

A&I

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Fucosidosis

Giant axonal neuropathy

orphan^anesthesia

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

SUPPLEMENT NR. 15 | 2020

OrphanAnesthesia –

ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesisten damit keine Erfahrungen gesammelt haben, so dass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

Bisher in A&I publizierte
Handlungsempfehlungen finden
Sie unter:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

OrphanAnesthesia –

a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

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orphananesthesia

Anaesthesia recommendations for Giant axonal neuropathy

Disease name: Giant axonal neuropathy

ICD 10: G60.8

Synonyms: GAN

Disease summary: Giant axonal neuropathy (GAN) is a rare, progressive, autosomal recessive neurodegenerative disorder. The disease is caused by variations in the gene GAN located on chromosome 16q24. The gene encodes gigaxonin, a protein involved in the dynamics of intermediate filaments and cytoskeletal framework. The defect in gigaxonin leads to an aberrant accumulation of neurofilaments within the axons leading to the development of progressive peripheral and central nervous system manifestations. Clinical features include a severe early-onset peripheral sensory motor neuropathy that might also involve the cranial nerves leading to facial weakness, optic atrophy and ophthalmoplegia. Patients generally present in early childhood with difficulty walking. By late teens, most are wheelchair bound with significant kyphoscoliosis. As the disorder worsens, the central nervous system is involved with intellectual disability, cerebellar ataxia, pyramidal signs and seizures. Visual and hearing disturbances may also develop. The nerves of the autonomic nervous system can become damaged by the accumulation of neurofilaments. Patients characteristically have tightly curled hair and a typical facial phenotype. Treatment is currently symptomatic and the average life expectancy is in the early twenties.

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

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Typical surgery

Patients may present for all types of elective and emergency procedures. Many patients will require elective surgery for orthopaedic conditions associated with the disorder, in particular spine surgery for correction of scoliosis.

Type of anaesthesia

Patients may receive both general and regional anaesthesia. Care must be taken with regional anaesthesia due to significant kyphoscoliosis that may result in a high or difficult block. If possible, an area of the spine that has minimal abnormal curvature but still provides adequate coverage for anaesthesia or pain control should be selected for epidural placement. If this is not possible, then epidural or spinal placement may still be attempted but patients should be aware of the possibility of multiple attempts and an increased risk of accidental dural puncture. Even after successful placement the spread of medication into the epidural space may be unpredictable and often patchy or one-sided [1].

Although use of peripheral nerve blocks may avoid many of the risks associated with general anaesthesia, patients with underlying neuropathy have an increased sensitivity to the complications of peripheral nerve blockade [2,3]. These include a prolonged block and increased neurotoxicity to local anaesthetic agents [4]. A comprehensive risk-benefit analysis should be completed preoperatively and patients and their relatives must be counselled about the increased risk associated with the procedure.

Necessary additional pre-operative testing (beside standard care)

Pulmonary function tests, including peak expiratory flow rate, are useful tests to assess respiratory function. Patients may have significant restrictive lung disease due to their scoliosis. A forced vital capacity of less than 30% is suggestive of potentially difficult postoperative extubation [5].

A sleep study is essential before scoliosis surgery. Confirmation of sleep disordered breathing, especially obstructive sleep apnoea, should lead to an echocardiogram looking for evidence of pulmonary hypertension. If present, appropriate measures such as non-invasive ventilation should be undertaken prior to surgery to optimise the outcome.

An electrocardiogram (ECG) should be performed if there is any evidence of autonomic dysfunction.

A history of poor swallow or choking should be sought to look for risk of aspiration.

Particular preparation for airway management

Airway management should be based on each patient individually, considering his or her underlying condition. Patients with GAN are noted to have micrognathia and limited mouth opening. Difficult endotracheal intubation with direct laryngoscopy has been reported [6]. Given this, equipment for dealing with a potential difficult airway should be readily available, including those for indirect laryngoscopy.

Patients are prone to aspiration due to poor pharyngeal tone, which may preclude the use of a laryngeal mask airway.

Particular preparation for transfusion or administration of blood products

There are no reports.

Particular preparation for anticoagulation

There are no reports.

Particular precautions for positioning, transportation and mobilisation

Meticulous patient positioning is essential for those with kyphoscoliosis. Pressure points must be well padded to avoid entrapment neuropathies and pressure sores [7].

Patient positioning can be challenging in scoliosis repairs for several reasons, including the abnormal body habitus of patients with advanced disease and the need for exposure of a large area of the spine for posterior approaches.

Interactions of chronic disease and anaesthesia medications

There are no current treatments for giant axonal neuropathy [8].

Patients with advancing disease may be on anti-epileptic medications. In patients with well controlled epilepsy, care must be taken to minimise disruption to their anti-epileptic drug regime. Patients should be advised to take their medication on the morning of surgery and to recommence therapies as soon as possible post-operatively [9].

Anaesthetic procedure

The provision of good peri-operative care begins with pre-operative assessment to identify end organ involvement. Patients with mental impairment require strategies to minimise anxiety in the perioperative period. This includes excellent communication explaining the peri-operative process, use of play therapists and distraction techniques as well as consideration of the use of anxiolytics.

Pre-operative benzodiazepines should be used with care. One case report using diazepam described prolonged muscle weakness post-operatively [10]. Benzodiazepines act at the level of the spinal cord to reduce skeletal tone, rather than at the neuromuscular junction [11]. Midazolam has been used for premedication with no reported problems [12]. If benzodiazepines are used, patients should be monitored pre-operatively to ensure hypoventilation or aspiration do not occur because of increased muscle weakness.

Patients are at risk of succinylcholine-induced hyperkalaemia and maybe of rhabdomyolysis but both volatile and total intravenous anaesthesia (TIVA) techniques have been reported for patients with GAN [6,10,12,13]. There is no evidence for a higher risk of malignant hyperthermia. Currently, there is no definitive data about the use of volatiles in GAN. One case report did not experience any problems [10], but some authors have concluded that TIVA is a safe technique for these patients [6,13]. Short-acting drugs should be chosen wherever possible to reduce the effects of residual anaesthetic agents on upper airway control and post-operative respiratory function. The use of bispectral index (BIS) or entropy to allow careful titration of anaesthetic agents is also beneficial.

The choice of neuromuscular blocking agent must be considered carefully. Patients with GAN have denervated muscle that may result in increased sensitivity to acetylcholine (Ach), suxamethonium and anticholinesterases. Suxamethonium must be avoided as the spread of Ach receptors across the entire sarcolemma may result in a massive potassium efflux on depolarisation leading to arrhythmias and potentially cardiac arrest [14,15].

The effects of non-depolarising muscle relaxants (NDMR) are unknown, however, they have been used safely so far [12]. Motor weakness increases susceptibility to NDMR. The patchy motor weakness that patients with GAN display limits the use of a peripheral nerve stimulator to assess recovery of nerve function [10]. If possible, train-of-four-response should be assessed before the first dose of NDMR. The use of rocuronium with full reversal with sugammadex has been described [12]. Several case reports have used TIVA with an intubating dose of remifentanil for scoliosis correction to avoid the complications of NDMR on neurophysiological monitoring [13].

Disease progression may lead to an autonomic neuropathy. Early on, this manifests with autonomic irritability with hypertension and arrhythmias in response to exogenous or endogenous catecholamines. Advancing involvement results in impaired cardiovascular reflexes with an inability to respond to hypotension due to blood loss, vasodilation or intermittent positive pressure ventilation [16]. Impaired thermoregulation has been reported [12]. Active intraoperative temperature monitoring and warming is essential to avoid hypothermia [17]. This is of particular importance in spinal surgery where patients often have a large surface area exposed for a prolonged amount of time. Patients should be kept warm pre-operatively, and active warming by use of warmed intravenous fluids, forced air warmers, and elevated room temperature should be used intra-operatively.

Care must be taken with ventilation strategies as patients are in danger of respiratory compromise due to restrictive lung disease secondary to kyphoscoliosis and respiratory muscle weakness. The use of respiratory support to avoid hypoventilation is important in these patients. Endotracheal intubation should be considered for all patients with poor bulbar function and a weak cough due to the risk of aspiration pneumonia.

Particular or additional monitoring

Routine monitoring including ECG, pulse oximetry, non-invasive blood pressure measurement, capnography and temperature should be used for all patients. For longer cases, a Foley catheter should be inserted for urine output monitoring. Invasive monitoring should be placed after consideration of both patient and the procedure. Patients with autonomic nervous system involvement will be more prone to haemodynamic instability and have an impaired response to hypotension secondary to e.g. haemorrhage, vasodilation or intermittent positive pressure ventilation. These patients are also more likely to have impaired thermoregulation predisposing them to peri-operative hypothermia. The potential for blood loss in scoliosis surgery is significant requiring arterial catheterisation for invasive

blood pressure monitoring, cardiac output monitoring and intra-operative blood tests. Central venous pressure monitoring can be used when peripheral intravenous access is difficult. It may also be useful to monitor right-ventricular function particularly in patients with moderate to severe pulmonary or cardiac dysfunction. Non-invasive cardiac output monitoring can also be considered and may help guide fluid resuscitation. BIS monitoring is reassuring when using TIVA rather than volatile anaesthesia and helps allow careful titration of anaesthetic drugs to minimise residual effects of anaesthetic agents on upper airway control and respiratory function. For patients with pulmonary hypertension as a result of obstructive sleep apnoea (OSA), close attention should be paid to factors that increase pulmonary vascular resistance, which could exacerbate right heart strain, such as acidosis, hypoxaemia, hypercarbia, and hypothermia.

In scoliosis surgery, monitoring of somatosensory (SSEP) and motor (MEP) evoked potentials enables assessment of the dorsal sensory and ventral motor columns. However, there have been two case reports describing poorly defined, unreliable, and poorly reproducible SSEP waveforms for patients with GAN [6,12]. The cause of this is unclear but it has been assumed to be due to disease progression. MEPs showed consistent responses in both cases and were used intra-operatively to monitor the integrity of the spinal cord [18,19]. The MEPs had a lower amplitude and prolonged conduction time. To overcome the lower amplitude waves, an increased number of stimuli and higher current stimulation have been recommended [13].

Possible complications

As described above, patients are at increased risk of respiratory complications including difficult intubation. Extubation is more difficult with $\text{FEV}_1 < 30\%$, or with peak inspiratory/expiratory pressures $< 30 \text{ cmH}_2\text{O}$.

Autonomic instability develops with disease progression, making patients susceptible to hypotension and arrhythmias.

Complications with the use of anaesthetic drugs may occur, including prolonged muscle weakness, with benzodiazepines, prolonged effects of NDMR, and hyperkalaemia with suxamethonium.

Post-operative care

Post-operative care depends on the pre-operative condition of the patient as well as the procedure performed. For short procedures, patients have been discharged from recovery to a high dependency unit [14]. The intensive care unit (ICU) may be chosen for patients with large operative procedures, high fluid shift expectations or need for post-operative mechanical ventilation [12].

Post-operative pulmonary complications can occur in scoliosis correction and are more likely in more severe disease. While scoliosis correction may prevent further decline in respiratory status, it does not improve baseline function in the immediate post-operative period [7]. A patient with a pre-operative vital capacity or $\text{FEV}_1 < 30\%$ of expected may require post-operative controlled ventilation, while a $\text{VC} \geq 70\%$ should have adequate pulmonary reserve to allow for immediate post-operative extubation [7]. Respiratory status should be optimised post-operatively because atelectasis, hypoventilation, secretion retention, immobilisation, and analgesic medications can all worsen underlying pulmonary disease.

Early post-operative mobilisation and aggressive physiotherapy helps mucus clearance and reduces respiratory complications. If possible, patients should be encouraged to use incentive spirometry and cough assist devices [9].

Post-operative pain management after surgery can be challenging. Optimising pain control for patient satisfaction and prevention of respiratory complications from hypoventilation is an important consideration. A multimodal approach to analgesia using paracetamol, NSAIDs, gabapentin, ketamine, opioids, and other available analgesics may improve outcomes. Patient-controlled analgesia has been reported to improve patient satisfaction.

Disease-related acute problems and effect on anaesthesia and recovery

Cardiac arrhythmias may be encountered either because of autonomic dysfunction or the use of suxamethonium and potassium efflux.

In patients with OSA and pulmonary hypertension hypoxia, acidosis, hypercarbia, or hypothermia can lead to cardiac decompensation and worsening right heart failure.

Ambulatory anaesthesia

Patients with GAN should be managed within an inpatient setting due to the significant risks of post-operative respiratory compromise.

Obstetrical anaesthesia

There are no reports.

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