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Madelung's disease

Metachromatic leukodystrophy

orphanaesthesia

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

SUPPLEMENT NR. 6 | 2023

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 Patientinnen und Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patientinnen und 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 Anästhesistinnen und Anästhesisten damit keine Erfahrungen gesammelt haben, sodass 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 eine Anästhesistin bzw. ein Anästhesist sowie eine weitere Krankheitsexpertin bzw. ein weiterer Krankheitsexperte (z. B. Pädiaterin bzw. Pädiater oder Neurologin bzw. Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, sodass 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

Metachromatic leukodystrophy

Disease name: Metachromatic leukodystrophy

ICD 10: E75.25

Synonyms: MLD

Disease summary: Metachromatic leukodystrophy (MLD) is an autosomal recessive lysosomal disorder caused by a gene mutation resulting in the reduced production of the enzyme arylsulfatase A (ASA). This deficiency results in the accumulation of sulfatides in the lysosomal deposits in the central and peripheral nervous system, which results in demyelination.

It is a rare disease seen in 1–4:100,000. There are three clinical subtypes, based upon age of onset of the first symptoms: late infantile, juvenile and adult forms. The late infantile subtype occurs before 30 months of age, with psychomotor regression resulting in ataxia and areflexia. Peripheral neuropathy can be the initial symptom, before central progression. As it progresses, it leads to dysphagia, drooling and the requirement of a gastrostomy for feeding. Painful spasms and seizures are common and death occurs within a few years. The initial symptoms of adult-onset MLD include memory loss and emotional instability with slower progression to the neurological deficits seen in the juvenile forms. Non-neurological symptoms result from the accumulation of sulfatides in visceral organs. This can lead to gallbladder issues such as gallstones and cholecystitis. Other organs affected include liver, kidney, pancreas and intestines.

The diagnosis of MLD is determined by progressing neurological dysfunction, widespread white matter changes in MRI, ASA enzyme deficiency in leucocytes, elevated urinary excretion of sulfatides as well as mutation analysis.

There are currently no curative treatment options for symptomatic patients with MLD. Haematopoietic stem-cell transplantation has been tested but results have been inconclusive. Gene therapy is approved for use in presymptomatic or very mildly affected children with the late infantile or early juvenile form of MLD.

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

Sedation for MRI, gastrostomy, gastro-oesophageal hernia repair, abscess drainage, endoscopy, central venous catheter placement and removal, tracheostomy, change of tracheostomy.

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia.

There is a relative contraindication to regional anaesthesia due to MLD causing scoliosis and marked spasticity. But there are reports of successful lumbar epidural anaesthesia.

Sedation is the most common form of anaesthesia for MRI (to assess disease progression) and the majority of cases require no airway intervention. Propofol and thiopental can be used safely.

Succinylcholine is avoided as it may risk hyperkalaemia and rhabdomyolysis.

Inhalation, intravenous and total intravenous anaesthesia have all been used safely.

Nitrous oxide can be used.

Necessary additional preoperative testing (beside standard care)

Monitoring of liver function tests as MLD patients are likely to be on multiple anticonvulsants. Optimisation of their medication and administration of anticonvulsants within the peri-operative period may require neurology input.

Therapeutic levels of anticonvulsants may be required.

Particular preparation for airway management

MLD patients are known to have gastro-oesophageal reflux, copious secretions, poor swallow and bulbar involvement with poor control of pharyngeal muscles. This creates a high risk scenario for aspiration and a rapid sequence induction (RSI) with cricoid is recommended. Use of a proton pump inhibitor or H2-receptor antagonist and antisialogue premedication (such as glycopyrrolate) are highly recommended.

Laryngeal mask airways have been used in patients with controlled reflux. Both cuffed and uncuffed endotracheal tubes are documented with patients that require an RSI.

Particular preparation for transfusion or administration of blood products

Not reported. Some anticonvulsants may cause pancytopenia, therefore it is advisable to check the patient's full blood count prior to anaesthesia.

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Particular preparation for anticoagulation

Severe seizure disorders requiring anticonvulsants can result in derangement of liver function and coagulation. Therefore, monitoring liver function and coagulation may be assessed preoperatively, if clinically indicated.

Particular precautions for positioning, transportation and mobilisation

Malnutrition and spasticity impacts on positioning MLD patients on the operating table. Care must be taken to pad bony prominences to prevent pressure necrosis. Iatrogenic fractures due to positioning must be avoided as best as possible.

Interactions of chronic disease and anaesthesia medications

As mentioned above, caution with patients on anticonvulsant medication and ensure continuation of these medications in the perioperative period. No documented interaction with anaesthetic sedative medications have been found in the literature review or experienced from patients with MLD anaesthetised in our unit. Note: Consider avoidance of succinylcholine due to a theoretical risk of hyperkalaemia.

Anaesthetic procedure

Preoperative medication of glycopyrrolate (for secretion management) and appropriate anti-reflux medication (such as ranitidine or omeprazole) are strongly recommended.

Although there is no documented proof of having to avoid succinylcholine, there are no reported cases of its use in MLD. This is due to the theoretical risk of hyperkalaemic cardiac arrest due to extrajunctional acetylcholine receptors, as is seen in many neurological motor diseases. In the immobile patients with marked spasticity, there is a risk of fasciculation causing iatrogenic bone fractures and, therefore, it should be avoided. Immobility also increases the risk of rhabdomyolysis.

Opiates, propofol, thiopental, sevoflurane, isoflurane and local anaesthetics have been used without any complications.

Non-depolarising neuromuscular agents (atracurium, vecuronium and rocuronium have been noted to be effective) can be safely used in these patients.

Ketamine and enflurane should be avoided due to their capability to lower the seizure threshold.

Inhalational induction, intravenous induction and total intravenous anaesthesia are all acceptable.

Antagonism of neuromuscular blockade with neostigmine is appropriate and documented.

Please note: Intraoperative doses of intravenous anaesthetic agents and muscle relaxants may need to be increased due to the increased hepatic enzyme activity seen in patients who are on anticonvulsant therapy.

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Particular or additional monitoring

Monitoring a neuromuscular blockade is recommended.

Monitor body temperature to avoid shivering and increased oxygen demand. Warming devices are advised.

Possible complications

Potential complications from sedation: hypoxia, vomiting, bradycardia, other major arrhythmias, convulsions.

Documented complications post extubation: postoperative hypothermia, aspiration pneumonia, bronchospasm.

Postoperative care

A critical care setting will often be required postoperatively as MLD patients will require frequent suctioning and positioning to avoid postoperative respiratory complications. Consider chest physiotherapy postoperatively. Postoperative pulse oximetry monitoring is recommended due to risk of aspiration/postoperative chest infection.

Documented cases suggest that the use of regional techniques for postoperative analgesia helps to reduce the use of parenteral opiates.

Post-sedation recovery requires no additional specific postoperative care. Thorough secretion management is advisable.

Disease-related acute problems and effect on anaesthesia and recovery

The increased risk of postoperative hypothermia, spasms, seizures and hypoxia is as has been documented above. Many patients will be on anticonvulsants and other chronic medication, requiring management during the perioperative period.

Ambulatory anaesthesia

Sedation for MRI is the most common procedure performed to assess disease progression in MLD patients. For those aged <3 years, thiopental is suggested. Propofol boluses can be given for children aged >3 years. Oxygen or airway intervention is often not required.

Obstetrical anaesthesia

MLD often presents in either an infantile of juvenile stage of life, inducing a rapid course of deterioration. Although an adult version of MLD exists, pregnancy in patients with MLD has not been reported.

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Please note that this recommendation has not been reviewed by an anaesthesiologist and a disease expert but by two disease experts instead.

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