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## Severe metabolic acidosis secondary to iatrogenic hyperglycaemia in secondary cytoreduction and hyperthermic intraperitoneal chemotherapy (HiPEC)

Sir,

Cytoreductive surgery (CRS)-hyperthermic intraperitoneal chemotherapy (HiPEC) is a popular topic of investigation for cancers with diffuse peritoneal metastasis.<sup>[1]</sup> Perioperative management for these patients is challenging for the anaesthesiology team. We report a case of hyperglycaemia and metabolic acidosis leading to delayed arousal from anaesthesia after CRS-HiPEC.

A 53-year-old female patient, weighing 52 kg, diagnosed with carcinoma ovary was posted for secondary cytoreduction followed by HiPEC. She had

no other co-morbidities. Inside the operating room, standard American Society of Anesthesiologists (ASA) monitors were connected, an epidural catheter inserted and general anaesthesia was induced with Inj. propofol 2 mg/kg, Inj. fentanyl 2 µg/kg and Inj. vecuronium 0.1 mg/kg intravenously (IV). Maintenance of anaesthesia was done on low flow nitrous oxide, oxygen and sevoflurane (2%) with intermittent Inj. vecuronium 0.02 mg/kg. This was followed by the insertion of a nasopharyngeal temperature probe, central venous catheter and right radial artery cannula. Warm intravenous fluids and warming blanket were used to prevent hypothermia. Secondary cytoreduction was performed for 6.5 hours. Total blood loss of 1100 ml was combated by 2.5 L of crystalloids (Ringer lactate), 500 ml colloid, and 2 units of packed red blood cells (RBCs). Surgery was followed by HiPEC, lasting another hour. Before commencing HiPEC, warm intravenous fluids were replaced with cold ones. Doxorubicin prepared in 5% dextrose at 42° was used as intraperitoneal dialysate. Adequate analgesia was provided by intravenous fentanyl, morphine and thoracic epidural infusion. Hourly urine output was adequate (>0.5 mL/kg/hour) throughout the surgery, with a desirable increase (3 ml/kg/hour)

during the HiPEC phase. Acute hyperthermia (up to 38.7° C) was witnessed during HiPEC and managed by reducing ambient temperature, using cold intravenous fluids and ice packs in the axilla. At the time of reversal, the patient was not taking spontaneous breaths despite 1 hr of the last dose of relaxant. Changes in vitals that were transient were attended and the temperature was restored to normal within the next 40 min. Arterial blood gas (ABG) analysis performed now revealed severe metabolic acidosis (pH = 6.96) and also severe hyperglycaemia (486 mg/dl), which was managed by 10 units of intravenous insulin. Lactic acidosis was managed by giving 2 mEq/kg of 8.4% sodium bicarbonate infusion over 30 min. After 90 min of active management, the parameters improved to pH = 7.29 and blood sugar = 268 mg/dl. The patient was successfully extubated and the rest of the postoperative period remained uneventful.

The main aim of intraperitoneal delivery of the cytotoxic drug in HiPEC is to achieve high drug concentrations in the local peritoneum with low systemic drug levels. Hyperthermia acts synergistically with chemotherapy by direct cytotoxic action and by increasing drug penetration.<sup>[2]</sup> Major anaesthetic challenges during CRS include blood loss, major fluid shifts, hypothermia, and prolonged surgery.<sup>[3]</sup> The concerns of HiPEC include acute hyperthermia, coagulation abnormalities, hypermetabolic state, raised intraabdominal pressure, fluid shifts, metabolic derangements and chemotherapeutic-induced nephrotoxicity.<sup>[4]</sup> The extensive surgery warrants good perioperative analgesic cover that can be done with opioids, epidural, paravertebral blocks and subcostal transverse abdominis plane (TAP) block.

The major challenge encountered by us was acute hyperthermia and severe hyperglycaemia with HiPEC. Significant stress-induced hyperglycaemia (of extensive surgery) was superadded with iatrogenic hyperglycaemia using 5% dextrose dialysate solution. Doxorubicin causes insulin resistance and hyperglycaemia by disrupting adenosine monophosphate activated protein kinase (AMPK) signaling pathways.<sup>[5]</sup> Haemodynamic instability (not requiring ionotropic support) during secondary cytoreduction owing to blood loss and massive fluid shifts lead to metabolic acidosis, which was exaggerated during HiPEC with a decreasing trend in pH and bicarbonate [Table 1].

We believe that our patient had Type-B lactic acidosis (unrelated to hypoperfusion) as she had received adequate pre-operative maintenance fluid (Ringer Lactate) and well-tailored intraoperative fluid therapy. After ruling out other causes, we believe that the culprit in our case was hyperglycaemia and acute hyperthermia causing increased metabolic rates, fluid shift and resultant delayed reversal.<sup>[4]</sup> Our perioperative management in this patient was guided by the Society of Onco-Anaesthesia and Perioperative Care consensus guidelines for CRS-HiPEC.<sup>[6]</sup> The utilisation of dextrose as a carrier for dialysate solution in HiPEC needs to be further explored considering the potential downbeat impact of perioperative hyperglycaemia and metabolic acidosis on patient outcomes. Anaesthetic care of patients undergoing CRS-HiPEC is challenging and even minor acts of omission can influence perioperative morbidity.

**Table 1: Comparison of various biochemical parameters in the patient depicting developing acidosis**

Parameters	Baseline	Intra-operative (3 h into surgery)	Post-secondary cytoreduction	Post HiPEC	At reversal
pH	7.38	7.34	7.28	6.96	7.29
PCO <sub>2</sub> (mm Hg)	33	36	35	38	36
HCO <sub>3</sub> <sup>-</sup> (meq/L)	21	20	19.9	8.2	17
LACTATE	1.0	1.0	1.1	4	1.3
BASE EXCESS	-3	-3	-9	-21	-8.7

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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#### Conflicts of interest

There are no conflicts of interest.

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**REFERENCES**

1. Helm CW. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Ovarian Cancer: World Experience. *Intraperitoneal Cancer Therapy*. Totova, NJ: Humana press; 2007. p. 147-62.
2. Gonzalez MS, Gonzalez BLA, Ortega PG. Hyperthermic intraperitoneal chemotherapy: Rationale and technique. *World J Gastrointest Oncol* 2010;2:68-75.
3. Garg R. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: Fluid and temperature remain the culprit! *Indian J Anaesth* 2018;62:162-5.
4. Kamal JM. The perioperative course and anesthetic challenge for cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. *Egypt J Anaesth* 2013;29:311-8.
5. de Lima Junior EA, Yamashita AS, Pimentel GD, De Sousa LG, Santos RV, Gonçalves CL. Doxorubicin caused severe hyperglycemia and insulin resistance, mediated by inhibition in AMPk signalling in skeletal muscle. *J Cachexia Sarcopenia Muscle* 2016;7:615-25.
6. Solanki SL, Mukherjee S, Agarwal V, Thota RS, Balakrishnan K,

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