ANAESTHESIA FOR MUSCLE BIOPSY CLINICAL PRACTICE GUIDELINES

BACKGROUND

General anaesthesia for a child with muscular disorders is a common clinical scenario. Once these patients have a confirmed diagnosis, it is possible to tailor management of general anaesthesia to minimize the risk of potentially life threatening complications. In many cases, diagnosis is made on muscle biopsy. These patients present for anaesthesia with no firm diagnosis. Anaesthetic management is therefore based on:

1. Likely diagnosis
2. Perceived risk of rare, complications in the absence of a clear diagnosis
    i. Malignant Hyperthermia (MH)
    ii. Anaesthesia Induced Rhabdomyolysis (AIR)
    iii. Propofol infusion syndrome
3. Risks associated with end organ effects of underlying disease of muscle
4. Requirements for the processing of the muscle biopsy specimen.

1. LIKELY DIAGNOSIS

Family history, clinical presentation and blood tests may suggest a diagnosis. For example Muscular dystrophy is more likely if there is a family history and an elevated CK. Mitochondrial myopathy is more likely if there is multi-systemic involvement and there is a pre operative elevated serum lactate. Encephalopathy suggests metabolic disease. Pre anaesthetic assessment should involve discussion with the treating neurologist and metabolic physician about the results of preoperative clinical assessment and testing.

2. PERCEIVED RISK OF RARE COMPLICATIONS

MALIGNANT HYPERTHERMIA (MH)

MH is a pharmacogenetic condition where exposure to volatile anaesthetic agents and suxamethonium triggers uncontrolled release of calcium from the sarcoplasmic reticulum. This leads to muscle rigidity, and a hyper metabolic state with hyperthermia, rhabdomyolysis and death.

Disease of Muscle Associated with MH:

A handful of the numerous diseases of muscle have been associated with MH.

1. Central Core Disease
2. Multiminicore Disease (Minicore disease)
3. Nemaline rod Myopathy
4. King Denborough Syndrome
5. Evans myopathy

Muscular Dystrophy and MH

The Muscular Dystrophies were thought to be associated with MH but a true MH association has not been found. Volatile agents are unlikely to trigger MH but may trigger rhabdomyolysis with a clinical picture difficult to distinguish from MH.

Mitochondrial Diseases and MH

Mitochondrial disorders, in isolation, have not been associated with MH. There has been one case report of MH in a patient with mitochondrial disease who received succinylcholine.

Succinylcholine

Use of depolarizing neuromuscular blocking drugs should be discouraged in patients with neuromuscular disease as these drugs are known triggers for MH and rhabdomyolysis.

ANAESTHESIA INDUCED RHABDOMYOLYSIS (AIR)

In susceptible individuals, exposure to volatile anaesthetic agents or succinylcholine can lead to skeletal muscle breakdown resulting in release of myoglobin, elevated serum CK and elevated serum potassium. Rhabdomyolysis can be acute resulting in hyperkalaemic cardiac arrest. A sub acute picture can also occur with delayed myoglobinuria and elevated serum CK. Delayed hyperkalaemic cardiac arrest can occur. Whilst AIR can resemble MH, it is recognized as being distinct from true MH. AIR is associated with Duchenne Muscular Dystrophy and Becker Muscular Dystrophy. If muscular dystrophy is suspected then avoiding halogenated agents is a first choice. Studies have shown that when halogenated agents are used in patients with suspected neuromuscular disease undergoing muscle biopsy, the risk of MH or rhabdomyolysis is 1 % or less. (Excludes patients with conditions known to be associated with MH).

PROPOFOL INFUSION SYNDROME

Propofol can impair mitochondrial function resulting in metabolic acidosis, rhabdomyolysis and lipidaemia. Cardiac failure, bradycardia and cardiac arrest can occur. This syndrome has been found to occur in children receiving high doses of propofol over long periods, (propofol infusion 4 mg/kg/hr for > 48 hours). This syndrome may occur at lower doses of propofol and after shorter infusion periods in children who have abnormal mitochondrial metabolism. Whilst the florid syndrome may not be apparent, short term propofol use may be associated with delayed recovery and need for ICU. If mitochondrial myopathy is suspected, propofol should be avoided. A single induction dose is probably safe.

3. RISKS ASSOCIATED WITH END ORGAN EFFECTS

The end organ effects of the underlying disease can have predictable effects which are amenable to optimal anaesthetic management.

i. Cardiac disease (Cardiac failure & abnormal cardiac conduction)
ii. Respiratory disease and respiratory failure
iii. Bulbar muscle weakness
iv. Difficult airway anatomy
v. Metabolic derangement

4. REQUIREMENTS FOR PROCESSING OF MUSCLE BIOPSY SPECIMEN

There are several types of muscle biopsies taken for analysis. Each has different requirements. For all biopsies, it is essential that local anaesthetic does not contaminate the specimen. A regional block can be performed if the site of infiltration is sufficiently distant from the biopsy site to ensure that no contamination occurs. Local anaesthetic infiltration can be performed after the specimen has been collected.

Malignant Hyperthermia Testing Biopsy

- A non – triggering anaesthetic is essential
- Live muscle preparation is taken and therefore coordination between RCH and the MH team at RMH is required.

Standard Anatomical Muscle Biopsy

- Usually performed if muscular dystrophy is suspected.
- No mitochondrial assay is performed therefore propofol is not an issue**.**
- Performed at Alfred and therefore timely transfer of specimen is important

Muscle Mitochondrial Enzyme Analysis

- Propofol and midazolam inhibit coupling between mitochondrial respiration and oxidative phosphorylation. (based on in vitro studies)
- Propofol may interfere with the enzyme assay resulting in a false negative.
- At higher than clinical doses, volatile anaesthetic agents reduce oxidative phosphorylation in isolated in vitro studies (It is not clear whether volatile anaesthetic agents interfere with enzyme analysis)

Metabolic – Liver, Muscle & Skin

Standard Anatomical Nerve Biopsy

- No specific anaesthetic requirements for the specimen.

In some situations specimens are collected for both anatomical studies and mitochondrial assays. This creates a conflict between the safe conduct of anaesthesia and the requirements for processing of the biopsy specimen.

ANAESTHETIC MANAGEMENT

PRE ANAESTHETIC ASSESSMENT

Patients presenting for anaesthesia for muscle biopsy often have complex, multi systemic disease. **They are a high risk group for general anaesthesia and should be referred for formal pre anaesthetic assessment**.

History and Examination

- **Discussion with neurologist / metabolic physician to determine likely diagnosis.**
- Assess for degree of cardiovascular insufficiency
- Assess for degree of respiratory insufficiency
- Assess for bulbar palsy, reflux and aspiration risk
- Anticipate difficult airway.

Investigations should include:

1. ECG
2. Echocardiogram
3. CXR
4. Respiratory function tests
5. Baseline Serum Potassium
6. Baseline Serum Lactate (Blood Gas)
7. Baseline Serum CK (indicator of muscle membrane integrity & potential for rhabdomyolysis)

Other Considerations:

1. These patients are usually not suitable for day case surgery
2. These patients may need an ICU/HDU bed for postoperative management.
3. Consult with metabolic physicians to guide peri operative fluid management.

- *Understand the Type of Biopsy required and potential anaesthetic requirements.*
- *A thorough risk versus benefit discussion with parents/guardians is essential.*

CONDUCT OF ANAESTHESIA

In general respiratory depressant drugs should be avoided peri-operatively. Regional techniques avoid the issue of general anaesthesia altogether. Pure regional techniques require cooperation and therefore are unlikely to be successful in children unless supplemented with agents such as ketamine, nitrous oxide or midazolam. There is emerging evidence that ketamine may be harmful to the developing brain. It is increasingly avoided in children under 1. The risk of a neuraxial technique in a child with an undiagnosed, evolving neuromuscular condition needs to be considered. Many anaesthetists would be reluctant to perform a neuraxial block in these children. When planning general anaesthesia for muscle biopsy, patients can be divided into four groups.

A. Known MH risk (MH Testing biopsy or likely congenital myopathy)

- Trigger free Anaesthetic.
- Prepare the patient and the operating theatre as for an MH susceptible patient.

B. Muscular Dystrophy Suspected

- Trigger free anaesthetic
- Prepare the patient and the operating theatre as for an MH susceptible patient.

C. Mitochondrial Myopathy Suspected

- If A & B are thought to be highly unlikely, volatile anaesthetic agents can be used.
- Propofol can't be used if mitochondrial enzyme assays are being performed.
- There is a small, un-quantified risk of propofol infusion like syndrome.
- Keep fasting to a minimum to avoid hypovolaemia and depletion of glucose.
- IV fluids should contain glucose (not higher than Dextrose 5%) and must not contain lactate (lactic acidosis).
- Avoid stress that may increase energy requirements (e.g. pain and hypothermia)

D. Patient to undergo standard anatomical biopsy and mitochondrial enzyme assay.

This creates a conflict between the type of anaesthetic associated with the lowest risk and the requirements for processing of the biopsy specimen.

- The evidence suggests that the risk of MH / rhabdomyolysis with volatiles is greater than the risks associated with short term use of propofol. However the requirements for specimen processing may stipulate the exclusion of propofol. Discussion with the pathologist is essential as there is no point doing the GA on safety grounds if the biopsy specimen cannot be used.
- If the decision is made to use volatile then this 1% risk of serious complications needs to be weighed against the benefit of the test itself.
- Alternatively Ketamine / N2O/ Regional could be considered. A remifentanil infusion can be used if a regional anaeshthetic is to be avoided with local anaesthetic infiltration after the biopsy specimen is taken. This is a technique less familiar to most experienced paediatric anaesthetists and may not be appropriate for very young patients. Again the risk needs to be weighed against the benefit.