Neurological conditions in the perioperative period

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Abstract

The wide spectrum of neurological disorders and their effects on the function of the central and peripheral nervous system can cause an extensive array of symptoms and significant morbidity and mortality. This morbidity and mortality is often amplified in the perioperative period with an elevated risk of anaesthetic complications and adverse events. However, the number of patients with neurological disease requiring surgery is unlikely to diminish, and therefore this anaesthetic risk needs to be met and managed effectively. Here we aim to examine a range of different neurological conditions, exploring the possible complications and complexities encountered in the perioperative period, in addition to discussing strategies to minimize the risk of adverse outcomes and ensure the delivery of safe anaesthesia and good perioperative care.

Keywords Neurological conditions; Guillain-Bare syndrome; motor neurone disease; multiple sclerosis; muscular dystrophy; neuro-anaesthesia; neurological disorders; perioperative care; perioperative management; spinal cord injury

Spinal cord injury

A spinal cord injury (SCI) is any insult to the spinal cord resulting in either transient or permanent loss of normal spinal motor, sensory or autonomic function. The mechanisms of injury resulting in SCI can be subdivided into primary or secondary. Primary SCI result from mechanical disruption to the spinal cord due to transection, penetration, vertebral fracture or vertebral displacement. This is often followed within minutes by a secondary SCI, where further cord damage occurs due to vascular disruption, thrombosis and hypoperfusion.

Additionally, the pathophysiological fallout of a SCI can divided into three distinct phases:

- Initial phase: a period of intense neuronal discharge within the first few minutes of injury due to direct cord stimulation, resulting in extreme hypertension and cardiac arrhythmias.
- Spinal shock phase: a loss of sympathetic tone results in profound hypotension and bradycardia with associated loss of muscle tone and reflexes distal to the level of the lesion (typically seen in high cord lesions above T7).
- Reflex phase: as neuronal 'rewiring' takes place efferent sympathetic innervation gradually returns along with muscle tone and reflexes.

Approximately 1000 people across the UK suffer a new SCI each year, with young to middle-aged males and elderly females being most at risk.[1] Causes of SCI are extensive, but common mechanisms include road traffic collisions, falls, assaults and sporting injuries.

The pattern of neurological deficits following SCI is highly variable, being dependent on the anatomical level and extent of cord disruption. The can range from self-limiting spinal cord concussion through to serious neurological damage such as paraplegia and tetraplegia or even neurogenic shock and death.

Perioperative considerations

Patients with SCI pose a set of unique anaesthetic challenges, whether that be in the hyper-acute phase as part of a trauma team receiving a SCI patient, inducing anaesthesia to permit damage control surgery or else planning for elective cases in those with a historical SCI, each instance requires a careful and considered approach.

In the acute phase, ensuring that a comprehensive physical examination has taken place, including both a primary and secondary survey in trauma cases, is essential to avoid the pitfalls of missing covert pathology, especially when distracting injuries are present. Up to one-third of patients with acute SCI may also have associated major injuries or other spinal fractures.

If the clinical situation allows, lung function tests should be considered mandatory for all those with SCI preoperatively. The potential for respiratory compromise in SCI is extensive and multi-factorial. The intense neuronal discharge of the initial phase of injury and resulting hypertension and arrhythmias can quickly result in significant pulmonary oedema, while denervation of the respiratory musculature can cause varying degrees of ventilatory impairment depending on the level of the lesion, as shown in Table 1.

Conduct of anaesthesia

If the mechanism of injury or initial assessment raises concerns of a c-spine injury, then manual in-line cervical spine stabilization (MILS) should be performed by a competent assistant prior to induction. This aims to minimize movement of the c-spine as

Level of SCI and effect on respiratory function[2]

Injury level	Resulting respiratory deficit	Vital capacity (% of normal)	Effect on cough
Above C3	Possible apnoea	<10%	Absent
C3–C5	Possible phrenic nerve denervation impairing diaphragm	10–30%	Weak
Above T8	Loss of inspiratory intercostal muscles	30–80%	Weak to Normal
Below T8	Loss of abdominal and lower expiratory intercostal muscles	80–100%	Weak to Normal

Table 1

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far as reasonably possible during laryngoscopy, once intubation has been achieved both the hard collar and head blocks should be re-sited. It is also advisable to ensure that difficult airway equipment is readily available prior to induction, intubation can prove challenging in the SCI patient, whether that be in the acute setting where views may be impaired by associated maxillofacial trauma, bleeding or swelling, or else in the chronic SCI patient where an inability to achieve adequate cervical extension can equally impair views.

In the acute spinal shock phase seen in high cord lesion, patients may experience a profound bradycardia and hypotension due to unopposed vagal tone. This can be countered with atropine or glycopyrronium and pre-loading with a fluid bolus prior to conducting a vagally stimulating procedure such as intubation. Ensuring an adequate blood pressure also helps reduce the risk of secondary cord injury due to hypoperfusion, achieving this may require vasopressor support. Some studies have suggested pursuing a mean arterial pressure of 80–85 mmHg over the initial 5–7 days is associated with better neurological outcomes; however, given the complications of prolonged inotropic support, most feel maintaining a blood pressure tailored to a patient's age and comorbidities is most appropriate.[3]

Following an upper motor neurone injury, over time the surface area of the motor end plate increases markedly as it extends to cover almost the entire muscle cell membrane. In such cases the administration of suxamethonium can induce a massive efflux of potassium from this elongated motor end plate, potentially resulting in life threatening arrhythmias. For this reason, suxamethonium should be avoided from 72 h from the point of injury onward.

Muscular dystrophy

The muscular dystrophies (MDs) comprise a number of congenital disorders characterized by progressive muscle wasting and weakness. The different disease subtypes are typically classified by their mode of inheritance and anatomical distribution.

- X-linked: Duchenne and Becker MD
- Autosomal recessive: limb–girdle, childhood and congenital MD
- Autosomal dominant: facioscapulohumeral and oculopharyngeal MD.

For the purpose of this article we narrow our focus to Duchenne MD (DMD), the more common and most severe form of the disease. Caused by a series of mutations to the dystrophin gene, DMD patients have a complete absence of the dystrophin protein, resulting in progressive degeneration of skeletal, cardiac and smooth muscle.

As an X-linked disorder, DMD is only clinically apparent in males, and affects up to 1 in 3600 new born males.

Clinical manifestations of the disease are usually detected between the ages of 2 and 5 years, when a child classically displays such signs as an abnormal gait, calf hypertrophy and difficulty arising from the floor. Progressive muscle weakness results in wheelchair dependence by 9.5 years on average, with premature death in the late teens to early twenties resulting from respiratory failure and cardiac complications.

Perioperative considerations

Impaired cardiac function is a common feature of DMD and is often evident by 6 years of age, with 50% of patients having a dilated cardiomyopathy by age 15. Myocardial degeneration can result in premature heart failure and predispose to mitral valve prolapse. Therefore, ensuring the patient receives an echocardiogram preoperatively is essential in order to assess valve patency and overall cardiac function.

As highlighted above, respiratory failure is a major cause of morbidity and mortality in DBD patients, weakness of respiratory muscles results in a progressive restrictive pattern of ventilation while a poor cough results in repeated episodes of pneumonia. Ensuring a preoperative chest X-ray to exclude sub-clinical pneumonia and performing spirometry helps to identify those most likely to require postoperative enhanced respiratory support, the risk of which is substantial, with a recent study of children undergoing spinal fusion surgery finding that 40% of DMD patients required postoperative ventilation.[4]

Conduct of anaesthesia

Following multiple case reports of hyperkalaemic cardiac arrest and perioperative rhabdomyolysis, it has been hypothesized that DMD patients are more likely to react adversely to anaesthetic volatile agents and suxamethonium. The exact mechanism of this reaction remains disputed, with favour shifting between malignant hyperthermia (MH) and anaesthesia-induced rhabdomyolysis (AIR). Irrespective of the underlying mechanism, consensus is that total intravenous anaesthesia with propofol and avoiding suxamethonium entirely is the safest method.

Due to the vulnerable respiratory baseline of many DMD patients, respiratory depressant effects of anaesthetic agents are enhanced, opiates especially should be used with caution and effects monitored closely. In an effort to reduce opioid use, regional analgesia should be considered where appropriate; however, the typical kyphoscoliosis of DMD patients may make performing a lumbar epidural technically difficult, in such cases a caudal epidural may prove easier to accomplish.

DMD patients are known to experience delayed gastric emptying as a result of decreased smooth muscle tone throughout the gastrointestinal tract, making them more susceptible to aspiration following induction. This risk can be reduced to some degree by premedicating with an antacid preparation and prokinetic such as metoclopramide.

Guillain-Barre Syndrome

Guillain-Barre Syndrome (GBS) is an immunologically mediated disorder resulting in acute demyelination and axonal degeneration. It is commonly preceded by an acute infective process, typically of the respiratory or gastrointestinal systems, leading to the theory that antibodies generated against the infecting pathogen also attack peripheral nervous tissues resulting in the clinical features of GBS.

A relatively rare disease, the incidence of GBS across Europe is between 0.8 and 1.9 per 100,000, with bimodal peaks between the ages of 15–35 and 50–75 years.

The clinical features of GBS are that of an acute and ascending progressive neuropathy, characterized by an areflexic motor

weakness and paraesthesia. GBS typically initially presents as a symmetrical weakness in the lower extremities, which then progresses proximally reaching peak severity after about 2 weeks. In its most severe form, GBS can progress to bulbar involvement and paralysis of the respiratory musculature, to that end a third of GBS patients require ventilatory support at some point during their illness.

Perioperative considerations

Respiratory failure can be a prominent feature of GBS, therefore respiratory function should be thoroughly assessed pre-operatively. Equally it should be anticipated that GBS patients may require ongoing ventilatory support extending in to the post-operative period and require level 2 or 3 care in order to facilitate this.

Epidural analgesia should be considered and planned for where appropriate, paraesthesia resistant to conventional analgesia can cause significant distress in GBS patients; however, epidural opiate has been shown to offer significant benefit while also reducing the systemic opiate requirement.

Conduct of anaesthesia

As is true with several of the neurological disorders already discussed, potential autonomic dysfunction makes the GBS patient vulnerable to developing marked hypotension on induction and when starting positive pressure ventilation. To mitigate this risk, fluid status should be optimized and vasopressor agents on hand prior to induction, equally, minute volume should be gradually increased on the ventilator until adequate volumes are achieved.

Depolarizing neuromuscular blocking agents should be avoided due to the risk of life-threatening hyperkalaemia. Non-depolarizing neuromuscular blocking agents may well not be required depending on the level and extent of motor weakness experienced, but if used they should administered with caution due to increased sensitivity to neuromuscular blockade.

Multiple sclerosis

Multiple sclerosis (MS) is an acquired cell-mediated autoimmune disorder of the central nervous system, characterized by repeated episodes of demyelinating inflammation of the nervous tissue within the brain and spinal cord. The cause of MS remains poorly understood, but the disease process is believed to stem from an abnormal immune response to an environmental trigger in genetically predisposed individuals.

With a mean age of onset of 30 years, MS is predominantly a disease which emerges in early adulthood, with a female to male ratio of 3:1 and prevalence estimated at 203.4 cases per 100,000 in the UK.

Clinical features of MS are highly variable, dependent on the disease subtype and the nerve fibres affected. Symptoms can range from isolated visual or sensory disturbance to limb weakness and paralysis, often interspersed with periods of remission. However, over time such episodes of remission become less complete, ultimately resulting in progressive neurodisability.

Perioperative considerations

Respiratory function warrants thorough assessment. Respiratory failure is a well-recognized feature of advanced disease due to both respiratory muscle failure and bulbar palsy. Bulbar involvement is known to reduce airway reflexes therefore increasing the risk of aspiration in the perioperative period. However, respiratory function requires careful consideration even in those without overt signs of respiratory involvement, as supported by one study which found over 35% of ambulatory MS patients had clinically detectable respiratory impairment when formally assessed.[5]

Baclofen is commonly used to treat spasticity and spasms associated with MS; however, it is also known to cause muscle weakness and can therefore predispose to extreme sensitivity to non-depolarizing muscle relaxants. Stopping baclofen preoperatively is an option, but abrupt cessation has been shown to cause agitation, delirium and convulsions, therefore gradual withdrawal over a 2-week period is advisable.

High-dose corticosteroid therapy is a further mainstay of MS management, and therefore an element of adrenal suppression should be anticipated. This therefore needs to be considered in the perioperative period, to ensure regular doses of corticosteroids are not omitted and 'sick day' rules are complied with if clinically indicated.

Conduct of anaesthesia

Depolarizing neuromuscular blocking agents such as suxamethonium should be avoided in debilitated patients due to the risk of an excessive transient rise in serum potassium post administration, potentially resulting in serious cardiac arrhythmias.

Furthermore, centroneuraxial blockade has been associated with recurrence of neuropathy, this risk can be reduced however by using minimal concentrations of local anaesthetic and opioid combinations.[6]

Temperature homeostasis during anaesthesia is a further vital consideration in MS patients. Demyelinated axons are more sensitive to raised temperatures, exposure to which can result in a marked worsening of neurological symptoms due to the blockade of demyelinated axons.[7] Continuous temperature monitoring and ensuring availability of cooling devices and antipyretics if indicated helps to mitigate this risk.

Autonomic instability is a known complication of MS, this can become particularly problematic perioperatively where anaesthetic drugs and hypovolaemia can prompt a marked hypotensive response. In order to detect and address such changes, continuous cardiovascular monitoring is essential during surgery and throughout the perioperative period.

Motor neurone disease

Motor neurone disease (MND) is a degenerative disorder of upper and lower motor neurones of unknown aetiology. It classically presents with peripheral muscle weakness, atrophy and fasciculations before progressing to axial and bulbar weakness, sparing of sensory function and a lack of cranial nerve involvement separates MND from other polyneuropathies.

With an annual incidence of approximately two cases per 100,000 of the population, MND is relatively rare condition despite its notoriety. It can present at any age but is more commonly encountered in those over 50 with a male to female ratio of 2:1.

MND typically advances rapidly, with median survival limited to between 2 and 4 years from diagnosis,[8] with patients normally succumbing to respiratory failure secondary to bulbar palsy and progressive weakness of respiratory musculature.

Perioperative considerations

As outlined above, impaired respiratory function is a common problem amongst MND patients, this trait becomes particularly problematic in the perioperative period. Bulbar palsy results in sputum retention and an increased risk of aspiration, MND patients are likely to require increased respiratory support both during surgery and postoperatively where atelectasis and weaning difficulties can result in a requirement for ongoing postoperative ventilation.

Conduct of anaesthesia

MND-induced autonomic dysfunction can result in a marked hypotensive response to the induction of anaesthesia or commencing positive pressure ventilation, it is therefore important to ensure that MND patients have their fluid balance optimized preoperatively and that vasopressor agents are immediately available before induction.

As is a common theme across upper motor neurone disorders, depolarizing neuromuscular blocking agents, namely suxamethonium, should be avoided due to the risk of massive potassium efflux already discussed. Equally, non-depolarizing agents, although safe to use should be administered at a reduced dose with the use of a nerve stimulator to monitor their effect due to increased sensitivity amongst MND patients.

Delirium

Delirium is defined as the acute onset of a fluctuating level of consciousness associated with confusion and inattention.[9] It can be subdivided into three subtypes:

- hyperactive delirium: where the patient displays abnormal agitation, excitability or exuberance
- hypoactive delirium: typified by inhibition of normal behavioural and locomotor activity with a muted response to external stimuli
- mixed delirium: where the patient fluctuates between a hyperactive and hypoactive state.

Delirium is thought to be detectable in up to 75% of critically unwell patients at some point during their illness.[10] The adverse implications of developing delirium can be extensive; studies amongst intensive care unit (ICU) patients have found those with co-existent delirium on average have more days on a ventilator, more failed extubations, a longer ITU stay and a higher ICU and 6-month mortality.[11]

The presentation of delirium is highly variable and largely dependent on which subtype of the condition is displayed. However, a number of common features set delirium apart from other disorders of consciousness:

- inattention: reduced ability to focus, sustain and shift attention appropriately
- impaired cognition: including memory deficit, disorientation, language disturbance and perceptual disturbance which cannot be accounted for by pre-existing disease
- rapid onset: typically develops over hours to days
- fluctuant course: the severity of impaired consciousness tends to vary throughout the day.

Perioperative considerations

As previously discussed, the potential for delirium to adversely influence morbidity and mortality is significant, it is therefore important to identify those patients at increased risk of perioperative delirium. Risk factors for the development of delirium include both modifiable and fixed factors, these can be considered as patient factors, acute illness factors and iatrogenic factors, as displayed in Tables 2 and 3.

After considering those patients at an increased risk, it is vital to consider a means to appropriately assess patients in order to diagnose delirium should it emerge. A number of different formal assessment tools, including some targeted specifically for use in ICU, namely the Intensive Care Delirium Screening Checklist (ICDSC) and the Confusion Assessment Method for the ICU (CAM-ICU).

The management of delirium requires a multi-faceted and multi-disciplinary approach. The initial task is to consider the

Common drugs known to contribute to delirium

CNS drugs	Amitriptyline, benzodiazepines, thiopental, opiates, pethidine, chlorpromazine, phenytoin
GI Drugs	Ranitidine, metoclopramide
CVS Drugs	Atenolol, digoxin, furosemide
Endocrine Drugs	Steroids
Synaptic Drugs	Atropine, hyoscine

Table 3

Risk factors for the development of delirium

Patient factors	Iatrogenic factors	Acute illness factors
Age >65 years	Polypharmacy	Hip fracture
Established cognitive impairment	Disturbed sleep	Metabolic disturbance
History of alcohol abuse	Immobilization	Malnutrition and dehydration
Visual or hearing impairment	Psychoactive drugs	Constipation
Male gender	ICU admission	Pain
Previous delirium	Major surgery	Infection

Table 2

possible underlying causes of the delirium, and where possible counter any modifiable factors identified. Management strategies for delirium can broadly be split into pharmacological and non-pharmacological methods. The initial and optimal method is non-pharmacological, often comprising of simple interventions such as taking steps to re-orientate a delirious patient, encouraging mobilization, promoting normal sleep patterns, ensuring spectacles/hearing aids are worn and facilitating regular visits from family and friends. However, if such steps fail pharmacological treatments may need to be considered, especially if a delirious patient poses a risk to their own safety or that of others. The spectrum of medications advocated to treat delirium is as broad as those known to induce it, and the choice of pharmacological management should be tailored to the individual patient and clinical situation. However, haloperidol is widely regarded as the first line drug of choice, recommended by both the Society of Critical Care Medicine and NICE.[12]

Summary

While most of these neurological conditions are rare, the development of supportive treatments and expansion of home ventilation services mean that it is likely that increased numbers of patients suffering from these conditions will present for unrelated elective and emergency surgery. It is important that both the surgeon and the anaesthetist has a good understanding of the potential complications that could arise in the perioperative period as a result of these conditions and takes steps to minimize these through thorough pre-assessment and proactive post-operative management. Delirium is a condition that can affect any patient in the healthcare system and has been shown to have a detrimental effect on patient experience and outcome so should be looked for in all settings (not just intensive care) and steps taken to mitigate against it. ◆

REFERENCES

1 https://www.nice.org.uk/guidance/ng41/chapter/Context.
2 Bonner S, Smith C. Initial management of acute spinal cord injury. *Cont Educ Anaesth Crit Care Pain* 2013; **13:** 224–31.
3 Ploumis A, Yadlapalli N, Fehlings MG, Kwon BK, Vaccaro AR. A systematic review of the evidence supporting a role for vasopressor support in acute. *Spinal Cord* 2009; **48:** 356–62.
4 Almenrader N, Patel D. Spinal fusion surgery in children with non-idiopathic scoliosis: is there a need for routine postoperative ventilation? *Br J Addict: Br J Anaesth* 2006; **97:** 851–7.
5 Grasso MG, Lubich S, Guidi L, Rinnenburger D, Paolucci S. Cerebellar deficit and respiratory impairment: a strong association in multiple sclerosis? *Acta Neurol Scand* 2000; **101:** 98–103.
6 Allman K, Wilson I, O'Donnell A. In: Allman Keith G, Wilson Iain H, O'Donnell Aidan M, eds. Oxford handbook of anaesthesia. Fourth edition/, 2016.
7 Lawden MC, Blunt S, Matthews T, Peatfield R, Kennard C. Recurrent confusion and ataxia triggered by pyrexia in a case of occult multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1994; **57:** 1436.
8 Chiò A1, Logroscino G, Traynor BJ, et al. Global epidemiology of amyotrophic lateral sclerosis: a systematic review of the published literature. *Neuroepidemiology* 2013; **41:** 118–30. https://doi.org/10.1159/000351153. Epub. 2013 Jul 11.
9 American Psychiatric Association. Diagnostic and statistical manual of mental disorders : DSM-5. 5th ed. Arlington, Va: American Psychiatric Association, 2013.
10 Bourne RS, Borthwick M. Guidelines on the detection, prevention and treatment of delirium. *J Intensive Care Soc* 2007; **8:** 76–8.
11 Milbrandt EB, Deppen S, Harrison PL. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med* 2004; **32:** 955–62.
12 Young J, Murthy L, Westby M, Akunne A, O'Mahony R, Guideline Development Group. Diagnosis, prevention, and management of delirium: summary of NICE guidance. *Br Med J* 2010; **341:** 247.