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REVIEW ARTICLE

Anaesthetic Considerations in the Perioperative Management of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Deepak B. Sheshadri[1] · **Murali R. Chakravarthy**[2]

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Abstract Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy has emerged as one of the primary modalities of treatment of diffuse peritoneal malignancies. It is a complex surgical procedure with the patients facing major and potentially life threatening alterations of haemodynamic, respiratory, metabolic and thermal balance with significant fluid losses and the perioperative management is challenging for anaesthesiologists and intensive care physicians. Though the alterations are short lived, these patients require advanced organ function monitoring and support perioperatively. The anaesthesiologist is involved in the management of haemodynamics, respiratory function, coagulation, haematologic parameters, fluid balance, thermal variations, and metabolic and nutritional support perioperatively. The chemotherapy instillate used are known to cause nephrotoxicity, cardiotoxicity, dyselectrolytemia and lactic acidosis. The preoperative polypharmacy for pain control, previous surgery and/or chemotherapy, malnourished status secondary to feeding problems and tumour wasting syndrome make the task all the more challenging. The anaesthesiologist also needs to consider the perioperative care from a quality of life perspective and proper preoperative counselling is important. The present overview summarizes the challenges faced by the anaesthesiologist regarding the pathophysiological alterations during the Cytoreductive surgery and Hyperthermic intraperitoneal chemotherapy in the preoperative, intraoperative and postoperative periods.

Keywords Peritoneal surface malignancies · Anaesthesia for cytoreductive surgery · Hyperthermic intraperitoneal chemotherapy

Introduction

Cytoreductive surgery (CRS) and Hyperthermic intraperitoneal chemotherapy (HIPEC) as a treatment modality for peritoneal surface malignancies has evolved the past two decades and is being increasingly used worldwide as the concerns of safety, morbidity and therapeutic considerations are better understood and addressed. This is a complex procedure wherein the physiologic and metabolic challenges of major abdominal surgery are compounded by the thermal stress induced by peritoneal surface instillation of heated chemotherapeutic solution. Patients undergo major haemodynamic, respiratory and metabolic alterations during the perioperative period which requires the constant attention and timely intervention of the anaesthesiologist. Despite a majority of the patient population in available reports [1–3] belonging to American society of anaesthesiologists physiologic status (ASA) I or II without significant systemic disorders/co-morbidities, the morbidity and mortality of the procedure remain as high as 65 and 12 % [1, 4]. A well-coordinated team of anaesthesiologists, surgeons and intensivists with adequate ancillary support services enable satisfactory outcomes. This overview attempts to summarize the challenges faced by the anaesthesiologist regarding the pathophysiological alterations during the Cytoreductive surgery and Hyperthermic intraperitoneal chemotherapy in the preoperative, intraoperative and postoperative periods.

✉ Deepak B. Sheshadri
ddbs25@gmail.com

[1] Fortis Hospital, 154/9, Opp. IIM (B), Bannerghatta Road, Bangalore, India 560076

[2] Department of Anaesthesia, Critical Care and Pain Relief, Fortis Hospital, 154/9, Opp. IIM (B), Bannerghatta Road, Bangalore, India 560076

Preoperative Considerations

Respiratory Function

Given the disease nature and progression of peritoneal malignancies, the expected ascites pleural effusion and their combined mechanical effects result in basal atelectasis developing over time, thus rendering these patients at risk of hypoxia preoperatively. In most patients a precise medical history and evaluation with a chest radiogram/computed tomogram usually suffices. Whenever indicated, preoperative arterial blood gas (ABG) analysis and pulmonary function tests would help to evaluate and optimize the patients, especially those with reactive airways. Educating the patients about the use of incentive spirometry would help to better manage the postoperative respiratory problems that can occur.

Cardiovascular Balance

Patients undergoing CRS with HIPEC experience a wide range of haemodynamic variations during the various phases of surgery. During the initial phase of Cytoreductive surgery, wherein the major debulking happens, large areas of raw peritoneal surface exposure occurs with substantial fluid losses due to evaporative loss and ascitic drainage along with significant blood loss. Maintaining normal intravascular volume may prove to be difficult as the fluid requirements far exceed the recommended 6–8 ml/kg/h [5] for major abdominal surgery. Across reports of fluid requirements, 12–20 ml/kg/h [6] are frequently observed guided by end organ perfusion targets (urine output of >0.5 ml/kg/h) or other advanced haemodynamic monitoring. The phase of HIPEC induces a hypermetabolic response with increase in heart rate, central venous pressure (CVP), cardiac index [2, 7–9] and increase in End tidal carbon dioxide (ETCO2) [2]. Increases in oxygen extraction and consumption have also been studied [8], which are the indicators of hypermetabolic physiology. These are also accompanied by a reduction in systemic vascular resistance (SVR) and mean arterial pressure (MAP) due to the peripheral vasodilation induced by hyperthermia, but have not been found to be statistically significant. Across the available literature, the changes noted correlated with the increasing core temperature and were significant at 30 min into the HIPEC. Secondarily, the increased intraabdominal pressure and resulting upward migration of the diaphragm contribute to decreased venous return and inferior vena cava collapse, as well as increased intrathoracic pressure making CVP and pulmonary capillary wedge pressure (PCWP) unreliable indicators of preload during HIPEC [7, 8]. Most patients for elective major abdominal surgery invariably undergo adequate preoperative assessment and evaluation, with echocardiogram and stress testing indicated in patients with reduced cardiac reserve and those with previous history of heart failure or chemotherapy induced cardiotoxicity. Patients with uncompensated cardiac disease have not been part of any studies on CRS and HIPEC in available literature. Such patients may have a poor risk benefit of treatment vs palliation and patient selection needs to be done with care.

Pain Management

In most cases, complete CRS and HIPEC necessitates a large incision (xiphisternum to pubic symphysis), lots of tissue manipulation and dissection and the massive exposure and scarring explains the intense pain experienced and pain control strategies adopted. Most reports in literature have a protocol of thoracic epidural analgesia for perioperative pain management [2, 3, 6, 8, 10]. Prospective randomised control trials have found epidural analgesia superior to intravenous patient controlled analgesia (IV-PCA) in appropriate indications [11–14]. These patients may also require local anaesthetics with opioids via epidural for longer time than the conventional 48–72 h, with Schmidt et al. [2] reporting median usage of 7 days continuous infusion.

Preoperative assessment should include disease progress and analgesic medication history. Patients with chronic pain/neuropathic pain need further evaluation. Thoracic epidural analgesia has been associated with shorter duration of postoperative mechanical ventilation [2] and higher patient satisfaction and better pain scores [11]. Across reported randomized control trails, 21–38 % patients [2, 15] did not receive epidural analgesia, but still had similar rate of perioperative complications and hospital stay and only an increased duration of postoperative mechanical ventilation and ICU stay were noted. Disorders of coagulation often occur secondary to nutritional deficiencies and occasionally patients are unwilling for the epidural, thereby excluding the option altogether.

Coagulation Homeostasis

The patient population undergoing cytoreductive surgery and hyperthermic peritoneal chemotherapy are always prone to some coagulation derangements in the perioperative period. These could range from a pathological decrease in the platelet count [2, 3, 10, 15] resulting from a preoperative chemotherapy regimen, to a prolongation of the Prothrombin time and international normalized ratio (PT-INR) due to preoperative nutritional deficiencies. Derangements of coagulation are of multifactorial origin. The prolonged nature of surgery, female gender, age (fifth and sixth decade of life) and malignancy per se contribute to the high thrombotic risk in these patients. Patients with gross ascites often lose in excess of two litres of ascitic fluid rich in protein (0.5–4 g/dL) which is primarily albumin. This perioperative loss causes oncotic pressure changes and could impair coagulation [16]. Across various reports of CRS and HIPEC, the preoperative protocol

followed was a panel of standard tests of coagulation including PT-INR, activated partial thromboplastin time (aPTT) and platelet count. Schmidt et al. [2] reported a correlating change in Antithrombin III with the other parameters.

Renal Function and Electrolyte Balance

Considering the extensive nature of surgery, fluid loss and infusions, thermal variations and effects of the chemotherapeutic agent and the solution used (Dextrose 5 % or peritoneal dialysate), significant electrolyte derangements are to be expected. Baseline preoperative electrolyte panel should be assayed and in cases of gross ascites or raised intra-abdominal pressure, ureteric stenting done prophylactically preoperatively reduces the risks of urological complications, but their patency needs to be ensured prior to surgery. As the chemotherapeutic agents also affect the renal function, preoperative renal function parameters should be assessed and serve as a guide to trend the perioperative changes.

Perioperative Thermoregulation

Perhaps one of the major impacts on the milieu interior due to the CRS and HIPEC is due to the thermal changes that occur intraoperatively, alongside the fluid shifts. During the initial debulking phase, due to the large area of surgical exposure [7], ascitic fluid loss and long duration of resection, patients are at high risk of hypothermia. It is imperative to regulate the body temperature intraoperatively with the use of convective warming devices such as the heated water driven thermal underbody mattress or forced air warming blankets (Bair hugger®) along with warm fluid infusions and ambient operating room temperature regulation. Continuous monitoring of the core body temperature (nasopharynx/oesophagus) and the abdominal cavity temperature during HIPEC are mandatory. Thermoregulation plays a significant role in maintaining the metabolic homeostasis, coagulation, anti-inflammatory cascade and neurological status intact [17].

In contrast to the initial hypothermic phase, during HIPEC the hyperthermic instillate causes a significant increase in core body temperature with values of up to 40.5 °C being described (mean 37.7 °C) [2, 9, 18, 19] Patients develop an increased metabolic rate characterized by increases in heart rate, end tidal carbon dioxide (ETCO2) levels, metabolic acidosis and elevated arterial lactate values, all these peaking at the end of HIPEC phase [7–9, 19] with increased cardiac index [8, 9]. One of the initial responses to the systemic hyperthermic insult is a peripheral vasodilatation with heat loss from the core to the periphery and environment. The increase in heart rate is in response to the decreasing systemic vascular resistance (SVR) [9] as well as increased systemic oxygen demand.

During this phase it is important that the anaesthesiologist should monitor and maintain normothermia by using cooled intravenous fluids, icepacks and setting the warming device to ambient or off mode [6, 8]. In some cases the mattress has also been used to cool the patient [15]. When the core temperature increases to 39 °C in spite of all other measures, the perfusionist is advised to reduce the instillate temperature. All recent reports have noted core temperatures in the range of 37–38.8 °C during HIPEC, indicating the proper attention and management which is demanded by the procedure. Upon completion of HIPEC and evacuation of the hyperthermic instillate, as the body temperature decreases the hyperdynamic circulatory state begins to normalise with time, though still remaining above the baseline.

Quality of Life (QoL) Perspective

In spite of the many improvements in strategy, technology and techniques, CRS and HIPEC still represent a radical treatment modality with curative intent in a patient who otherwise has no definitive cure in sight. Patients benefit immensely in preoperative counselling in making a decision of their treatment modality with a correct understanding of the pros and cons of the procedure. Notwithstanding a high perioperative morbidity and mortality, [1, 4] studies show significant improvement in median survival for colorectal cancers [20, 21] and a quality of life similar to baseline or exceeding that (ovarian cancers and massive ascites) [21] following CRS and HIPEC. McQuellon et al. [22] reported that among long term survivors no patient regretted having undergone the procedure from a quality of life perspective.

Intraoperative Period

Respiratory Function

These patients often have a decreased functional residual capacity (FRC) due to raised intra-abdominal pressure and volume, thus predisposing them to rapid oxygen desaturation. Adequate preoxygenation at induction of anaesthesia is important. Due to the raised intra-abdominal pressure and possible bowel obstruction in colonic malignancies, these patients are also at a risk of regurgitation and aspiration of gastric contents at induction of anaesthesia. Ensuring adequate preoperative fasting, employing a rapid sequence induction and intubation safeguards against these risks. Ventilatory strategies of smaller tidal volumes, positive end expiratory pressure and recruitment manoeuvres are recommended as the physiological conditions mimic that during long duration laparoscopy surgeries [23]. Open abdomen (Coliseum) technique for HIPEC is recommended over a closed technique whenever a preoperative evaluation reveals a gross reduction in FRC with altered pulmonary function tests [7]. During the phase of HIPEC, impaired oxygenation ratio and tissue oxygenation

occur along with raised airway pressures up to 30 mm Hg due to the cephalad displacement of diaphragm [3, 17, 19]. These changes only reverse partially following completion of HIPEC and evacuation of the peritoneal instillate.

Cardiovascular System

Given the duration of surgery and the large fluid shifts and frequent necessity of vasopressor support, intraoperative haemodynamic changes need constant and adequate attention, even though they are transient in nature. Intraoperative monitoring of haemodynamics are multipronged and across literature reports of CRS and HIPEC, the monitoring modalities used are at least a central venous pressure (CVP) line, invasive arterial pressure monitoring line and hourly urine output. Few centres employed invasive monitoring such as a pulmonary artery catheter [8, 19], transoesophageal echo Doppler [7, 9, 10] and continuous cardiac output by transthoracic thermodilution method [6]. Other minimally invasive devices such as the pulse contour analysis (LiDCO) and Vigileo (Flotrac) ® [24] which uses the peripheral arterial line for analysis, have also been helpful in guiding transfusion and fluid replacement therapy. The pulse contour analysers may exhibit faster response to sudden changes in volume but may be impaired in septic shock and vasodilation. Volume responsiveness can also be assessed by measuring the beat to beat stroke volume variations and pulse pressure variations, but may not be accurate in patients with impaired systolic function during hypovolemia. In the midst of so many technological advances of perioperative haemodynamic parameter monitoring, the primary goals remain to ensure adequate preload replenishment, ensure end organ perfusion and prevent fluid overload. In this context few authors have debated that CVP and pulmonary capillary wedge pressure (PCWP) do not reflect the preload reliably due to the mechanical effects of patient positioning and intra-abdominal pressure increase (especially during HIPEC) [7, 9, 25]. Urine output (commonly used as an indicator of end organ perfusion) maybe reduced due to the intra-abdominal pressure or the renal toxicity of the chemotherapeutic agents. The support of circulation with inotropes/vasopressors has not presented definite recommendations. Common practice in the setting of vasodilation is the use of noradrenaline and methoxamine in a few studies and usually depends on institutional protocols.

The use of low dose Dopamine has been recommended earlier based on reported increase of renal perfusion during laparoscopic procedures [26], and has also been suggested in CRS and HIPEC [9, 15]. However, the standardized use of furosemide [9] and low dose dopamine [6] is inadvisable as other studies have demonstrated no change in creatinine values during CRS and HIPEC with just maintenance of normovolemia and adequate urine output [2]. Several trials have also shown a lack of benefit of low dose dopamine in improving renal function, especially in patients with acute oliguric renal dysfunction [27] along with having adverse effects on the immune, endocrine and respiratory systems [28]. Choice of intraoperative fluid infused is a subject of intense debate in scientific circles and no definitive directions have emerged [29]. Common practice followed is a balanced infusion therapy to maintain preload, colloid oncotic pressure, end organ perfusion (urinary output) and maintain electrolyte homeostasis. Perioperative albumin infusions are usually restricted to severe reductions in plasma albumin levels and fresh frozen plasma (FFP) transfusions are restricted to clinically manifest bleeding disorders. Thus, to prevent haemodynamic imbalance and reductions in end organ perfusion, the main aim of the anaesthesiologist should be adequate fluid replacement with fluid and blood loss adjustment and maintaining euvolemia.

Pain Management

In the intraoperative period, pain management is usually a balance of epidural analgesia (where feasible) and intravenous opioid boluses or infusions. In the patients who accept an epidural pain management, continuous local anaesthetic infusions through the epidural catheter with or without opioids would be the ideal choice. However it is not without its concerns, as expressed by several authors [15, 30]. The concerns voiced mainly referred to the high potential of continuous infusions to worsen the hypotension caused by sympathetic blockade acting in synergy with the reduction in systemic vascular resistance due to hyperthermia during the phase of HIPEC. However, Schmidt et al. [2] have described the lack of any adverse effect of epidural analgesia during the phase of HIPEC and systemic hyperthermia. The beneficial effect of thoracic epidural for both acute and long term pain prevention (6 month follow-up) has been described [31]. Whether the thoracic epidural analgesia has a similar effect in CRS and HIPEC is still a matter of speculation and debate. There are also lot of emerging data which suggest that the use of epidural analgesia in the perioperative period may prolong time to tumour relapse or decrease the incidence of relapse. Among the studies concerning CRS and HIPEC, deOlivera et al. [32] found a significantly longer time to recurrence in the patients that had an activated thoracic epidural analgesic during the phase of CRS, but not during HIPEC alone or during only the postoperative period in patients with ovarian cancers. One proposition to the beneficial effect is that it is secondary to the hyperfunction of the nK cells (natural killer cells) whenever surgical stress response is reduced and large quantities of intravenous opioids are avoided [33, 34]. Also, large amount of intravenous opioids may prolong the intensive care unit (ICU) stay due to their depressant action and bowel atony [35]. Better analgesia and faster return of bowel function have been shown for thoracic epidural analgesia compared to intravenous patient controlled analgesia (IV-PCA) in elective open colectomy surgeries [36, 37]. Patients undergoing CRS and

HIPEC are at risk of pulmonary complications due to impaired diaphragmatic and abdominal muscle function similar to all major abdominal surgeries. If analgesia is inadequate, the smaller tidal volumes generated result in inadequate oxygenation, ineffective expectoration and unsatisfactory participation in physiotherapy [38].

The physiological benefit of epidural analgesia is by promoting parasympathetic drive by sympathetic blockade and thus faster recovery of bowel function and improving pulmonary function by attenuating spinal reflex inhibition of diaphragmatic function. It also provides adequate analgesia with lower pain scores which enables patients to participate in and respond better to physiotherapy [39, 40].

Coagulation Homeostasis

In the intraoperative period, the anaesthesiologist has to deal with multiple coagulation related issues in a short time span. These include dilutional coagulopathy due to large quantities of crystalloid and colloid solutions administered and red cell transfusions to replace blood loss itself causing transfusion coagulopathy, along with pre-existing coagulopathy due to protein abnormalities resulting from nutritional deficiencies and ascites evacuation. This multifactorial scenario complicates the coagulation profile evaluation as we normally understand it in terms of the international normalized ratio (INR), aPTT and platelet count. In view of dilutional coagulopathy, the platelet function analyser or thromboelastogram (TEG) may give a better evaluation of integrity of the coagulation system. TEG guided transfusion of blood component has shown to reduce bleeding and more appropriate component transfusion and requirements in major surgeries [41, 42].

Renal Function and Electrolyte Balance

Debate over type of fluids infused, infusion strategies and targets and end points achieved during major abdominal surgeries have been ongoing since decades. Balanced isotonic crystalloid infusion with goal directed rather than liberal or massive fluid infusion is what is presently followed. Additionally, colloids (hydroxyethyl starches or 5 % albumin) when used appropriately help achieve specific therapeutic end points of haemodynamics/end organ perfusion and optimal coagulation.

Urine output is an accepted non-invasive measure of end organ perfusion during all types of surgeries. During CRS and HIPEC, ensuring adequate urine output especially during HIPEC assumes all the more significance in view of the ongoing thermal and haemodynamic changes. There is also the additional concern of nephrotoxic insult by the chemotherapeutic agent used in HIPEC. The use of loop diuretics to enhance urine output and facilitate renal excretion of the absorbed chemotherapeutic drug has also been described [6, 9, 15]. Though many centres employ high dose loop diuretics during chemotherapy (especially platinum compounds) as a standard protocol, definitive association of renal protection due to high dose loop diuretic has not been proven [43]. The special interest group on cancer care of European society of clinical pharmacology recommends a brisk diuresis during platinum infusions and in the immediate postoperative period by saline infusions. However, the use of diuretics as a standard of care still has a role as long as euvolemia is maintained with invasive haemodynamic monitoring and loop diuretics are not contraindicated [16]. Unfortunately, acceptable urine output has not been quantified and link between intraoperative urine output and postoperative creatinine elevation remains unclear. The importance of euvolemia is repeatedly stressed as repeated use of diuretics can be misleading as they produce good urine output but cause unrecognised renal dysfunction due to hypoperfusion. Drug clearance is dependent on renal blood flow and not just the urine output.

During the phase of HIPEC, the recommendations are to maintain urine output of at least 100 ml every 15 min. This is ensured by maintaining euvolemia with infusion of crystalloids and colloids up to 1800 mL/h. The “renal dose dopamine” has no relevance as already discussed under cardiovascular function. Various electrolyte and acid base disturbances have been noted and attributed to the procedure of HIPEC and it is important for the anaesthesiologist to know the acute systemic toxicity of chemotherapeutic agents used, as well as the composition of the peritoneal instillate used. Cisplatin and oxaliplatin are known to cause hyponatremia, calcium and magnesium leaching into the peritoneal solution, renal toxicity and lactic acidosis. Ifosfamide causes haemorrhagic cystitis and Adriamycin is known to cause cardiotoxicity.

The commonly used peritoneal instillate carrier solutions are either Dextrose 5 % or peritoneal dialysate solution (containing Dextrose 1.5 %). Most common problem with these solutions is hyperglycemia which can be quite significant, even though it is short lived, especially with oxaliplatin HIPEC which mandates Dextrose 5 % instillate. Hyponatremia is known to occur due to two mechanisms, one due to diffusion into the peritoneal solution and second due to intravascular fluid shift due to hyperglycemia. This hyponatremia is rapidly correctable with glycaemic correction. Cisplatin and mitomycin when used in 1.5 % dextrose containing peritoneal dialysate caused less significant hyperglycemia and no significant electrolyte abnormality but are more nephrotoxic. Saver et al. [44] reported these abnormalities of hyperglycemia, hyponatremia and also lactic acidosis which they attributed to metabolic relationship between glucose and lactate. Increased glucose turnover indicated that lactate production could be entirely secondary to increase glucose metabolism irrespective of any anaerobic metabolic state [45]. Intraoperatively, approximately 15–20 min before the start of HIPEC, a set of laboratory investigations should be obtained including serum electrolytes, haemoglobin, arterial blood gas and blood sugar. Patients frequently require

electrolyte replacements during and after HIPEC, most commonly calcium, potassium and magnesium. Glycaemic control is more difficult as the glycaemic changes are very rapid and short lived. Thus, reassessment of electrolytes and blood glucose every 30 min during and up to two hours after the chemotherapy phase is frequently followed.

Following is a commonly observed checklist, done 15 min prior to initiation of hyperthermic chemotherapy.

1. All fluid warmers switched off
2. Body warmer set to ambient
3. Laboratory studies of serum electrolytes, blood gas analysis, coagulation, haemoglobin and blood sugar are done
4. Intravenous fluid infusion increased to approximately 1800 mL/h
5. Antibiotics repeated
6. Supplementary drugs administered (e.g. MESNA for Ifosphamide, leucovorin for intravenous 5-fluorouracil)
7. Ensure availability of blood components and albumin
8. Continuous temperature evaluation and documentation of urine output every 15 min throughout the period of HIPEC

Postoperative Management

In view of CRS and HIPEC being a long and complex procedure, all patients need intensive postoperative monitoring and care in the ICU irrespective of the predominantly short lived physiological changes. Though majority of the patients are amenable to tracheal extubation in the operating theatre at the end of surgery, the possibility of postoperative ventilator support as well as continuous positive airway pressure which hastens recovery [46] should be discussed with the patients and family preoperatively. The possible postoperative respiratory complications should also be counselled about. Various reports describe varying requirements of postoperative ventilator y support (0–38 %) [10, 15]. Schmidt et al.[2] observed that effective epidural analgesia reduced the duration of postoperative mechanical ventilation (3.1 vs 10.3 h without epidural) and more patients' tracheal extubation in the operating theatre (41 vs 14 % without epidural). Haemodynamic instabilities are usually short lived postoperatively, but some patients still need a vasopressor support and management in the ICU at the end of surgery. Fluid losses continue postoperatively and mainly occur through the abdominal/thoracic drains, with up to 4 l per day being reported [3]. This complicates the assessment of fluid requirements. Adequate replacement of fluid loss along with appropriate use of vasopressor is necessary for preventing end organ hypoperfusion. Cooksley et al. [10] reported that though 26 % patients were on vasopressors postoperatively, none of them developed renal failure or difficulty to wean off vasopressors. Epidural analgesia is continued in the postoperative period up to 72 h at most centres and the due benefits and concerns already discussed. Strict asepsis must be ensured in care and handling of the epidural catheter and drug infusion system. Development of chronic pain may necessitate referral to a chronic pain service or a palliative care centre.

Coagulation parameters continue to need attention postoperatively and need up to 5 days or more to return to baseline values [15]. Many patients may need component transfusions of fresh frozen plasmas or platelets postoperatively even though the intraoperative period may have been uneventful. Renal dysfunction, dyselectrolytemia and hyperglycaemia occur frequently in the first 48 h postoperatively. Though transient, they need correction as they are invariably inter-related and depend on the fluids infused, end organ perfusion targeted and use of diuretics as well as the sequelae of the chemotherapeutic agents used in HIPEC.

Conclusions

CRS and HIPEC are an important development in the management of peritoneal surface malignancies. The anaesthesiologist has to deal with the relevant fluid, blood and protein losses, raised intraabdominal pressures, thermal imbalances and raised metabolic rate during CRS and HIPEC. The onus remains on maintaining and restoring integrity of the milieu interior by volume infusions, component transfusions, supplementary thoracic analgesia and appropriate patient monitoring. With a better understanding of the respiratory and haemodynamic derangements and their control along with thermal regulation through new devices or techniques, the perioperative morbidity is decreasing. Given the perioperative blood and fluid shifts and duration of surgery, future studies need to focus on how to improve outcomes through better understanding of the coagulation derangements and issues concerning pain patterns, nutritional replenishment and improving quality of life.

Compliance with Ethical Standards

Conflict of Interest No conflicts of interest declared.

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