orphanaesthesia

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 3 clinical subtypes, based upon age of onset of the first symptoms: late-infantile, juvenile and adult forms. Late infantile 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. Adult onset MLD initial symptoms 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 pre-symptomatic 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

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 pre-operative 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 anti-sialogue pre-medication (such as glycopyrrolate) are highly recommended.

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

Particular preparation for anticoagulation

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

Particular precautions for positioning, transportation and mobilisation

Malnutrition and spasticity impacts on positioning of 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 peri-operative period. No documented interaction with anaesthetic sedative medications found in the literature review or from patients with MLD anaesthetised in our unit. Note consider avoidance of succinylcholine due to theoretical risk of hyperkalaemia.

Anaesthetic procedure

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

Although there is no documented proof of the requirement 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 extra-junctional acetylcholine receptors, as 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 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 those on anticonvulsant therapy.

Particular or additional monitoring

Monitoring of 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: post-operative hypothermia, aspiration pneumonia, bronchospasm.

Post-operative care

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

Documented cases suggest use of regional techniques for post-operative analgesia helps to reduce the use of parenteral opiates.

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

Disease-related acute problems and effect on anaesthesia and recovery

Increased risk of post-operative hypothermia, spasms, seizures and hypoxia as documented above. Many patients will be on anticonvulsants and other chronic medication, which require management during the peri-operative period.

Ambulatory anaesthesia

Sedation for MRI is the most common procedure performed for MLD to assess disease progression. 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 with a rapid course of deterioration. Whilst there is an adult version of MLD, 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.