PATHOLOGY

Relationship Between Occlusal Features and Enzyme Replacement Therapy in Patients With Mucopolysaccharidoses

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Purpose: The aim of this study was describe the relation between occlusal features and enzyme replacement therapy in patients with mucopolysaccharidoses.

Materials and Methods: A cross-sectional study was conducted. The sample consisted of 20 patients with mucopolysaccharidoses, 10 of whom were undergoing treatment at a hospital in northeast Brazil. Occlusal features were evaluated by clinical examination and panoramic radiography. A structured questionnaire was administered to evaluate the dental care of each patient. Pearson χ^2, Fisher exact, and Mann-Whitney tests were used for data analysis, with a level of significance of 5%.

Results: Marked overjet (75%) and anterior open bite (70%) were the most frequent occlusal alterations, and 15% had Class III disorders. Radiography visualized the presence of impacted teeth (75%) and prolonged retention of deciduous teeth (65%). Patients with enzyme replacement therapy had a lower average maximum protrusion (P = .033). A total of 75% of mothers said they had not been advised to take their children to the dentist and 10% of children had never been to the dentist.

Conclusion: Patients with mucopolysaccharidoses exhibited notable occlusal alterations, especially marked overjet and anterior open bite. Enzyme replacement therapy seems to influence the maximum protrusion of patients.

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Mucopolysaccharidoses (MPSs) are a group of hereditary disorders characterized by the accumulation of glycosaminoglycans (GAGs) in multiple organs caused by a deficiency in the lysosomal enzymes necessary for the degradation of these polysaccharides. The accumulation of GAGs results in different clinical manifestations. MPSs are rare, with a worldwide prevalence of 3.5 to 4.5 per 100,000 live births. Eleven enzymatic

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defects causing different types of MPS have been reported in the literature and are listed in Table 1.[1-6] Most MPSs are of autosomal recessive inheritance, except for MPS II, whose inheritance pattern is linked to the X chromosome. Recessive autosomal MPSs affect male and female individuals equally. The parents of an affected child are asymptomatic carriers of the disorder; that is, they carry a normal gene and a mutated gene (defective) that encodes the deficient enzyme. Thus, the individual carrier (heterozygote) does not present the disease.

MPSs are clinically heterogeneous disorders. Different residual enzymatic activities can result in different phenotypes of the same MPS disorder, from severe to attenuated. The most frequent manifestations are macrocephaly, hepatosplenomegaly, umbilical and inguinal hernias, bone dysplasia, delayed motor development, hearing loss, breathing difficulties, heart disease, limited joint movement, and facial and dental alterations.[3,7-9] In the oral cavity, the accumulation of GAGs in tissues is responsible for the occurrence of different alterations, such as anterior open bite associated with macroglossia, gingival hyperplasia and hypertrophy of the alveolar processes, high-arched palate, delayed tooth eruption and impacted permanent teeth, hyperplastic dental follicles, and the presence of dentigerous cysts.[1,6,10-13]

One treatment option for MPS is enzyme replacement therapy (ERT), which consists of periodic intravenous administration of the deficient enzyme. This therapy is available for only 3 types of MPS: I (laronidase), II (idursulfase), and VI (galsulfase); the other MPS types still do not have treatment.[5,10,11]

The oral manifestation of MPSs should be known and studied by dentists to provide adequate dental treatment to patients with the disorder. However, studies investigating oral alterations in MPSs are sparse. Therefore, the objective of the present study was to describe the occlusal features of MPSs and the influence of ERT on lessening the severity of these alterations.

Materials and Methods

This study was approved by the research ethics committee of the Federal University of Campina Grande (Campina Grande, PB, Brazil; protocol number 20111304-008) and was conducted in accordance with Resolution 466/12 of the National Health Council. Consent was obtained from patients and the study was performed in accordance with the Declaration of Helsinki.

A cross-sectional, observational, and exploratory study was conducted using a convenience sample that consisted of patients with MPS 4 to 31 years of age and their mothers. Participants, treated and untreated, were recruited from the endocrinology outpatient clinic of a referral hospital in northeast Brazil. The study was conducted over a period of 8 months (April to November 2011).

The criterion for inclusion in the study was the biochemical or molecular diagnosis of any type of MPS (Table 1). Exclusion criteria were patient conditions that did not permit dental or radiographic examination and previous dental treatment. The initial sample consisted of 27 patients; 7 patients were excluded because of varying degrees of neurologic impairment that prevented them from performing the tests necessary for participation in the study. The final sample was composed of 20 patients with MPS,

Table 1. CLASSIFICATION OF MUCOPOLYSACCHARIDOSES

MPS Type	Eponym	Deficient Enzyme	GAG Excreted in Urine
I	Hurler, Hurler-Scheie, Scheie	α-L-iduronidase	Dermatan sulfate, heparan sulfate
II	Hunter	Iduronidase sulfatase	Dermatan sulfate, heparan sulfate
III	Sanfilippo A	Heparan-N-sulfatase	Heparan sulfate
	Sanfilippo B	α-N-acetylglucosaminidase	
	Sanfilippo C	Acetyl-CoA:α-glucosaminide N-acetyltransferase	
	Sanfilippo D	N-acetylgalactosamine-4-sulfatase	
IV	Morquio A	N-acetylgalactosamine-6-sulfatase	Keratan sulfate, chondroitin 6-sulfate
	Morquio B	β-galactosidase	Keratan sulfate
VI	Maroteaux-Lamy	N-acetylgalactosamine-4-sulfatase	Dermatan sulfate
VII	Sly	β-glucuronidase	Dermatan sulfate, heparan sulfate, chondroitin-4,6-sulfate
IX	Natowicz	Hyaluronidase	Hyaluronic acid

Abbreviations: GAG, glycosaminoglycan; MPS, mucopolysaccharidosis.

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