

## Mucopolysaccharidosis: Anaesthetic Considerations and Clinical Manifestations

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**Abstract:** Mucopolysaccharidosis (MPS) are a group of inherited metabolic disorders. These disorders are uncommon yet an important topic in continuing education in clinical anaesthesiology. Therefore there is a need to study their clinical features and effect of these features on anaesthetic management with special reference to airway management. In the last few years many scientific studies have been published emphasizing the risks involved in anaesthetic management of such patients. These are patients of potential difficult airway and entire anaesthetic management revolves primarily around proper assessment of clinical features leading to difficult airway and judicious use of available airway equipment. We want to review the literature as regards the clinical features and anaesthetic complications especially involving intubation difficulties and techniques and equipment used in managing these difficulties. We want to study the literature as regards the use of latest gadgets available for managing difficult intubation in these patients in a procedural manner so as to improve the quality of care and minimize anaesthetic complications when handling such kind of patients.

**Material Method:** A thorough literature review was undertaken to locate all the relevant articles that described the clinical features and anaesthetic management of MPS. We searched the pub med EMBASE™, google scholar, Wiley online and medline plus for relevant articles using the following search terms- Mucopolysaccharitosis, Anaesthesia, management, morquios, hurlers, huters syndrome.

**Conclusion:** MPS disorders are characterized by progressive craniofacial, joint and skeletal deformities, progressive cardiac involvement and early death from pulmonary infection or cardiac failure. Patients of MPS are short statured with skeletal deformities like short broad metacarpals and phalanges, kyphosis, scoliosis, immobile cervical and temporomandibular joint and coxa vara..

Children with MPS should be handled by anaesthesiologists and surgeons who are aware of the expected complications of this disease. Before subjecting such a patient to anaesthesia a proper informed consent should be obtained, difficult airway cart should be ready and available and even a surgeon standing by ready to do an emergency tracheostomy. Inhalational induction with maintenance of spontaneous ventilation is preferred but in mentally retarded and uncooperative patients intravenous induction is more satisfactory. A fiberoptic technique of intubation for children of MPS using laryngeal mask airway has been described<sup>15</sup>. LMA allows a good airway control without tracheal intubation.

Anaesthesia should ideally be administered by experienced anaesthesiologist and in a set up which has facility for paediatric intensive care unit. Recovery after general anaesthesia in such cases may be accompanied by periods of breath holding, apnoea, bronchospasm, cyanosis and respiratory arrest.<sup>16</sup> A fiberoptic technique of intubation for children of MPS using laryngeal mask airway has been described<sup>15</sup>. LMA allows a good airway control without tracheal intubation.

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Date of Submission: 22-03-2018

Date of acceptance: 09-04-2018

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### I. Introduction

Mucopolysaccharidosis (MPS) are a group of genetic disorder in which lysosomal enzyme deficiency leads to intralysosomal deposition of glycosaminoglycans in nearly all cell types, tissues and organs. This causes cellular enlargement, structural and functional disruption in oral cavity, airway, cornea, brain, heart, liver, spleen, bones, ligaments and skin causing various symptoms<sup>1,2</sup>

Typical clinical manifestations include coarse facial feature, skeletal dysplasias, growth impairment, cervical instability and spinal cord compression, organomegaly, hernias, cardiorespiratory disease, impaired vision and hearing and joint contractures<sup>3</sup>. Most MPS patients require surgical interventions and anaesthetic exposure for management of their disease. Data from MPS-I registry (N=544) showed at least one surgical procedure in 75% of patients, with a median of three to four surgeries per patient<sup>4</sup>

This group of diseases are known to cause major problems in anaesthesia due to difficult airway, cervical spine disease and an increased prevalence of cardiovascular manifestations<sup>5</sup>

**Pathophysiology**

Glycosaminoglycans are long- chain complex carbohydrates consisting of repeating sulfated acidic and amino sugar disaccharide units. They are usually linked to proteins to form proteoglycans, which are the major constituents of the ground substance of connective tissues, lubricant in joint fluid, and the surface coating that initially binds growth factors to cells. The major GAGs are chondroitin-4-sulphate, chondroitin-6-sulphate, heparin sulphate, dermatan sulphate, keratan sulphate, and hyaluronic acid. In the organism, these substances are degraded by the sequential action of lysosomal enzymes leading to a stepwise shortening of the terminal sulphate, acidic, and amino sugar residues. Deficient/dysfunctional activity of the degradative enzymes result in MPS disorder of which there are eleven types based on levels of severity. The clinical phenotype of the disorder depends upon the distribution and turnover of the substrate effected by the deficiency, rather than be distribution of the enzyme<sup>6,7,17</sup>

**Classification**

Of the total 11 MPS disorders, there are 7 major types classified 1 through IX. MPS V, formerly, Scheie syndrome, and MPS VII are no longer recognized<sup>7</sup>. The MPS disorders are differentiated by clinical features and age at presentation and biochemically by associated enzyme deficiency. Table I shows classification of MPS .

**Table I:** Specific classification and features of MPS

Number	Eponym	Enzym deficiency	GAG stored	carinofacial abnormalities	joint and skeletal deformities	cardiac involvement	Visceral, visual and neurologic manifestations
(Mps I (severe) Dominant feature: soft tissue storage and skeletal disease	hurler syndrome	alpha- L- iduronidase	dermatan sulfate, heparan sulfate	macrocephaly coarse facies macroglossia hydrocephalus	stiff joints, thoracolumbar kyphosis, possible odontoid deformity, hypoplasia, short neck, short stature	coronary intimal and valvular thickening, mitral regurgitation, cardiomegaly	hepatosplenomegaly; umbilical and inguinal hernias; corneal clouding severe mental retardation
mps (attenuated)	scheie syndrome	alpha- L- iduronidase	dermatan sulfate, heparan sulfate	coarse facies, macroglossia prognathia	short neck, Normal stature	aortic regurgitation	hepatosplenomegaly, umbilical and inguinal hernias, corneal clouding
Mps II (severe) Dominant feature: soft tissue storage and skeletal disease	hurler - scheie syndrome	iduronate sulfatase	dermatan sulfate, heparan sulfate	Macrocephaly, coarse facies, macroglossia, hydrocephalus	diffuse joint limitation, short neck, short stature	coronary intimal and valvular thickening, mitral regurgitation, cardiomegaly	hepatosplenomegaly, no corneal clouding
Mps II (attenuated)	hunter syndrome (severe)	iduronate sulfatase	dermatan sulfate, heparan sulfate				
Mps IIIA (syptoms appear after the first year of life) Dominant features: primarily CNS disease	hunter syndrome (mild)	heparan N sulfatase	heparan sulfate	coarse facies, heavy eyebrows that meet in centre in the face above the nose	mild stiff joints, short stature, dysphagia	minimal to none	severe retardation, behavioral problems, diarrrhea
Mps IIIB Dominant features: primarily CNS disease	Sanfilippo B syndrome	alpha- N acetyl glucosaminidase	heparan sulfate	coarse facies	mild stiff joints, short stature, lumbar vertebral issues, dysphagia	minimal to none	developmental delay, behavioral problems
Mps IIIC Dominant features: primarily CNS disease	Sanfilippo C syndrome	acetyl co alpha- glucosaminidase	heparan sulfate	coarse facies	mild stiff joints, short stature, lumbar vertebral issues, dysphagia	minimal to none	developmental delay, behavioral problems

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Mps IIID Dominant features: primarily CNS disease	Sanfilippo syndrome	N-acetylglucosaminase 6 sulfatase	heparan sulfate	coarse facies	mild stiff joints, short stature, lumbar vertebral issues, dysphagia	minimal to none	developmental delay, behavioral problems
Mps IVA Dominant features: primarily skeletal disease	Morquio syndrome, type A	galactose sulfatase	keratan sulfate, chondroitin-6-sulfate	coarse facies	joints laxity, severe kyphoregurgitation scoliosis, odontoid hypoplasia, short neck, C1-C2, C2-C3 cubluxation, short stature	aortic regurgitation	mild corneal opacities, hepatosplenomegaly
Mps IVB Dominant Feature: Primarily skeletal disease	Morquio syndrome, type B	beta galactosidase	Kertan sulfate, chondroitin-6-sulfate	coarse facies	joints laxity, severe kyphoregurgitation scoliosis, odontoid hypoplasia, short neck, C1-C2, C2-C3 cubluxation, short stature	aortic regurgitation	mild corneal opacities, hepatosplenomegaly
Mps VI Dominant Features: soft tissue and skeletal disease	Maroteaux-Lamy syndrome	N-acetylglucosaminase-4-sulfatase	dermatan sulfate, heparan sulfate	Macrocephaly, coarse facies, macroglossia, hydrocephalus	mild joint stiffness, kyphoscoliosis, odontoid hypoplasia, short stature	mitral and aortic valve thickening and regurgitation	
Mps VII Dominant feature: soft tissue storage and skeletal disease	Sly syndrome	beta glucuronidase	dermatan sulfate, heparan sulfate, chondroitin 4,6 sulfate	Macrocephaly, coarse facies, macroglossia, hydrocephalus	joints flexion, concentrated thoracolumbar deformity, hip dysplasia, odontoid hypoplasia, short stature	mitral and aortic valve thickening and regurgitation	
Mps IX		hyaluronidase	hyaluronan				

(Modified from Diaz JH, Belani KG. Perioperative management of children with Mucopolysaccharidoses. *Anaesth Analg* 1993;77:126-70)

Figure 1



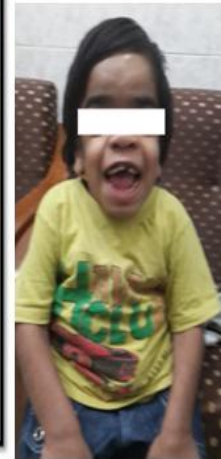
10 YEAR OLD PATIENT OF HUNTERS SYNDROME (MPS II) WITH COARSE FACIES AND SHORT STATURE.

Figure 2



16 year boy with morquios syndrome (MPS-IV) patient having primarily skeletal deformities

Figure 4



Patient of MPS II having coarse facies and poor dentition

### Identifying Anaesthetic Risk Factors in MPS

When planning surgery in MPS patients, one should carefully evaluate anaesthetic risks preoperatively.

#### Airway

Child with MPS represent a major challenge to the anaesthesiologists. The upper airway in MPS patients can be narrowed due to accumulation of GAG, causing adenotonsillary enlargement, macroglossia, thickened soft tissue in nasopharynx and laryngopharynx. Progressive upper airway narrowing can be compounded by deformities of the skull or spine, such as short neck, flattened nose bridge, mandibular abnormalities or abnormal cervical vertebra<sup>8,9,10,11</sup>. Multilevel airway obstruction may occur if there is GAG accumulation in trachea or upper airway obstruction is accompanied by tracheobronchomalacia.<sup>9,12,13,14</sup> Children with MPS represent a major challenge to the anaesthesiologist. A survey of airway complications in this group of patients at the Royal Manchester Childrens Hospital (Manchester, United Kingdom) showed an overall incidence of difficult intubation of 25% of all subgroups and a failed intubation rate of 8%<sup>15</sup>. They reviewed airway problems encountered during anaesthesia in MPS children for surgical procedure from 1986 to 1991. Tracheal intubation was accomplished using conventional laryngoscopy. 1996, Moores et al<sup>1</sup> reported seven children with MPSIIH after stem cell transplantation undergoing 16 anaesthetic procedures. Conventional intubation was difficult in 72% and failed in 29%. In patients of MPS there is deposition of mucopolysaccharides in tongue, tonsils, adenoids, epiglottis, glottis and trachea thereby changing anatomy of airway and leading to difficulty in maintaining the airway<sup>2,16,17</sup>. The oropharynx may be obstructed by a large tongue with or without tonsillar hypertrophy. These patients also have excessive tracheobronchial secretions with frequent upper respiratory infections.<sup>2</sup> These patients may have abnormal dentition, gingival hyperplasia, thickened and overhanging epiglottis, short neck and limited movement at temporomandibular joint. The uniqueness of their anatomy may result in failed tracheal intubation and bronchospasm even after successful intubation.<sup>18</sup> Chest deformities along with deposits in lower respiratory tract may increase chances of failed tracheal intubation. Upper airway obstruction and decreased pulmonary reserve lead to obstructive sleep apnoea.

MPS patients who have a history of severe obstructive sleep apnoea (OSA) are at high risk of emergencies during anaesthesia. OSA occurs in more than 80% of MPS patients<sup>19, 9,20</sup>. Preoperative obstructive symptoms are a good indicator of post extubation respiratory difficulty<sup>21</sup> Table 2 shows Serious anaesthetic complications that may occur during anaesthesia in patients with MPS

**Table 2:** Serious anaesthetic complications related to airway that may occur during anaesthesia in patients with MPS:

S.no.	
1	Inability to ventilate or intubate
2	Temporary airway obstruction: can cause negative pressure (mostly during introduction or at extubation) : can cause profound
3	Hypoxaemia and cardiac arrest
4	Post-intubation problems:
5	Stridor
6	Lower airway collapse/infection
7	Need for reintubation or tracheostomy

### Respiratory system

Respiratory abnormalities are a result of airway obstruction ,neurologic compromise, recurrent infections, Skeletal restrictions. And /or organomegaly , all of which can lead to pulmonary insufficiency,severe sleep apnoea and sudden death from central apnoea. MPS patients often develop restrictive pulmonary disease due to thoracic –cage abnormalities or compromised excursion of diaphragm due to enlarged liver and/or spleen or compromised neuromuscular function.<sup>23,22,9</sup> Obstructive defects have also been suggested to contribute to respiratory compromise<sup>20</sup>. Restrictive pulmonary disease , often in combination with airway obstruction, can lead to OSA, hypoventilation,pulmonary hypertension,cor pulmonale and eventually respiratory failure<sup>24</sup> MPS IV patients are especially prone to high cord compression secondary to atlantoaxial instability and odontoid dysplasia ,which can lead to depressed respiration or sudden respiratory arrest. Patients of MPS may have recurrent pneumonias secondary to increased volume and poor clearance of airway secretions.

Respiratory dysfunction can be highly disproportionate to the patients clinical appearance.It can be detected preoperatively using respiratory function testing (e.g. spirometry), but these tests are difficult to interpret in MPS patients due to lack of reference data. Standard reference equations based on data from normal patients may not apply on these patients with systemic skeletal dysplasia and short stature, but it is useful to follow absolute values longitudinally in a single patient.To evaluate the extent or severity of airway infiltration and anaesthetic risk, fiberoptic bronchoscopy can also be performed.

Yeung et al published a retrospective study on 27 patients between 1984 and 2004.70% patients that is 19 patients had significant upper airway obstruction,diagnosed on the basis of clinical results such as snoring, noisy breathing, OSAS history, desaturation and polysomnography. Pulmonary function tests in 15 out of 19patients revealed reduced FEVI, forced vital capacity and an increase in airway resistance<sup>65</sup>.

Surgical interventions such as adenotonsillectomy are sometimes performed to removing upper airway obstruction.In addition use of continuous positive airway pressure (CPAP) to maintain airway patency has been beneficial. Tracheostomy may be necessary for some patients of MPS either as treatment for severe obstructed sleep apnoea or in rare cases to facilitate safer anaesthesia.

### Cardiac Abnormalities

Valvular disease is caused by progressive thickening of the mitral and aortic valves and leads to insufficiency more often than stenosis<sup>25</sup> It is common in MPS 1, II, VI.Azevedo et al<sup>26</sup> reported mitral regurgitation (96%),tricuspid regurgitation(71%)and aortic regurgitation (43%) in 28 patients with MPSVI disease.Stenosis occurred in mitral and aortic valves in 7% of these patients.Colour flow and Doppler interrogation of cardiac valves during cardiac ultrasound determines the severity of valve disease based on published guidelines<sup>27</sup> and should be performed routinely in MPS.Subacute Bacteria E ndocarditis prophylaxis with antibiotics is recommended for all patients of MPS with valvular cardiac lesions<sup>2</sup>. Cardiovascular lesions are common in Hunters syndrome(MPS II),the prevalence and age at onset of main cardiovascular signs and Symptoms as reported in HOS are shown below in table-III

Table III Prevalence and reported age at onset (median and 10<sup>th</sup>-90<sup>th</sup> percentiles) of the main cardiovascular manifestations of mucopolysaccharidosis type II (Hunter syndrome) in a cohort of 82 patients in HOS, the Hunter Outcome Survey.

Cardiac manifestation	n	Prevalence(%)	Age at onset (years )
Valvular disease	34	53	6.2(2.9-13.8)
Murmur	32	52	6.4(3.7-12.3)
Cardiomyopathy	4	9	7.6(5.2-27.3)
Any cardiovascular sign / symptom	49	72	6.0(2.9-13.7)

Taken from:-J Edmond Wraith, Scarpa M, Beck M et al. Mucopolysaccharidosis type II(Hunters Syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement <sup>64</sup>

### **Electrocardiographic Abnormalities**

Electrocardiograms are frequently abnormal in patients with MPS VI <sup>2</sup>The most common abnormalities are sinus tachycardia, right axis and left axis deviation and atrial enlargement.

The spontaneous development of complete heart block has been described for MPS types II, III and VI <sup>29,30</sup>

### **Coronary Artery Disease**

Coronary artery disease has been described for only for MPS I. Also systemic hypertension is common in patients with MPS I <sup>31</sup> In patients of MPS coronary vessel narrowing secondary to intimal deposition of GAG develops and impairs coronary vessel flow.

Cardiac ischaemia results. Identifying MPS patients who may be at risk of having myocardial ischemia during anaesthesia can be very difficult, as clinical signs may be masked preoperatively due to inactivity and communication difficulties, Coronary angiography can detect completely obstructed vessels <sup>28</sup> but may underestimate severe diffuse coronary artery disease, which can result in sudden cardiac death during anaesthesia. Pulmonary hypertension may exacerbate right heart failure <sup>32,33</sup>

Decompensated heart failure associated with systolic dysfunction has been reported for different types of MPS <sup>34,35,36,37,38,39</sup>

patients, especially those who are untreated and have OSA, may develop pulmonary hypertension due to chronic hypoxaemia <sup>19,40</sup>

Left ventricular hypertrophy may be present in MPS patients but Cardiomyopathy is rare.

### **Skeletal abnormalities**

Skeletal and connective tissue complications develop as GAGs accumulate in bones, joints, and ligaments. Dystosis multiplex and odontoid hypoplasia are known to affect the patients with MPS I, II, VI, VII, and MPS I, IV and VII respectively. Dystosis Multiplex is used to describe the radiological skeletal deformities seen in patients with MPS. Radiographic signs may include point shaped metacarpal bones, dysplastic femoral head, defective development of the vertebral bodies with anterior beaking, widening of the ribs and short, irregular clavicles. Hypoplasia can lead to atlantoaxial instability, C1-C2 subluxation and high spinal cord compression. Spinal cord compression may also occur due to spinal cord narrowing at cervicocranial and thoracolumbar regions in patients with MPS I, II, IV and VI. <sup>41,42</sup> Patients with MPS IV and to some extent those with MPS VI, are at risk of atlantoaxial instability due to odontoid hypoplasia <sup>43,44,45,6</sup> In addition, abnormally shaped vertebral bodies (flattening, beaking) may produce spinal nerve entrapment or acute spinal cord injury related to spondylolisthesis, kyphosis, scoliosis and increased lumbar lordosis.

Clinically, skeletal involvement may be evident since birth when a gibbus deformity or dorsolumbar kyphosis is present as a result of anterior hypoplasia of vertebral bodies at thoracolumbar junction. Short stature is a common finding in all types of MPS.

Progressive arthropathy may affect all joints and lead to severe restriction of motion. The hip joint appears to be particularly vulnerable and severe erosive hip dysplasia can be especially disabling. Poor hand function, due to the characteristic claw hand deformity, carpal tunnel syndrome and interphalangeal joint stiffness is also common.

Abnormal joint function is largely a result of both metaphyseal deformities and thickened joint capsules. Patients with a combination of poorly formed pelvis, dysplasia of the femoral heads, and coxa valga are at a risk of developing progressive and debilitating hip disease. Symmetrical stiffness, pain, and flexion contractures of the elbows, shoulders, hips and knees lead to decreased range of motion and gait abnormality. Walking ability decreases and toe walking can be observed. Ultimately, patients may become wheelchair bound as a result of hip or spine disease. temporomandibular joint



Fig 5: Chest x-ray view with skull mild widening of metacarpals and slanting distal articular  
 Fig:6 Chest x-ray lateral view with skull  
 Figure 7: Wrist joints AP view showed surfaces of radius and ulna

Of patient of morquios syndrome f patient of morquios syndrome Citation: Shivajirao TP, Wasmatkar NP, Gore PG, Lakhe JN, Vinayak SR. Anesthetic considerations in Morquio syndrome: A case report. *Anaesth Pain & Intensive Care* 2013;17(1):75-78

Chest x-ray PA view and lateral view with skull (Figures 3 and 4) showed 'mild flaring and widening of ribs, platyspondyly (flattening of vertebral bodies) and anterior beaking of all vertebrae, short thick clavicles, pectus carinatum (increase in AP d

stance of thoracic cage), focal narrowing of airway seen at the level of hypopharynx just posterior to epiglottis measuring 5mm at this level, 10mm above it and 15mm below it in AP diameter and hypoplastic maxilla with prominent mandible.

Citation: Shivajirao TP, Wasmatkar NP, Gore PG, Lakhe JN, Vinayak SR. Anesthetic considerations in Morquio syndrome: A case report.

### Neurological Manifestation

Developmental delay and progressive neurologic decline occurs in severe forms of MPS I,II,III,VI and VII. Due to deposition of mucopolysaccharides in the brain cells they may develop progressive mental retardation of varying degree. Thickening of meninges may lead to hydrocephalous and hypertrophic pachymeningitis that may result in myelopathy associated with nerve root compression.<sup>16</sup> Pachymeningitis cervicalis is progressive thickening and scarring of meninges around the cervical spinal cord. This thickening may form a sleeve around the spinal cord that impedes the flow of cerebrospinal fluid and progressively compresses the cervical cord. Cord compression from cervical pachymeningitis and odontoid dysplasia can result in progressive ascending paresis and paralysis.<sup>9</sup> Communicating hydrocephalous frequently develops in MPS I,II,III,VI and VII due to the engorgement of arachnoid granulations by storage material impeding resorption of cerebrospinal fluid and increasing intracranial pressure. The diagnosis of communicating hydrocephalous by computed tomography or MRI is not an easy task because ventricular dilation may be related to cervical atrophy and direct measurement of central nervous system pressure may be required.



CLAW HAND  
DEFORMITY

### **Ophthalmic and Auditory complications**

Ophthalmologic manifestations include corneal clouding and potentially blindness may develop. Corneal opacity is generally a feature of MPS I and VI but has also been reported in MPS II<sup>46</sup>. This occurs as a result of GAG accumulation both intra and extracellularly in corneal epithelium, keratocytes, stroma and endothelium with subsequent disruption of optically important collagen fibrils<sup>47,48</sup>. Ocular hypertension and glaucoma occur in MPS due to GAG accumulation within anterior chamber structures. This can lead to narrowing of the anterior chamber angle<sup>49,50</sup> and deposition within trabecular cells may lead to obstruction of outflow. Retinal degeneration resulting in decreased peripheral vision and poor dark adaptation is common in MPS II. Also, disc oedema, uveal effusions and epiretinal membranes have all been reported in MPS II as a part of variable ocular pathology<sup>51,52,53</sup>. Optic nerve abnormalities are reported to be common in MPS<sup>54</sup>.

Auditory manifestations include conductive and neurosensory deafness. Hearing loss is common in patients with MPS II. It is attributable to frequent ear infections, defective ossification in the middle ear, scarring of tympanic membrane and damage to eighth nerve.

### **Gastrointestinal Complications**

Gastrointestinal complications include progressive hepatosplenomegaly due to storage of GAGs in liver and spleen. This may cause recurrent inguinal and umbilical hernias. Surgical repair is often performed and may have to be repeated<sup>32,33</sup>. In Hunter's Syndrome, patients are prone to periodic bouts of watery diarrhea, which occur without apparent cause and are not associated with malabsorption. Rectal biopsies in affected patients have demonstrated storage within gut neural cells, an autonomic cause for episodes of diarrhoea has been postulated<sup>64</sup>. Gastric reflux has been described in Hunter's Syndrome. A case report by Michalek et al in 2008<sup>67</sup> describes fiberoptic intubation through an I-Gel Supraglottic Airway in two patients with predicted airway difficulty and intellectual disability. One of the patients in their case report was of Hunter's Syndrome with history of gastric reflux.

### **Anesthetic Considerations**

#### **Preoperative evaluation**

Preoperative evaluation and planning can be considered the most important part of the process.

Preoperative Consideration includes airway inspection, neurologic, cardiac, skeletal, and visceral assessment. A complete and accurate history of the patient should be taken with particular regard to previous anaesthetic management, and time to present examination, this is to obtain an accurate risk scoring<sup>59</sup>. The type of MPS syndrome is ascertained for effective planning of anaesthetic procedure. For instance in Hurler's Syndrome, MPS I, airway problem has been described as the worst in paediatric anaesthesia<sup>6</sup>. History of snoring and sleep apnea is enquired. Objective examination of the airway, ear, nose and throat, cardiac and neurological system should be done. Neck and temporomandibular joint movements should be assessed preoperatively. Flexion-extension cervical films may confirm the potential for subluxation and demonstrate tracheal collapse on flexion. Atlantoaxial subluxation contraindicates cervical extension during intubation. The potential risks of an operation should also be discussed with patients and their families, who should be involved in the decision whether or not to initiate the procedure<sup>6</sup>. Child's intelligence and behavior are important. Behavior of a child with MPS may vary from uncooperative belligerent to placid, cooperative and lovable. Preoperative investigations should include arterial blood gas analysis, complete blood count, blood chemistry serum electrolytes liver



enzymes and renal function tests. Also, chest , cervical spine and skeletal radiographs, electrocardiography, echocardiography and pulmonary function tests should be done Polysomnography is gold standard investigation for OSA evaluation. Semenza and Pyeritz retrospectively studied 21 patients and scored an incidence of 50% according to clinical history and 90% on the basis of polysomnography<sup>20</sup>. In patients with kyphoscoliosis and chronic chest infections optimization of lung capacity should be done with preoperative chest physiotherapy, pulmonary toilet and antibiotics<sup>1,2,32</sup>. Patients presenting with abnormal gait , sensory changes or weakness in lower extremities should be evaluated by a neurologist<sup>1,2,32</sup>. 2D echocardiography should be done in all patients of MPS and if patient experiences chest pain in clinical symptoms that suggest ischaemia , more invasive tests like angiography are suggested. Somatosensory evoked potentials for detecting early cord compression and measurement of CSF pressure if communicating is suspected<sup>60</sup> Other factors to be considered preoperatively are previous anaesthetics and treatment haematopoietic stem cell transplantation .

### **Intraoperative Anaesthetic Management**

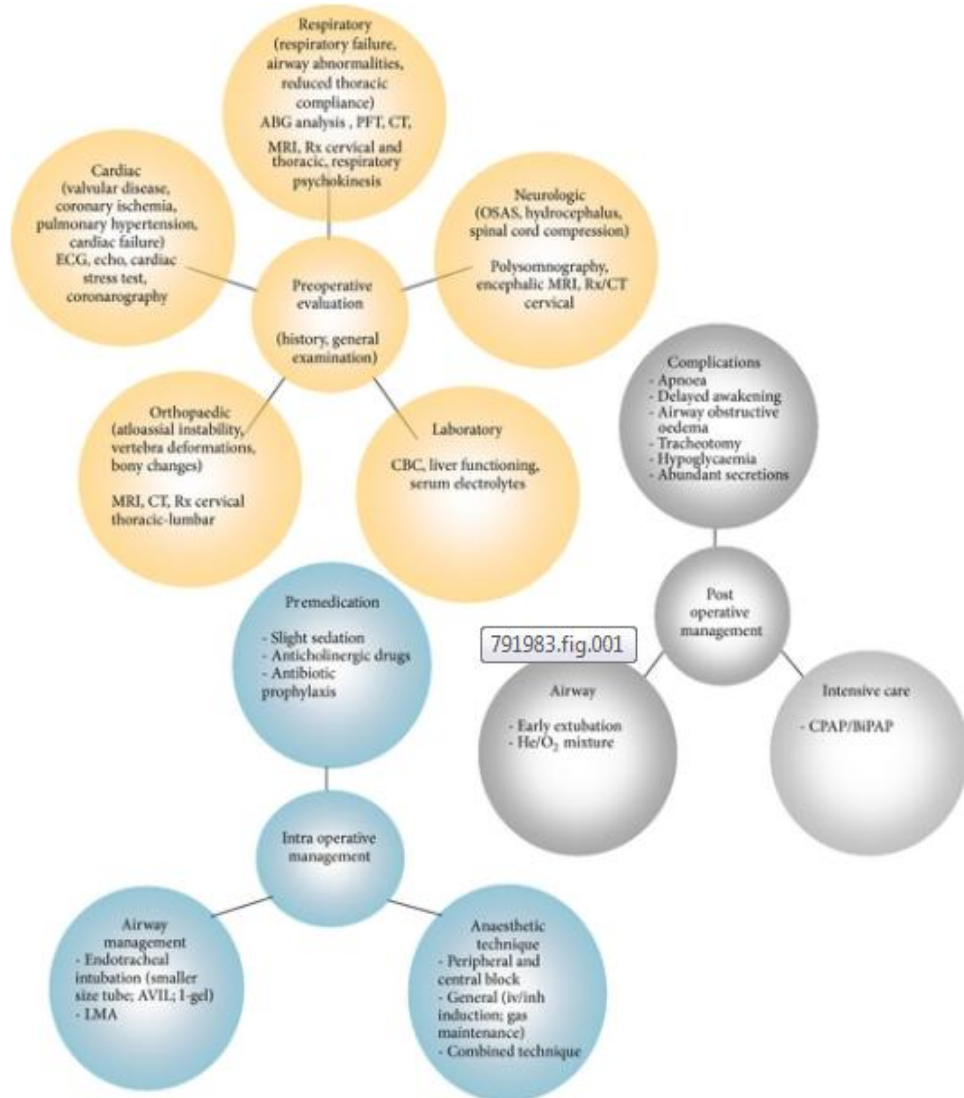
Normally , surgery in MPS patient requires general anaesthesia , although local anaesthesia may be an option for older patients with normal intelligence<sup>6</sup>. General anaesthesia should be administered in a set up which is fully equipped with latest gadgets of difficult intubation like videolaryngoscope, fiberoptic bronchoscope and intubating LMA etcetra. Also an expert team of doctors comprising of experienced anaesthesiologist (preferably paediatric anaesthesiologist), ENT specialist and Intensivist (intensive care backup) should be available to handle a case of MPS scheduled for surgery. It is advisable to discuss the anaesthesia plan with the team before the start of procedure, which often results in a plan A and a backup plan B.

Sedative premedicants should not be used as there may be risk of upper airway obstruction, respiratory depression, hypercarbia and cardiorespiratory arrest. Using nitrous oxide to sedate a patient in order to place an intravenous catheter can be a safe alternative. Opioids should be avoided as they may cause respiratory depression. Oropharyngeal secretions can be controlled by anticholinergics such as scopolamine and glycopyrrolate.<sup>2,21</sup> Patients with MPS can be difficult to ventilate secondary to abnormal facies. An air cushioned paediatric face mask may be applied upside down , with the broad chin edge of the mask over the patients brow and nose and the narrow nasal bridge of the mask over the open mouth and protruding tongue<sup>2</sup>. As mentioned earlier, atlantoaxial subluxation secondary to odontoid hypoplasia/dysplasia with spinal cord compression may occur during cervical hyperextension<sup>2</sup>. Cervical traction can be used to prevent manipulation of the neck. Inhalational induction with maintenance of spontaneous ventilation is preferred but in mentally retarded and uncooperative patients intravenous induction is more satisfactory. In patients of MPS spontaneous ventilation should be maintained until the airway is secured as after administration of muscle relaxant muscle tone is lost and the thickened supraglottic tissue and large tongue obstruct the airway and act as ball valve mechanism during manual ventilation leading to airway obstruction,<sup>1,55,56</sup>. The choice of technique depends on the anaesthesiologists skill to maintain spontaneous breathing until intubation. Intravenous induction is possible (thiopentone, propofol, ketamine) as well as inhalational induction (halothane or sevoflurane) or fiberoptic intubation in awake patient (topical anaesthesia) with light sedation. Ketamine can be used for achieving light levels of anaesthesia and facilitating fiberoptic intubation without significant airway obstruction. Spontaneous ventilation techniques using oxygen and high concentration of volatile anaesthetic have also been used but require a skilled team to manage the airway if airway obstruction increases. Insertion of a laryngeal mask airway will often improve ventilation and so will a nasal airway. Patients of MPS can develop ventilation and intubation difficulties during induction (or after administration of muscle relaxant ), requiring emergency tracheostomy<sup>1</sup>. In case of difficult airway, Intubation of trachea should be done with the help of fiberoptic bronchoscope. Use of LMA can give sufficient time for bronchoscopy.<sup>6,15</sup> A selection of endotracheal tubes is needed since age adjusted and anatomic formulae for endotracheal tube size do not apply to patients with MPS due to unique configurations of the laryngeal inlet and subglottic area. Laryngeal and tracheobronchial cartilage narrowing requires use of smaller endobronchial tubes than those commonly used<sup>33</sup>. A fiberoptic technique of intubation for children of MPS using laryngeal mask airway has been described<sup>15</sup>. LMA allows a good airway control without tracheal intubation. This device has been used by some authors in MPS patients<sup>61</sup>. Osthaus et al<sup>62</sup> identified ten children (three males, seven females) suffering from MPS IH who received 41 general anaesthetics from 2004-2010. They used videolaryngoscope successfully on five occasions in four children . Recovery after general anaesthesia in such cases may be accompanied by periods of breath holding, apnoea, bronchospasm, cyanosis and respiratory arrest.<sup>16</sup>

Extubation can be problematic in patients with advanced clinical manifestations, especially in MPS I, II, VI. Preparation for extubation should include use of intraoperative steroids, full reversal of muscle relaxants and placement of a nasopharyngeal airway to reduce upper airway obstruction after extubation. A tube changer can be positioned in endotracheal tube to facilitate reintubation in cases where successful extubation is uncertain.

**Postoperative management**

Postoperatively, continued airway management and monitoring to detect airway obstruction episodes and desaturation is recommended until the patient regains full consciousness. Extubation should not be performed before the patient is fully awake, coughing vigorously, breathing adequately and moving deliberately<sup>57</sup>. Patients are best extubated early after surgery. Utilizing a fiberoptic intubation and then leaving the endotracheal tube in place immediately postoperatively, minimizes airway complications, in particular for those patients who do not meet all the extubation criteria. After tracheal extubation, humidified O<sub>2</sub>, chest physiotherapy, and postural drainage should be instituted and continued until the patient is ambulatory and able to expectorate excessive secretions<sup>2,21</sup>



Taken from :- Spinello CM, Lorena MN ,Pitino S et al Review Article Anaesthetic Management in Mucopolysaccharidoses . ISNR Anaesthesiology2013<sup>66</sup>;

**Figure 8:** Algorithm of patients with MPS. ABG analysis: arterial blood gas analysis; PFT: pulmonary function test; MRI: magnetic resonance imaging; CT: computed tomography; CBC: complete blood count; ECG: electrocardiogram; Echo: echocardiogram; AVIL: angled video intubation laryngoscope; LMA: laryngeal mask airway; CPAP: continuous positive airway pressure; BiPAP: Bi-level positive airway pressure.

**II. Conclusion**

MPS disorders are characterized by progressive craniofacial, joint and skeletal deformities, progressive cardiac involvement and early death from pulmonary infection or cardiac failure Patients of MPS are short statured with skeletal deformities like short broad metacarpals and phalanges , kyphosis, scoliosis,immobile cervical and temporomandibular joint and coxa vara..

Children with MPS should be handled by anaesthesiologists and surgeons who are aware of the expected complications of this disease. Before subjecting such a patient to anaesthesia a proper informed consent should be obtained, difficult airway cart should be ready and available and even a surgeon standing by ready to do an emergency tracheostomy. Inhalational induction with maintenance of spontaneous ventilation is preferred but in mentally retarded and uncooperative patients intravenous induction is more satisfactory. A fiberoptic technique of intubation for children of MPS using laryngeal mask airway has been described<sup>15</sup>. LMA allows a good airway control without tracheal intubation.

Anaesthesia should ideally be administered by experienced anaesthesiologist and in a set up which has facility for paediatric intensive care unit. Recovery after general anaesthesia in such cases may be accompanied by periods of breath holding, apnoea, bronchospasm, cyanosis and respiratory arrest.<sup>16</sup>

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Dr Vandana chugh "Mucopolysaccharidosis: Anaesthetic Considerations and Clinical Manifestations." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 17, no. 4, 2018, pp 33-44.