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Anesthetic management of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC): The importance of hydro-electrolytic and acid-basic control

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ABSTRACT

JUSTIFICATION AND OBJECTIVES: Patients affected by gynecological or gastrointestinal tract neoplasms that evolve to peritoneal carcinomatosis experience a significant drop in their quality of life, high morbidity and short survival times with currently available chemotherapeutic schemes. The surgical treatment based on cytoreduction and the employment of hyperthermic intraperitoneal chemotherapy in the intra-operative period is a true challenge to anesthesiologist.
CASE REPORT: A 67 years old patient diagnosed with mucinous adenocarcinoma of the Appendix associated with mucinous carcinomatosis, was submitted to cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), under general anesthesia and epidural block. Volume replacement was performed with crystalloids, colloids and blood products to support an important ascites volume drained during the procedure. The target was the strict control of hydro-electrolytic and acid-basic equilibrium. The patient was referred to the ICU and evolved to a hospital discharge on the third postoperative day.
CONCLUSION: The neoplastic compromise of the peritoneum has long been considered to be a pre-terminal state. The advent of CRS/HIPEC represent an alternative promising with numerous challenges to the anesthesiologist regarding the metabolic and hemodynamic adjustment, which once again demand training and ongoing study from the perioperative team.

1. Introduction

Patients affected by gynecological or gastrointestinal tract neoplasms, that evolve to peritoneal carcinomatosis, experience a significant drop in their quality of life, high morbidity and short survival times with currently available chemotherapeutic schemes [1]. With the objective of treating these patients, who frequently present local tumoral spread associated with the absence of distant metastases, oncologists have developed a treatment method that consists of cytoreductive surgery and the continuous hyperthermic peritoneal perfusion with chemotherapeutic agents. The procedure, which administers high doses of chemotherapeutic drugs locally, favors the local control of the disease and minimizes the effects of systemic toxicity [2]. In contrast, the surgery involves blood loss, significant fluid mobilization, deterioration of gaseous exchanges, metabolic changes and coagulation disorders that must be promptly identified and managed by the anesthesiologists in the intra-operative period.

2. Case report

This case report describes a 67 years old, hypertensive patient, diagnosed with mucinous adenocarcinoma of the Appendix associated with mucinous carcinomatosis, who was submitted to cytoreductive surgery (CRS) and paleative hyperthermic intraperitoneal chemotherapy (HIPEC), under general anesthesia combined with a non-continuous epidural block.

The patient was admitted to the operating room while conscious, oriented, eupneic, after adequate fasting, presenting an ascitic abdomen. After providing written Informed Consent, the patient was monitored with electrocardiogram, non-invasive blood pressure, bispectral index and pulse oximetry. Two large venous lines in the upper limbs was provided. Subsequently, the patient was positioned in the right lateral decubitus for an epidural block

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in T9-T10, through the administration of 0.5% of ropivacaine in the volume of 40 mL associated with 2 mg of morphine and 150 μg of clonidine. A balanced general anesthesia was induced with 70 μg of fentanyl, 60 mg of lidocaine, 100 mg of propofol and 9 mg of cisatracurium. Then, the monitoring was complemented with an esophageal thermometer, invasive arterial pressure monitoring and central venous access, while sevoflurane at 1.5% was started when the surgical procedure began; with a duration of 4 h and 15 min.

Successive blood gas analyses were necessary in the intra-operative period for the correction of metabolic disorders and hydroelectrolytic disturbances, the maintenance of low doses of noradrenaline and remifentanil through continuous infusion, which ensured the hemodynamic stability during the infusion of the chemotherapeutic fluid based on Cisplatin. 30 mg/kg of tranexamic acid was administered along with the antibiotic prophylaxis before the surgical incision. Volume replacement was done with 8500 mL of crystalloids, 500 mL of colloids (hydroxyethyl starch at 6%), 01 red blood cell concentrate unit and 50 mL of albumin at 20% due to an important ascites of approximately 10L, drained during the procedure. Diuresis at the end of the procedure was 1600 mL (rate of 400 mL/h) and the central venous blood gas test demonstrated a SVO2 of 83.5%. A replenishment of calcium with 10% of calcium gluconate and a glycemic correction with regular intravenous insulin (Δglycemia: 214–148) was also necessary.

Body temperature ranged between 34.6 °C and 36.9 °C (Fig. 1) and the patient maintained moderate metabolic acidosis during the intra-operative period (Δ pH 7.3–7.21).

At the end, the patient was extubated without incidents and forwarded to the ICU while eupneic, without the use of vasoactive drugs and with complaint of a mild pain in the abdominal region. She evolved to leave the ICU after 24 h and was discharged from the hospital on the third postoperative day, without complaints. She maintains a clinical follow up with the Oncology Service.

3. Discussion

HIPEC is being increasingly performed around the world, with rising safety levels and lower rates of morbidity as the intra-operative variables are better understood and managed. This management challenges the anesthesiologist because patients are submitted to a long surgical procedure with an extensive surgical incision and great loss of fluids.

Most patients present a large volume of ascitic fluid to be drained, in addition to a hyperdynamic circulatory state inherent of the procedure itself. The acute changes in body temperature, associated with an increased intra-abdominal pressure by the administration of the chemotherapeutic fluid (3 to 5 L of solution at 42 °C) can promote severe hemodynamic disorders, with increased cardiac output, a reduction of systemic vascular resistance and an increase in the cardiac index and EtCO2 [3]. The maintenance of a proper pre-loading during such intra-operative changes requires a more liberal volume replacement rate, between 1220 mL/h and 1770 mL/h [4], which enables the provision of an effective circulatory volume despite the reduced systemic vascular resistance and the peripheral vasodilation, caused by the increase in temperature because of the chemotherapeutic infusion.

It is also important to consider the nephrotoxicity of cisplatin and the need to prevent renal injury, which makes an average diuresis rate of 500 mL/h desirable, mainly at the time of the drug-based fluid infusion, with often the administration of low doses of furosemide and dopamine being recommended, in addition to

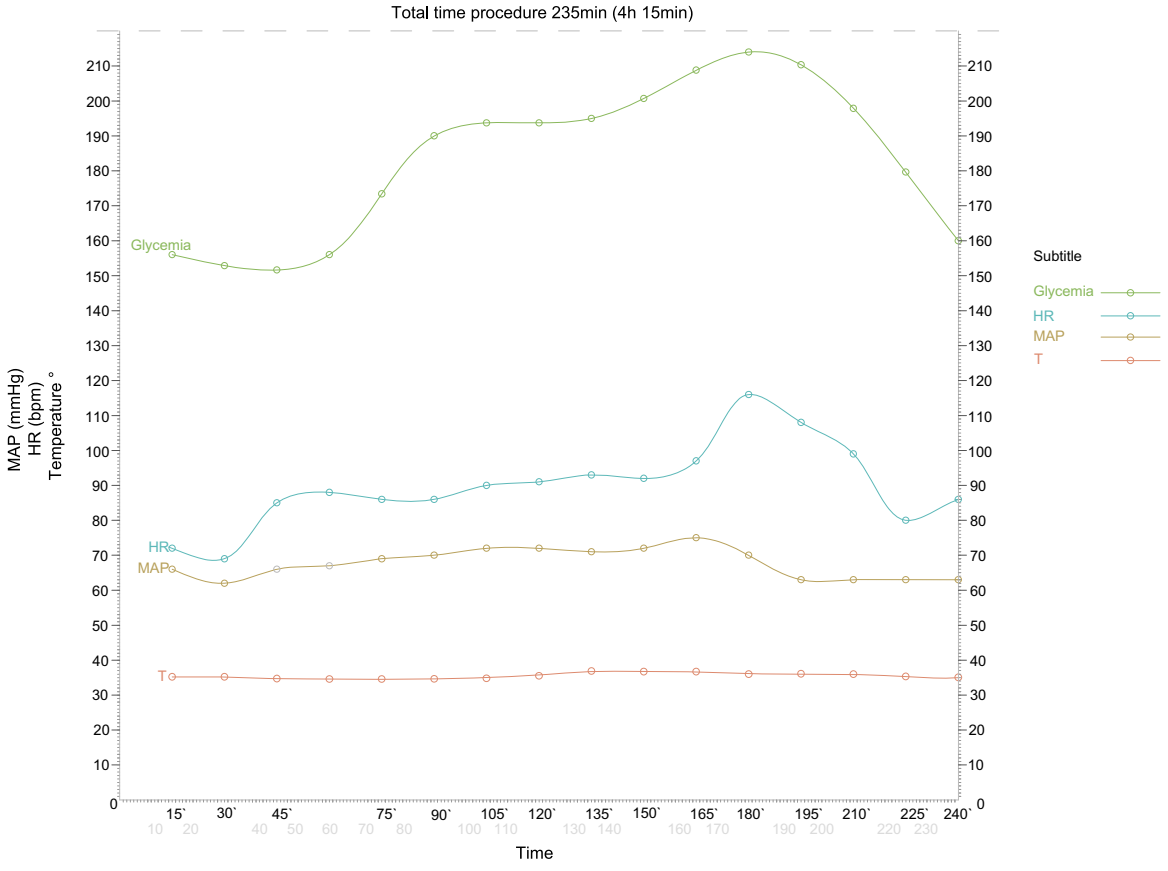

Fig. 1. Perioperative hemodinamic behavior. MAP: Mean arterial pressure; HR: heart rate; T: temperatura.

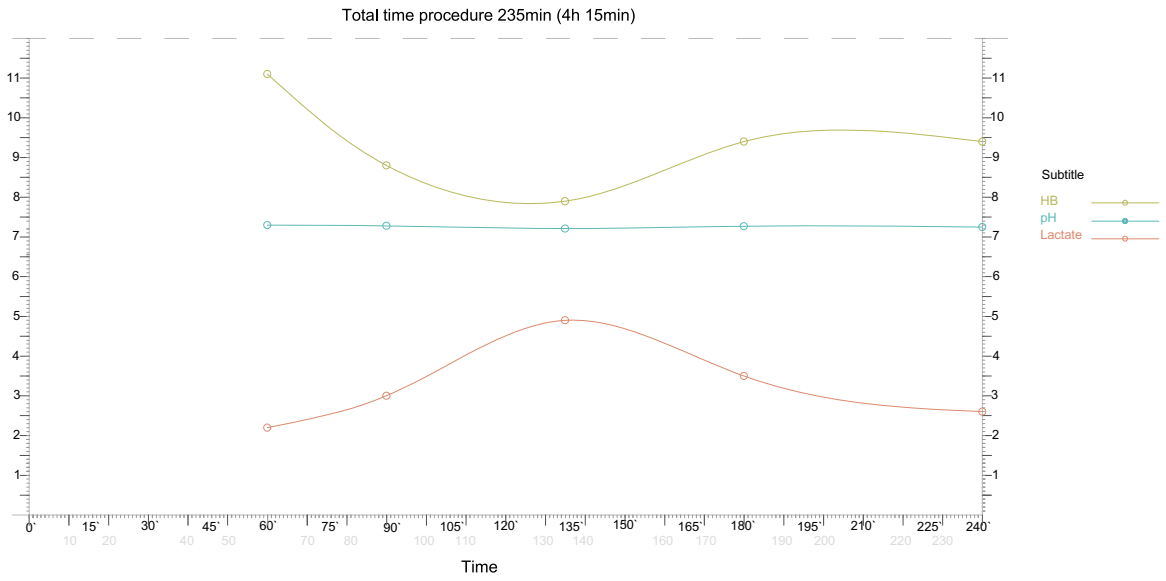

Fig. 2. Perioperative metabolic behavior. HB: hemoglobin.

urine alkalinization and the use of halopurinol in cases of renal disease or in patients with high risk of developing tumor lysis syndrome [5]. The increase in body temperature is also one of the culprits for the metabolic acidosis and elevation in the serum lactate levels (Δ2.2– 4.9) observed in the patient (Fig. 2) [6].

The development of coagulation disorders is frequent, which is why we opted for not using an epidural catheter [7]. Regarding the hyperdynamic state induced by the chemotherapy in the genesis of the metabolic disorders and hydroelectrolytic disturbances, one should also consider other factors that influence the metabolic imbalances, such as the intensity of the surgical trauma, the age group (there is no difference in the distribution of water and electrolyte by age) and the pre-operative state. To such factors, the metabolic acidosis of multifactorial etiology is added. The massive and abrupt release of cellular components after the rapid tumor lysis promoted by cisplatin [8] is the mechanism that generates the organic acids responsible for high anion gap acidosis. There is also a hypermetabolism generated by the surgical trauma, hyperthermia and by the chemotherapeutic agent itself to elevate the lactic acid serum levels, contributing to the perpetuation of acidosis [9].

That scenareo may become severe, with a reduction of the threshold for malignant ventricular arrhythmias, centralization of the blood volume with increased risk of pulmonary edema, a reduction of myocardial contractility and of the cardiovascular response to catecholamines, with a consequent decrease in cardiac output, blood pressure and renal and hepatic perfusion, factors that accentuate and perpetuate the already established lactic acidosis, in addition to aggravating the existing insulin resistance, hyperkalemia and protein catabolism [10].

Surgical patients are subject to stress hyperglycemia and a good intra-operative glycemic control is therefore recommended. In these cases, euglycemia is not the most appropriate target [11], which has been previously advocated in studies by Van den Berghe [12,13], but the level of 140–180 mg/dL recommended by the study NICE-sugar [14]. Hyperglycemia and insulin resistance are common findings in patients submitted to surgical stress due to the increased secretion of counter-regulatory hyperglycemic substances, in addition to the decrease of insulin production by the pancreatic beta cells [15]. The intravenous administration of insulin has a more predictable absorption when compared to the subcutaneous use, and it enables faster adjustments, with a more accurate glycemic control [16].

For analgesia, the epidural block with morphine is a suitable option that is regularly used to avoid the excessive use of intravenous opioids, in addition to reducing the need for prolonged mechanical ventilation and facilitating early hospital discharge, with benefits also being reported in the reduction of thromboembolic events. In addition, the use of combined anesthesia may result in lower use of intravenous anesthetics, shorter time of anesthesia and better analgesia [17].

4. Conclusion

The neoplastic compromise of the peritoneum has long been considered to be a pre-terminal state. The advent of CRS/HIPEC represent an alternative promising with numerous challenges to the anesthesiologist regarding the metabolic and hemodynamic adjustment, which once again demand training and ongoing study from the perioperative team.

Conflicts of interest

The authors declare there were no conflicts of interest.

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Ethical approval

This is a case report. Approval by ethics committee was not required.

Consent

Written consent was obtained from the patient.

Author contribution

All authors contributed to data acquisition, manuscript preparation, manuscript editing, manuscript review.

Guarantor

The first author, Fabricio Tavares Mendonça

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