ORIGINAL RESEARCH

DOI: 10.5336/worldclin.2016-50697

Overview on Anesthetic Management of Children with Mucopolysaccharidoses (MPSs)

Gürcan GÜNGÖR,[a]
Pervin BOZKURT SUTAŞ[a]

[a]Department of Anesthesiology and Reanimation,
İstanbul University
Cerrahpaşa Faculty of Medicine,
İstanbul

Received: 03.02.2016
Accepted: 03.05.2016

Correspondence:
Gürcan GÜNGÖR
İstanbul University
Cerrahpaşa Faculty of Medicine,
Department of Anesthesiology and Reanimation,
İstanbul, TURKEY
gugungor@yahoo.com

This study was presented as an oral presentation at The Meeting of Asian Society of Paediatric Anaesthesiologists (ASPA 2014), 8-10 May 2014, İstanbul, Turkey.

ABSTRACT Objective: Mucopolysaccharidoses (MPSs) are hereditary disorders characterised by the accumulation of glycosaminoglycans (GAGs) due to the deficiency of lysosomal enzymes. These substrates accumulate in the skin, brain, heart, bone, liver, spleen, blood vessels, cornea and tracheobronchial airways. Patients with MPS disorders require several surgical interventions related to the deposition of GAGs most frequently otolaryngologic and ophthalmologic procedures. A well-known problem with MPS disease is high incidence of difficult airway. Airway obstruction, difficulty in ventilation and oxygenation elevate the mortality rates of these patients under general anesthesia. **Material and Methods:** Charts of nine children with MPS who received general anesthesia performed by the authors at the otolaryngology and ophthalmology departments in the past five years were retrospectively reviewed. **Results:** Nine children received general anesthesia for 12 surgical procedures. One child died at preinduction, one case could not be intubated at his second surgery and it was cancelled, another case could not be intubated and an otolaryngologist performed an emergency tracheostomy in the emergency department for status epilepticus and respiratory distress. the others were uncomplicated under general anesthesia. **Conclusion:** An experienced anesthetic team should undertake anesthesia of all MPS cases. Awareness of MPS among anesthesiologists should be increased regarding to the problems of both syndrome and treatment in order to reduce morbidity and mortality.

Key Words: Mucopolysaccharidoses; anesthesia, general; child

World Clin J Med Sci 2017;1(1):30-5

Mucopolysaccharidoses (MPSs) are hereditary lysosomal storage diseases related to the accumulation of glycosaminoglycans (GAGs) in different tissues due to the deficiency of lysosomal enzymes. These GAGs consist of dermatan sulphate, heparan sulphate and keratan sulphate. These substrates accumulate in the skin, brain, heart, bone, liver, spleen, blood vessels, cornea and tracheobronchial airways. Clinical manifestations of MPS are coarse facial features, short immobile neck, limited mobility of the cervical spine and temporomandibular joints, ear, nose and throat problems, impaired vision and hearing, organomegaly and cardiopulmonary diseases.[1,2]

The symptoms of MPS usually occurs in childhood and cause mainly otitis media, hearing loss and airway obstruction.[3] Patients with MPS disorders require general anesthesia for several surgical interventions and they

are frequently admitted to otolaryngology departments for serous otitis media, adenoid and tonsil hyperplasia and ophthalmology departments for vision defects. Cardiomyopathy, coronary artery diseases and valvular heart diseases are also common in these patients as well as orthopedic and dental problems.4Well-known feature in anesthetic management is difficulty in providing safe airway. Airway obstruction, difficulty in ventilation and oxygenation increase the mortality rate of MPS patients.

In the past five years, the authors managed 9 children with MPS who had undergone 12 surgical procedures at the departments of otolaryngology and ophthalmology. The characteristics and anesthetic management of these patients were reported and discussed here.

MATERIAL AND METHODS

The parents of each patient were informed about the difficulties in airway management and anesthesia complications before surgery and written informed consent was obtained for presenting their child's anesthesia management because MPS disease was a rare condition. Anesthetic charts of these cases were retrospectively reviewed and preoperative conditions and perioperative events were reported. A standardized approach had been provided for all of the MPS cases following catastrophic experience in the first case presented here. Both the surgical and anesthesia teams were briefed about the scheduled MPS cases. Difficult airway cart was prepared for scheduled elective surgery in the operating room, which included laryngoscope blades (both Macintosh and Miller), different sizes of endotracheal tubes (ETT), supraglottic airway devices (LMA), fiberoptic bronchoscope and transtracheal jet ventilator. Other than first case all patients received 0.2-0.3 mg/kg midazolam by oral route (IV formulation Dormicum® Roche 5mg/ml) added to 5 ml paracetamol syrup (Calpol® Glaxo-Smithkline, 5 mg/ml paracetamol) as premedication with parental presence. In the operating room electrocardiogram, noninvasive blood pressure, pulse oximeter and body temperature probes were attached, and if possible intravenous (IV) access was obtained. Anesthetic induction was provided by sevoflurane 4-8% with slow increments in 80% oxygen-air mixture. After motionlessness was provided by inspired sevoflurane, anesthetic gas was decreased to 3-4% sevoflurane in 40% oxygen-air mixture through facemask. An orophrayngeal airway was placed in case of difficulty in ventilation. IV access line was obtained while the child was under anesthesia if previously not present. Pulse oximeter oxygen saturation (SpO_2), heart rate, noninvasive blood pressure and body temperature were constantly monitored. A quick look performed by Macintosh laryngoscope blade. If view was satisfactory tracheal intubation was attempted before giving muscle relaxant under deep sevoflurane anesthesia. After the success of intubation, the relaxation was achieved by rocuronium bromide 0.5 mg/kg or atracurium besilate 0.5 mg/kg. Anesthesia was maintained with 2% sevoflurane in 40% oxygen-air mixture.

RESULTS

Nine children with MPS underwent general anesthesia for 12 ear, nose and throat (ENT) and ocular procedures who had been admitted to otolaryngology and ophthalmology department. The youngest patient was 2.5 years and the oldest was 14 years old. The demographic and anesthetic properties of MPS patients as well as type of the syndrome were summarized in Table 1a and 1b. The most frequent type of MPS was Hunter Syndrome -MPS II (Table 1a and 1b). All cases were numbered according to the chronological order of their admission for surgery. Specific features of cases were summarized below.

Case 1: -A 7-year-old boy with Marateaux Lamy syndrome (MPS VI) was admitted for adenoidectomy and ventilation tube insertion due to adenoid hyperplasia and serous otitis media. He had mitral valve regurgitation and copious airway secretions because of upper airway infection. After 7 days of antibiotic therapy he was allowed to undergo surgery under endocarditis prophylaxis by pediatricians. Unpremedicated child was admitted to the operating room and monitored. SpO2 fell from 96% to 50% gradually while applying 80%

TABLE 1a: Demographic and anesthetic properties of MPS patients.

Patient Number	1	2	3	4	5
Gender	M	M	M	M	M
Study age	7	4 and 6	6 and 7	4	2.5
Weight (kg)	18	20	21	25	18
MPS type	Maroteaux- Lamy-MPS VI	Hurler-MPS I	Hunter- MPS II	Hunter- MPS II	Hunter- MPS II
Number of anesthesia	null	2	2	1	1
Difficult intubation	No	Yes	No	No	No
Can not be intubated	No	At the second operation	No	No	No
Operation	Adenoidectomy, ventilation tubes insertion	Adenoidectomy, ventilation tubes insertion	Adenoidectomy, ventilation tubes insertion	Adenoidectomy, ventilation tubes insertion	Adenoidectomy, ventilation tubes insertion
Post anesthesia	Exitus before operation	Ward	Ward	Ward	Ward
Enzyme therapy	No	No	Yes	Yes	Yes

TABLE 1b: Demographic and anesthetic properties of MPS patients.

Patient Number	6	7	8	9
Gender	M	F	M	F
Study age	6, 8 and 9	7	12	14
Weight (kg)	30	24	35	40
MPS type	Hunter- MPS II	Hurler-Scheie-MPS I	Hunter- MPS II	Sanfilippo- MPS III
Number of anesthesia	3	null	2	1
Difficult intubation	No	Yes	Yes	No
Can not be intubated	No	Yes	Yes	No
Operation	Adenoidectomy, ventilation tubes insertion	Eye examination	Emergency tracheostomy- decannulation	Eyelid repair
Post anesthesia	Ward	Ward	Post anesthesia care unit	Ward
Enzyme therapy	Yes	No	No	No

oxygen via facemask before anesthesia induction in supine position. Oxygen concentration raised to 100% and I.V line was inserted urgently. The child was intubated with 5.0 ID endotracheal tube immediately. Cardiopulmonary resuscitation (CPR) was initiated after worsening bradycardia and hypotension. Manuel ventilation was not effective because of excessive secretions and high airway pressure. Following atropine and adrenaline administration he was defibrillated 3 times with 100, 100 and 150 joules following detection of ventricular tachycardia. The last blood gas analysis during resuscitation demonstrated a pH: 6.71, PaO_2: 26.6 mmHg, $PaCO_2$: 44.1 mmHg, HCO_3: 4.7 mEq/L and SO_2: %16.3 on an FiO_2: 100%. CPR was continued for 90 minutes but the patient's condition deteriorated rapidly and followed shortly by death.

Case 2: -A 4-year-old boy with Hurler syndrome (MPS I) was admitted for adenoidectomy and ventilation tubes insertion because of adenoid hyperplasia and serous otitis media. Premedication provided as defined and induction was carried out with 8% sevoflurane in 40% oxygen-air mixture. After sufficient depth of anesthesia, the Cormack-Lehane grade 3 was obtained by direct laryngoscopy and he was intubated after three attempts hardly without neuromuscular blocker agent by a senior anesthesiologist. The operation ended without any problem. The child was extubated after the surgical procedure.

He was admitted for ventilation tube placement for serous otitis media once again 2 years later. Induction was carried out in the same way but he could not be intubated after many attempts. He received enzyme therapy throughout this period but he had limited movements of his neck and jaw at that time. The operation was cancelled and he was ventilated until he was fully awake.

Cases 3-6; four boys with Hunter syndrome (MPS II) and Case 9; a mentally retarded 14 years old girl with Sanfilippo syndrome (MPS III) had undergone operations uneventfully and they were

extubated successfully at the end of the operations when they were fully awake. All the devices providing re-intubation and the whole team were available in the operating room at the time of extubation.

Case 7: -A 7-year-old girl with Hurler-Scheie syndrome (MPS I H/S) was referred to ophthalmology department for an eye examination under general anesthesia. Her physical examination revealed a short neck with limited mobility, an inability to open her mouth fully and demonstrated a Mallampati IV airway. Parents were informed about the difficulties of intubation. The patient was assured and calmed down by her family for eye examination. She did not need any operation for her eye after the examination. The family reported complaints associated with inguinal hernia. She was referred to pediatric surgery department but due to severe anaemia her operation was postponed two years. Another group of anesthesiologists provided anesthesia for inguinal hernia repair. The information obtained from the patient's reported chart that her intubation was very difficult but the surgery were copleted without any problem. At the end of the operation she was extubated but her spontaneous breathing was inadequate. She deteriorated and required re-intubation but she could neither be in-tubated nor ventilated and died in the intensive care unit (ICU).

Case 8: -A 12-year-old boy with Hunter syndrome and epilepsy was admitted to emergency department for status epilepticus and respiratory distress. Due to his big tongue and difficulty in visualization of the larynx (Cormack- Lehane Grade 3) he could not be intubated and an otolaryngologist performed an emergency tracheostomy. The patient was admitted to the operating room for tracheostomy revision and control of bleeding after this procedure by the authors. General anesthesia was induced with propofol, fentanyl and rocuronium. Anesthesia was maintained with oxygen, sevoflurane, fentanyl and rocuronium boluses. He was sent to ICU after the revision of his tracheostomy.

He was scheduled for the decannulation of tracheostomy 20 days later. He was ventilated through the tracheostomy stoma after the induction of anesthesia with sevoflurane. The tracheostomy cannulae was changed but was not decannulated. The operation was terminated after the bleeding control. He was taken to the post anesthetic care unit fully awake with tracheostomy.

DISCUSSION

11 MPS disorders are reported in the literature and 7 of those are major types.5We presented 9 patients classified into 5 different MPS types. Preoperative anesthetic evaluation, airway, respiratory and cardiovascular system examination before the operation minimize the anesthetic risks of MPS patients. Respiratory and cardiovascular diseases pose a high anesthetic risk for these patients.

Cardiorespiratory failure causes death in severe types of MPS. Myocardial hypertrophy, ventricular dysfunction and cardiomyopathy result from accumulation of GAGs in the myocardium and frequently cause congestive heart failure and death.5 Cardiorespiratory failure and as a result death was encountered in case 1 before anesthesia in the operating room. Collaboration between the department of pediatrics and anesthesiology increased following the death of first case, meetings regarding MPS were attended and detailed survey of literature was analyzed to improve anesthetic management. Preoperative anxiety aggravated cardiac disease in case 1. After that incidence, a good psychological preparation of the child was achieved in the presence of their parents by the anesthesiologist covering the case and decided to use oral midazolam at tapered doses before anesthesia, which did not depress respiration. An anesthesiologist accompanied the patients after midazolam intake during transfer to the operating room.

Airway obstruction during intubation and extubation is a major anesthetic complication in MPS patients. The accumulation of GAGs in different tissues due to the deficiency of an enzyme can cause airway management problems.6 In addition to GAG deposition in the oropharynx; prominent mandible or maxilla, limited mouth opening,

macroglossia, tonsils and adenoid hyperplasia, short neck and scoliosis contribute to the difficult airway.[7] Preoperative diagnosis and awareness of difficult airway problem is important in MPS patients in order to take all precautions by providing necessary devices and experienced team of anesthesiologists and surgeons in the operating room. Difficult intubation was encountered in cases 2, 7 and 8. In case 2, team failed to intubate the patient two years after the first operation and the second operation was cancelled. Tavlan et al. stated that ETT was placed into trachea at third attempt to a child with Hurler syndrome.[8] Isık et al. and Erkal et al. placed laryngeal mask airway (LMA) instead of ETT to the patients with Hurler syndrome.[9,10] Atıcı et al. reported that a child with MPS could not be intubated but retrograde intubation was successfully performed using modified knot technique without any complication.[11] Case 7 did not undergo an eye operation, but anesthesiologists assured the patient and her parents to avoid general anesthesia for simple procedures. Asutay et al. published that a child with MPS received an eye exam under general anesthesia, he was ventilated using face mask and bag but he was not intubated.[12] Case 8 required intubation because of respiratory distress. MPS cases are very difficult in elective surgery settings. These cases pose worst scenarios in emergency settings as expected. Case 8 could not be intubated and an emergency tracheostomy was performed. Walker et al. stated that estimated incidence of difficult intubation is 25% of cases and of failed intubation 8%.[2]

Chan et al. preferred inhalation induction to intravenous because their patient had severe somatic involvement.[4] Authors preferred inhalation induction with sevoflurane to intravenous induction because of its beneficial to MPS patients who have needle phobias, difficult venous access and potential for airway obstruction. Induction of anesthesia with sevoflurane compared with propofol is also associated with a lower incidence of apnea and a shorter time to establish spontaneous ventilation.[13] Kaur et al. used ketamine for anesthesia induction and maintained with sevoflurane in a child with Hunter syndrome and tracheal intubation was successful with a smaller size of ETT in the third attempt. They reported that they were unable to ventilate the lungs after giving muscle relaxant to their patient but they could ventilate with face-mask before giving muscle relaxant.[14] Use of muscle relaxants before intubation were avoided in cases reported here because of difficulty in securing the airway. Yeksan et al. and Yagmurdur et al. used muscle relaxants after sufficient depth of anesthesia and evaluation of Cormack- Lehane grade by direct laryngoscopy for intubation.[15,16]

Chaudhuri et al. chose smaller size of ETT in MPS patients because these patients have mucopolysaccharide deposition in their airway with subglottic stenosis.[17] Multiple intubation attemps will predispose a MPS patient to glottic oedema. Similarly, smaller size of ETT was used for intubation in this series of patients here because repated tracheal intubation attempts may lead to the possibility of subglottic stenosis and airway collapse.

Cases 3, 4, 5 and 6 were taking enzyme replacement therapy (ERT) with idursulfase. These children were given general anesthesia seven times because of adenoid hyperplasia and serious otitis media. These cases encountered neither difficult mask ventilation nor endotracheal intubation. ERT with idursulfase had provided improvements in respiratory function, organomegaly and joint mobility.[18] Authors think that ERT helps endotracheal intubation to be easy and successful. Early diagnosis and treatment with ERT are essential to optimize outcome.[19] Meticulous efforts to provide best conditions for handling difficult intubation (laryngeal mask, fiberoptic bronchoscope), extubation, knowledge about the disorders of all other systems and the evolvement in the treatment of MPS by several enzyme therapies increase the success rate of general anesthesia.

Endotracheal extubation is as difficult as intubation in MPS patients. Hemodynamic stability, airway protection and gas exchange should be evaluated before extubation. Patients should be fully awake and all devices and team should be available in the operating room at the time of extubation.

CONCLUSION

It is well known that difficult airway and systemic complications are always together with MPS patients. Teamwork is essential for patient safety and patient outcomes in anesthesia of these cases. Anesthesia plan should be made preoperatively in elective procedures, all team members should be educated and anesthetic management skills should be enhanced. An experienced anesthetic team should undertake anesthesia of all MPS cases. Authors also recommend that anesthesiologists should increase awareness of MPS in order to reduce morbidity and mortality.

Conflict of Interest

Authors declared no conflict of interest or financial support.

Authorship Contributions

Idea/Concept: Constructing the hypothesis or idea of research and/or article: *Gürcan Güngör, Pervin Bozkurt Sutaş;* ***Design: Planning methodology to reach the conclusions:*** *Gürcan Güngör, Pervin Bozkurt Sutaş;* ***Control/Supervision: Organizing, supervising the course of progress and taking the responsibility of the research/study:*** *Gürcan Güngör, Pervin Bozkurt Sutaş;* ***Data Collection and/or Processing: Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments:*** *Gürcan Güngör, Pervin Bozkurt Sutaş;* ***Analysis and/or Interpretation: Taking responsibility in logical interpretation and conclusion of the results:*** *Gürcan Güngör, Pervin Bozkurt Sutaş:* ***Literature Review: Taking responsibility in necessary literature review for the study:*** *Gürcan Güngör, Pervin Bozkurt Sutaş;* ***Writing the Article: Taking responsibility in the writing of the whole or important parts of the study:*** *Gürcan Güngör, Pervin Bozkurt Sutaş;* ***Critical Review: Reviewing the article before submission scientifically besides spelling and grammar:*** *None;* ***References and Fundings: Providing personnel, environment, financial support tools that are vital for the study:*** *None; Materials:* ***Biological materials, taking responsibility of the referred patients:*** *None.*

REFERENCES

1. Frawley G, Fuenzalida D, Donath S, Yaplito-Lee J, Peters H. A retrospective audit of anesthetic techniques and complications in children with mucopolysaccharidoses. Paediatr Anaesth 2012;22(8):737-44.
2. Walker RW, Darowski M, Morris P, Wraith JE. Anaesthesia and mucopolysaccharidoses. A review of airway problems in children. Anaesthesia 1994;49(12):1078-84.
3. Santos S, López L, González L, Domínguez MJ. [Hearing loss and airway problems in children with mucopolysaccharidoses]. Acta Otorrinolaringol Esp 2011;62(6):411-7.
4. Chan YL, Lin SP, Man TT, Cheng CR. Clinical experience in anesthetic management for children with mucopolysaccharidoses: Report of ten cases. Acta Paediatr Taiwan 2001;42(5): 306-8.
5. Sam JA, Baluch AR, Niaz RS, Lonadier L, Kaye AD. Mucopolysaccharidoses: anesthetic considerations and clinical manifestations. Middle East J Anaesthesiol 2011;21(2):243-50.
6. Walker RW. Management of the difficult airway in children. J R Soc Med 2001;94(7):341-4.
7. Muhlebach MS, Wooten W, Muenzer J. Respiratory manifestations in mucopolysaccharidoses. Paediatr Respir Rev 2011;12(2):133-8.
8. Tavlan A, Köstekçi H, Otelcioğlu S. [Anaesthetic approach to Hurler syndrome]. Selçuk Tıp Derg 2006;22:39-41.
9. Işık B, Tekgül ZT. [Anaesthetic aproach towards a patient with Hurler syndrom in the magnetic resonans imaging area]. İnönü Üniv Tıp Fak Dergisi 2004;11(4):259-63.
10. Erkal H, Çıplaklıgil E, Özyurt Y, Arıkan Z. [Anesthetic management of Hurler's syndrome: a case report]. Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi 2003; 14(2):115-6.
11. Atıcı Ş, Doruk N, Yapıcı D, Çolak Ç. [Retrograd intubation applied by a modified knot technique may be a choice for difficult airway management in children]. Türk Anest Rean Der Dergisi 2008;36(6):381-4.
12. Göktuğ A, Uyar E, Çetinsoy BC, Kotanoğlu M, Baltacı B. [Anesthesia management in a patient with mucopolysaccharidoses]. Türk Anest Rean Der Dergisi 2006;34(6):405-8.
13. Thwaites A, Edmends S, Smith I. Inhalation induction with sevoflurane: a double-blind comparison with propofol. Br J Anaesth 1997;78(4):356-61.
14. Kaur J, Swami AC, Kumar A, Lata S. Anesthetic management of a child with Hunter's syndrome. J Anaesthesiol Clin Pharmacol 2012;28(2):255-7.
15. Yeksan AN, Akçıl EF, Dilmen ÖK, Yentür E, Kafadar A, Hanımoğlu H, et al. [Morquio syndrome: case report]. Turk J Anaesth Reanim 2013;41:101-3.
16. Yağmurdur H, Cıngıllı C, Başar H. [Anaesthetic management of a child with mucopolisaccharidosis type II and congenital hypothyroidism]. Türk Anest Rean Der Dergisi 2007;35(1):68-71.
17. Chaudhuri S, Duggappa AK, Mathew S, Venkatesh S. Safe intubation in Morquio-Brailsford syndrome: A challenge for the anesthesiologist. J Anaesthesiol Clin Pharmacol 2013;29(2):258-61.
18. Scarpa M, Almássy Z, Beck M, Bodamer O, Bruce IA, De Meirleir L, et al. Mucopolysaccharidosis type II: European recommendations for the diagnosis and multidisciplinary management of a rare disease. Orphanet J Rare Dis 2011;7(6):72.
19. Valayannopoulos V, Wijburg FA. Therapy for the mucopolysaccharidoses. Rheumatology (Oxford) 2011;50 Suppl 5:v49-59.