Anesthetic Management in a patient with Complex I Mitochondrial Deficiency and Malignant Hyperthermia Susceptibility

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Summary

Mitochondrial disorders are estimated to have a lifetime prevalence of 1 in 5,000 and are the most common group of neuro-metabolic diseases. They require a different approach to the anesthetic management, with avoidance of multiple drugs we typically use for anesthesia. We present a case of anesthetic management in a 4 year old male with Complex I mitochondrial disorder and possible Malignant Hyperthermia (MH) susceptibility undergoing a gastrosotaneous fistula closure.

Case Description

4 year old male with PMHx significant for mitochondrial disorder and RYR1 mutation presented for a gastrosotaneous fistula closure. Muscle biopsy confirmed a pronounced defect in complex III enzyme activity. The patient was evaluated in POCC clinic prior to surgery.

Past Medical History: Complex I mitochondrial disorder; RYR1 mutation; prior OSA that is now resolved; Cardiology evaluation with no RVH, small PDA

Allergies: Egg-containing compound (vomiting) and Peanuts (vomiting)

Anesthesia: General Anesthesia [MH cart at bedside]

Induction: Oral midazolam premedication was given prior to going to the operating room. A peripheral 20G IV was placed with supplemental inhaled nitrous oxide. Intravenous induction of anesthesia with midazolam 0.1 mg/kg, fentanyl 1 mcg/kg, dexmedetomidine 1 mcg/kg and rocuronium 0.5 mg/kg. Direct laryngoscopy was performed with a Mac 2 laryngoscope. The patient was intubated awake with no complications. Postoperatively, glucose level was normal. He was then monitored in PACU for four hours prior to discharge home.

Maintenance: Patient was placed on a 50:50 nitrous oxide and oxygen mixture. Intravenous medications included midazolam 0.1 mg/kg, fentanyl 1 mcg/kg, remifentanil 0.2 mcg/kg/min, dexmedetomidine 0.8 mcg/kg/hr and remifentanil 0.2 mcg/kg/min. After surgery was complete, neuromuscular blockade was reversed with glycopyrrolate and neostigmine. The patient received a total of 50ml NS 0.9% and 30 ml Dextrose 10% with minimal EBL. Lactated ringer was avoided due to the addition of exogenous lactate. The patient was extubated awake with no complications. Postoperatively, glucose level was normal. He was then monitored in PACU for four hours prior to discharge home.

Discussion

Mitochondria generate ATP and energy production through the electron transport chain (ETC), among many other functions. The ETC is made up of 5 enzyme complexes; mutations in any of the DNA codes can result in defective oxygen phosphorylation and have variable clinical presentations. High energy dependent organ systems that rely heavily on ATP display symptoms of mitochondrial disease.

Anesthesia and surgery impair the mitochondria’s ETC, resulting in energy deficits and reactive oxygen species. The reactive oxygen species increase membrane permeability, ultimately leading to apoptosis. This is thought to be a factor in anesthesia-induced neurotoxicity.

Preoperative concerns are focused on assessing organ system functional reserve. Common manifestations include:

- CNS: encephalopathy, seizures, or ataxia with greater susceptibility to anesthetics
- Cardiac: cardiomyopathy/conduction abnormalities and risk of sudden death
- Pulmonary: respiratory function compromise and postoperative ventilation
- GI: dysphagia and risk of aspiration
- Hepatorenal: prolonged drug effects; renal tubular necrosis secondary to exogenous lactate
- GI: dysphagia and risk of aspiration
- Metabolic: hypothyroidism, lactic acidosis, diabetes and glucose fluctuations

Intraoperative Considerations:

- General endotracheal anesthesia and avoid spontaneous ventilation
- Adequate anesthetic and analgesia to avoid high energy requirements
- Avoid succinylcholine secondary to hyperkalemia risk in patients with myopathy
- Use dextrose-containing fluids; Ringers are avoided due to the addition of exogenous lactate
- Monitor glucose levels closely
- Postoperative Management
- Consider postoperative ICU care
- Monitor glucose levels closely
- Peri-operative Adverse Events: stroke, coma, seizures, respiratory failure, arrhythmias, and death

Anesthetic Medications and Effects on Mitochondria:

- Volatile Inhalational Anesthetic Agents
  - Propofol inhibits acylcarnitine transferase and Complex III
  - Ketamine, barbiturates and Etomidate inhibit Complex I
  - Midazolam inhibits complex I, II and III
  - Local Anesthetic disrupt oxidative phosphorylation
  - Short-acting opioids (avoid morphine due to mitochondrial effects)

MH triggering medications to avoid:

- Succinylcholine
- Volatile Inhalational Anesthetic Agents

References