The Dilemma in Anesthetic Management of Patients with Concurrent Diagnoses of Mitochondrial Disease and Malignant Hyperthermia Susceptibility

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Introduction

- Successful anesthetic management of patients with Malignant Hyperthermia Susceptibility (MHS) involves the use of “safe” agents for prevention of Malignant Hyperthermia (MH). However, some of the “safe” anesthetic techniques for MHS patients may have detrimental effects in patients with other rare genetic diseases, such as mitochondrial disease.
- Propofol has been shown to inhibit mitochondrial function and uncouple oxidative phosphorylation, increasing the risk of perioperative complications in patients with mitochondrial diseases.
  - Increased risk of respiratory depression, cardiac arrhythmias, and neurologic defects

Case 1

- 10-year-old 37.8 kg female presented for an electrophysiologic study and ablation in the cardiac catheterization lab due to palpitations, arrhythmias, and ablation in the cardiac catheterization lab due to palpitations, -93.
- Whole exome sequencing revealed
  - MH mutation - Ryanodine Receptor RYR1 c.7300G>A (p.G2434R)
  - Paroxysmal nonkinesigenic dyskinesia (PNKD) mutation - autosomal dominant disorder which leads to sudden involuntary movements and associated with mitochondrial dysfunction
  - Mitochondrial tRNA translation optimization 1 (MTO1) gene carrier
- Anesthesia induction: midazolam (0.16 mg/kg total in divided doses), fentanyl (2.6 mcg/kg total in divided doses), ketamine (0.8 mg/kg), and rocuronium (1 mg/kg)
- Anesthesia maintenance: ketamine infusion at 1-2 mcg/kg/hr and 50% oxygen/50% nitrous oxide
- Perioperative considerations: Short NPO time, glucose containing IVF without lactate, lactate & glucose monitoring
- Discharged home after 6 hours recovery with no complication

Case 2

- 12-year-old 25 kg male with history of episodic dysautonomia with associated failure to thrive and fatigue, presented to the operating room for a cleft palate repair
- Exome sequencing revealed ATP8 gene (G8519A) mutation which is associated with mitochondrial disease
- Two prior episodes of clinical relevant MH requiring the use of succinylcholine
- Anesthesia induction: fentanyl (2 mcg/kg), rocuronium (1 mg/kg), and etomidate (2 mg/kg)
- Anesthesia maintenance: remifentanil (0.2 mcg/kg/min) and 50% oxygen/50% nitrous oxide
- Perioperative considerations: Short NPO time, glucose containing IVF without lactate, lactate & glucose monitoring
- Discharged home on POD1 with no complication

Discussion

- Malignant Hyperthermia recommendations:
  - avoiding the use of triggering agents, which includes volatile agents and succinylcholine
  - replacing the circuit and carbon dioxide absorbent
  - utilizing activated charcoal filters
  - flushing the machine at 10 liters per minute for at least 15 minutes, depending on the ventilator manufacturer
- Mitochondrial myopathy recommendations:
  - minimizing preoperative fasting to avoid hypovolemia and hypoglycemia
  - increasingly cautious use of muscle relaxants
  - Succinylcholine: risk of hyperkalemic cardiac arrest
  - Nondepolarizing NMBD: prolonged effect
  - avoiding the use of lactate as some patients have difficulty metabolizing lactate and may become acidic
  - avoiding tourniquets and pressure points to minimize regions of poor perfusion and may become acidotic
  - slow titration of volatile and parenteral anesthetics to minimize regions of poor perfusion and oxygen delivery
  - avoiding swings in body temperature – defects in thermogenesis
- No increased sensitivity to MH in patients with mitochondrial disorders, and volatile agents appear safe in patients with mitochondrial disorders
- Mitochondrial disease have hundreds of defects with different phenotypes and reactions to anesthetics
  - Every general anesthetic can depress mitochondrial function
  - Genetic screening of entire exome may become more prevalent and useful for anesthesiologists to better predict reaction to medications and safely deliver care

References

Malignant Hyperthermia Association of the United States. mhaus.org