orphanaesthesia

Anesthesia recommendations for patients suffering from

Morquio Syndrome

Disease name: Morquio Syndrome

ICD 10: E76.219

Synonyms: Morquio-Brailsford Syndrome; Mucopolysaccharidosis IV; MPS IV type IVA

Morquio Syndrome (MS) or mucopolysaccharidosis (MPS) type IVA is a progressive lysosomal storage disorder with autosomal recessive inheritance. Literature may combine MPS type IVA and B and refer to them as Morquio Syndrome, although type IV B is extremely rare and presents a far less aggravating course. A deficiency of the enzymes N-acetyl-galactosamine-6-sulphat sulphatase and beta-galactosidase compromises the catabolism of the glycosaminoglycans (GAGs) keratan sulphate and chondroitin-6-sulphate/chondroitin-4-sulphate . The GAGs accumulate excessively in soft tissue, cartilage, and bone causing severe skeletal dysplasia and a distinct phenotype. Features include dwarfism, significant pectus carinatum and kyphoscoliosis, hypoplasia of the odontoid process causing atlanto-axial instability and cervical subluxation, cervical stenosis, and deformity of joints with limited mouth opening and genu valgum ("jockey stance"). Accumulation causes deformation of the oropharyngeal and laryngeal structures, macroglossia, sleep apnea, bulgy soft tissue prone to bleeding and hypertrophic tonsils and adenoids, GAGs have a predisposition for the trachea and cornea, especially keratan sulfate (the predominant GAG in patients with MS) which accumulates in the hyaline cartilage of the anterior tracheal rings causing tracheal stenosis and tracheomalacia with position-depending obstruction.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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

Disease summary

Co-morbidity is common in MS. Thoracic deformities result in severe restrictive pulmonary disease, reduced alveolar capacity, and recurrent infections. Accumulation in the coronary arteries, heart valves, and myocardium is described leading to cardiomyopathy, myocardial ischemia, and valve dysfunction. Vital organs can be affected, in particular hepato- and splenomegaly. Other co-morbidity is neurological due to the spinal cord impact, skeletal, ophthalmological, and otolaryngological. In general MS patients are wheel-chair bound as teenagers but have a normal intelligence. In most cases life span is limited to the second or third decade of life, pulmonary and cardiac impact being responsible for the early demise. However, life sustaining surgery and improved medical treatment have increased the life expectancy and recommendation towards prophylactic stabilising cervical fusion suggest that more MS patients will undergo general anaesthesia in the future. Already, patients with MS undergo multiple surgical procedures majority of which are orthopaedic, heart valve, and ear-nose-throat related.
Airway management is challenging and general anaesthesia is a high risk procedure involving the risk of death. Much information is emerging detailing airway abnormalities that may have an impact on anaesthetic management.

Typical surgery

Fusion and decompression of cervical spine, in particular craniocervical junction, VEPTOR instrumentation and repeated lengthening of the VEPTOR rods, (the use of Veptor instrumentation is controversial. Because of very small vertebrae the complication rate (dislocation of material; tetraparesis) is high. In general Veptor instrumentation is questionable and if indicated only be done in the most experienced centers) kyphoscoliosis surgery, correction of genu valgum, and hip arthroplasty, heart valve surgery, tonsillectomy and adenoidectomy, sedation for MRI and in future central venous access for enzyme therapy.

Type of anaesthesia

Currently there are no definitive recommendations for general versus regional anaesthesia. However, literature reporting successful regional anaesthesia is limited. One report describing 28 patients undergoing over 140 procedures (paediatrics) with MS described 6 successful regional anaesthetics in 8 patients attempted. Authors preferred a caudal approach when possible due to the known abnormalities of the neuraxial structures including kyphoscoliosis, rendering caudal approach safer by keeping the point of needle entry further from the termination of the dural sac.

More recently there have been four cases (one published case by Calvin et al and three others known to this author via personal communication) of spinal cord infarction in the area of C7-to T-7 which occurred following lower extremity procedures (3/4) and cervical spine surgery (1/4). All four patients were in their teenage years and the three patients who had lower extremity procedures had an epidural placed in the operating room. Due to the devastating nature of such an event and the lack of any warning signs to avert such an occurrence in these patients we no longer recommend epidural anesthesia for children with Morquio Syndrome.

Sedation is often provided for radiological procedures for these children most commonly for Magnetic Resonance Imaging (MRI). Sedation which often exceeds 'conscious sedation' should be considered a high risk procedure in MS patients. Due to a high degree of known upper airway difficulties including difficulty in intubating the trachea, the provider of the sedation should be an anaesthetist with experience in MS patients.

Necessary additional diagnostic procedures (preoperative)

The main goal of the additional preoperative evaluations is to delineate the upper and lower airway anatomical and functional abnormality. Otolaryngology (ENT) examination of upper airways, sleep study to estimate obstructive and central sleep apnea, pulmonary evaluation including lung function test and spirometry (if the patient is old enough to cooperate) and cardiac evaluation are important. In addition fluoroscopy of the airways to detect functional and structural obstruction (real time) to breathing is preferred by some centers. Coronal and axial MRI or CT of the airways are recommended in order to assess tracheal stenoses which can be found in a very proximal position.

In addition to echocardiography cardiac evaluation may need to include an MRI to evaluate aortic root dilatation especially in older MS patients (>20 years). Bear in mind that silent cardiac abnormalities are common in MS patients with predominantly left-sided valve involvement, especially in children. Reported valvular abnormalities include aortic valve insufficiency, which is the most common valve disease present in MS and is a result of GAG deposits that thicken and deform heart valves. Factor et al. studied the coronary arteries by light and electron microscopy in a 15-year-old boy (postmortem) with MS and showed that intimal sclerosis was a prominent feature of MS. Rarely, deposits in the myocardium itself can cause a decrease in myocardial compliance.

Currently, mortality and morbidity from MS continue to be of respiratory and neurological origin; however, the advent of enzyme therapy for MS may increase life expectancy and other organ failures may become more evident.

Particular preparation for airway management

The most important aspect of the anaesthetic management of the MS patients is airway management. Anticipation of difficulties and preparation are of paramount importance. Difficult mask ventilation is common and 'two person' technique may be necessary. Airway tools necessary to manage difficult airway should be readily available. Equipment that displaces soft tissue in a definitive and rigid manner is preferable in children with MS. This includes Video Laryngoscope, Laryngeal Mask Airway (LMA) and endoscopy mask (used to provide mask ventilation while a fiberoptic intubation is being performed). Fiberoptic Bronchoscope should always be available due to its ability to add additional modes of intubation if other quicker modes such as Video Laryngoscope fail. The fiberoptic scope has also been used using LMA as a conduit in MS patients when video laryngoscope has failed. In a patient with very difficult airway one may fail to visualize the larynx in spite of best efforts. When appropriate, an ENT surgeon may be made available to perform a tracheostomy in the event that all else fail and airway becomes an emergency. Placement of tracheostomy, electively, should only be after considerable discussion due to difficulty of not only of the surgical technique but of maintaining the tracheostomy in such patients. Another important aspect of the Morquio airway is that they have smaller calibre airway and therefore anticipate using smaller endotracheal tubes.

Particular preparation for transfusion or administration of blood products

Not a particular concern in MS patients.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transport or mobilisation

Transportation of Morquio patients requires knowledge of the stability of the individual patient's cervical spine. If in doubt one may assume the possibility of an unstable cervical spine due to a high prevalence and known risk of cervical subluxation (Such situation may arise if a MS patient is being transferred from the site of a trauma or motor vehicle accident where the patient's history may not be readily available. Thus, all measures may be taken to stabilize cervical spine while transporting MS patients following an incident such as a 'fall' or major trauma)

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

Not a significant reported problem.

Anaesthesiologic procedure

Parameters to consider when deciding induction of anesthesia are:

- severity of disease related to airway such as history of obstructive sleep apnoea or history of snoring
- prior history of anesthetic difficulty
- history of cervical fusion (most patients have cervical spine surgery when they are children)

It is prudent to obtain an intravenous line using topical anesthetic creams avialable both in United States and Europe. Nitrous oxide mixed with oxygen may also be used to obtain analgesia to start intravenous line. In United States a combination of slow inhalational anesthesia (sevoflurane) combined with small doses of Intravenous agent (propofol used most commonly) are used to increase the level of anesthesia in such patients, assessing airway patency. Whether to maintain spontaneous ventilation or not, is a clinical judgement made by the Anesthesiologist and is based on the criteria that patient will be ventilated using a face mask using positive pressure ventilation till trachea is intubated. It is important to examine a patient's previous anesthetic history in all such situations.

Use of muscle relaxants is a step that should take into consideration the risk of losing the airway if ventilation is not possible via mask and if intubation is not achieved in a timely fashion. This is a crucial step in the anesthetic management and requires careful

consideration. There are patients who may be easier to intubate once relaxed using neuromuscular blockers (such as rocuronium).

Concerns related to induction of anaesthesia are related to upper airway management and intubation of trachea. Ventilating with mask may be fraught with obstruction due to tongue and GAG deposits in naso and oropharngeal area. A second anesthesia provider should be available to help and two person mask ventilation may often be necessary; where one individual manages the mask with anterior displacement of the tongue while the second individual applies positive pressure breaths. Displacing the tongue with a piece of gauze (or a ring forceps) may be necessary to adequately ventilate and oxygenate the patient. Use of a laryngeal mask airway (LMA) in a failed intubation may be possible but is not guaranteed to provide adeqaute ventilation, but may be an option for a short period of time (eg., while waiting to awaken the patient in the event that intubation failed and surgery is cancelled). If LMA doesnot provide air entry after placement it is almost always due to the posteior tongue blocking the LMA aperture. It is also possible to intubate via an LMA which is well placed. It is reasonable to consider an awake fiberoptic intubation in the event that all other methods of intubation have failed. When nasal fiberoptic intubation is attempted, bleeding from the nostrils can obliterate the view. Application of a vascular constrictor can be considered (i.e. an adrenalin infused piece of gauze). An ENT surgeon is made available in situations where considerable difficulty is anticipated and tracheostomy may be a consideration. Tracheostomy placement is also made more diffciult in Morquio patients due to tracheal wall abnormalities and due to very short neck. In line stabilization is required during airway manipulation in a patient who may have C1-C2 instability.

Neurophysiological monitoring may also be provided if significant concern of spinal cord compromise exists during intubation.

When intubating the trachea regardless of the choice of instrument being used a simple but effective manoeuvre to facilitate visualizing the larynx is to displace the tongue anteriorly

C1-C2 reduction and fusion in patients with MS is a procedure of significant perioperative concern. Careful attention needs to be given to the alignment of the head and neck and the ‘‘head should be positioned posterior to the body and looking up.’’ This head and neck alignment is favoured by patients themselves because it optimizes airway patency and facilitates unobstructed breathing, giving the patients a somewhat peculiar posture that is easily discernible on examination. The airways of patients with MS easily obstruct when the neck is flexed, demonstrated by flow–volume loop, tracheal tomography, and fiberoptic tracheography reported by Pritzker et al. They noted anterior buckling of the posterior tracheal wall during flexion of the head, which caused a slit-like narrowing of the tracheal lumen. The need for a posture of optimal head and neck extension cannot be overemphasized in children with MS. While the causative mechanism is unknown, it might be attributed to a loss of tensile integrity of the tracheal walls due to a combination of abnormal hyaline cartilage composition and GAG deposits in the sub mucosal tissue. Other structural and morphological airway abnormalities result from sub-mucosal GAG deposits in the upper airways (tongue, floor of mouth, epiglottis, ary-epiglottis folds, and tracheal wall), all of which combined impart a rigid anatomy. Although rare, vocal cord paralysis has also been described in children with MS

Based on our study and experience with perioperative anesthetic care of patients with MS, we recommended the following in a manuscript published by this author:

- airway evaluation in patients with MS, not only in regard to intubating the trachea, but also to facilitate optimal head and neck position for postoperative care;
- otolaryngology consult to document abnormalities of airway and pulmonary consult to evaluate respiratory function;

- glidescope to intubate trachea when difficulty with direct laryngoscopy is anticipated;
- awareness that some patients with MS will be very difficult to intubate, regardless of choice of equipment;
- evoked potentials monitoring during intubation in the sub-population where spinal cord compromise is a concern;
- manual displacement of the tongue anteriorly during intubations;
- expectation of difficulty with nasal FOB because of narrow nasopharyngeal path;
- cardiac consult to evaluate structural and functional abnormality.

Particular or additional monitoring

Monitoring spinal cord integrity during spinal fusion procedures using somatosensory (SSEP) and motor evoked potentials (MEP) are recommended by some although practices vary Spinal cord compromise is an ever present threat to MS patients during anaesthesia. . There are reports of ischemic spinal cord injury not adjacent to the surgical site in MS children. (I would refrain from using this sentence. The reference list should be adequate in my opinion.)

Possible complications

Complications related to airway management: (1) failure to adequately ventilate and oxygenate the patient (2) failure to intubate trachea resulting in cancellation of the surgery or worse hypoxic injury to the patient (3) trauma to the larynx and trachea from repeated and traumatic attempts to secure airway (4) regional anaesthesia has been described but may lead to late recognition of spinal cord injury (data not published)??? (5) Profuse epistaxis from attempts at nasal intubation) Cervical flexion causing airway obstruction or spinal cord injury (8) Airway obstruction following extubation of trachea.

Postoperative care

Extubation of the patient requires careful consideration, especially following a difficult intubation and long/extensive surgical procedures: accessing the larynx and trachea may have altered due to the cervical fusion surgery. If intubation was difficult prior to cervical fusion then greater difficulty should be anticipated after. An awake patient able to obey commands (take a deep breath; put your tongue out) is re-assuring when preparing for extubation. Watch patient's respiratory pattern to ensure that no diaphragmatic or other respiratory muscle weakness has ensued from the surgical manipulation of the spine during surgery. All difficult airway equipment should be readily available along with the same skilled personnel who were present during intubation. Extubation over a tube exchanger is recommended. An Otolaryngologist present at induction of anaesthesia and extubation of the trachea is desirable; however this practice varies between institutions and countries. If the anaesthesiologist chooses to transfer the patient to intensive care with endotracheal tube in place to be extubated at a later period, such extubation should receive the same cautious considerations as described above.

To further enhance safety, other steps that may be taken are: extubation over a tube exchanger, administration of steroids for preventing laryngeal oedema, and postponing extubation 24 hours after extensive airway manipulation to secure all swelling is settled.

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 diseases, e.g.:

n/a

Ambulatory anaesthesia

In MS patients there are no minor anaesthetics even when surgery may be 'minor'. There are case reports of airway difficulties during minor surgery such as myringotomy and tube placement. The airway difficulties usually progress and worsen with age along with progression of cardiac and respiratory mechanics. Utmost caution should always be exercised during all anaesthetics including ambulatory anesthesia and the skilled anesthesia providers experienced in the care of MS patients should provide care. IN United States, care of MS patients in ambulatory centres is not recommended. I consider a similar recommendation very appropriate in your website.

Obstetrical anaesthesia

There are no publications specifically addressing the anaesthetic care of MS patients during labour and delivery. As the life expectancy of MS patients increases such reports may be forth coming. Regarding epidural anaesthesia one should bear in mind that neuraxial spinal stenosis is to be expected especially in older patients. **In addition, we no longer think epidural anesthesia is appropriate for Morquio patients.** For explanation, please see page 3, under ‘types of anesthesia’.

Literature and internet-links

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