Anesthesia for Diagnostic Muscle Biopsy to R/O Mitochondrial Cytopathy: Less is More

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Introduction
Mitochondrial disorders could present as myriad of symptoms affecting the neurologic, cardiac, musculoskeletal and endocrine systems. High-energy requiring tissues are uniquely dependent on the energy delivered by the mitochondria and therefore have the lowest threshold for displaying symptoms of mitochondrial disease. Anesthetic agents exert their primary effect in tissues that have high-energy requirements. Essentially every general anesthetic studied has been shown to depress mitochondrial function and it is unclear that any particular anesthetic regimen is safer than another. We believe adverse events of mitochondrial cytopathies under general anesthesia may be underreported. Several small case series have reported rare adverse events with general anesthesia in the mitochondrial patients. However, from our experience and communication with parents, we are aware of adverse events such as respiratory depression, muscle weakness, cardiac dysrhythmias, seizures and prolonged emergence requiring unplanned hospital admissions. Our case series reports a previously undescribed homogenous anesthetic protocol that has led to very successful postoperative outcomes.

Method
Between December 2006 and November 2010, pediatric patients with suspected mitochondrial disease undergoing diagnostic muscle biopsy to diagnose mitochondrial disorders were enrolled under a separate IRB protocol. A single anesthesiologist administered anesthesia for all of these enrolled patients with assistance by either a resident, fellow or nurse anesthetist. All patients were prescribed a specific anesthetic protocol as detailed below.

- Slow mask induction with sevoflurane titrated to a BIS of 50-60
- Maintenance of anesthesia with sevoflurane to BIS of 50-60
- Ultrasound guided fascia ilaca block on the same lower extremity of muscle biopsy
- Avoidance of propofol, opioids, and lacedtating ringers
- Caution with muscle relaxants
- IV ketorolac and ondansetron at the end of the procedure

Prior to induction of anesthesia, a BIS monitor was placed. Mask induction of anesthesia was slowly induced by increasing the concentration of sevoflurane 0.5% every 30 seconds until a BIS of below 60 was achieved. A saphenous IV was placed and a VBG was drawn at induction and at the end of the procedure, whenever possible.

Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tr>
<td>Gender</td>
<td>Male 29 (69%), Female 13 (31%)</td>
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<tr>
<td>Age (years)</td>
<td>*&lt; 5 years 14, 5-10 years 9, 11-12 years 19, &gt;12 years 9</td>
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<td>Duration of anesthesia (mins)</td>
<td>98.6 (23.2)</td>
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Adherence to Protocol

- All patients received slow mask induction with sevoflurane to BIS of 50-60
- Sevoflurane closely titrated to maintain BIS of 50-60 for maintenance of anesthesia for all patients
- All patients received regional anesthesia with fascia ilaca blocks with either bupivacaine 0.25% or ropivacaine 0.2%. The mean volume injected was 0.67 mL/kg (SD = 0.25)
- None of the patients received midazolam or propofol.

Results

- The mean duration under anesthesia was 98.6 mins (SD = 23.2 mins).
- All patients were extubated unexpectedly at the end of the procedure.
- None of the patients required additional treatment for PONV in the PACU except for one patient who did not receive intravenous ondansetron intraoperatively.
- The average preoperative lactate level was 1.6 mmol/L and postop was 1.52 mmol/L with a mean change of -0.01 mmol/L.
- Of the 42 patients, 19 patients were found to have abnormal findings in their muscle biopsies and are currently under review for the precise mitochondrial cytopathology diagnosis.

References

Discussion
Among the patients who presented to us for muscle biopsies for the diagnosis of mitochondrial cytopathies, most of them (74%) present with neurologic symptoms. This represents patients who are present with developmental delays, seizures, or encephalopathy. The second most common presenting symptom is myopathy, that is 64% of patients. This closely mirrored the presenting symptoms presented by Driesen et al, that is 76% of patients presented with neurologic symptoms followed by 27% of patients with myopathy. We, however, did not have any patients who presented with preoperative cardiomyopathy. Anesthetics have their primary effect in tissues that have high-energy requirements, similar to tissues most affected by mitochondrial disorders. Patients with mitochondrial disorders are more sensitive to both intravenous and inhaled anesthetic agents.

Our anesthetic protocol utilizes multimodal analgesia to minimize the use of anesthetic agents and opioids. In addition to intravenous NSAIDs (i.e ketorolac in our protocol), the use of fascia ilaca block in this protocol allowed us to minimize, if not, exclude opioid use for intraoperative and postoperative pain. It also allowed us to use as little anesthetic agent as possible to maintain anesthesia.

The use of regional anesthesia technique has been a proven technique to minimize both opioids and anesthesia requirements. We also hypothesize that patients with mitochondrial disorder are more sensitive to anesthetic agents and have lower requirements than patients of otherwise similar age and demographics.

We chose to induce all of our patients with inhaled anesthetics as we believed it to be a more reliable titration to a BIS scale, which have been validated in the pediatric population. We chose to avoid propofol as it has indiscriminate effects on the mitochondria, inhibiting both multiple electron transport chain complexes as well as fatty acid transport. In addition, there is concern for propofol infusion syndrome.

While this small cohort of complex patients did well with this anesthetic regimen it is worth reminding the reader that mitochondrial disease represents probably a myriad of different defects, both genetic and environmental in origin, and is thus difficult to characterize from any limited case series.