Neuromuscular disorders and anaesthesia.
Part I: generic anaesthetic management

Sarah Marsh MB ChB FRCA
Nicola Ross MBBS BSc FRCA
Alison Pittard MB ChB FRCA MD FFICM

Patients with neuromuscular disorders are a concern for anaesthetists and intensivists alike, as well as their parent medical or surgical team. Although it is impossible to negate risk altogether in these patients, an understanding of the pathophysiology underlying each condition facilitates preoperative, perioperative, and postoperative planning. A precise diagnosis before anaesthesia is ideal, but this is not always possible—anaesthesia may be required for muscle biopsy to complete investigations. Complications associated with high morbidity and mortality should be planned for with regard to prevention and subsequent management should they arise. This article follows on from a previous article in this journal Anaesthesia for Children with Neuromuscular Disease by detailing the anaesthetic management for patients with generic neuromuscular disorders and the anaesthetic management of specific neuromuscular disorders in the accompanying article. These together should provide both paediatric and adult anaesthetists with a core level of information on how to proceed.

Key points
Neuromuscular disorders are a heterogenous group of diseases.
Thorough preoperative assessment and investigation is vital.
Depolarizing neuromuscular blocking agents may result in life-threatening hyperkalaemia.
Complications can include rhabdomyolysis, autonomic dysfunction, and myotonias.
Significant cardiac and respiratory involvement is common.

History
Neuromuscular disease was first described in 1836 by Conte in Naples, Italy. Conte reported in the Annal of the Ospendale degl’Incurabili di Napoli on two brothers with an unknown kind of muscular paralysis. A British physician, Edward Meyron, systematically studied the condition in the nineteenth century. In Paris, in 1868, Guillaume Armand Duchenne de Boulogne described the disease as ‘pseudo hypertrophic muscular paralysis’, and it was his name that was assigned to the most common childhood muscular dystrophy. Myotonia congenita was first described in 1876 by Dr Thomsen who mapped it in himself and family. Myotonic dystrophy, the most common of the myotonic syndromes, was described as a separate disorder in 1909 by Steinert. From this time, there has been an ever-expanding identification of separate disease processes resulting in neuromuscular disease.

Classification
Neuromuscular disorders consist of a heterogenous group of diseases that affect skeletal muscle via abnormalities at multiple sites. These can be classified into hereditary conditions and acquired syndromes as well as anatomically with regard to the site that the disease process affects (e.g. pre-junctional, junctional or synaptic, and post-junctional).

Box 1
Hereditary disorders:
- Pre-junctional
  - Peripheral neuropathies
    - Charcot-Marie-Tooth
    - Friedreich ataxia
  - Post-junctional
    - Dystrophicas
    - Duchenne
    - Becker’s
- Myotonias
- Myotonic dystrophy
- Myotonia congenita
- Hyper, hypokalaemic periodic paralysis
- Metabolic/mitochondrial disorders

Continuing Education in Anaesthesia, Critical Care & Pain | Volume 11 Number 4 2011
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Acquired disorders:
- Pre-junctional
  - Motor neurone disease
  - Multiple sclerosis
  - Guillain–Barré syndrome
  - Peripheral neuropathies—diabetes mellitus
- Junctional
  - Myasthenia gravis
  - Eaton–Lambert syndrome
- Post junctional
  - Inflammatory myopathies
  - Critical illness polyneuropathy and myopathy

**Anaesthetic management of neuromuscular disorders**

**Preoperative management**

- Precise diagnosis
- Full discussion with patients and family members regarding potential risks and complications
- Thorough pre-assessment of function and associated conditions
- Anaesthetic strategies and preparation
- Planning of postoperative care

As for any anaesthetic preoperative assessment, a thorough history and examination should be performed. Particular importance should be placed on respiratory and cardiac function. There is a high incidence of respiratory complications in patients with neuromuscular disease due to involvement of respiratory and pharyngeal muscles, progressive spinal deformities, and potentially difficult airways. The patient may be unaware of any underlying cardiac dysfunction, as they are often not capable of stressing the heart daily due to their underlying muscular disorder. The severity of the patient’s underlying cardio-respiratory function does not correlate with the progression of the neuromuscular disorder and investigations into the extent of their physiological reserve should be sought. These may include:
  - ECG
  - CXR
  - Echocardiogram
  - Pulmonary function tests
  - Baseline arterial blood gases
  - Baseline blood tests including haematology, urea, electrolytes, and creatinine kinase.

Premedication may be beneficial to some and detrimental to others. Short-acting agents such as benzodiazepines may be ideal in patients in whom crying or fear may precipitate muscle spasms due to catecholamine release. However, agents causing central respiratory depression or reduced respiratory muscle tone should be given in reduced doses with close continuous monitoring.

**Perioperative management**

**Monitoring**

Monitoring should be established according to the AAGBI standards, including ECG, oxygen saturation monitoring, and capnography. Invasive monitoring of arterial blood pressure may be indicated to allow beat-to-beat observations in the potentially unstable patient, and in addition being used for blood sampling.

**Thermoregulation**

Temperature measurement and control is extremely important. Patients with neuromuscular disorders can be vulnerable to both hypo- and hyperthermia.

Hyperthermia may develop due to reduced heat production from immobile muscles. This state may be compounded by the peripheral vasodilatation that occurs with general and regional anaesthesia. Patients should be normothermic before induction of anaesthesia and their temperature maintained throughout with the use of warmed fluids and forced air warmers if necessary. In some neuromuscular disorders, hyperthermia can exacerbate myotonia, increase sensitivity to non-depolarizing neuromuscular blocking agents and potentially aggravate rhabdomyolysis as well as more recognized complications such as bleeding and arrhythmias.

Hyperthermia may occur due to increased muscle activity seen in myotonia, iatrogenic causes, or malignant hyperthermia. A high index of suspicion should exist for patients with muscular dystrophies and myotonias for concomitant malignant hyperthermia. Unexplained tachycardia with an increase in end-tidal carbon dioxide concentration should alert the anaesthetist to a potential hyperthermic complication, which should be treated aggressively.

**Regional anaesthesia**

Regional anaesthesia offers advantages to those with significant respiratory or cardiac involvement. A thorough preoperative neurological assessment must be performed however, and the technique should perhaps be avoided in those with rapidly progressing neurological deterioration to be able to distinguish regional blockade from disease progression. Autonomic dysfunction may be exacerbated by sympathetic blockade, requiring the use of invasive monitoring and careful titration of agents to control blood pressure.

**General anaesthesia**

The use of volatile agents is considered controversial for a number of reasons. Volatile agents have been contraindicated in the past due to the association of malignant hyperthermia with some neuromuscular disorders such as Duchenne muscular dystrophy (DMD).
Although the link between DMD and malignant hyperthermia is now thought to be tenuous, a total i.v. anaesthetic with a clean anaesthetic machine to avoid rhabdomyolysis is recommended. Further to this, cardiovascular decompensation may be caused by the use of volatile agents due to their cardio-depressive and arrhythmogenic properties.4,5

I.V. anaesthesia may offer many benefits to patients with neuromuscular disorders as the agents used are short acting and relatively easy to control. Caution must however be exercised due to the potential for autonomic dysfunction and cardiovascular collapse.

### Neuromuscular block

Both depolarizing and non-depolarizing neuromuscular blocking agents should be used with caution. Depolarizing neuromuscular blocking agents are not recommended for use in patients with neuromuscular disease for a number of reasons. Succinylcholine activates nicotinic acetylcholine receptors, leading to an influx of cations into the sarcolemma. In muscle that has been denervated or immobile for prolonged periods, extra-junctional receptors can occur. This leads to an increase in the number of Ach receptors, which spread throughout the muscle membrane. Fetal y isoforms of the nicotinic acetylcholine receptor subunits may also develop in neuromuscular disease. Activation of both these receptor groups by succinylcholine will lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis. Furthermore, in the myotonias, the fasciculations caused by the administration of succinylcholine may lead to membrane depolarization, and potentially massive K\(^+\) efflux. This can cause fatal hyperkalaemia, muscle fibre swelling, and rhabdomyolysis.

In contrast to other neuromuscular disorders, succinylcholine may be used in myasthenia gravis. The required dose may need to be increased by up to two-fold, as those with the disease show a relative resistance to the drug.

The use of non-depolarizing agents can often be avoided by judicious use of i.v. induction agents. Many patients with neuromuscular disorders show sensitivity to non-depolarizing neuromuscular blocking agents, which can result in respiratory weakness and inability to wean, sputum retention, and dysphagia. However, if absolutely required, they should be given in reduced doses (10–20% of recommended dose) and the degree of neuromuscular block monitored. Agents such as mivacurium and atracurium are preferred due to their degradation process.

Anticholinesterases are not recommended in muscular dystrophies because they, like succinylcholine, may lead to hyperkalaemia.

### Postoperative management

Patients with neuromuscular disorders are unsuitable for day case surgery. Admission, where possible, should be appropriately planned. Postoperative admission to high dependency or intensive care is mandatory, with access to physiotherapy, positive pressure circuits, and appropriate analgesia.

### Complications

#### Rhabdomyolysis

Depolarizing neuromuscular blocking agents have the potential to cause rhabdomyolysis in most patients with neuromuscular disorders. After administration, there can be massive changes in ion distribution with muscle contraction, swelling, and consequent damage which lead to rhabdomyolysis. Myotonias may also spontaneously induce rhabdomyolysis due to sustained muscle contraction. Volatile agents have been implicated with rhabdomyolysis in the past, due to their association with malignant hyperthermia, but it is now thought that this is a separate disease process to most neuromuscular disorders other than Central Core Disease.4

Signs of rhabdomyolysis include metabolic acidosis, hyperkalaemia, myoglobinuria, and creatinine kinase > 10 000 units litre\(^{-1}\). Treatment involves cessation of potentially causative drugs and correction of life-threatening hyperkalaemia. Aggressive volume resuscitation to remove myoglobin should commence to maintain a urine output of >1 ml\(^{-1}\) kg\(^{-1}\) h\(^{-1}\). The urine may be alkalized using sodium bicarbonate. If hyperthermia is present, the use of dantrolene should be considered.

#### Autonomic dysfunction

Autonomic dysfunction is not uncommon in neuromuscular disorders and can be responsible for severe hypotension on induction and after regional anaesthesia. Gastric dysmotility can lead to regurgitation and aspiration during general anaesthesia. Sympathomimetic drugs should be available for use but doses may need to be reduced due to increased sensitivity of alpha- and beta-receptors.4

#### Myotonias

Myotonic contractures can occur with the dystrophic and non-dystrophic myotonias. The contractures are caused by repeated action potentials leading to a permanent sodium influx or chloride efflux across the muscle membrane, rendering it hyperexcitable. Myotonic contractures can be caused by a number of agents including succinylcholine, anti-cholinesterases, and opioids. Environmental factors also play a part with alterations in temperature, acidosis, and shivering capable of triggering a contraction.4

Should a myotonia be triggered, they are not classically responsive to neuromuscular block, regional or peripheral nerve blockade. After correction of environmental and physiological conditions, drugs which block sodium channels, such as local anaesthetics and antiarrhythmic agents, are considered to be the drugs of choice.3,4
Cardiac and respiratory complications

Cardiomyopathies and conduction abnormalities can cause serious morbidity and mortality in the peri- and postoperative period. Perioperative catecholamine release may further precipitate arrhythmias and potentiate cardiac failure. Adequate preoperative screening should aid the diagnosis of underlying abnormalities, but regardless of findings the patient should be treated as a high cardiac risk, with appropriate access to invasive monitoring, inotropic drugs, and high-level care postoperatively.

Respiratory failure is the commonest cause of death in patients with neuromuscular disorders. The reasons for this are:

- Bulbar muscle weakness leading to repeated aspirations
- Poor pharyngeal and respiratory muscle tone
- Obstructive sleep apnoea and progressive spinal deformities lead to a restrictive lung defect.

Extubation should be achieved as early as possible to prevent further weakening of respiratory muscles but weighted against the risk of atelectasis, aspiration, infection, and respiratory failure, which may ensue. The majority of patients with neuromuscular disorders will have some underlying respiratory dysfunction and again should be appropriately investigated preoperatively.

Malignant hyperthermia

Historically, patients with neuromuscular disorders are felt to be at increased risk of developing malignant hyperthermia during anaesthesia. Myotonia congenita, Schwartz–Jampel syndrome, hypokalaemic periodic paralysis, DMD, central core myopathies, and King Denborough syndrome have all been associated with malignant hyperthermia in the past. However, it is now felt that there may be two distinct conditions of true malignant hyperthermia and a contracture-related rhabdomyolysis and acidosis. A recent literature review of muscle physiology and the pathophysiology of malignant hyperthermia and neuromuscular disorders suggests that the risk of myotonic patients developing malignant hyperthermia is equivalent to the general population, with the exception of hypokalaemic periodic paralysis and central core disease. Clinicians should act on the side of caution, with a high index of suspicion in patients with muscle disease however.

Conflict of interest

None declared.

References


Please see multiple choice questions 1–4.