orphananesthesia

Anaesthesia recommendations for patients suffering from

Hurler syndrome

Disease name: Hurler syndrome

ICD 10: E 76.0

Synonyms: Mucopolysaccharidosis (MPS) I-H, α-L-iduronidase deficiency; Pfaundler-Hurler syndrome

Hurler syndrome is a rare lysosomal storage disease belonging to the group of mucopolysaccharidoses type I (MPS I) with an autosomal recessive transmission. MPS I is subdivided into three phenotypes of increasing severity: Scheie syndrome being the mildest, Hurler-Scheie syndrome (MPS I-HS) intermediate and Hurler syndrome (MPS I-H) the most severe. The genetic defect in MPS I-H results in a complete deficiency of the enzyme α-L-iduronidase. This leads to progressive accumulation of glycosaminoglycans causing multi-organ dysfunction. Prevalence of MPS I-H is estimated at 0.7-1.6/100,000.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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Disease summary

Patients presenting with MPS I-H have progressive cognitive impairment and somatic disorders. The skeletal abnormalities (cervical spine instability, loss of joint range of motion, restricted mobility, growth slowing or arrest in childhood, short stature, typical facial features with a short and stiff neck) seen in these patients are collectively referred to as dysostosis multiplex. Other signs and symptoms include cardiac disease (cardiomyopathies, valvular dysfunction), restrictive lung disease, frequent and recurrent respiratory infections, different types of hernias, communicating hydrocephalus, compression of the spinal cord, corneal clouding, loss of hearing and all types of organomegaly. The airway is obstructed at all levels due to hypertrophy of the soft tissue with narrowed nasal passage, adenotonsillar hypertrophy, macroglossia and thickened laryngeal and pharyngeal structures, subglottic narrowing and tracheobronchomalacia. These pathologies often result in severe obstructive sleep apnoea (OSA). There might also be odontoid dysplasia and stiff temporomandibular joint with reduced mouth opening.

Life expectancy for untreated MPS I-H is usually under 10 years. Although haematopoietic stem cell transplantation is associated with several risks, it is the only therapeutic option to preserve intellectual development and also improves cardiac and respiratory function and the problems of airway obstruction. It has to be performed before the age of 2 years. Skeletal abnormalities show no improvement.

The enzyme substitute (laronidase) obtained EU marketing authorisation as an Orphan drug in 2003. Given through weekly infusions, it leads to improvement of lung function and joint mobility. However, the neuropsychological manifestations are not influenced by enzyme replacement therapy.

Typical surgery

- Inguinal, umbilical, ventral hernias
- Adenotonsillectomy
- Cardiac surgery
- Carpal tunnel release
- Corneal grafting
- VP-Shunt
- C-spine fusion
- Contracture release in major joints
- Bone marrow transplantation
- Cardiac catheterization

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Type of anaesthesia

The indication for anaesthesia for surgery or diagnostics has to be thoroughly evaluated. Surgery in MPS patients is associated with a 30-day mortality rate of up to 4.2%! This high mortality is mainly due to respiratory problems such as difficult mask ventilation, difficult intubation and obstructive and restrictive disorders of ventilation, which can be problematic in all phases of anaesthesia. General as well as regional anaesthesia are possible.

In MPS I-H patients with severe OSA, premedication with benzodiazepines or clonidine should be avoided or used judiciously.

There are no disease-specific limitations regarding the commonly used drugs in anaesthesia. After securing the airway, basically all anaesthetics, analgesics and muscle relaxants can be used with consideration to possible or known organ dysfunctions.

Short-acting drugs such as Sevoflurane, Propofol and Remifentanil should be preferred. For short procedures, Midazolam or Propofol in combination with Ketamin offers the option of preserving spontaneous ventilation and airway control. In any case, you have to be prepared for serious airway obstruction.

Local or regional anaesthesia should be used as an adjunct to reduce cardio- and respiratory-depressant drugs when possible. Case reports about the use of regional anaesthesia in MPS I-H nevertheless are rare. Successful spinal and caudal anaesthesia have been reported as well as successful and failed epidural analgesia. Possible mechanisms for failure could be mucopolysaccharide deposition in the epidural space or in the sheath of the nerve fibers preventing the direct access of the local anaesthetic to the nerve.

Performing regional anaesthesia often is considerably impeded by altered anatomical conditions. Therefore, ultrasound should be used for guidance whenever possible.

Necessary additional diagnostic procedures (preoperative)

Before proceeding with anaesthesia, the patient should be inspected systemically on cardiovascular, pulmonary, neurological und musculoskeletal systems.

Preoperative investigation should include:

- arterial blood gases, coagulation test, serum electrolytes, biochemistry,
- chest and cervical spine x-ray,
- radiographic studies of the neck in flexion und extension to assess cervical instability,
- neurologic examination to detect spinal cord compression or communication hydrocephalus, if necessary CT scan or MRI,
- a cardiac evaluation including ECG and echocardiography, and if possible cardiac catheterization to assess cardiac abnormalities. These include cardiomyopathy, endocardial fibroelastosis, valvular regurgitation, diffuse narrowing of the coronary arteries and irregular lesions of the aorta,

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- in some cases an evaluation of the airway by flexible bronchoscopy under local anaesthesia and sedation could be helpful,

- pulmonary function tests and polysomnography to evaluate obstructive sleep apnea due to soft tissue thickening in nose and pharynx, storage within tonsils and adenoids, abnormalities in tracheal cartilage as well as skeletal abnormalities.

Particular preparation for airway management

Patients suffering from Hurler´s syndrome possibly present the most challenging airway in paediatric anaesthesia. Difficulties in airway management are reported in up to 54% and failed intubation in up to 23% of these patients. Difficult laryngoscopy with a Cormack & Lehane grade ≥ 3 are described in 30 - 40%. Fortunately, haematopoietic stem cell transplantation at an age younger than 2 years significantly reduces airway complications by reducing the accumulation of glykosaminoglykans in the tissues of the airway.

Due to the typical facial dysmorphology standard paediatric face masks may not fit properly. In ventilation difficulties with a face mask an oropharyngeal tube should be used, and a two-hand mask ventilation approach could be beneficial. The most important airway device in MPS-I-H is the laryngeal mask airway. Although ventilation can be difficult with the use of an LMA, oxygenation is almost always possible.

Additionally to the standard intubation equipment the following should be available:

- different kind of face masks and laryngeal mask airways

- flexible paediatric bronchoscope

- rigid intubation tracheoscope (Bonfils/Brambrink)

- videolaryngoscope.

Tracheostomy is the last resort to secure the airway. For this reason, an ENT surgeon should be on standby. In some cases, preoperative assessment may reveal the need for elective tracheostomy to avoid the problems associated with emergency tracheostomy. It is important to note that tracheostomy may be extremely difficult at times and will not necessarily relieve airway obstruction as tracheal narrowing may be located distal to the tracheostomy.

Particular preparation for transfusion or administration of blood products

No disease specific bleeding diathesis is known in patients with Hurler syndrome.

In patients after allogenic stem cell transplantation caution is advised regarding the transfusion of cellular blood components. The German Medical Association recommends the use of irradiated blood after HSCT for at least six month or until full recovery of immunologic function. Patients after GvHD should also receive irradiated blood.

Particular preparation for anticoagulation

There is no evidence to support the need of particular anticoagulation. Prevention of thrombosis should be accomplished as usual for the given surgical procedure. Caution is advised in patients suffering from prolonged immobilization and/or cardiac disease requiring anticoagulation.

Particular precautions for positioning, transport or mobilisation

Spinal cord compression may occur due to spinal canal narrowing at the cervicocranial and thoracolumbar regions in patients with MPS I. Although rather typical for MPS IV and VI, atlantoaxial instability due to odontoid hypoplasia has previously been described in Hurler syndrome and should be considered.

Probable interaction between anaesthetic agents and patient's long-term medication

No specific interactions are known so far. Data from studies regarding compatibility and interactions with other drugs are currently not available.

Anaesthesiologic procedure

Anaesthesia for patients suffering from MPS I-H should be performed by a very experienced team, which should consist of two anaesthesiologists and at least one anaesthesia nurse. The anatomical abnormalities of this disease mandate a comprehensive plan including airway management as well as management options if complications develop and ample backup support.

In case of elective surgery, the young patient should be affected by upper airway infections as least as possible. According to this, it is appropriate to defer the intervention to a period of less respiratory impairment. Pharmacologically, a full preoperative atropinisation has been recommended to control excessive secretion.

Induction of anaesthesia can be performed inhalational or intravenous.

Even in case of inhalational induction, intravenous access has to be established prior to induction. As placement of an intravenous line often is substantially hindered, material for intraosseus cannulation should be readily available.

Some anaesthesiologists prefer an inhalational induction with Sevoflurane under maintenance of spontaneous ventilation and application of PEEP because it provides good control of the upper airway.

Propofol slowly and carefully titrated to effect permits a smoother and also safe induction. Propofol 0.5 % is the induction agent of choice, as it reduces injection pain.

Muscle relaxants should be used with caution until the airway is secured.

Rocuronium offers the advantage of being reversed immediately by Sugammadex, which can be advantageous in emergencies.

Laryngeal mask airways usually offer sufficient ventilation conditions in nearly all cases by splinting the supraglottic airway. If the ventilation is sufficient, and if the LMA is appropriate for the type of surgery performed, the device should be the airway of choice. Additionally the laryngeal mask can be used as a conduit for flexible fiberoptic intubation, if an endotracheal tube is necessary.

If mask ventilation is possible without difficulties, fibreoptic intubation can alternatively be performed with the help of a "Mainzer-Adapter" or "Frei-mask". Although the use of awake fiberoptic intubation is often recommended for tracheal intubation in adult patients with difficult airway, in the case of MPS I-H children it is nearly impossible to get close cooperation of these patients as needed.

MPS patients have friable mucosal structures, and bleeding could obscure the fiberoptic view. Trauma to the subglottic structures by endotracheal intubation in an already narrowed airway can have deleterious consequences and should be avoided by choosing appropriate endotracheal tube size, measuring of cuff inflation pressure and minimizing intubation attempts.

Direct laryngoscopy should be only done with caution, and reclination of the neck should be avoided by reason of atlantoaxial instability.

The use of videolaryngoscopic devices with age adapted blades offers a good option to avoid traumatic direct laryngoscopy and reclination of the neck.

Emergence and extubation is another critical point as multilevel airway obstruction easily occurs in patients with Hurler syndrome. Extubation therefore should be preferably performed in an awake patient.

Particular or additional monitoring

Additional monitoring is dependent on the stage of the disease. Arterial and central venous lines should be considered in patients with severe cardiorespiratory compromise.

Possible complications

Multilevel airway obstruction and the resulting difficulties in airway management.

Airway collapse is common, and negative pressure pulmonary edema has been described.

Difficult ventilation from obstructive and restrictive lung disease.

Cardiocirculatory compromise due to pre-existing pathologies.

Compression of the cervical spine.

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Postoperative care

Degree of postoperative monitoring is depending on surgical procedure and preoperative condition of the patient. Intensive care is not mandatory but should be available even for minor surgery in case of cardiologic or respiratory complications.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

Massive upper airway obstruction and urticaria have been reported with the use of laronidase for ERT three hours after infusion. This seems to be of allergic nature and Ig-E mediated. Therefore, elective anaesthesia should never be given on days ERT.

Ambulatory anaesthesia

Experienced centres manage less affected patients as day-case anaesthesia. Data on possible complications after ambulation are not available.

Obstetrical anaesthesia

The necessity of consistent myeloablation for prevention of engraftment failure after allogenic bone marrow transplantation (BMT) with high-dose busulfan usually results in significant impairment of fertility in women who undergo BMT after the onset of puberty. However, very little is known about the ovarian toxicity when this regimen is administered before the onset of puberty, as it usually is in patients suffering from MPS I-H. To date there are only three case reports about pregnancies in women with MPS I-H. One reports the successful completion of caesarean section under epidural anaesthesia. Other reports on obstetric anaesthesia are lacking. Given the high incidence of problems in managing the airway in Hurler syndrome and the well-known changes in the upper airway of labouring women, implementation of a regional anaesthetic technique seems most reasonable.

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