

Anaesthesia and the paediatric muscle disorders

Gray RM, MBChB(UCT), DA(SA), FCA(SA)

Specialist Anaesthetist, Red Cross War Memorial Children's Hospital

Correspondence to: Rebecca Gray, e-mail: rebecca.gray@uct.ac.za

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Abstract

Paediatric muscle disorders have significant implications for anaesthetists. Their effects extend beyond skeletal muscle and manifestations in other organ systems are frequently seen; in addition, adverse reactions to anaesthetic drugs may result in fatality if unrecognised or inadequately treated. In the past, it was thought that muscular dystrophies and myopathies put a patient at increased risk of malignant hyperthermia, however, the link between these conditions has largely been dismissed and other anaesthetic catastrophes, such as anaesthesia-induced rhabdomyolysis, are now recognised. Undiagnosed muscle disorders put children at risk of experiencing adverse reactions to anaesthesia. A high index of suspicion should be exercised during preoperative review to facilitate anaesthetic choices and guide intraoperative management.

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Introduction

Paediatric muscle disorders encompass myaesthetic syndromes, myotonias, dystrophies and mitochondrial myopathies. Each of these groups of conditions will be considered, with a particular focus on the last two. Finally, the child with an undiagnosed muscle disorder presenting for general anaesthesia will be considered.

Myaesthetic syndromes

Congenital myaesthetic syndromes, implicated in certain cases of sudden infant death syndrome, are extremely rare (< 1:500 000).¹ Where anaesthesia is required, caution with the administration of muscle relaxants is prudent, and awareness of the sensitivity of the respiratory system to depression by anaesthetic agents important.

Myotonias

Myotonias may be inherited, or may arise from a spontaneous mutation in the gene coding for calcium, sodium or potassium channels. All are characterised by sustained myotonic contraction which may be triggered in theatre by muscle stimulation (by diathermy), cold, pain or stress. The myotonias can be subdivided into two

groups: dystrophic, in which progressive wasting of muscle mass and strength accompanies myotonic episodes, and nondystrophic.

Steinert's muscular dystrophy is the most common form of congenital myotonia. In addition to progressive skeletal muscle weakness and wasting, patients manifest respiratory insufficiency, incoördinate swallowing (bulbar weakness), cardiac (conduction disturbances, enlargement, and fibrosis) and cerebral (seizures and retardation) involvement.

Preoperative assessment of these patients should be directed at evaluating the severity of their condition and its effect on organ systems, identifying triggers, and ensuring normal electrolyte levels.

Intraoperatively, all triggers of myotonic contraction should be avoided. To this end, suxamethonium is contraindicated. Muscle relaxation can be challenging in these patients. Their chronic medication (quinine or procainamide) and the disease process itself may make them sensitive to nondepolarising muscle relaxants, which should be titrated to effect, and reversal with neostigmine may precipitate a myotonic episode. Muscle relaxants will not prevent myotonic contraction as this is triggered distal to the neuromuscular junction. Volatile anaesthetics may directly

counteract the myotonia to an extent, but their respiratory depressant effect must be anticipated in the spontaneously breathing patient. Masseter spasm on induction may make airway instrumentation difficult. Diaphragmatic and intercostal spasm will interfere significantly with ventilation. Good analgesia is the key to preventing myotonic contraction in the intra- and postoperative periods. Opiate sparing medications and regional anaesthesia should be used wherever possible.²

Muscular dystrophy

Duchenne and Becker muscular dystrophy, the most prevalent of the muscular dystrophies, are X-linked recessive conditions in which the muscle-stabilising protein, dystrophin, is abnormal. Duchenne muscular dystrophy has an incidence of approximately 1:3 500 live male births, and most patients will be symptomatic by five years of age. It is characterised by delayed milestones, progressive muscle weakness with calf pseudohypertrophy, mental retardation in one third and the development of a cardiomyopathy. Over 50% of patients will have a clinically relevant dilated cardiomyopathy by 15 years of age.³ Death is expected in early to mid-adulthood because of progressive cardiomyopathy or respiratory insufficiency.

Becker muscular dystrophy is milder, and weakness may only become apparent in adolescence. Cardiomyopathy develops concurrently and death is expected between the fourth and seventh decades.

Female carriers of both mutations may have mild musculoskeletal abnormalities (scoliosis) and are at risk of cardiomyopathy.

The anaesthetic risks that relate to these disorders are varied and substantial. A difficult airway may be anticipated because of macroglossia in Duchenne muscular dystrophy. The respiratory system requires careful preoperative assessment and optimisation. Kyphoscoliosis, causing restrictive lung disease, is compounded by respiratory muscle weakness that predisposes the patient to recurrent lung infections. Postoperative noninvasive ventilation may be useful, especially after major surgery such as scoliosis repair, but requires preoperative preparation of the patient.

Cardiac dysfunction may manifest clinically as a resting tachycardia or other arrhythmia. An echocardiogram is notoriously unreliable at predicting the severity of myocardial dysfunction,⁴ and cardiac magnetic resonance imaging or a dobutamine stress echocardiogram may be preferable as patient weakness prevents a traditional stress echocardiogram. Preoperative optimisation with angiotensin converting enzyme-inhibitors may be indicated. Patients who have been identified with cardiomyopathy preoperatively should be invasively monitored and have

adequate venous access intraoperatively. Hypovolaemia may precipitate cardiac arrest in the context of severe cardiomyopathy so meticulous attention to fluid status is crucial. Myocardial depressants, such as volatile anaesthetics and propofol, should be used cautiously. Early intervention with inotropes may be life-saving.

Patients with Duchenne muscular dystrophy are reported to have an increased bleeding risk which manifests most obviously during major surgery, such as scoliosis repair. This has been postulated to be because of impaired vascular reactivity.⁵ Adequate venous access should be secured preoperatively and blood products should be available. A cell saver is recommended. Cyclokapron infusion has been shown to reduce transfusion requirements.⁶

Patients with Duchenne muscular dystrophy are susceptible to “malignant hyperthermia (MH)-like” reactions and much academic ink has been spent exploring the link between the two conditions.⁷⁻¹⁰ Two systematic analyses of the literature have failed to demonstrate an increased risk of susceptibility to malignant hyperthermia in Duchenne muscular dystrophy and Becker muscular dystrophy, compared to the general population.^{11,12} Instead the potentially fatal condition of anaesthesia-induced rhabdomyolysis (AIR) has been described.

Acute rhabdomyolysis, following the administration of suxamethonium, is well described, and for many years the drug has been contraindicated for use in patients with known or suspected muscular dystrophies. Although many patients who are known to have Duchenne muscular dystrophy or Becker muscular dystrophy have received volatile anaesthesia without event¹³ and only a small minority of muscular dystrophy patients will develop AIR in response to volatile anaesthesia (despite some previously having had an uneventful volatile anaesthetic), current recommendations are for a “trigger-free” anaesthetic and a “clean” anaesthetic machine.¹² The reason for the variation in susceptibility is poorly understood.

AIR may present as acute hyperkalaemia and cardiac arrest, postoperative rhabdomyolysis without arrest, or as a gradual increase in temperature and heart rate, without the signs of hypermetabolism or muscle rigidity. Many of the cases of hyperkalaemia and cardiac arrest or rhabdomyolysis without arrest are reported to have occurred in the recovery room after awakening and apparent return to lucidity and movement.

It is postulated that the abnormality in dystrophin renders the muscle membranes frail and susceptible to damage. Dystrophic muscles have reduced mitochondrial metabolic capacity, putting them at risk of rhabdomyolysis in conditions of fasting. Many anaesthetic drugs have been associated with rhabdomyolysis, including propofol,

ketamine, thiopentone, nonsteroidal anti-inflammatory drugs and benzodiazepines,¹⁴ but volatiles appear to have the most direct action on muscle membranes. Younger patients (often undiagnosed) may be most at risk of severe hyperkalaemia from rhabdomyolysis by virtue of the fact that they have more muscle mass and a greater proportion of fibres attempting regeneration (which makes the muscle fibres more vulnerable to destruction).

If AIR is suspected:

- Discontinue any volatile anaesthesia and convert to total intravenous anaesthesia (TIVA). Change to a “clean” anaesthetic machine.
- Check serial serum potassium, creatinine kinase (CK), myoglobin and urine myoglobin concentrations.
- If potassium concentration is > 5.5 mmol/l, give NaHCO₃, as well as insulin with 10% dextrose. It is necessary to hyperventilate to shift the potassium intracellularly. Kayexelate can be given via nasogastric tube.
- A urinary catheter should be placed to monitor urine output.
- Intravenous fluids should be given, as well as mannitol to maintain urine output ≥ 1 ml/kg/hour to minimise the risk of renal impairment.

If cardiac arrest develops, or is the presenting event:

- Intravenous calcium chloride should be given to antagonise the cardiac effects of hyperkalaemia.
- Treat potassium as above, until it is within normal limits, then continue to monitor serially until within normal limits for 24 hours.
- Resuscitation should be continued until the potassium returns to normal.

Renal dialysis and heroic measures, such as the institution of cardiopulmonary bypass, may be required. Dantrolene appears to be of no benefit in this context.

Patients who are known or suspected to have muscular dystrophy should be given a TIVA. They must be prepared for this preoperatively with anxiolysis as required. EMLA® cream should be applied timeously. If there is reason to suspect a difficult airway or venous access, a volatile induction could be considered with conversion to TIVA once the airway and venous access are secured. In these cases, monitoring for potential AIR using serial serum potassium measurements should be considered.

Mitochondrial myopathies

The mitochondrial myopathies encompass a variety of multisystem disorders in which any one of the mitochondrial oxidative complexes is abnormal. These genetic diseases have variable expression and family members who are afflicted by the same genetic mutation may have differing clinical pictures and varying responses to anaesthetic drugs.

As muscle and nerve tissues are uniquely dependent on mitochondria for energy, the clinical features of these disorders often include myopathy, cardiomyopathy, encephalopathy, seizures and gastrointestinal symptoms. In circumstances in which adenosine triphosphate levels become inadequate (for example, inadequate oxygen delivery or increased oxygen demand), acidosis and cell breakdown occurs. Patients may exhibit these exaggerated metabolic responses to stresses such as fasting, fever, shivering and increases in sympathetic tone (pain).

Preoperative assessment should establish the degree of severity of involvement of each organ system. Baseline serum lactate, electrolyte and CK levels should be checked.

The anaesthetic recommendations revolve around preventing deterioration to lactic acidosis, and include:

- Giving intravenous glucose-containing fluids preoperatively when *nil per os*.
- Premedicating to avoid anxiety in theatre.
- Treating pain adequately.
- Keeping haematocrit near normal to facilitate oxygen delivery.
- Aiming for normotension.
- Keeping warm.
- Checking glucose, pH, lactate and electrolytes regularly.
- Avoiding lactated fluids.
- Avoiding respiratory depressants and supporting ventilation to prevent respiratory acidosis and hypoxaemia.
- Avoiding tourniquets.

The association between mitochondrial myopathies and malignant hyperthermia has now been largely dismissed.¹⁵ Expert opinion on specific drugs and techniques stems from case reports, series^{16,17} and theory. Those with mitochondrial myopathies are thought to be at risk of a propofol infusion syndrome-like clinical picture that may develop more rapidly than the classically described syndrome.¹⁸ Although incident-free propofol exposure has been shown in several case reports, it is recommended that in known or suspected mitochondrial myopathy, propofol should be avoided. Sevoflurane, the least respiratory depressant of the volatiles, may be the best choice for general anaesthesia. A case report of rhabdomyolysis following suxamethonium implies that this drug is best avoided, and a variable response to nondepolarising muscle relaxants has been reported.

The undiagnosed child

Knowing that a patient has a specific neuromuscular disorder enables specific anaesthetic tailoring, but what of the undiagnosed child who presents for incidental surgery or the hypotonic child needing a muscle biopsy?

Vigilance is essential. In all boys, a family history of neuromuscular disease or adverse reaction to anaesthesia should provoke suspicion. Developmental milestones should be assessed and examination must assess tone and include an inspection for calf hypertrophy. If any suspicion arises, a screening CK may guide management. The absence of family history in a hypotonic child with other organ system involvement should provoke suspicion of mitochondrial myopathy, in which case preoperative lactate levels may be useful.

Conclusion

Anaesthesia for children known to have muscular disorders is a challenging balance between meeting anaesthetic and analgesic requirements, while avoiding excessive suppression of neuromuscular, cardiovascular and respiratory systems. It is possible that the greatest challenge lies in managing the undiagnosed patient who may develop a catastrophic reaction to a chosen anaesthetic. Preoperative vigilance may raise suspicion, and intraoperative vigilance lead to early diagnosis and management, with possible avoidance of adverse outcome. Postoperative observation is essential.

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