Guidelines for the Management of Mucopolysaccharidosis Type I

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Mucopolysaccharidosis type I (MPS I) is the prototype of the MPS disorders, a subgroup of lysosomal storage diseases. The incidence of MPS I in Brazil is unknown, but a retrospective population study in Australia conducted between 1980 and 1996 yielded an overall prevalence of 1 in 22 500 for all MPS types.[1] In British Columbia, cases ascertained between 1952 and 1986 determined that the frequency of MPS type I Hurler, the most severe form of the disease, was approximately 1 in 144 000 newborns,[2] a result similar to that found in The Netherlands.[3] A recent analysis of data collected by the Society for Mucopolysaccharides in the United Kingdom in patients with MPS I found a prevalence of 1.07 per 100 000 births.[4]

MPS I is characterized by a deficiency in α-L-iduronidase enzyme activity, leading to buildup and urinary excretion of high levels of glycosaminoglycans (GAGs), specifically dermatan and heparan sulfates. The disease is genetically determined and shows autosomal recessive inheritance.[5,6] MPS types were initially named by using eponyms, but after the advent of biochemistry, specific enzymatic deficiencies were established for each MPS type. MPS I, first described by Hurler as a severe form of MPS and by Scheie as a mild form, were subsequently identified as the same disease. Although MPS I is classically referred to as Hurler, Hurler-Scheie (intermediate presentation between the Hurler and Scheie extremes), or Scheie syndromes, there is no biochemical or molecular basis for this classification, and the disease encompasses a continuum of severity, with varying degrees of skeletal, cardiac, digestive, respiratory, and central nervous system involvement, all resulting from the same underlying enzymatic deficiency.[7] Common symptoms include atypical facies, progressive infiltration of tissues, normal intelligence or developmental delay and mental retardation, growth retardation, short stature, multiple dysostosis multiplex, joint stiffness, corneal clouding, cardiomyopathy, valvular compromise, respiratory insufficiency, hepatosplenomegaly, and recurrent respiratory infections.[5-7] Patients with MPS I have a reduced life expectancy. Without treatment, patients with the most severe form of the disease have a median survival of 6.8 years.[4] Patients with a more attenuated form of the diease (Hurler-Scheie and Scheie) survive to adolescence or adulthood, but with significant morbidity.[5]

ADLs	Activities of daily living	ERT	Enzymatic replacement therapy
ATR	Abdominal thorax rebalance	GAG	Glycosaminoglycans
BAEP	Brain stem auditory evoked potential	GVHD	Graft versus host disease
BHM	Bronchial hygiene maneuvers	HR	Heart rate
BMT	Bone marrow transplant	HSCT	Hematopoietic stem cell transplant
CFP	Federal Psychology Council	IDUA	Alpha iduronidase
CH	Communicating hydrocephalus	LSD	Lysosomal storage disorders
CHF	Congestive heart failure	MNR	Magnetic resonance
CNS	Central nervous system	MPS	Mucopolysaccharidoses
CPAP	Continuous positive airway pressure	MPS I	Mucopolysaccharidoses type I
CT	Computerized cranial tomography	OSAHS	Obstructive sleep apnea-hypopnea syndrome
CTMA	Cetyltrimethylammonium	RFLP	Restriction fragment length polymorphism
EFA	Expiratory flow acceleration maneuver	ROM	Range of movement
EMEA	Evaluation of medicinal products	RR	Respiratory rate
		ST-s	ST segment
		UARS	Upper airway resistance syndrome

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Clinical Manifestations of MPS I

As a multi-systemic disease, MPS I requires early intervention and multi-disciplinary management for optimal patient quality of life, treatment response, and survival. Patient and family disease education are essential.[8] Each patient's treatment and follow-up plan should be individualized according to the patient's unique situation and clinical status.[7-9]

Airway Manifestations

Thoracic cage limited mobility and deformities in tracheal or bronchial cartilage cause the pulmonary problems in these patients. Nasal secretion and tracheal thickening are frequent. Other head and neck manifestations include craniofacial abnormalities, depressed nasal bridge, chronic rhinitis, shortened neck, enlarged tonsils and adenoids, protruding tongue, infiltration of glottis tissues, abnormal epiglottis, tracheal compression, and bronchial narrowing.[10]

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by partial or total obstruction of upper airways during sleep, accompanied by alterations in arterial blood gases and in sleep architecture, with characteristic clinical symptoms and long-term complications.[11] Snoring and disturbed sleep are the most common symptoms of OSAHS in children. Night sweats and bedwetting may also be observed. Daytime symptoms include mouth breathing, morning headache, excessive drowsiness, and behavioral disorders such as hyperactivity and aggressiveness. The latter is often confounded with, or worsen, behavioral alterations already present.[12] Possible complications are impaired learning, developmental delay, growth retardation, systemic arterial hypertension, pulmonary hypertension, or both,[13] and sudden death. The gold-standard diagnosis of OSAHS is polysomnography or sleep study. Pediatric studies must be staged and interpreted according to the appropriate criteria for patient age.[14-18] In addition to cyclic obstructive apnea, many children have partial and persistent upper airway obstruction associated with hypoxemia and hypercapnea. This is combination is known as obstructive hypoventilation and is especially common in children <3 years of age, the critical age at which symptoms appear in children with MPS I. Upper airway resistance syndrome (UARS) has also been described in both children and adults. Patients with UARS have snoring and excessive daytime drowsiness, but no apnea or alteration in arterial gases on polysomnography.[19]

The nasofibrolaryngoscopy allows visualization of the entire nasal cavity, nasopharynx, soft palate, tongue root, palatine tonsils (often not visible in oropharynx examination with macroglossia), epiglottis, and larynx. This allows dynamic evaluation of swallowing, phonation, and respiration. In addition to OSAHS, patients with MPS tend to have recurrent respiratory infections (otitis media, sinusitis, and tonsillitis).[20,21]

Recurrent and excessive rhinorrhea is a frequent complaint in this patient group.[10,22,23] Excessive build-up of mucus and increased viscosity common in MPS may lead to secretion stasis and alteration in paranasal sinus drainage, causing secondary infections and chronic alterations in nasal mucosa. Although an unusual finding, formation of nasal polyps may occur as a result of chronic inflammation of nasal mucus, associated to mucus stasis.[24]

Alternatives in diagnosing respiratory problems, besides polysomnography and nasolaryngoscopy, include full lung function tests, arterial blood gases, pulse oximetry, hemoglobin levels, and imaging examinations (computerized cranial tomography [CT], magnetic resonance [MNR]), which can contribute toward locating the obstruction site and assessing pulmonary structure.

Treatment

The aim of clinical treatment is to control recurrent airway infections. Normally, nasal isotonic or hypertonic saline solution is used to eliminate crusts and secretions, improve cilia mobility, and reduce mucus edema. Nasal topical decongestants may be used for acute episodes in which nasal obstruction is very intense, bearing in mind the reduced effect of the medicine when used for periods longer than a week. Systemic decongestants must be used sparingly so secretions are not further thickened.[25] Antibiotics (10- to 15-day courses) are used for treating purulent nasal secretion or acute bacterial infection such as acute otitis media or tonsillitis. Systemic corticosteroids for brief periods may help reduce the edema and facilitate drainage of secretions.

The most frequent surgical procedures include adenotonsillectomy, surgery of the nasal shells, tracheostomy, laser surgery of tracheal lesion, and uvulopalatopharyngoplasty. Because airway blockage in MPS is multi-factorial, the outcomes of adenotonsillectomy vary, but substantial short- to medium-term improvements in respiratory quality are seen in most cases. However, as the disease progresses, tracheostomy or nasal continuous positive airway pressure (CPAP) may become necessary.

Airway surgery can be complicated by macroglossia, limited mouth opening, a restricted operation margin, and instability of the cervical column, making it difficult to visualize the operative field. Neck hyperextension in these patients can cause an acute cord compression. An alternative option to performing adenoidectomy when access via the oral opening is impaired is endoscopic surgery through the nasal route.[26] Definitive or temporary tracheotomy may be performed before other surgeries to facilitate airway control. Tracheostomy should be avoided whenever possible because of difficulties in surgical technique, stiffening of the trachea, significant anatomic alterations with a short neck, and the possibility of postoperative complications such as tracheitis, recurrent pneumonia, and blockage of the tracheostomy by thick excretions.[10] Swallowing, already impaired by the anatomic alterations and neurological compromise tends to worsen, increasing aspiration risk.[27] The challenges of managing a tracheostomy in these patients, with the difficulty in acceptance by the patient and family, should also be taken