orphanaesthesia

Anesthesia recommendations for

Pelizaeus-Merzbacher disease

Disease name: Pelizaeus-Merzbacher disease

ICD-10: E75.2; **ICD-11:** 8A44.0

ORPHAcode: 702

OMIM: 312080

Synonyms: Hypomyelinating leukodystrophy type 1; Diffuse familial brain sclerosis; Pelizaeus-Merzbacher brain sclerosis; Sudanophilic leukodystrophy (Pelizeus-Merzbacher type)

Brief disease summary: Pelizaeus-Merzbacher disease (PMD) is a type of hereditary hypomyelinating leukodystrophy caused by variants in the PLP1 gene on the X chromosome. It is characterized by progressive and degenerative central nervous system abnormalities caused by myelination defects. PMD results in developmental delay, nystagmus, hypotonia, spasticity, and varying degrees of intellectual disability. PMD follows an X-linked pattern of inheritance and generally affects males; however, adult females may also exhibit mild to moderate symptoms as “carriers.” Based on age of onset and severity, it is classified into three subtypes: connatal, transitional, and classic PMD. Classic PMD, the most common form, initially presents with nystagmus within the first 3 months of life. PLP1-related disorders may be associated with duplications, point mutations, missense mutations, and null mutations within the PLP1 gene. Although the diagnosis is primarily based on MRI findings and clinical characteristics, a definitive diagnosis is made through genetic testing in nearly half of the patients. On MRI, bilateral diffuse hyperintensity in the white matter is observed on T2-weighted images. Laboratory tests reveal abnormalities in auditory brainstem responses (ABR) in 90% of patients. The prognosis for patients with PMD depends on the severity of the condition. With appropriate care, life expectancy can extend into their 30s. Many PMD patients also have dysphagia and epilepsy. In a retrospective cohort of 164 patients with possible congenital hypomyelinating leukodystrophies, 17% of patients had undergone tracheostomy with laryngotracheal separation, and an additional 8% required mechanical ventilation. In addition, 27% of patients, including those who had undergone gastrostomy, required tube feeding. Nearly 30% of patients were taking antiepileptic drugs and/or muscle relaxants.

Diagnosis may be incorrect; if uncertainty exists, the diagnosis should be re-evaluated.

Every patient is unique; individual circumstances must always guide clinical care.

Medicine is in progress; new clinical knowledge may not be yet reflected in this recommendation.



Recommendations are not rules or laws; they provide a framework to support clinical decision-making. Although this recommendation has passed a structured review process, it does not meet the formal criteria of a guideline.

Translations may not always reflect the most recent updates of the English version.



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

Emergency information

A	**AIRWAY / ANESTHETIC TECHNIQUE**	The vast majority of reports describe procedures performed under general anesthesia (GA). In selected cases, regional anesthesia with light sedation is well tolerated.
B	**BLOOD PRODUCTS (COAGULATION)**	No specific recommendations exist.
C	**CIRCULATION**	No specific recommendations exist.
D	**DRUGS**	Suxamethonium should be avoided, as it can cause hyperkalemia.
E	**EQUIPMENT**	Train-of-four (TOF) monitoring is useful to confirm recovery of neuromuscular function and detect spasticity.

Additional disease information

PMD is the most common of 11 recognized forms of congenital leukodystrophy caused by the dysmyelination of the central nervous system [1-3]. It is characterized by nystagmus and head tremors in early infancy, and over time, varying degrees of cognitive impairment, spastic quadriplegia, dystonia, and cerebellar ataxia may also occur. The frequency in Europe and the United States is reported to be one in 200,000 to 500,000 live births and the number of patients in Japan is estimated to be about 200 [4].

The prognosis for patients with PMD depends on the severity of the condition [5]. Patients with the congenital form typically survive into childhood. Some of these patients die very early due to respiratory complications. With appropriate care, life expectancy can extend into their 30s. Patients with classic PMD may live into their 70s. On the other hand, patients with milder forms of the disease have a life expectancy that is nearly normal.

Many patients with PMD have dysphagia and epilepsy as comorbidities. 17% of patients had undergone tracheostomy with laryngotracheal separation; an additional 8% required mechanical ventilation; and 27% of patients, including those who had undergone gastrostomy, required tube feeding. Nearly 30% of patients were taking antiepileptic drugs and/or muscle relaxants [4].

Since PMD follows an X-linked (sex-linked) pattern of inheritance, it generally affects males; however, females may also exhibit mild to moderate symptoms as “carriers” [3].

Typical surgery and procedures

Not reported.

Type of anesthesia

There are no restrictions on the use of anesthetic agents and analgesics during general anesthesia in patients with PMD [6,7]. There is little definitive evidence to support or negate the use of regional anesthesia in patients with PMD. However, it would be prudent in both peripheral nerve blocks and nerve trunk blocks to reduce the concentration and total dose of local anesthetics to the minimum necessary level. Thus, the use of regional anesthesia and analgesia in patients with pre-existing neuropathy should be carefully decided considering the potential risks and benefits. One case report described the successful use of caudal anesthesia [8].

Necessary additional preoperative testing (beside standard care)

The risk of airway complications must be assessed prior to surgery. In particular, the risk of aspiration should be assessed.

Particular preparation for airway management

Rapid sequence induction (RSI) is essential when the risk of aspiration due to gastroesophageal reflux or decreased pharyngeal muscle tone is high.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilization

Not reported.

Interactions of chronic disease and anesthesia medications

Not reported.

Anesthetic procedure

Suxamethonium can cause unpredictable reactions such as hyperkalemia and should be avoided in rapid induction [6-10]. Considerations in anesthesia should include efforts to prevent complications associated with abnormal muscle tone due to spasticity, airway complications due to decreased pharyngeal muscle strength, aspiration, and convulsions. RSI is essential when the risk of aspiration due to gastroesophageal reflux or decreased pharyngeal muscle tone is high. We recommend using rocuronium instead of suxamethonium (due to the risk of hyperkalemia). Prolonged neuromuscular blockade is a major concern in patients with PMD; routine use of neuromuscular monitoring is strongly recommended. Case reports have described the uneventful use of volatile anesthesia or total intravenous anesthesia (TIVA) for maintenance.

Spasticity causes muscle contractions that may lead to respiratory failure, hypertension, dehydration, and rhabdomyolysis [6,7]. If exacerbation of spasticity is observed, benzodiazepines may be effective. To prevent convulsions, it is better to avoid high concentrations of anesthetics and hyperventilation [7]. Anesthesia and analgesia should be considered to minimize adverse effects on postoperative respiratory function, and regional anesthesia is useful to reduce opioid use [7,8].

For postoperative nausea and vomiting (PONV) prophylaxis, dexamethasone as well as ondansetron (or similar antiemetics) should be safe. Antidopaminergic drugs (metoclopramide, droperidol) for prophylaxis should be avoided due to the higher risk of interaction with chronic medication.

Particular or additional monitoring

During emergence from general anesthesia, exacerbation of spasticity is the most common PMD-related complication and may persist after neuromuscular blockade has ceased; TOF monitoring is useful to confirm recovery of neuromuscular function and detect spasticity and should be used in all patients receiving pharmacological muscle relaxation [7]. Prolonged PACU stay may be necessary in some patients.

Possible complications

Complications associated with abnormal muscle tone due to spasticity. Airway complications due to decreased pharyngeal muscle strength, aspiration, and convulsions.

Postoperative care

There are theoretical risks that new neurological symptoms may develop, or existing symptoms may worsen after surgery, because of exposure to multiple exacerbating factors, regardless of the anesthetic technique chosen.

Disease-related acute problems and effect on anesthesia and recovery

During emergence from general anesthesia, exacerbation of spasticity is the most common PMD-related complication and may persist after neuromuscular blockade has ceased. Spasticity causes muscle contractions that may lead to respiratory failure, hypertension, dehydration, and rhabdomyolysis [7]. If exacerbation of spasticity is observed, benzodiazepines may be effective. To prevent convulsions, it is better to avoid high concentrations of anesthetics and hyperventilation [7]. Strategies for anesthesia and analgesia should be tailored not to interfere with postoperative respiratory status. Regional anesthesia is useful to reduce opioid use [7,8].

Ambulatory anesthesia

Not reported. We recommend planning ambulatory care only after an interdisciplinary discussion and an individual risk-benefit analysis.

Obstetric anesthesia

Not reported.

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