# ANESTHETIC MANAGEMENT DURING HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC)

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## Introduction

HIPEC is used to treat abdominal malignancies that have spread throughout the peritoneum. The procedure can be thought of in two stages: the cytoreductive stage, and the HIPEC stage.

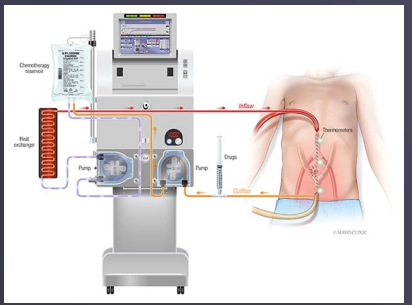
The cytoreductive stage involves opening the abdomen to debulk as much of the tumor as possible. The purpose of cytoreduction is to reduce any large and visible tumor so that cytotoxic medications can be more effective, as these medications can only reach through 5mm of tissue.[3,4]

The HIPEC portion of the procedure involves the infusion of heated chemotherapeutic agents into the abdomen. This can be done using an open or closed abdomen technique, and allows cytotoxic medications to be distributed within the peritoneum for approximately 90 minutes. Chemotherapeutic agents that may be used include mitomycin, cisplatin, doxorubicin, and carboplatin.[4]

The entire procedure lasts up to 10 hours and is dependent on how extensive tumor debulking is. There are several unique anesthetic considerations during a HIPEC procedure involving significant shifts in fluids, electrolytes, and temperature, as outlined below.

## Learning objectives

- Understand the physiologic changes that occur with the infusion of heated chemotherapeutic agents
- Considerations for fluid and electrolyte shifts
- How to manage temperature during a HIPEC procedure




## Patient Presentation

A 61 year old female with a past medical history of epilepsy treated with phenytoin presented for abdominal tumor debulking and HIPEC for diffuse colon cancer. The patient had previously undergone a diagnostic laparoscopy which revealed appendiceal cancer invading into the retroperitoneum and parietal abdominal wall. She was initially treated with 8 cycles of systemic chemotherapy. Her most recent CT scan showed improvements and the patient was considered optimized for surgical resection. On the day of surgery, surgeons planned for the removal of sections of the peritoneum, omentum, small and large intestines, and retroperitoneal muscle prior to infusion of hyperthermic mitomycin.

A thoracic epidural was placed in pre-op for post-operative pain management. Once in the operating room, standard ASA monitors were placed. General anesthesia was induced using fentanyl, lidocaine, propofol, and rocuronium. A post-induction arterial line was placed for serial monitoring of hemodynamics and blood gases. Two large-bore IVs were also placed given the potential for significant blood loss. Anesthesia was maintained using sevoflurane. Analgesia was primarily achieved through epidural bupivacaine and hydromorphone, as well as small amounts of intravenous ketamine.

A goal directed fluid therapy strategy was used to manage fluid shifts throughout the procedure. Using this strategy, the patient received a total of 4.25 liters of lactated ringers. In addition to fluid therapy, a phenylephrine infusion was utilized to maintain blood pressure within a normal range. The patient received potassium and magnesium supplementation according to intraoperative chemistry panel results. During the cytoreductive stage, temperature was maintained using a forced air warmer. During the HIPEC stage, the patient was actively cooled using a polar cube, ice packs around the axilla, and a forced air cooler. The patient was successfully weaned from pressors prior to an uneventful extubation, and immediately brought to PACU. She was later discharged on post-operative day 7 with no notable complications.

# Discussion

## Why Hyperthermia?

Hyperthermia enhances the effectiveness of cytotoxic medications by several mechanisms. Heat increases malignant cell membrane permeability and therefore improves drug uptake and tissue depth of medications.[4,6] Hyperthermia also works synergistically with cytotoxic medications to inhibit RNA synthesis and mitosis, and increase lysosomal enzyme activity.[4,6] Hyperthermia appears to selectively target malignant cells as compared to benign cells. This is hypothesized to be due to the increased sensitivity of mitochondria membranes of cancer cells.[6]

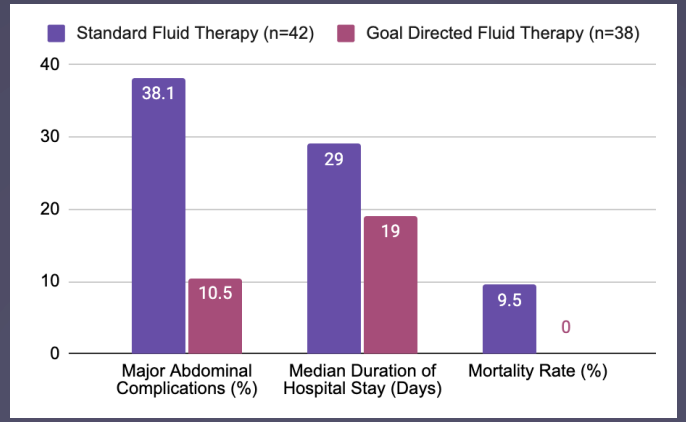



**Figure 1.** Complications associated with standard fluid therapy (8269 +/- 1452ml) vs goal directed fluid therapy (5812 +/-1244ml).[1]

## Physiologic Changes During the HIPEC

- Lactic acidosis: hyperthermia induces a hypermetabolic state and increased oxygen demand by tissues which predisposes patients to lactic acidosis.[3,4]
- Decreased SVR and MAP: this can be expected due to two mechanisms. First, hyperthermia causes vasodilation. Additionally, damaged cancer cells release inflammatory markers that also contribute to vasodilation and a potentially significant drop in SVR.[4,5]
- Increased cardiac output: this can be anticipated as a compensatory response to a drop in SVR.[4,5]

Of note, the physiologic and hemodynamic changes that occur during a HIPEC can somewhat resemble sepsis.

## Fluid Management

Multiple retrospective analyses have shown that a liberal fluid management strategy during a HIPEC is associated with increased morbidity and mortality.[1,2] However, fluid restriction can lead to organ hypo-perfusion and increase the incidence of AKI, one of the most common complications associated with this procedure.[4] Therefore, practice guidelines generally recommend goal directed fluid therapy.[1,2,4] Several patient factors and monitors can be used to help guide fluid replacement, as detailed below.

## Helpful Monitors of Fluid and/or Electrolyte Status

- Arterial line: recommended to monitor ABGs frequently (every 30-45 min) during the HIPEC stage as there can be significant electrolyte shifts.[4] Base deficit may also be a helpful indicator of fluid status (check baseline).
- Urine output: minimum goal of 0.5 mL/kg/h pre-HIPEC, and 2-4 mL/kg/h during the HIPEC portion[3,4]
- Pulse pressure variation: measures the ventilator-cardiac interaction to estimate fluid responsiveness
- Dynamic fluid monitor (ie FloTrac): stroke volume, stroke volume variation, cardiac output, cardiac index
- TEE: not always indicated, but may be helpful to monitor fluid status in a patient at increased risk of fluid overload, including those with heart failure

## Electrolyte Changes and Management

In addition to vasodilation, the release of inflammatory markers by damaged cells leads to increased vascular permeability. This can result in significant shifts in both fluid and electrolytes during the HIPEC portion of the procedure. Some electrolyte changes that may be encountered include the following:[3,4,5]

- Hypomagnesemia- presents a concern for perioperative arrhythmias.
- Hypokalemia- presents a concern for perioperative arrhythmias including atrial fibrillation.
- Hyperkalemia- may occur secondary to cell lysis from cytotoxic agents, although it is more common to see hypokalemia
- Hypocalcemia- transfusion of blood products may also contribute to this

Since electrolyte abnormalities are common, ABG's should be monitored and supplemental magnesium, potassium, and/or calcium should be administered if needed.

## Temperature Management

Chemotherapeutic agents are heated to 41-43 degrees Celsius. As discussed, hyperthermia is necessary to improve the effectiveness of treatment. However, hyperthermia can have detrimental systemic effects. Specifically, there is concern over the potentially damaging effects of hyperthermia to brain cells. This is why it is essential to accurately monitor and regulate patient temperature.

Goal of temperature monitoring

- Maintain core temperature below 39 degrees Celsius (this number may vary slightly by institution).[4] If this temperature is exceeded, the temperature of heated chemotherapy should be decreased.

Temperature monitoring sources

- Practice guidelines recommend two sources of temperature monitoring throughout the procedure, as temperature can fluctuate significantly[3]
  - A bladder temperature probe closely resembles the temperature of the chemotherapeutic agent and the temperature within the abdomen.
  - Core temperature should also be monitored using an esophageal or nasopharyngeal temperature probe

Strategies for controlling temperature

- Ice around the head/ polar cube
- Ice packs around the axilla
- Cold IV fluids
- Bair hugger
- Underbody mattress

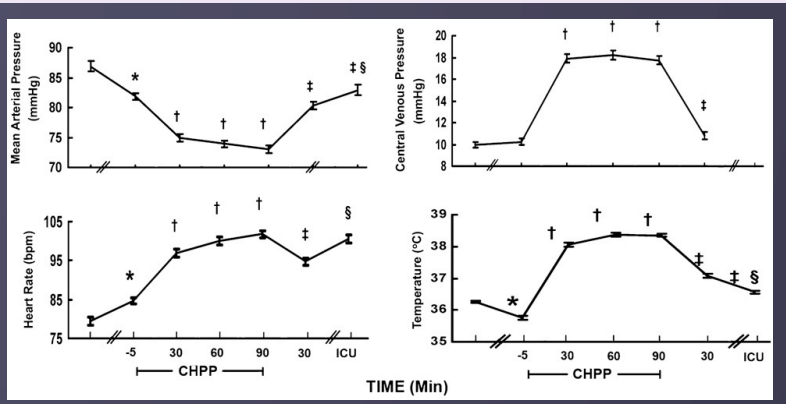



**Figure 2.** Data from 169 patients undergoing cytoreduction w/ HIPEC (CHPP). Note that from induction until the end of the cytoreductive stage, there is a significant increase in HR, as well as decreases in temperature and MAP. After the start of the HIPEC stage, there are significant increases in temperature, CVP, and HR, and a decrease in MAP (Miao et al., 2009).

References

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