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Multiple myeloma

Pantothenate kinase-associated neurodegeneration

orphanaesthesia

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

SUPPLEMENT NR. 22 | 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 Orphan Anesthesia 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 recommenations 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.

Find a survey of the recommendations published until now on:

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orphananesthesia

Anaesthesia recommendations for

Pantothenate kinase-associated neurodegeneration

Disease name: Pantothenate kinase-associated neurodegeneration

ICD 10: G23.0

Synonyms: Hallervorden-Spatz disease; neurodegeneration with brain iron accumulation type 1

Disease summary: Pantothenate kinase-associated neurodegeneration (PKAN) is a rare autosomal recessive disorder that was first described by the neuropathologist Julius Hallervorden and the neurologist Hugo Spatz in 1922 [1]. The active involvement of Hallervorden in euthanasia in Germany during World War II and the discovery of the defective gene (mutation in pantothenate kinase 2 gene, located on chromosome 20p13) removed the name "Hallervorden-Spatz disease" to PKAN (2,3). Prevalence is estimated at 1–3/1,000,000 [4]. It has a variable phenotype that is mainly age-dependent. The classic form has early onset (usually before six years of age) and rapid progression. Children usually present with gait abnormalities, followed by severe dystonia, seizures, dysarthria, spasticity, retinopathy and learning disorders [5]. Atypical PKAN (25% of cases) has a later onset and slower progression. Speech abnormality and psychiatric symptoms are more common in this form. Dyskinetic symptoms may be mild [5]. PKAN has a characteristic brain MRI pattern called ''eye-of-the-tiger sign'', which is a low signal intensity region surrounding a central high signal intensity region in the globus pallidus [6]. Histopathologic findings reveal iron deposition in the globus pallidus and pars reticulata of the substantia nigra [7]. Oropharyngeal dystonia can lead to pulmonary aspiration, dynamic upper airway obstruction and breathing difficulty [8]. Severe dystonia usually fails to respond to pharmacological therapy and intrathecal baclofen pump or stereotactic pallidotomy can be considered. Patients requiring general anaesthesia with this syndrome may have many symptoms that influence the pre-anaesthetic management, the induction of anaesthesia and the post-operative care.

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

- Stereotactic procedures, deep brain stimulation, pallidotomy
- Intrathecal baclofen pump implantation
- Orthopaedic surgery (for bone fractures)
- Orodental surgery (for self-mutilation of the orofacial mucosa due to intense spasms)
- Spine surgery
- Sedation (for MRI, gastric tube placement, tracheostomy)
- Ophtalmologic surgery

Type of anaesthesia

Regional anaesthesia is not suitable for these patients because of the presence of involuntary movements, rigidity and seizures. Scoliosis and contractures, causing position difficulties, are common late complications of dystonia. Patients may be mentally disabled and uncooperative.

General anaesthesia with volatile or intravenous anaesthetics can be performed [9–12].

Sedative agents must be chosen carefully because of risk of dynamic airway. Dexmedetomidine can be a viable option without comprising airway and haemodynamics [13].

Necessary additional pre-operative testing (beside standard care)

The detailed pre-anaesthetic evaluation is very important in patients with PKAN. However, because of compromised articulation, dementia or severe mental retardation, the medical history usually cannot be obtained from the patient, and cooperation with family members is necessary. The presence of medical personnel may induce anxiety leading to exaggerated dystonic movements. Assessment of auscultation, respiratory rate, chest X-ray and arterial blood gases are limited. Sedation of the patient is sometimes needed for this evaluation.

Patients in an advanced stage of the disease show severe involvement of the pulmonary system. Dystonia may involve oromandibular muscles leading to dysphagia and impairment of swallowing. Malnourishment, chronic pulmonary aspiration, pneumonia and compromised gas exchange can be seen [8]. Blood gas analysis and X-ray of the thorax should be done. Cardiac function tests including electrocardiography and echocardiography should be performed looking for cardiomyopathy and arrhythmias due to electrolyte imbalance.

Rhabdomyolysis and myoglobinaemia, causing acute renal failure and metabolic acidosis may occur after dystonic storms as well as hyperpyrexia and dehydration [14]. Renal function tests are important in these patients.

Particular preparation for airway management

PKAN is characterised by periods of life-threatening dysfunctional breathing that can include dynamic upper airway obstruction. The mouth opening is reduced with oromandibular rigidity. Extrapyramidal signs like chorea, dystonia, rigidity and tremor usually disappear with the induction of anaesthesia [8,9]. However, chronic repeated dystonic movements can lead to excessive stress on the cervical spine, resulting in degenerative changes [15]. Muscle

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contractures may fix the jaw or cervical spine, so that mobility could be limited even in the presence of muscle relaxants. Endotracheal intubation may be difficult. Awake intubation techniques are not suitable as noxious stimulation intensify the dystonia and involuntary movements. Physicians should be aware that emergency tracheostomy can be necessary.

Increased risk of gastric aspiration in patients with PKAN makes endotracheal intubation the gold standard for securing the airway. There is one single report about the successful administration of ProSeal laryngeal mask airway in a child with PKAN undergoing ophthalmic surgery [16].

Involuntary movements may reappear on emergence from anaesthesia. Re-intubation or a delayed tracheal extubation can be needed [9,12]. Patients should be monitored longer than usual in the recovery room or admitted to the intensive care unit and sedated to allow slow, gradual emergence. However, there is a case report that intrathecal baclofen may help post-anaesthetic pulmonary care by attenuating dystonia and rigidity and can be an adjuvant for anaesthesia care in patients with PKAN [17].

Particular preparation for transfusion or administration of blood products

There is no special consideration for transfusion or administration of blood products in patients with PKAN. Acanthocytosis has been reported in some patients [18]. This is a condition of the blood that presents with some red blood cells that are spiked, or possess various abnormal thorny projections. Acanthocytes have a reduced red blood cell survival. This may give rise to a mild haemolytic anaemia. But it usually does not require special treatment.

Particular preparation for anticoagulation

There is no evidence to support the need of particular anticoagulation. But the impaired mobility of patients may suggest a higher risk of post-operative thrombosis.

Particular precautions for positioning, transportation and mobilisation

Repeated dystonic movements cause extra stress to the spine, leading to degenerative changes and neurologic symptoms. The positioning of the neck during intubation and surgery must be performed with extreme care.

Muscle spasms combined with decreased bone mass can result in bone fractures, not caused by trauma or accident [19]. Patients with PKAN are often malnourished and accordingly, the skin is at risk of injury from compressive and shearing forces of surgical positioning. Meticulous patient positioning and padding is important.

Interactions of chronic disease and anaesthesia medications

Patients of PKAN could be on any one or more of the following medications: Anticholinergics, antiepileptics, baclofen, deferiprone, levodopa and benzodiazepines. These drugs are to be continued during perioperative period. Any discontinuation can precipitate withdrawal.

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Baclofen withdrawal is a life-threatening condition that may be associated with reflex spasticity, dysautonomia, hyperthermia, rhabdomyolysis, multiple organ dysfunction, and death [20].

Sedation with an increased dose of benzodiazepines can be helpful at the day of surgery controlling for involuntary movements. But the risk of aspiration and respiratory depression on the treatment of sedatives should not be forgotten.

Anaesthetic procedure

Sedative premedication with benzodiazepines and the presence of the parents during induction may be helpful in controlling involuntary movements of children with PKAN [12].

Propofol, thiopental, fentanyl, remifentanil, N_2O and volatile anaesthetics have been used without adverse effects [8]. When venous conditions are difficult, inhalational induction of anaesthesia can be considered. The agent mostly used is sevoflurane [9].

Non-depolarising neuromuscular blocking agents can be used safely. Hyperkalaemic cardiac arrest induced by succinylcholine is always a possibility, because skeletal muscle wasting and diffuse axonal changes in the brain that involve upper motor neurons could accentuate the release of potassium [8,10]. However, Keegan et al. reported the administration of succinylcholine without problems [9]. The possibility of difficulties in intubation determines the anaesthetic management.

Madhusudhana et al. reported a successful use of dexmedetomidine, without comprising airway and haemodynamics, as a sole sedative agent for MRI in a patient with PKAN [21].

In most case reports, dystonia reappeared post-operatively after the anaesthetics wore off. Re-intubation may be required due to muscular rigidity, spasticity and respiratory disability.

Patients should be monitored longer than usual in the recovery room or admitted intubated to the intensive care unit [12]. Emergency tracheostomy may even be needed [9].

Particular or additional monitoring

Standard monitoring is indicated. Arterial cannulation for invasive blood pressure measurement is recommended in case of high-risk surgery, major fluids shifts, advanced disease or multiple blood sampling.

A urinary catheter may be beneficial to assess fluid status during anaesthesia.

Possible complications

Patients with PKAN requiring surgery under general anaesthesia are usually in a status of uncontrolled dystonia and rigidity. This state is life-threatening and often requires intensive care.

Involuntary movements and seizures can complicate catheter cannulations. Dystonia may lead to spontaneous fractures, rhabdomyolysis and renal failure.

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Oromandibular rigidity, contractures and severe tongue protrusion can cause difficult airway. Emergency tracheostomy may be needed.

Due to immobility, hyperkalaemic cardiac arrest induced by succinylcholine is always a possibility.

Dysphagia and difficulties in swallowing raise the risk of aspiration and pneumonia. Sedatives used for the control of dystonia can also cause respiratory depression.

Hayashi et al. described a spontaneous presentation of neuroleptic malignant syndrome in a patient with PKAN in the absence of neuroleptic drugs and suggested that dopaminergic hypoactivity, which is characteristic of PKAN, could trigger episodes of this syndrome [22].

Post-operative care

Anaesthetists should be aware that delayed tracheal extubation or re-intubation may be required due to muscular rigidity, spasticity and respiratory disability. Patients should be monitored longer than usual in the recovery room or admitted to the intensive care unit. Emergency tracheostomy may be needed.

Disease-related acute problems and effect on anaesthesia and recovery

- Post-operative respiratory problems (DD of dynamic upper airway obstruction corresponding to the underlying disease versus residual opiate or neuromuscular blockers effect)
- Emergency tracheostomy

Ambulatory anaesthesia

Due to the significantly higher risk for post-anaesthetic adverse airway events, ambulatory anaesthesia is not recommended.

Obstetrical anaesthesia

Not reported.

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