Case Report

Anaesthetic management of extra-pleural pneumonectomy and hyperthermic intrathoracic chemotherapy procedure

Address for correspondence:
Dr. Jalaja Koppa Ramegowda,
#75, 80 Feet Road, Opposite M.S. Ramaiah Hospital,
Raj Mahal Vilas 2nd Stage,
Bengaluru - 560 094,
Karnataka, India.
E-mail: jalaja1975@gmail.com

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/0019-5049.171574

Quick response code

Jalaja Koppa Ramegowda, Mohammed Abdul Salam, Vasant Nayak, Shabber Zaveri[1]

Departments of Anaesthesiology and [1]Surgical Oncology, Manipal Hospital, Bengaluru, Karnataka, India

ABSTRACT

Malignant pleural mesothelioma is a rare tumour with survival of 9–17 months after diagnosis. Radical surgical resection by extra-pleural pneumonectomy combined with hyperthermic intrathoracic chemotherapy has shown to improve patient survival and better microscopic tumour control. Anaesthetic management of this procedure is challenging due to the complex pathophysiological changes associated with prolonged duration of surgery, one- lung ventilation, haemodynamic instability due to major blood loss, temperature variations including heat loss during pneumonectomy and rapid rise in temperature during hyperthermic chemotherapy, cardiac arrhythmias due to exposure to heated chemotherapeutics, cisplatin toxicity and acid-base changes. Intra-operative management involves protective ventilation, regulation of temperature and haemodynamics along with prevention of complications associated with 'heated chemotherapeutics'. Thorough pre-operative assessment and preparation, advanced intra-operative monitoring with prompt corrective interventions, will help in improved patient outcome in the immediate post-operative period. We present one such case done for the 1st time in India.

Key words: Extra-pleural pneumonectomy, hyperthermic intrathoracic chemotherapy, malignant pleural mesothelioma, plethysmographic variability index

INTRODUCTION

Malignant pleural mesothelioma (MPM) is a rare tumour with survival of 9–17 months after diagnosis.[1] Extra-pleural pneumonectomy (EPP) with *en-bloc* removal of the parietal and visceral pleura, lung, pericardium and diaphragm is done to achieve macroscopic clearance of MPM. Recently, EPP has been combined with hyperthermic intrathoracic chemotherapy (HITHOC) to achieve microscopic tumour control and improved patient survival.[2,3]

EPP with HITHOC is a complex procedure of prolonged duration involving one-lung anaesthesia added on with the complications induced by intrapleural instillation of the heated chemotherapeutic solution. There are wide variations in haemodynamics, temperature, metabolic and coagulation parameters during the perioperative period.[4] We present a case of MPM, planned for EPP followed by HITHOC.

CASE REPORT

A 58-year-old male presented with 4 months history of dyspnoea, weight loss and change in voice. He had tachypnoea, woody dullness and reduced breath sounds over the whole of right hemi-thorax. Airway and other systemic examinations were normal. He had no other medical co-morbid conditions. Computed tomography, positron emission tomography and cytological studies established the diagnosis of right-sided MPM with middle and lower lobe collapse along with the right upper, lower paratracheal and subcarinal lymphadenopathy. Room air oxygen

How to cite this article: Ramegowda JK, Salam MA, Nayak V, Zaveri S. Anaesthetic management of extra-pleural pneumonectomy and hyperthermic intrathoracic chemotherapy procedure. Indian J Anaesth 2015;59:807-10.

saturation was 97%. His haemoglobin concentration was 15.5 g%. Coagulation profile, renal function tests, liver function test, electrocardiogram and two-dimensional echocardiography were normal. Pulmonary function tests showed moderate restrictive dysfunction. Pre-operative blood gas showed mild respiratory alkalosis. He was posted for right thoracotomy with EPP and HITHOC.

Intra-operative monitoring included electrocardiography, arterial blood pressure, central venous pressure, end-tidal carbon-dioxide, neuromuscular monitoring, entropy, Masimo™ Rad-7 pulse-oximeter with plethysmographic variability index (PVI),[5] nasopharyngeal and peripheral temperature monitoring. Intravenous access was secured with two 16 gauge intravenous cannulae. Bolus intravenous infusion of dexmedetomidine (1 μg/kg) was given over 10 min followed by maintenance infusion of 0.5 μg/kg/h. After pre-oxygenation with 100% O_2, anaesthesia was induced with intravenous propofol 100 mg, fentanyl 125 μg and atracurium 35 mg. A 37 Fr left sided double lumen endotracheal tube (Mallinckrodt™ Covidien Ilc, MA, USA) was placed and its position confirmed with fibreoptic bronchoscopy. Anaesthesia was maintained with propofol 100–150 μg/kg/h, fentanyl 50 μg/h and atracurium 20 mg/h. Patient was placed in left lateral position for right thoracotomy. One-lung ventilation was started 1 h after induction of anaesthesia with 50–60% inspired oxygen, tidal volume of 300–325 ml, respiratory rate of 12–14 breaths/min and a positive end-expiratory pressure (PEEP) of 5 cm H_2O.

During EPP, blood loss was 2500 ml, which was replaced with 3 units of packed red blood cells (PRBCs) and 3 units fresh frozen plasma. Temperature was maintained at around 35.0°C during cytoreduction by using warm intravenous fluids, warming blanket and forced-air warmer. The cytoreduction, which lasted for 9:30 h constituted EPP, lymph node clearance, pericardiectomy and right hemi-diaphragmatic resection and repair using a polytetrafluoroethylene graft. Towards the end of EPP, before starting HITHOC, the patient was actively cooled to bring down the core body temperature to 34°C. The ambient temperature was set at 18°C. Forced-air warmer and fluid warmers were switched off. Hemotherm® blanket was switched to cooling mode at 12°C. Cold intravenous fluids (at 10°C) were infused along with dopamine infusion (at 2–4 μg/kg/min). Open HITHOC technique using high dose Cisplatin, (150 mg/m^2 body surface area total dose-260 mg) in 3.5 L perfusate at 42.5°C was circulated for 60 min in the right hemi-thorax at a rate of 900 ml/min using Belmont® hyperthermia pump (Billerica, MA, USA). During the HITHOC period, temperature, urine output and haemodynamics were continuously monitored. Urine output was maintained above 100 ml/15 min with 5–10 mg increments of intravenous furosemide and 1800 ml/h of intravenous fluid infusion. The temperature increased from 34.2°C at the start of HITHOC to 37°C at the end. To prevent the drop in temperature after HITHOC, the cooling process was stopped towards the end of HITHOC and warming devices were restarted. Serial blood gases showed no major abnormalities. Throughout the procedure, the patient was haemodynamically stable and had no arrhythmias. Intravenous calcium gluconate 10% 10 ml and $MgSO_4$ 1 g, were administered. Total surgical duration was 13 h with total blood loss of 3000 ml. Total fluid infusion amounted to 7000 ml of balanced salt solution, 1000 ml 6% hydroxyethyl-starch 130/0.4 and 2100 ml of blood products. Patient had an uneventful recovery, was extubated on the table and shifted to the Intensive Care Unit.

On the first post-operative day, the patient had mild hypokalaemia and haemoglobin dropped to 8 g%, which was corrected with potassium-chloride infusion and single unit PRBCs transfusion. A marginal increase in serum creatinine was noted during first five post-operative days, which normalised later. Pain control was achieved with intravenous acetaminophen (1 g 6th hourly) and patient-controlled analgesia using fentanyl for 5 days. The right-sided chest drain remained clamped to prevent mediastinal shift and to facilitate filling of the right hemi-thorax with exudate. It was removed on the 7th post-operative day. He was discharged from the hospital on 10th post-operative day.

DISCUSSION

Anaesthetic management in EPP with HITHOC is challenging due to potential complications associated with prolonged duration of surgery, one-lung ventilation, haemodynamic instability due to major blood loss and fluid shifts, temperature variations including heat loss during EPP and rapid raise in temperature during HITHOC, arrhythmias due to direct handling of the heart and exposure to heated chemotherapeutics, cisplatin-induced nephrotoxicity, electrolyte-imbalance and acid-base changes. Therefore, a thorough pre-operative cardiopulmonary evaluation, intensive intra-operative monitoring

combined with immediate corrective interventions throughout the surgical period is mandatory. Our patient was managed with total intravenous anaesthesia. Arterial blood pressure, central venous pressure and PVI were used for continuous haemodynamic monitoring and as a guide for fluid management. There is a strong correlation between liberal fluid administration and increased incidence of coagulopathy, post-operative acute lung injury and increased mortality. Goal-directed fluid management based on PVI has shown to reduce complications and improve patient outcome.[5-7] Therefore, we set a goal of urine output >0.5 ml/kg/h, PVI <14 and mean arterial pressure >65 mmHg for fluid management during the prolonged EPP phase. Nephrotoxicity, acid-base abnormality, hypomagnesaemia and hypokalaemia are noted complications following cisplatin use in hyperthermic intraperitoneal chemotherapy.[8] During HITHOC, renal protection measures such as rapid fluid infusion (2 L/h), low dose dopamine and furosemide were used to maintain a urine output of >100 ml/15 min in addition to calcium, magnesium and potassium supplementation.

Lung isolation was achieved with a left sided double lumen tube. Protective one-lung ventilation strategy of low tidal volume (5 ml/kg), plateau pressure limitation and application of PEEP (5–7 cm H_2O) was employed to ensure adequate oxygenation and prevention of acute lung injury.[4] During EPP, forced-air warmer, fluid warmer and hemotherm were used to maintain the core temperature around 35°C. During HITHOC, chemotherapeutic agents mixed with 2–3 L of peritoneal dialysis fluid, is circulated through the thoracic cavity at 41–42°C for 60 min through a pump capable of generating rapid flow rates (1000 ml/min) to achieve microscopic tumour clearance.[2] This process causes a rapid increase in core temperature, which is countered by various cooling manoeuvres. In a similar procedure (hyperthermic intraperitoneal chemotherapy), there were significant increases in mean temperature despite the intense cooling measures. 18% patients had an increase in core temperature >39°C which could precipitate myocardial infarction, cardiac arrhythmia, acute lung injury and neurological damage.[9] In our case, with all the cooling measures, we could prevent an excessive rise in temperature during the 60 min HITHOC phase (core temperature increased from 34.2°C to 37°C) [Figure 1].

Hyperthermic intrathoracic chemotherapy patients are at risk of reduced pulmonary reserve which would influence the decision about immediate post-operative extubation. Kerscher *et al*.[4] have reported that 75% of their HITHOC patients were extubated in the operation room and the rest required elective ventilation up to 8 days post-operatively. Since our patient had recovered adequately, he was extubated in the operation theatre. Large fluid loss (up to 4 L/day) from the drains is expected to occur for 3 days post-operatively.[2] Liberal intravenous fluids along with inotropic support may be required to maintain haemodynamic stability. In addition, these patients need correction of coagulation abnormalities, electrolyte imbalance and control of blood sugar for the next 5 post-operative days. Hence, HITHOC patients require ICU care during the first post-operative week.

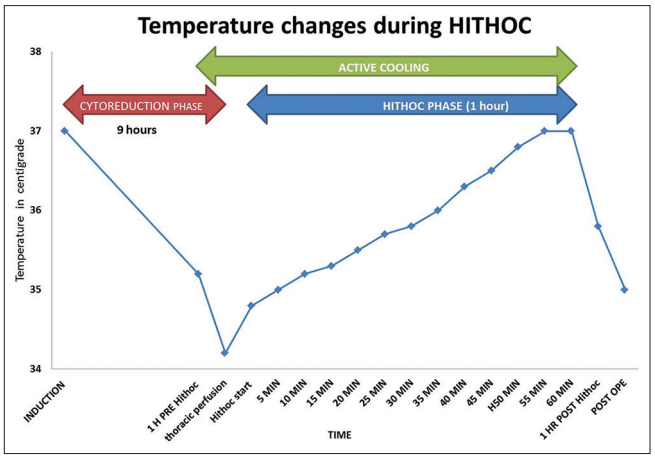

Figure 1: Temperature variations that occurred during cytoreduction and hyperthermic intrathoracic chemotherapy (HITHOC) phases of the procedure. Cytoreduction lasted for 9 h and patient's core temperature was maintained around 35°C. Active cooling of patient was started approximately 1 h before HITHOC and continued throughout the 60 min HITHOC period

CONCLUSION

Anaesthetic management of EPP with HITHOC involves lung isolation with protective ventilation, control of temperature and haemodynamic variations along with prevention of complications associated with 'heated chemotherapeutics'. Thorough pre-operative assessment and preparation, advanced intra-operative monitoring with prompt corrective interventions will help in improved patient outcome.

REFERENCES

1. Tsao AS, Wistuba I, Roth JA, Kindler HL. Malignant pleural mesothelioma. J Clin Oncol 2009;27:2081-90.
2. Ried M, Potzger T, Braune N, Neu R, Zausig Y, Schalke B, *et al*. Cytoreductive surgery and hyperthermic intrathoracic chemotherapy perfusion for malignant pleural tumours:

Perioperative management and clinical experience. Eur J Cardiothorac Surg 2013;43:801-7.
3. Kyaw MA, Hu W. Effect of cytoreductive surgery combined with intraoperative intra-thoracic hyperthermic chemotherapy in patients with advanced non-small cell lung cancer. J Cancer Res Treatment 2014;2:1-5.
4. Kerscher C, Ried M, Hofmann HS, Graf BM, Zausig YA. Anaesthetic management of cytoreductive surgery followed by hyperthermic intrathoracic chemotherapy perfusion. J Cardiothorac Surg 2014;9:125.
5. Forget P, Lois F, de Kock M. Goal-directed fluid management based on the pulse oximeter-derived pleth variability index reduces lactate levels and improves fluid management. Anesth Analg 2010;111:910-4.
6. Brandstrup B, Tonnesen H, Beier-Holgersen R, Hjortso E, Ording H, Londorff-Larsen K, *et al*. Danish study group on perioperative fluid therapy: Effects of intravenous fluid restriction on postoperative complications: Comparison of two perioperative fluid regimens: A randomized assessor-blinded multicenter trial. Ann Surg 2003;238:641-8.
7. Licker M, de Perrot M, Spiliopoulos A, Robert J, Diaper J, Chevalley C, *et al*. Risk factors for acute lung injury after thoracic surgery for lung cancer. Anesth Analg 2003;97:1558-65.
8. Hakeam HA, Breakiet M, Azzam A, Nadeem A, Amin T. The incidence of cisplatin nephrotoxicity post hyperthermic intraperitoneal chemotherapy (HIPEC) and cytoreductive surgery. Ren Fail 2014;36:1486-91.
9. Kamal JM, Elshaikh SM, Nabil D, Mohamad AM. The perioperative course and anesthetic challenge for cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. Egypt J Anaesth 2013;29:311-8.

Source of Support: Nil, **Conflict of Interest:** None declared

Announcement

ANNOUNCEMENTS FOROM ISA NATIONAL SECRETARIAT

1. The Annual National Conference of ISA will be in November from 2016
   - Workshops 25th November
   - CME 26th November
   - Conference inauguration 26th November evening
   - Orations 27th November forenoon
   - AGBM 28th November Afternoon
   - Valedictory function 29th November noon
2. ISA Android App is live now. Members can download it from Google Play store by searching "ISA" in Google Play store Apps or by clicking the following link

   https://play.google.com/store/apps/details?id=dotweb.isa&hl=en

   Member can use their ISA login details for Login to App. (Your ISA No is log in ID & the password id same as ISA log in password)
3. Members are requested to visit www.isaweb.in regularly to get information on various ISA Awards, Fellowships, Conferences, member details, decisions of GC / GB etc.
4. SMS is sent from ISANHQ regularly to pass messages to members
5. Online election for ISA National President elect & GC members is from 8.00 a.m on 1st December 2015 to 5.00 p.m. on 5th December 2015.
6. ISA Protocols are published in www.isaweb.in Please go through.
7. ISA Member details is published in www.isaweb.in Please go through and update if required.
8. Members are requested to update their details (Branch Transfer, ALM to LM conversion & Address change etc) by logging in at www.isaweb.in
9. ISA membership is online only & membership Fee payment is also through online payment only.
10. All City & State Branch Office Bearers are requested to update their details with ISA National & also send their Bank details to transfer Grant in Aid.

Dr. Venkatagiri K. M.
Hon. Secretary, ISA National