preoperative considerations: Standard coagulation evaluation (INR, aPTT, platelets count, list of antithrombotic drugs) is enough.

Intraoperative considerations: Thromboelastography (TEG) gives the possibility of a thorough evaluation of the coagulation profile and it is probably more useful in this type of surgery than in others. TEG-guided transfusion of blood products may substantially reduce bleeding and eventually blood-products requirements similarly to what happens in other major surgeries.

Postoperative considerations: The coagulation profile takes at least 5 d to get back to baseline values so surveillance and timely transfusion is needed. Temperature control is of utmost importance as it is directly related to the gravity of deregulation in the hemodynamic and coagulation balance.

RENAL STATUS, TEMPERATURE AND METABOLISM:

Standard evaluation: If ureteral stents are positioned preoperatively to be used as landmark during CRS phase it should be advisable to check for their bilateral patency.

Intraoperative considerations: Calcium, potassium, sodium and magnesium are routinely checked. Forced diuresis by the use of high dose loop-diuretics is still considered "standard of care" during chemotherapy. Hypovolemia can be easily detected and corrected if invasive monitoring is ensued and there is no clear evidence "against" the use of loop-diuretics. There's a need for the anesthesiologist to know the composition of the perfusate and to prevent possible electrolyte unbalances due to the abdominal perfusion itself. Temperature control devices and strategies need to match the different requirements during the CRS and HIPEC phase of the procedure. During the cytorreduction hypothermia must be prevented using all the warming devices available. On the contrary patients must be cooled down during the HIPEC phase when the warm infusate is delivered into the abdominal cavity. Cold fluids, ice packs, cooling mattress have been used to cool the patients during the HIPEC procedure.

Postoperative consideration: None of these disturbances is reported to be long lasting after the completion of the procedure so just standard care is needed.

POSTOPERATIVE CARE : Postoperative respiratory support is not always necessary even if CPAP periods can be useful to get back to baseline respiratory function. Our patient got extubated on POD 1. Presence of a working epidural analgesia was significantly associated with a reduction in the mechanical ventilation period.

NUTRITIONAL SUPPORT : All malnourished patients should have a nutritional consultation before surgery and should start a nutritional support to reach a better metabolic profile before surgery. Although

little is known about the effect on small bowel physiology of the hyperthermic intrabdominal chemotherapy, it is advisable that these patients should be treated according to the guidelines about perioperative nutritional support after major surgery.

CONCLUSION: CRS and HIPEC are complex procedures. High morbidity and mortality rates are reported. Respiratory and hemodynamic derangements were the first ones to be extensively evaluated. Morbidity related to these two systems failure is decreasing since pathophysiology of hyperthermia is better understood and better temperature, hemodynamic and respiratory control is achieved through new devices or technique.

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