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MUCOPOLYSACCHARIDOSIS AND ANAESTHESIA: THE IMPACT OF ENZYME REPLACEMENT THERAPY ON MODERN AIRWAY MANAGEMENT IN ASIAN EXPERIENCE

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ABSTRACT

Background: Mucopolysaccharidoses (MPS) are hereditary storage diseases, and airway management is typically worse in these patients as disease progresses. The impact of enzyme replacement therapy (ERT) on the incidence of difficult airway management has not been adequately documented in Asian patients.

Methods: A retrospective chart review of 28 patients (13 patients receiving ERT) with MPS who had received 72 anaesthetics at Mackay Memorial Hospital between January 2004 and February 2014. The first endpoint of this study is to evaluate the impact of ERT on bronchoscopic findings and airway management. The second endpoint is to examine airway problems during anaesthesia and determine the role of the new intubation device in MPS patients.

Results: A problem in airway management at induction of anaesthesia occurred in 10 of 67 (15%) anaesthetics in 6 of 28 patients (21%). The success rates of use of the intubation device for MPS patients were 89%, 90%, 83%, 100% and 100% for the classic laryngoscopy, laryngeal mask airway, awake fibre-optic bronchoscopy, video laryngoscopy and rigid bronchoscopy, respectively. Three patients were still documented as having difficult intubation even after long-term ERT. Interestingly, 54% of MPS patients could have a stationary airway condition, evident from preoperative bronchoscopic evaluation, and have a smooth anaesthesia intubation scenario after long-term ERT even having undergone therapy since they were teenagers.

Conclusions: Long-term ERT in Asian MPS patients might help maintain the airway condition in a steady state even having undergone therapy since they were teenagers. Choice of the newer alternative intubation device might help greatly in this scenario.

KEYWORDS : anaesthesia; mucopolysaccharidoses; airway management; enzyme replacement therapy

Introduction

Mucopolysaccharidoses (MPSs) are rare progressive genetic disorders characterized by defects in glycosaminoglycan (GAM) metabolism. Accumulation of GAM in various body tissues results in anatomic abnormalities and organ dysfunction that can increase the risk of anaesthesia complications. MPSs are well-documented as having an association with difficult airway management and have been described as the worst airway problems in paediatric anaesthesia.[1] Before, we analyzed our experience at Mackay Memorial Hospital in administering anaesthesia to MPS patients between July 1, 1998, and October 31, 2008, and emphasise that airway management for MPS patients should be conducted by experienced anaesthesiologists, with assistance from an otolaryngologist when necessary.[2]

Enzyme replacement therapy (ERT) via intravenous infusion of recombinant human enzyme is available for MPS I, II, VI, and VI. ERT may improve joint mobility, walking ability, endurance and pulmonary and respiratory functions, as evidenced by data from pivotal trials and extension studies.[3] ERT might have a positive influence on the safety of anaesthesia by improving soft-tissue changes in the upper airway. Currently, the available literature consists of single or small sample sizes and a lack of data on Asian patients.

Materials and methods

This retrospective study (14MMHIS051) was approved by the Human Research Review Committee and conducted at Mackay Memorial Hospital in Taipei, Taiwan. Data were collected from chart review of MPS children who underwent anaesthesia at our institution between January 2004 and February 2014. For each patient, the following additional information was obtained from the medical record: age, gender, MPS type, surgery, preoperative bronchoscopy evaluation (when available), intraoperative airway management and history of ERT.

The first endpoint of this study is to evaluate the impact of ERT on bronchoscopic findings and airway management. The second endpoint is to examine airway problems during anaesthesia and determine the role of the new intubation device on MPS patients.

Results

During the study period, 28 patients with MPS were anaesthetized, including 2 patients with MPS I Hurler syndrome, 15 patients with MPS II Hunter syndrome, 4 patients with MPS III Sanfilippo syndrome, 4 patients with MPS VI Maroteaux-Lamy syndrome, and 3 patients with MPS VI. Thirteen patients with MPS received ERT during the study period, including two patients with MPS I, five patients with MPS II, three patients with MPS IV and three patients with MPS VI. (Table.1)

Induction of anaesthesia

A total of 72 anaesthetics were performed. Patients with MPS I were anaesthetized 9 times, patients with MPS II 31 times, patients with MPS III 8 times, patients with MPS IV 15 times and patients with MPS IV 9 times. (Table 1) Six of 72 anaesthetics were originally planned as regional anaesthesia, and two of them were changed to general anaesthesia due to fail block. Inhalation induction (sevoflurane + oxygen +/- N_2O) was used in 45 of 68 (66%) anaesthetics, intravenous induction with propofol was used in 10 of 68 (14.7%) anaesthetics and intravenous induction with ketamine was used in 7 of 68 (10.3%) anaesthetics. (Table 2)

Airway management

A problem in airway management at induction of anaesthesia occurred in 10 of 67 (15%) anaesthetics in 6 of 28 patients (21%). (Table 3)

Maintaining the airway with a laryngeal mask airway (LMA) was attempted in 10 anaesthetics and failed in 1 (90% success rate). Tracheal intubation using a classic laryngoscope was attempted in 19 anaesthetics and reported difficult in 8 of 19 (42%) anaesthetics and failed in 2 (89% success rate). Tracheal intubation with video laryngoscope was performed successfully in eight anaesthetics (100% success rate). Fibre-optic intubation was attempted in six anaesthetics and performed without difficulty in two, with difficulty in three and failed in one (83% success rate). Tracheal intubation with rigid bronchoscope was successfully performed in six anaesthetics (100% success rate).

In four anaesthetics, the primary chosen intubation technique failed; a different intubation technique was subsequently done. Maintaining the airway with an LMA failed in one anaesthetic, and the patient was subsequently successfully intubated using video laryngoscope. Tracheal intubation using classic laryngoscope failed in two anaesthetics, and one was subsequently successfully intubated using a Macoy blade. In another anaesthetic, intubation was done successfully using the LMA as a conduit for the fibre-optic scope. Tracheal intubation with fibre-optic scope failed in one anaesthetic, and the patient was subsequently successfully intubated using classic laryngoscope. Emergency tracheotomies were not performed during the study period.

Impact of ERT on airway

The characteristics of 13 MPS patients under ERT are shown in Table 4. One MPS I patient (No. 9) received ERT since 6 months of age, and his preoperative bronchoscopic picture is mild and stationary. The patient still has difficult intubation even after 34 months of ERT therapy. One MPS VI patient (No.17) received ERT since 14 years of age for 56 months and still had a severe preoperative bronchoscopic picture and even failure of awake fibre-optic intubation. Another MPS VI patient (No.18) received ERT since 9 years of age and has severe preoperative bronchoscopic finding even after ERT for 60 months.

In contrast, 7 of 13 patients (54%) showed stationary condition after long-term MPS therapy, including 4 MPS II patients (No.3, No.5, No.15 and No.21) after ERT 23~50 months, 2 MPS IV patient (No.7 and No.11) after ERT 12~26 months and 1 MPS VI patient (No.14) after ERT 23 months. These seven patients were all successfully intubated with first-choice intubation device.

Discussion

Even now, airway management in MPS patients is still a challenge for anaesthesiologists. In our study, problems in airway management at induction of anaesthesia occurred in 10 of 67 (15%) anaesthetics in 6 of 28 patients (21%). Compared with a previous study by Walker[4], which reported an overall difficult airway rate in all MPS disorders of 25% and an overall failed intubation rate of 8%, our report showed a difficult airway rate of 15%. A possible explanation for this lower rate may be that the clinical anaesthesiologists in our institution prefer the alternative intubation device as the first anaesthesia intubation plan other than classical laryngoscope for MPS patients.

ERT may improve walking ability, endurance and pulmonary function for MPS patients.[3] Questions about the effect of ERT on soft-tissue changes in the upper airway and dose ERT offer positive influence on the safety of anaesthesia are still controversial. Kirkpatrick[5] stated that patients with the attenuated form of MPS I on ERT still have a high incidence of airway problems at 57% and a failed intubation rate of 3%. Megens[6] reported the incidence of perioperative respiratory problems did not increase with age or decrease after starting ERT followed by haematopoietic stem cell transplantation. Frawley[7] also showed that ERT was initiated late in the clinical course of MPS II and VI and induced improvements in upper airway patency but did not reduce the incidence of difficult airway management in Australian children with MPS. It appears that many of the consequences of these secondary pathogenic events, while they may improve on treatment, cannot be fully corrected even with long-term exposure to enzyme, thereby supporting the treatment of patients with MPS before the onset of clinical disease.

In this study, we attempt to determine ERT's effect on Asian children with MPS, but the result is still controversial. Three patients were still documented as having difficult intubation even after long-term ERT. Interestingly, 54% of MPS patients could have stationary airway condition, evident from preoperative bronchoscopic evaluation, and have smooth anaesthesia intubation scenario after long-term ERT even having undergone therapy since they were teenagers

With the advancement of modern anaesthetic technique and new intubation device, many anaesthesiologists change clinical practice in first-choice airway management of MPS patients. Awake fibre-optic intubation is more difficult in MPS patients because most are also have intellectual disability. The judicious use of sedative agents in MPS patients is therefore worth considering. LMA might be useful not only be a good airway but acts as a conduct for fibre-optic intubation. Video laryngoscope is a useful tool in a variety of paediatric patients with difficult airways because it provides a wider field of view and does not require alignment of the eye to the larynx axis.[1,8,9,10] In this study, the success rates of use of the intubation device for MPS patients were 89%, 90%, 83%, 100% and 100% for the classic laryngoscopy, LMA, awake fibre-optic bronchoscopy, video laryngoscopy and rigid bronchoscopy, respectively.

This study has some limitations. It is a retrospective case chart review and has missing data. The study considered relatively few patients, which is inherent in patient group studies.

In conclusion, effect of long-term ERT in Asian MPS patients is still controversial. Choice of the newer alternative intubation device might help a lot in this scenario.

Table 1. Patient profile

MPS type		I	II	III	IV	VI
Patient numbers		2	15	4	4	3
Gender (Male/Female)		0 / 2	15 / 0	3 / 1	3 / 1	2 / 1
ERT / No ERT treatment		2 / 0	5 / 10	0 / 4	3 / 1	3 / 0
Anaesthetics		9	31	8	15	9
Pre-op bronchoscope						
	Adenoid hypertrophy	3	17	-	14	6
	Laryngomalacia	8	9	5	1	4
	Subglottic stenosis	-	3	-	5	3
	Lower airway deposit/malacia	-	6	3	13	3
	N/A	-	11	3	1	3
Surgery						
	ENT	6	11	5	8	8
	Dental	-	1	-	-	1
	Orthopaedics	1	2	-	3	-
	General surgery	1	19	1	2	-
	Cardiac/thoracic surgery	-	-	1	-	-
	Neurosurgery	1	-	-	-	-
	Obs/Gyn	-	-	1	-	-
	MRI	-	2	-	1	-

Table 2. Methods used for induction of anaesthesia (exclude 4 regional anaesthesia)

MPS type		I	II	III	IV	VI	total
IV induction	Propofol	0	3	3	3	1	10
	Ketamine	2	2	1	0	2	7
Inhalation induction	Sevoflurane±N2O+O2	7	20	3	9	6	45
Awake fibre-optic intubation		0	3	0	3	0	6

Table 3. Airway management at induction in 72 anaesthetics

MPS type		I	II	III	IV	VI
Anaesthetics		9	31	8	15	9
Regional anaesthesia		0	3	1	0	0
No difficult intubation (documented)		5	5	3	7	1
Difficult intubation (documented)						
	No ERT		1	2		
	Pre-ERT				1	1
	Post-ERT 1~24 months	1				
	Post-ERT for 24 months	2				2
Tracheostomy		0	6	0	0	1
Alternative intubation method		1	14	2	11	1
	LMA	-	7	-	1	1
	Rigid bronchoscope	1	1	2	0	2
	Awake fibre-optic intubation	-	3	-	3	-
	Video laryngoscope (Glidescope)	-	3	-	5	-
Fail fibre-optic intubation		-	-	-	1	-
Fail LMA		-	-	-	1	-
Fail regional anaesthesia		-	2	-	-	-

Table 4. Characteristics of 13 patients receiving ERT

Patient number	MPS type	Age starting ERT	Surgery post-ERT interval	Airway management (1) Preoperative bronchoscope (2) Intubation situation
No.3	II	16y/o	23m, 45m	(1) Mild condition (2) Video laryngoscope; LMA (after failed spinal anesthesia)
No.5	II	6y/o	23m	(1) Moderate stationary condition (2) Video laryngoscope
No.6	II	25y/o	<12m	(1) Severe bronchoscopy picture (2) Classic laryngoscope, no documented difficult intubation
No.7	IV	8y/o	2m, 12m, 26m, 38m, 43m	(1) Progress before 12-month ERT therapy, but stationary during 12 to 43 months ERT therapy. (2) Video laryngoscope (after failed LMA)
No.9	I	6m/o	3m, 20m, 34m, 40m	(1) Mild condition (2) Documented difficult intubation even after 34 months ERT therapy

No.11	VI	9y/o	23m	(1) Mildly condition (2) Rigid bronchoscope
No.14	IV	18y/o	26m, 27m, 38m	(1) Moderate stationary condition (2) Awake fibre-optic intubation
No.15	II	4y/o	36m	(1) Mild condition (2) Classic laryngoscope
No.17	VI	14y/o	56m	(1) Severe bronchoscopy picture (2) Classic laryngoscope (after failed awake fibre-optic intubation)
No.18	VI	9y/o	20m, 60m, 73m	(1) Progress even after 20-month ERT, but dramatic improvement after 73 months of ERT (2) Documented difficult intubation even after 73 months of ERT
No.19	I	9y/o	3m	(1) Mild condition (2) Documented difficult intubation
No.21	II	13y/o	50m, 86m	(1) Moderate stationary condition (2) Classic laryngoscope, no documented difficult intubation
No.22	IV	13y/o	1m	(1) Mild condition (2) Video laryngoscope

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