TOTAL INTRAVENOUS ANESTHESIA (TIVA) FOR CARCINOID SYNDROME

- A Case Report -

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Carcinoid tumors are rare slow-growing tumours that originate in the cells of the neuroendocrine system either enterochromaffin or Kulchitsky cells[1]. The nerve cells rarely undergo hyperplasia or neoplastic transformation, whereas cells in the endocrine glands and in disseminated sites in the mucous membranes and skin may undergo a tranformation commonly known as carcinoid tumors[2].

There are three main areas of origin for carcinoid tumors: foregut carcinoid tumours start in the lungs, bronchi, or stomach; midgut carcinoid tumours start in the small intestine, appendix, or proximal large bowel; and hindgut carcinoid tumours start in the distal colon or rectum[3]. The appendix is the most common site of carcinoid tumors, followed by the rectum, ileum, lungs, bronchi, and stomach[4].

The annual incidence of carcinoid tumors is approximately 0.28 per 100.000 population[5]. However, the overall prevalence in the United States is estimated to be one to two cases per 100.000 persons[3,4]. Because many carcinoid tumors are indolent, their true prevalence may be higher[6]. Data derived from a five-decade analysis of 13,715 carcinoid tumors revealed an overall increase in incidence over the past 30 years, with 67.2 percent of patients having a five-year survival rate regardless of the site of the tumor[2].

Prognosis varies widely depending stage of the tumor[2,3]. The disease is considered to be more aggressive and to have a worse prognosis than was thought previously[3].

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Remifentanil has been used for anesthesia for resection of other endocrine tumors[7] and reported used for carcinoid syndrome[1] but this is the first report of use of TIVA (total intravenous anesthesia) with Propofol and Remifentanil in a patient with carcinoid syndrome.

Case Report

A 64-yr-old woman with a history of appendicectomy and laparotomy at young age, sterilisation procedure and in 1988 a total hysterectomy and cholecystectomy at the same operation, presented in 1993 with epigastric discomfort, reflux symptoms, abdominal bloating and colicky pain. Gastroscopy was unremarkable. The patient presented in November 1994 as an emergency with small bowel obstruction and initial laparotomy revealed a terminal stricture, which was resected. Pathology report showed a 15 cm segment of terminal ileum containing a carcinoid tumor with lymphatic and vascular permeation and lymph node metastases. 24 hours urinary 5-hydroxy-indoleacetic acid (5HIAA) 5 days after surgery was normal at 0.9 umol/1.

The anesthetics for this procedure were uneventful with fentanyl, thiopentone, suxamethonium, N_2O and isoflurane. In 1998 laparotomy with division of adhesions was performed to relieve the erratic bowel activity and precipitous diarrhea. In December 2005, 24-hour 5HIAA showed elevation at 228.0 umol/24 hours (normal reference: 0-60 umol/24 hour) and CT-scan of thorax, abdomen and pelvis. March 2006 demonstrated liver (4.5 cm tumor involving segment 2 and 3 and 1.5 cm tumor involving segment 4) and pelvic (2 large vascular deposits within the lower mesentery) carcinoid lesions. Isotope bone scan September 2006 showed no evidence of skeletal metastases. Intractable diarrhea, nausea and fecal incontinence have since been the main problems. Fecal elastase was therefore measured November 2006 due to suspicion of steatorrhea and this was satisfactory (302 mikg/g) and 5HIAA was 195 umol/24 hours. Due to small bowel obstruction laparotomy was performed April 2007. Patient's current medication was subcutaneous octreotide 200 µg prn, vitamin B Calfec BD and ondansetron 4 mg prn.

Premedication included subcutaneous octreotide 100 μg, oral chlorpheniramine 4 mg and ranitidine 150 mg. I.V access was initially established with a 14-gauge cannula peripherally and an arterial line was inserted, after Allen's test, at right radial artery. An epidural catheter was placed at T9-10 interspace with the patient awake and sitting. A 2 ml test dose of bupivacaine 0.5% was injected to exclude intrathecal placement. Then a 5 ml bolus of bupivacaine 0.5% was given epidurally. Remifentanil was commenced at 1.2 mcg/kg/min and anesthesia was induced with a bolus of propofol 200 mg. No neuromuscular blockage was given. Anesthesia was maintained with continuous infusion of Remifentanil 3 mcg/kg/min and propofol (Diprivan 1% w/v AstraZeneca prefilled syringe) with target concentration 4 μg/ml (patients weight 51 kg) using a IVAC TCI Diprifusor (Alaris Medical Systems). A central venous line was placed ultrasound guided (Sonosite 180 Plus) in right internal jugular vein and a urinary catheter and nasogastric tube inserted. Continuous infusion of 5 ml/hour of bupivacaine 0.5% epidurally was started after induction and reduced to 4 ml/h 1 hour after induction. After 30 min, propofol was reduced to a target concentration of 3 μg/ml. Remifentanil was continued throughout the procedure at 3 mcg/kg/min. Additional drugs included cefuroxime 1.5 g and metronidazol 500 mg. Octreotide was available as well as vasopressors (ephedrine, phenylephrine and arginine vasopressin[8] and vasodilators (glycerylnitrate), but none was required except ephedrine. The entire procedure lasted 2.5 hours; arterial pressure, heart rate and central venous pressure (8-13 mmHg) was stable until the last 30 min where considerable pelvic bleeding occurred (blood loss of 1500 mls) and ephedrine 6 mg twice was given together with 2 units of packed red cells. Intraoperative fluids consisted of 2.5 litres Hartmann Solution and 1 litre Gelofusin. As hemostasis was poor in the pelvis, it was decided to pack the pelvis and an intubated and ventilated overnight-stay at the intensive care unit (ICU) was initiated.

Laparotomy confirmed extensive adhesions throughout the abdomen, and obstructed small bowel due to distal ileal loop adhering to one of the pelvic tumors. There were two nodular pelvic tumors each 8 cm. On patient arrival at ICU continuous infusion of epidural analgesia was provided with

bupivacaine 0.125% and fentanyl 4 μg/ml at a rate of 6 ml/hour together with propofol sedation 15 ml/hour and respirator setting (Draeger Evita) with FiO_2 30%, peep 5 cm H_2O, Pasb 5 cm, RR 12 and SpO_2 100%. The following day the pack was removed and closure of the rest of abdomen was performed. Postoperative course included total parenteral nutrition (TPN) support and was uneventful with discharge 14 days after initial surgery.

Discussion

Anesthetic considerations in patients with carcinoid syndrome include the prevention of mediator release. It was shown that these tumors release multiple hormones and mediators including tachykinins, bradykinins, prostaglandins, adrenocorticotropic hormone, vasoactive intestinal peptide, substance P, dopamine and neurotensin[9,11-13]. Avoiding triggering factors and preparation for the management of perioperative carcinoid crisis is the anesthetic aim[9].

Studies have been previously inconclusive on the effectiveness of prophylactic treatment with cyproheptadine, kentanserin, and aprotinin[14-17] and have recommended pre-treatment with octreotide and histamine blockers only[14,18-20]. Octreotide exerts pharmacologic actions similar to the natural hormone, somastatin. It is a potent inhibitor of growth hormone, glucagons, and insulin. Like somastatin, it also suppresses luteinising hormone response to gonadotropin relieving hormone, decreases splanchnic blood flow and inhibits release of serotonin, gastrin, vasoactive peptide, secretin, motilin, and pancreatic polypeptide. Because of these pharmacological actions, octreotide has been used to treat the symptoms of metastatic carcinoid tumors and vasoactive intestinal peptide secreting adenoma. We included the use of histamine blockers since histamine release is found mostly in gastric carcinoid tumors[21]. Octreotide in a dose of 100 μg three times daily for three weeks prior to surgery has been recommended[23]. We believed this treatment to be redundant since the patient had received a long-acting dose. Nevertheless octreotide was ready in the surgical suite in the case of an intraoperative complication.

A study noted that 43% of patients received vasopressors, either phenylephrine or ephedrine, and 38% of patients required intraoperative octreotide[5]. The pharmacodynamic profile of remifentanil, its elevated potency and low histamine releasing potential, mean that this opioid offers novel advantages during general anesthesia[10]. Remifentanil infusion has the advantages of good suppression of the intubation response, adequate analgesia, rapid titrate-ability and the ability to control any intraoperative hypertension. A potential disadvantage is the occurrence of hypotension, especially at higher infusion rates. At an infusion rate of 0.12-0.3 mcg/kg/min, the hemodynamic variables were virtually unchanged in this patient who is consistent with previous reports[1].

TIVA with propofol and remifentanil has been proved to be particularly suited for abdominal surgery. Its major advantages are hemodynamic stability, significantly shorter times of emergence and the exceptional acceptance by the patients[24]. Propofol TIVA results in a clinically relevant reduction of postoperative nausea and vomiting compared with isoflurane-nitrous oxide anesthesia (number needed to treat = 6)[25]. Anesthesia costs however, were more than three times greater for propofol TIVA, without economic gains from shorter stay in the post-anesthesia care unit[25].

Epidural anesthesia could cause hypotension, triggering mediator release and a carcinoid crisis[22]. However, the successful use of epidural anesthesia for transurethral resection of the prostate in a patient with carcinoid syndrome has been reported[23]. Epidural analgesia was adequate and did not produce any adverse hemodynamic consequences during the postoperative period of 72 h, after which the catheter was removed. The use of epidural analgesia is only advised in carcinoid patients who have been adequately treated before surgery with octreotide and provided that local anesthetic is administered in a graded manner with careful hemodynamic monitoring. A diluted concentration of bupivacaine 0.1% is advised in the postoperative period. However, further studies will be required to confirm the favourable outcome observed in this patient.

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