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CASE REPORT

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Cytoreduction with Hyperthermic Intraperitoneal Chemotherapy and Renal Insufficiency Related to Diabetes Mellitus: An Anesthetic Challenge

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Abstract

Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) improves the prognosis in selected patients with peritoneal surface malignancies but it is an extensive procedure predisposing to major complications. Among them renal toxicity was reported. Severe renal insufficiency is considered a contraindication for this complex procedure. We present a patient with diabetic nephropathy with renal insufficiency KDOQI 3 and peritoneal metastasis from sigmoid adenocarcinoma with a good clinical outcome after CRS with HIPEC, highlighting the anesthetic precautions considered for this particular clinical case.

Keywords: acute renal failure, cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, diabetes mellitus

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Introduction

Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) improves the prognosis in selected patients with peritoneal surface malignancies [1]. It is an extensive procedure with significant hemodynamic, metabolic, hematological unbalances predisposing to major complications. A recent manuscript highlighted that diabetes predicted significant more major complications and increased mortality following CRS/HIPEC [2]. Among them renal toxicity was reported to occur with a frequency ranged between 1.9-5.7%, depending on chemotherapy [3-5]. Severe renal insufficiency is considered a contraindication for this complex procedure [6]. Scare literature data address a debate regarding the peri-operative anesthetic management of patients with moderate renal insufficiency related to diabetes mellitus that are considered for CRS with HIPEC. We present a patient with diabetic nephropathy and chronic renal failure stage 3 Kidney Disease Outcomes Quality Initiative (KDOQI 3) and peritoneal metastasis from sigmoid adenocarcinoma with a good clinical outcome after CRS with HIPEC, highlighting the anesthetic precautions considered for this particular clinical case.

Case report

A 64-year-old ASA II (American Society of Anesthesiologists) patient known with sigmoid adenocarcinoma pT4bN0M0L0V0R0 treated with sigmoid resection and chemotherapy was proposed for CRS with HIPEC considering the development of peritoneal metastases 10 months later. His past medical history was signifi-

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cant for blood hypertension, diabetes mellitus treated with insulin, hypertensive and diabetic nephropathy with renal insufficiency KDOQI 3.

At admittance in hospital the clinical examination revealed an obese patient with BMI of 34.5 with controlled blood pressure and diuresis of 1500 ml daily. Blood analyses revealed, a blood glucose level of 165mg/dl, a creatinine level of 2.25mg/dl corresponding to a GFR of 49.98.

The CRS with HIPEC procedure was performed in general anesthesia. Anesthesia was induced with fentanyl 3μg/kg and propofol 2mg/kg, intubation being facilitated with atracurium 0.5 mg/kg. Anesthesia was maintained with isoflurane and supplemented with intravenous fentanyl or epidural bupivacaine according to the patient's individual needs.

The cytoreductive phase consisted in extensive peritoneal resections together with segmental colonic and ileal resections, reestablishing digestive continuity through L-L ileo-transverso-colonic anastomosis. After cytoreduction before initiation of HIPEC, we ensured that fluid warmers and warming blankets were turned off. HIPEC was performed using an open technique (COLISEUM). For HIPEC phase oxaliplatin at 41-43°C for 30 min was used, being associated with intravenous administration of 5-fluorouracil and leucovirin. We monitored the core body temperature that was maintained by using warming blankets and infusing warm fluids.

The duration of the whole procedures was 720 min with 100ml blood loss.

The main purpose during the procedure was to maintain hemodynamic stability (MAP≥65 mmHg) and euvolemia (CVP between 3 and 5 mmHg). Hemodynamic stability was achieved by continuous infusion of low dose of noradrenaline (0,03-0,05 μg/kg/min).

Crystalloids at the rate of 10-15 ml/kg/h were infused and urine output (62.5 ml/15 min) was used as a guide for fluids administration. It was noticed a brief metabolic acidosis and a transient increase in arterial lactate levels (ph = 7.2, lactate = 1.8mmol/l). Calcium, potassium, sodium and magnesium were also checked intraoperatively and the values were normal.

The patient was monitored in intensive care unit for 5 days without any significant complications. We focused on the renal function, the diuresis being approximately 2500 ml daily, and creatinine level dropped at 1.3 mg/dl in the 5th day after surgery and then stabilizes at 1.6 mg/dl at discharge from hospital [Fig 1-Fig 3]. He was discharged from hospital 10 days after the procedure in good clinical condition.

At 6 months follow-up there were no signs of tumor recurrence and the creatinine level was similar with the basal values of the patient.

Discussions

CRS with HIPEC is an extensive procedure with significant hemodynamic, metabolic, hematologic alterations that predispose patients to a wide variety of postoperative complications. Among them renal toxicity was reported to occur with a frequency ranged between 1.9-5.7%, depending on the type of chemotherapy [3-5]. Severe renal insufficiency is considered a contraindication for this complex procedure [6]. Diabetes pre-

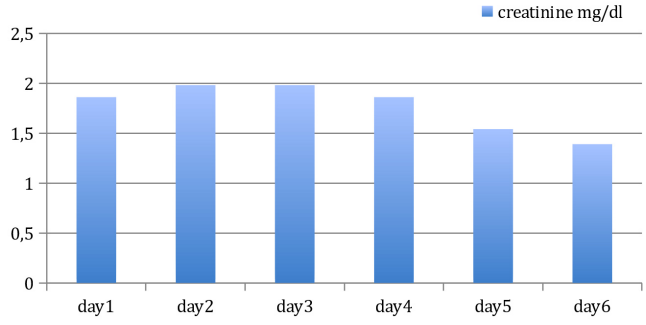

Fig. 1. Creatinine values in postoperative period

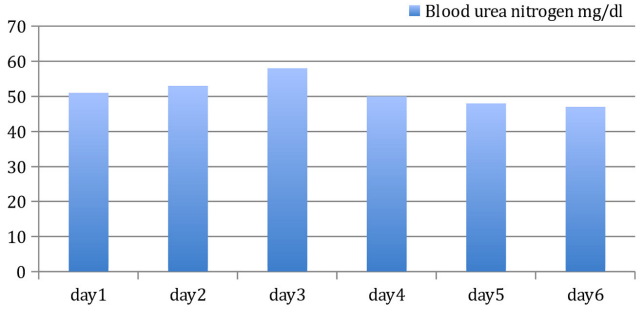

Fig. 2. Blood urea nitrogen values in postoperative period

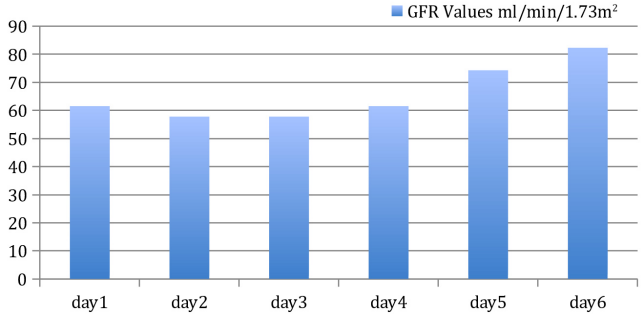

Fig. 3. GFR values in postoperative period

disposes to significantly more major complications and increased mortality following CRS/HIPEC [2].

Literature data are lacking in protocols regarding the peri-operative anesthetic management of patients with moderate renal insufficiency related to diabetes mellitus that are considered for CRS with HIPEC. We report for the first time a case of renal insufficiency KDOQI 3 in a diabetic patient who tolerated well a 12-hour intervention of CRS with HIPEC for peritoneal metastasis from sigmoid adenocarcinoma, highlighting the anesthetic precautions considered for this particular clinical case.

The risk factors for renal failure after CRS with HIPEC are: chemotherapy, surgical technique, hemodynamic instability, fluid losses and temperature.

Oxaliplatin is a chemotherapeutic agent that affects renal function by direct toxicity, or through hemolytic mechanism [7].

The closed technique of CRS with HIPEC can affect the renal function by raising the intra-abdominal pressure (IAP). It was showed that there is a signicantly decreased GFR in patients with elevated intraabdominal pressure (8).

HIPEC produces a hyperdynamic vasodilated state leading to increase in heart rate and increase in intra-abdominal pressure, especially in the closed technique with reduction in the cardiac output [9, 10]. Considering the extent of this type of intervention large fluid shifts can explain the renal impairment. Hyperthermia may cause consumptive coagulopathies, arrhythmias, liver/renal injury, peripheral neuropathies, and seizures [10, 11].

Our intraanesthetic management to prevent further renal function deterioration consisted of achieving hemodynamic stability by continuous infusion of low dose of noradrenaline, maintaining euvolemia by crystalloid infusion (10-15 ml/kg/h). For this patient we preferred the open technique to prevent the increase in intra-abdominal pressure. In the HIPEC phase we monitored the urinary output and try to achieve a flow of 50-70-ml/15 min using crystalloids and loop and osmotic diuretics. We also used anesthetic drugs with low impact on the renal function. The total amount of crystalloid used was 11000ml/12h and we obtained a diuresis of 3000ml/12h.

There is a debate in literature regarding the use of furosemide to enhance urine output to clear as much chemotherapeutic agent as possible [9,12-14]. Forced diuresis by the use of high dose loop-diuretics is still considered "standard of care" during chemotherapy with compound derived from platinum, even without definitive evidence. Corbella et al highlighted the role of invasive monitoring of euvolemia, as drug clearance is mainly linked to renal blood flow and not to plain urine output; this approach permitted the use of loop diuretics in accordance with maintaining euvolemia [9]. Our management was similar as we used only 80 mg of Furosemide administered bolus in the first 3 postoperative days.

Postoperative management was also focused on maintaining euvolemia (CVP between 3 and 7 mmHg) and an adequate diuresis using loop and osmotic diuretics (100mg mannitol 20% in the first 3 postoperative days) that were gradually stopped as the renal function stabilized (creatinine level dropped from 2.26mg/dl to 1.3mg/dl in the 5th day and stabilized to 1.6 mg/dl at discharge from hospital). At 6 months follow up there were no signs of tumor recurrence and the creatinine level was similar with the basal values of the patient.

Conclusion

In patients with renal failure that need CRS with HIPEC we recommend that intraoperative management should be focused on maintaining euvolemia by measuring parameters that give information about it (lactate, SVV, CVP) and maintenance of hemodynamic stability (MAP> 65 mmHg) using vasopressors.

We also recommend the administration of diuretics (loop diuretics and osmotics) both intraoperatively during the HIPEC phase of the procedure and in the first 3 days postoperatively.

With this management CRS (open technique) with HIPEC can be performed safely to patients with renal failure KADOQI 3 related to diabetes mellitus.

Conflict of Interest

None declared.

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