ORIGINAL RESEARCH

Dental Considerations for the Treatment of Patients with Morquio Syndrome

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Abstract

Aim: Morquio syndrome, also called Mucopolysaccharidosis IV (MPS IV), is a rare autosomal recessive metabolic lysosomal disorder that results in the deposition of glycosaminoglycans (GAGs) in various tissues and organs, resulting in an array of signs and symptoms. The aim of the study was to systematically record the clinical features with a special emphasis on oral manifestations of patients diagnosed with MPS IV and asses the dental treatment implications of the disease manifestations.

Materials and methods: A cross-sectional study was conducted on patients diagnosed with MPS IV (n = 26). A complete clinical and oral examination was done and the findings were systemically recorded.

Results: The study showed that the patients diagnosed with MPS IV have multiple treatment challenges owing to the range of disease manifestations. Furthermore, they have higher oral health care needs because of the anatomical and pathological changes.

Conclusion and clinical significance: Dental professionals must be aware of the implications of the disease manifestation and their accompanying challenges while treating patients with MPS IV. The oral health needs are higher for these patients and regular dental evaluation and treatment must be incorporated into their health care regimen.

Keywords: Morquio syndrome, Mucopolysaccharidosis, Oral health needs, Treatment implications.

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Introduction

Morquio syndrome (MPS IV) was first described independently by Morquio and Brailsford in 1929 and the clinical, biochemical, and molecular heterogeneity was demonstrated by Dale in 1931.[1] It is a rare autosomal recessive lysosomal storage disorder that causes accumulation of GAGs due to deficiency or absence of enzymes responsible for the catabolism of GAGs.[2] The reported point prevalence ranges from 1:1,872,000 in Malaysia to 1:599,000 in the United Kingdom, whereas the birth prevalence ranges from 1:71,000 in the United Arab Emirates to 1:500,000 in Japan.[3] The lack of turnover and subsequent accumulation of GAGs causes a cascade of events leading to the progressive damage of cells, tissue, and organs, primarily affecting cardiovascular, respiratory, and skeletal organ systems. Additionally, ophthalmological and auditory manifestations are regularly seen.[2] MPS IV is further subclassified as MPS IV A and IV B, with MPS IV B being a more attenuated phenotype (Table 1). Depending on the nature and site of mutation, MPS IV has a wide phenotypic presentation with a vast array of symptoms and signs. Typically, patients are normal at birth and start manifesting symptoms by 2–4 years of age.[4] Until recently, the treatment of MPS IV was limited to supportive symptomatic care, including symptom-based treatment, physical therapy, surgery, and rehabilitation. However, with the emergence of new modalities for treatment, the life expectancy and quality of life have substantially improved for the affected individuals. Subsequently, oral health, which is a major contributor to quality of life, is becoming increasingly important. There is very limited literature available, as case reports and small cohort studies, on the oral health needs and dental treatment implications and considerations while treating these patients.[5] Thus, the aim of this study was to systematically record the clinical findings, assess their oral health needs and to determine the treatment considerations while treating patients diagnosed with MPS IV.

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Materials and Methods

A cross-sectional study was conducted from May 2018 to December 2019. Ethical clearance was obtained from the teaching institution and informed consent was obtained from the parents/guardian of the patients who participated in the study. A preliminary diagnosis was made by analyzing urine/blood GAGs accumulation, followed by confirmatory genetic and biochemical

Table 1: Subsets of Morquio syndrome

Classification	*Deficient enzyme*	*Genes involved with chromosome loci*	*Deficient enzyme*
MPS IV A	*N*-acetyl-galactosamine-6-sulfatase (GLANS)	GALNS on 16q24. 3	Keratan sulfate chondroitin-6-sulfate
MPS IV B	β-galactosidase (GLB1)	GLB1 on 3p22.3	Keratan sulfate

Table 2: General characteristics of the participants

	Age of the participant		
	N	*Minimum (years)*	*Maximum (years)*	*Mean (years)*
Cases	26	2	15	8.5
Gender-wise distribution of the subjects			
	Frequency		Percentage
Female	11		42.3
Male	15		57.7
History of consanguineous marriage in the family			
Consanguineous marriage	18		69.2
Non-consanguineous marriage	08		30.8

Table 3: Overview of common clinical manifestations of Morquio syndrome

	Frequency	*Percentage*
Delay in developmental milestones	22	84.6
Abnormal gait	17	65.4
Atlantoaxial dysfunction		
(not treated)	08	30.8
(surgically treated cases)	11	42.3
Wrist hyperextensibility	19	73.1
Genu valgum (knock knees)	17	65.4
Scoliosis/kyphoscoliosis	17	65.4
Cardiovascular system disorders	21	80.8
Respiratory compromise	22	84.6
Hepatosplenomegaly	22	84.6

Table 4: Common extra/intraoral findings in the participants

	Frequency	*Percentage*
Extraoral findings		
Coarse facies	19	73.1
Incompetent lips	20	76.9
Corneal clouding	21	80.7
Auditory disorders	20	76.9
Short neck	22	84.6
Intraoral findings		
High arched palate	18	69.2
Macroglossia	17	65.4
Enlarged adenoids	14	53.8
Gingival diseases	22	84.6
Dental caries	20	76.9
Thin enamel with pointed cusps	17	65.4
Delay in eruption	26	100
Anterior open bite	18	69.2
Spaced dentition	19	73
Hypoplastic enamel	10	38.4
Posterior crossbite	15	57.7
Tongue thrusting	17	65.4
Mouth breathing	17	65.4

assays to check for the activity of the deficient enzyme. The clinical findings were systematically recorded by a single investigator. Oral examination was done with the help of sterile mouth mirrors and explorers. Complete soft tissue and hard tissue examination were done and the findings were recorded.

Results

A total of 29 patients agreed to partake in the study, of which three patients were excluded due to very young age, below 2 years of age ($n = 26$). Table 2 shows the general characteristics of the participants. Table 3 exhibits the commonly observed clinical manifestations in the subjects. Table 4 illuminates the common extra/intraoral findings in the study participants.

Discussion

In the present study, a cohort of 26 patients ailing from different parts of the Indian subcontinent was included with six pairs of affected siblings. The patients included in the study were from 2 to 15 years of age, with the majority of them having a history of first/second-degree consanguineous marriage in their pedigree.

Although a consanguineous marriage does not result in increased allele frequency, there is an unquestionably higher probability that the next generation will inherit disorders as there is mating between two mutant alleles of two individuals heterozygous for the same mutant allele.[6] This has contributed to an increased burden of rare genetic diseases, especially autosomal recessive disorders like MPS IV. However, the disease manifestation could also be due to sporadic mutation in a child born to unrelated noncarrier parents.[7,8]

In the present study, seven patients in the cohort were diagnosed primeval in routine examination or were examined as

their siblings were known cases of MPS IV. Hence, these patients manifested very mild or no symptoms at all, as the disease usually manifests only in 2–4 years.[4]

Patients included in the study showed abnormal gait, increased knee flexion, genu valgum, scoliosis/kyphoscoliosis, pectus carinatum, wrist hyperextensibility, and atlantoaxial dysfunction, which was corroborated with previous studies.[9,10] The skeletal manifestations are collectively called the dysostosis multiplex group of dysplasia and are a classical feature of MPS IV.[9] The abnormal gait resulted from reduced stride length, reduced cadence, external tibial torsion, genu valgum, and in later stages due to hip dysplasia. The dental management for these patients is a challenge for dental professionals. Older children and adolescents must always be requested to be accompanied by caregivers for the ease of transfer of the patient to a dental chair, or if the patient is more comfortable in the chair, treatment must be commenced in the wheelchair itself. The hyperextensibility of the wrist affects the patient's range of motion and results in reduced strength, grip, pinch strength, and making carrying and grasping objects difficult.[11,12] This makes practicing oral hygiene measures difficult. Hence, the dentist must recommend electric toothbrushes or toothbrushes with modified handles for more efficient oral hygiene measures. Atlantoaxial dysfunction results due to excessive independent movement between the anterior arch of C1 and C2, and most of the patients undergo corrective surgery in late childhood as the failure of treatment might result in the compression of the spinal cord.[13] Dental professionals must compulsorily provide neck support while treating patients, especially those with the untreated condition, as it might result in posterior tilting of the dens and compression of the spinal cord.

The participants in the present study also exhibited various cardiovascular diseases, including valvar dysfunction, coronary artery disease, and conduction abnormalities varying in onset and severity, which is in accordance with the findings in the literature.[10,14] The medications prescribed, like calcium channel blockers and angiotensin-converting enzyme inhibitors, often result in xerostomia and inevitably increase the risk of dental caries, as stated in the literature.[15] It is critical to get a medical consult and consent from the concerned medical care professional as the risk of infection for these patients is considerably higher than for the rest of the population. Preprocedure antibiotic prophylaxis must be considered in patients with a higher risk of infection.

Although not as common as in other subsets of MPS IV, hepatosplenomegaly can be observed in patients with MPS IV.[10,16] In the present study, hepatosplenomegaly was commonly observed. Dentists must be critically aware of the pharmacokinetics of the drugs routinely prescribed to avoid toxicity due to improper metabolism of the drugs. Furthermore, the patients might manifest anemia and increased bleeding,[17] thus the dental professionals must request the patient a complete blood profile to rule out complications, especially during invasive treatments.

The respiratory manifestations include nasal mucosal hypertrophy, reduced chest wall compliance, tracheomalacia, bronchomalacia, and enlarged and redundant supraglottis.[10,18] This results from the deposition of GAGs in the lung parenchyma resulting in the development of symptoms.

The extraoral findings commonly observed in patients who partook in the study are substantiated by previous literature.[10,19] The corneal clouding and auditory disturbances like recurrent infections and conductive hearing loss might be taxing to the dentist as traditional behavior management techniques like tell show do and desensitization might not be effective. Hence, modifications of routine behavior management and shaping techniques should be implemented. Similarly, modification in the means of communication might be necessary.

Treating patients under general anesthesia is rather challenging due to difficulty in endotracheal intubation-extubation change and reduced oxygen saturation due to tracheomalacia, enlarged adenoids, and macroglossia. Furthermore, tracheostomy, if required, might be arduous due short neck and thickened soft tissue of the neck in these patients.[20]

The present study bolstered the finding that patients with MPS IV have enlarged adenoids and macroglossia due to the deposition of GAGs resulting in the development of habits like obstructive mouth breathing and tongue thrusting.[19] Mouth breathing can result in the development of the high arched palate and incompetent lips.[21] Similarly, the macroglossia can result in tongue-thrusting, which subsequently proceeds to the development of anterior open bite. Furthermore, these nonnutritive habits result in the development of posterior crossbite.[22] The correction of deleterious oral habits can result in the correction of the developing malocclusion. Similarly, treatments like a rapid maxillary expansion for the correction of the narrow and deep palate can result in enlargement of the nasal cavity and improvement in nasal breathing. During the development of teeth, deposition of the GAGs causes disturbances in the formation of enamel resulting in disturbances like hypoplastic lesions, thinner enamel, and delayed eruption. This finding was ratified by the results of the present study.[16,19] The study showed that the majority of the participants had high caries prevalence, which was consistent with studies by Ponciano et al.[23] and Robert et al.[2] This could be ascribed to the hyposalivation, mouth breathing, xerostomia causing medicaments for cardiac ailments like calcium channel inhibitors, increase in *Streptococcus mutans* and *Candida* species; alterations in the immune system, and reduction in pH and vitamin D deficiency.[23–26] The importance of oral hygiene must be emphasized to patients as well as caregivers. In the present study, even though the patients presented with a high caries rate and poor oral hygiene, there was a very lower number of filled teeth, and revealing neglected oral care. The parents must be made aware of infant oral care programs and encouraged to establish an early dental home. Risk assessment tools like Caries Management by Risk Assessment must be used early on and subsequent recall visits must be planned accordingly. The anticipatory guidance approach, which is designed to take advantage of time-critical opportunities to implement preventive health practices and reduce the child's risk of preventable oral disease, must be given emphasis.

A piece of thorough knowledge of the manifestations of the disease and the risk factors associated with the disease is necessary for efficient and adequate treatment. Dental professionals must be aware of the precautions and care that need to be taken while treating these patients.

Dental treatment must be integrated into multidisciplinary management in order to improve the quality of life of patients and their families. It is important to encourage regular visits to dentists in order to avoid complicated invasive treatments. Treatment should be based on a preventive protocol promoting the use of pit and fissure sealants, fluoride, dietary control, and good oral hygiene habits. Moreover, parents must be made aware of the role of habit-breaking appliances and their effect on growing craniofacial structures.

Conclusion

MPS IV has an array of signs and symptoms affecting many organs and organ systems. Dental professionals treating these special children must be acutely aware of the implications of the disease manifesting and its accompanying challenges. Moreover, the oral health needs of these patients are higher, requiring more attention and care, and thus, oral health care must be incorporated into their treatment regimen.

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