

# Anesthesia for Peritonectomy with Hyperthermic Intraoperative Peritoneal Chemotherapy. Case Report

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**Summary:** Pretto G, Grando M, Chella Junior N, Bergold RA, Castro RAC, Santiago A – Anesthesia for Peritonectomy with Hyperthermic Intraoperative Peritoneal Chemotherapy. Case Report.

**Background and objectives:** Pseudomyxoma peritonei is a rare condition related to epithelial neoplasia of the appendix and ovaries. Surgical cytoreduction, peritonectomy, and hyperthermic intraoperative peritoneal chemotherapy (HIPEC) is the treatment of choice. Maintenance of normovolemia, normothermia, postoperative pain management and coagulation status are all responsibility of the anesthesiologist. The objective of this report was to describe a case of peritonectomy with HIPEC.

**Case Report:** This is a 37 year-old female, ASA I, with a history of appendectomy 3 months ago with an anatomopathological report of mucinous cystadenoma. After review of the pathological sample, a pseudomyxoma peritonei was diagnosed with indication of peritonectomy with HIPEC. An epidural catheter (T11-T12) was placed and a test-dose, as well as morphine, was administered. Anesthesia was induced with remifentanyl, 0.4  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , propofol, and rocuronium, besides rapid-sequence orotracheal intubation. Remifentanyl, sevoflurane, and rocuronium were used for anesthesia maintenance according to the TOF. Ropivacaine 50 mg, and fentanyl 10  $\mu\text{g}$ . in 10 mL were administered through the epidural catheter 10 minutes before incision. During the surgery, CVP,  $\text{SpO}_2$ ,  $\text{FeCO}_2$ , temperature, heart rate, MAP, and urine output maintained stable levels within normal limits, including during HIPEC. Reduction of the hematocrit and  $\text{SvO}_2$ , increased PT, and thrombocytopenia were corrected by administering blood products. After 13 hours of surgery, the patient was admitted to the ICU under controlled ventilation. She was extubated on the 1<sup>st</sup> postoperative day, being discharged from the hospital on the 17<sup>th</sup> day of hospitalization.

**Conclusions:** Surgical cytoreduction and peritonectomy with HIPEC goes back to the decade of 1990 with several studies showing a significant increase in survival. Due to the complexity of the procedure and large surgery the vigilance of the anesthesiologist is fundamental for maintenance of clinical and laboratorial parameters, and recognition and treatment of any changes.

**Keywords:** ANESTHESIA, General, Epidural; CHEMISTRY, Chemotherapy; Hypovolemia; Pseudomyxoma Peritonei.

[Rev Bras Anesthesiol 2010;60(4): 551-557] ©Elsevier Editora Ltda.

## INTRODUCTION

Pseudomyxoma peritonei is a rare condition commonly associated with epithelial neoplasias of the appendix and ovary, showing indolent intraperitoneal dissemination with recurrent relapses over months or years, evolving to death. Systemic chemotherapy does not show satisfactory results for this type of tumor. The treatment of choice is surgical cytoreduction associated with hyperthermic intraoperative peritoneal chemotherapy (HIPEC)<sup>1</sup>. This therapeutic modality is based on the fact that surgical reduction of tumor foci to a minimum follo-

wed by heat, which presents cytotoxic activity, provides more efficacy of chemotherapeutic agents<sup>1,2</sup>. Due to the size of the surgery, patient sedation should be judicious and the medical-hospital structure should provide proper conditions for adequate perioperative management, with the participation of a multidisciplinary team composed of oncology surgeons, anesthesiologists, intensive care physicians, clinical oncologists, physical therapists, and nutritionists, all with experience in the management of patients undergoing large surgeries.

Cytoreduction surgery with HIPEC is a long procedure associated with significant blood losses due to exposure of a wide surgical field and bleeding, which frequently evolve to coagulation changes in the cytoreduction phase, and a series of pathophysiological changes described during the hyperthermic chemotherapy phase, such as increase in intra-abdominal pressure (IAP) leading to an increase in airways pressure and central venous pressure (CVP), as well as body temperature and the consequent increase in heart rate (HR), exhaled fraction of  $\text{CO}_2$  ( $\text{FeCO}_2$ ), arterial lactate, and metabolic acidosis<sup>2,3</sup>.

It is up to the anesthesiologist to foresee, prevent, recognize, and control any changes that represent a risk to the patient. Maintenance of normovolemia and of the activity of the coagulation system is the main goal during the cytoreduction

Received from the CET/SBA Serviço de Anestesiologia de Joinville (SAJ), and Hospital Regional Hans Dieter Schmidt.

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Submitted on February 2, 2010.  
Approved on May 3, 2010.

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phase, while hemodynamic, metabolic, and ventilatory vigilance is the priority during the HIPEC phase.

Control of postoperative pain should be planned by the anesthesiologist, since it is a very painful procedure, which has better results with epidural analgesia, reduction in the consumption of systemic opioids, and need of mechanical ventilation for a shorter period<sup>3</sup>. The objective of the present report was to describe the case of a patient with pseudomyxoma peritonei who underwent peritonectomy with HIPEC.

## CASE REPORT

M.L.R., a 37-year old female, underwent an appendectomy in January 2009 with the anatomopathological diagnosis of mucinous cystadenoma. After review of the anatomical specimen, pseudomyxoma peritonei was diagnosed. She developed several episodes of intestinal subocclusion during the follow-up and preoperative period, which resolved without surgery. She did not undergo any neoadjuvant treatment.

The patient was seen in the preoperative evaluation in March of the same year, and she denied comorbidities, allergies, or prior anesthetic interurrences. On that occasion, the patient did not show abnormalities in the physical exam and, therefore, she was classified as physical status ASA I. She weighed 56 kg, had a height of 155 cm (BMI 23.3), and had a Mallampati degree 2. Ancillary tests, electrocardiogram, and chest X-rays were all normal.

Upon arrival to the operating room, a venoclysis with a 14G catheter was performed in the left upper limb, followed by the intravenous administration of 2 mg of midazolam and 100 µg of fentanyl, for sedation, with posterior infusion of a complementary dose of midazolam, 1 mg. Before inserting the epidural catheter, 2 g of ampicillin with 0.5 g of sulbactam (half of this dose would be repeated every 6 hours during the surgery) and 500 mg of hydrocortisone (to modulate the systemic inflammatory response), were administered. The epidural catheter was introduced in the T11-T12 intervertebral space and a test-dose of 60 mg of lidocaine with vasoconstrictor and 2 mg of morphine were administered.

Anesthesia was induced with continuous infusion of remifentanyl, 0.4 µg.kg<sup>-1</sup>.min<sup>-1</sup>, a bolus of propofol, 2 mg.kg<sup>-1</sup>, and a bolus of rocuronium, 1 mg.kg<sup>-1</sup>, followed by rapid-sequence tracheal intubation under cricoid pressure with a 8.5 orotracheal tube with balloon. Anesthesia was maintained with continuous infusion of remifentanyl, with the rate ranging from 0.05 to 0.2 µg.kg<sup>-1</sup>.min<sup>-1</sup>, sevoflurane, with an exhaled fraction of 1 to 1.5%, and bolus rocuronium at 25% of the initial dose, according to neuromuscular monitoring (TOF).

Before beginning the surgery, a triple lumen catheter was introduced in the right subclavian vein. The right femoral artery was punctured and an 18G catheter was introduced to monitor the mean arterial pressure (MAP) and to collect blood for intraoperative laboratorial exams. Monitoring consisted of: esophageal temperature, urine output, gas analyzer, FeCO<sub>2</sub>, pulse oximetry, cardioscope, CVP, and MAP. Laboratorial

exams were performed every hour. A thermal mattress and a warming fluid system were used to prevent hypothermia during the cytorreduction phase of the surgery.

Ten minutes before beginning the surgery, 50 mg of ropivacaine and 100 µg of fentanyl diluted in 10 mL of solution were administered through the epidural catheter.

The cytorreduction phase of the surgery lasted 9 hours and 30 minutes, period during which the pelvic peritoneum was resected en bloc, including uterus and adnexa, retosigmoid colon, right hemicolectomy with resection of 15 cm of the terminal ileum, peritonectomy in the right and left upper quadrant, including resection of the spleen, gallbladder, hepatic capsule, parietocolic gutters, subdiaphragmatic regions, and greater omentum. The patient had a blood loss of 1,360 mL of blood and 360 mL of urine (0.7 mL.kg<sup>-1</sup>.h<sup>-1</sup>). During this phase of the surgery, 10,500 mL of crystalloids and 1,000 mL of colloids were administered. When the INR was about 1.83 (5 hours of surgery), 50 mL of fresh-frozen plasma (FFP) were administered and repeated at 9 hours of surgery. Platelet count reached 56,000 platelets after 7 hours of the procedure, being corrected with the infusion of 10 U of platelets. Two units of packed-red blood cells (PRBC) were administered after 9 hours of surgery, when the venous oxygen saturation (SvO<sub>2</sub>) reached 72% and hematocrit 16%. Blood replacement was restrictive, based on the SvO<sub>2</sub> and aiming at levels greater than 70%. Hemodynamic parameters (HR 60-90 bpm; MAP 60-75 mmHg; CVP 13-16 mmHg), esophageal temperature (35.3-36.1 °C), and FeCO<sub>2</sub> (29-34 mmHg) remained stable and within normal levels during this phase of the surgery.

In the HIPEC phase, which lasted 60 minutes, intra-abdominal mitomycin at 42 °C, through a mechanism of extracorporeal circulation by closed technique, was administered. During this phase, 500 mL of crystalloids were administered, and the patient urine output reached 50 mL (0.9 mL.kg<sup>-1</sup>.h<sup>-1</sup>). Hemodynamic parameters (HR 80-85 bpm; MAP 65-75 mmHg; CVP 13 mmHg), as well as FeCO<sub>2</sub> (32 mmHg), remained stable. As expected, esophageal temperature increased significantly (37.5-38.8 °C) without reaching levels above what would be tolerable.

After those phases the abdominal cavity was washed, followed by colorectal anastomosis and protective loop ileostomy, which lasted 2 hours. During this phase, 1,000 mL of crystalloids were administered and the patient had a urine output of 200 mL (1.8 mL.kg.h).

The patient was transferred to the ICU intubated at the end of the surgery where she remained for 6 days; however, she was extubated in the first postoperative day. She received daily doses of 2 mg of morphine and 10 mg of bupivacaine with vasoconstrictor administered by the anesthesiology team until the 6<sup>th</sup> postoperative day, when the epidural catheter was removed. She was asymptomatic and in good nutritional status when she was discharged from the hospital on the 17<sup>th</sup> postoperative day.

Five months after the surgery, the patient underwent reconstruction of the intestinal tract, and she is on monthly follow-up with the surgical team, showing good postoperative recovery.

## DISCUSSION

Pseudomyxoma peritonei is one of the tumors that show best results with cytoreduction surgery followed by HIPEC regarding improvement of survival and quality of life indices. However, due to its complexity and long duration, this technique is not devoid of risks<sup>1</sup>.

Peritonectomy with HIPEC can be divided into two phases, each with its respective physiological changes and, therefore, with particularities that deserve attention from the anesthesiologist. In the present report, the cytoreduction phase lasted 10 hours presenting as expected a large blood loss (around 1,500 mL), besides the loss of fluid from diuresis and large exposure in the surgical field. Those losses were replaced with infusion of crystalloids and colloids, reaching a mean of  $16.7 \text{ mL.kg}^{-1}.\text{h}^{-1}$ , which was higher than reported in a previous study of  $11.9 (6.1-25.5) \text{ mL.kg}^{-1}.\text{h}^{-1}$ <sup>3</sup>. It was also necessary to replace blood components (FFP, platelets, and PRBC) as a consequence of changes in laboratorial levels of coagulation, platelet count, hematocrit and  $\text{SvO}_2$ . Replacement of blood components is frequently necessary in this type of surgery<sup>2,3</sup>. Besides, replacement of blood losses with maintenance of volemia is also impor-

tant before the onset of HIPEC to maintain hemodynamic stability in this phase of the surgery<sup>3</sup>.

The HIPEC phase lasted 60 minutes. During this phase an increase in heart rate<sup>2,3</sup> is expected, which was not observed in this case, contrary to the elevation in body temperature and airways pressure. Monitored parameters were never outside normal levels.

Similar to other reports<sup>2,3</sup>, the patient was transferred to the ICU intubated, being extubated in the immediate postoperative period. Postoperative analgesia was programmed with a daily combination of boluses of opioids and local anesthetics through the epidural catheter, besides intravenous analgesics, with good pain control. The patient presented good evolution during the postoperative period; she underwent reconstruction of the intestinal tract, and she is now being followed-up on an outpatient basis. In the present case, it was demonstrated that this therapeutic modality, although complex, offers benefits to the patient.

To conclude, peritonectomy with HIPEC is a therapeutic modality that might improve survival and quality of life of patients with pseudomyxoma peritonei, but due to the size and peculiarities of the surgery, permanent vigilance and immediate control of any clinical change is the responsibility of the anesthesiologist.

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**Resumen:** Pretto G, Grando M, Chella Junior N, Bergold RA, Castro RAC, Santiago A –Anestesia para Peritonectomia con Quimioterapia Intraperitoneal Hipertérmica Transoperatoria. Relato de Caso.

**Justificativa y objetivos:** El seudomixoma peritoneal es una condición rara, relacionada con neoplasias epiteliales de apéndice y ovario. El tratamiento de elección es la citorreducción quirúrgica, peritonectomía y quimioterapia intraabdominal hipertérmica transoperatoria (QIAHT). Le concierne al anestesiólogo mantener la normovolemia, normotermia, el manejo del dolor postoperatorio y el estado de coagulación. El objetivo de este estudio fue describir un caso de peritonectomía con QIAHT.

**Relato del Caso:** Paciente femenina, 37 años, ASA I, con apendicectomía hace 3 meses, con laudo anatomopatológico de cistoade-

noma mucinoso. Después de revisada la pieza, quedó evidenciado el pseudomixoma peritoneal, con una indicación de peritonectomía con QIAHT. Se instaló un catéter epidural (T11-T12), dosis de test y morfina. Se procedió entonces a la inducción anestésica con remifentanil  $0,4 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , propofol y rocuronio, además de intubación orotraqueal en secuencia rápida. El mantenimiento se hizo con remifentanil, sevoflurano y rocuronio, conforme al TOF. Fueron administrados vía catéter epidural 10 minutos antes de la incisión ropivacaína 50 mg y fentanil 100  $\mu\text{g}$  en 10 mL. Durante toda la cirugía, PVC,  $\text{SpO}_2$ ,  $\text{FeCO}_2$ , la temperatura, frecuencia cardíaca, PAM y diuresis mantuvieron valores estables dentro de la normalidad, inclusive en el período de la QIAHT. Reducción en el hematocrito y  $\text{SvO}_2$ , el ensanchamien-

to del TAP y la plaquetopenia fueron corregidos con la administración de hemocomponentes. Después de 13 horas de cirugía, la paciente fue admitida en la UCI en ventilación controlada. Se extubó el 1º día del postoperatorio, con alta al 17º día del ingreso.

**Conclusiones:** La citorreducción quirúrgica y la peritonectomía con QIAHT surgieron en la década de 1990, con diversos estudios revelando el aumento significativo de la sobrevida. En función de la complejidad del procedimiento y de la gran demanda quirúrgica, es fundamental que el anestesista vigile el mantenimiento de los parámetros clínicos, laboratoriales, el reconocimiento y el tratamiento de cualquier alteración.