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ORIGINAL RESEARCH

Oral manifestations in children with mucopolysaccharidosis

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BACKGROUND: Patients with mucopolysaccharidosis have several changes of the stomatognathic complex, representing a challenge for dentists.
OBJECTIVE: The study aimed to evaluate and characterize oral health in patients with mucopolysaccharidosis in a reference center of Portugal.
METHOD: The sample consisted of twelve participants with mucopolysaccharidosis followed in Metabolic Diseases Unit of the S. João Hospital Centre and twelve healthy participants followed at Faculty of Dental Medicine, University of Porto. The clinical oral evaluation was performed by a complete extra-oral and intra-oral examination to assess the presence of oral pathologies, gingival index and occlusion status.
RESULTS: Mucoplysaccaridosis patients and controls presented similar age ranges and sex distribution. In comparison to controls, children with mucopolysaccharidosis presented a higher prevalence of tooth decay, gingival bleeding, macroglossia, dental hypoplasia, lingual interposition, delayed tooth eruption, anterior open bite, right and left posterior cross-bite, limitation of mouth opening, alteration on the size and shape of the teeth, diastemata and maxillary compression.
CONCLUSIONS: Patients with mucopolysaccharidosis have a high prevalence eruption delay, teeth morphology alterations, occlusal problems, dental caries and bleeding gums, highlighting the need of oral health care providers to improve diagnostics and preventive protocols to overcome the factors that limit the oral health of these patients and promote together with parent/caregiver efficient oral care strategies.

KEYWORDS: Mucopolysaccharidosis, oral health, pediatrics, dental manifestations

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INTRODUCTION

Mucopolysaccharidosis (MPS) are a heterogeneous group of genetic disorders that can affect brain, eyes, oral cavity, face and skeleton, among other systems;[1-6] they are lysosomal storage disorders caused by deficiency of the enzymes responsible for the degradation of glycosaminoglycans, causing the accumulation of these macromolecules in the lysosome present in various tissues and organs. The intracellular and extracellular accumulation of these non-metabolized substances causes dysfunction in multiple organs and systems.[1-6]

MPS are classified into seven major groups (I, II, III, IV, VI, VII, IX) according to the deficient enzyme and the accumulated substrate.[1,7] Type II is linked to chromosome X, whereas all the others are autosomal recessive disorders.[1,8,9] It is estimated that the overall incidence of MPS is around 4 per100,000 live births (0.04%).[10-12]

Each type of MPS is associated with a wide range of clinical heterogeneities; however, all possess some common characteristics such as multisystemic, chronic and progressive deterioration, with osteoarticular, audiovisual and cardiovascular changes. Mental retardation is rare in types IV and VI. Patients may appear normal at birth and manifest symptoms later.[1-4,6-9,13-15] Among the various features that characterize MPS patients,

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the most common are dwarfism, umbilical and inguinal hernias, macrocephaly, coarse facial changes, delayed motor skills, corneal clouding, glaucoma, dysostoses, bone dysplasias, heart disease, respiratory distress (obstructive/restrictive disease), hepatosplenomegaly, progressive neurodegenerative disease, limited joint mobility as well as hearing loss.[1-4,6-9,13-15]

The average life expectancy in the most severe forms is between ten to twenty years, though in attenuated forms survival may be normal.[1-4,6-9,13-15] Death is usually a result of either respiratory tract infection or cardiac disease, which are caused by the deposition of mucopolysaccharides.[1-4,6,15,16] Diagnosis and management are often challenging because of the considerable variability in symptom presentation and rate of progression.[1-4,6,15,16]

MPS patients also present oral manifestations that are observed either clinically or radiographically. The accumulation of mucopolysaccharides impacts the stomatognathic system, leading to changes in oral health and to the development of the dentition of patients with this disease.[3,7-9,13-15,17-27]

Craniofacial features consist of coarse facial features high prominent forehead, snub nose with a depressed nasal bridge, broad nasal tip, and anteverted nostrils.[3,7-9,13-15,17-27] Thick lips with an open mouth posture are also features associated with this syndrome.[3,7-9,13-15,17-27]

Few studies have reported the oral and dental changes in MPS patients. The reported alterations include a short and broad mandible, macroglossia, anterior open-bite, high arched palate with pronounced rugae, spaced dentition, lip hypotonia, gingival hyperplasia and enlargement of the alveolar process. Teeth have been described as misshapen, peg-shaped, small, malformed, short, and hypoplastic. Radiographic features that have been reported include short mandibular rami with abnormal condyles; reports also include delayed eruption teeth related to the presence of multiple unerupted teeth with large thickened dental follicles secondary to excessive dermatan sulfate and collagen deposition.[3,7-9,13-15,17-27]

Notwithstanding, to date there are no studies comparing oral features of patients with mucopolysaccharidosis with controls without the disease. The evaluation of dental conditions in patients with MPS is scarce considering that in literature only clinical cases are described. Epidemiological studies with all types of MPS are rare, specially multicenter studies performed for the collection of more comprehensive data. Finally, there are no studies of dental characteristics of patients with mucopolysaccharidosis in Portugal.

So, the present study aimed to evaluate and characterize the prevalence of oral pathology in patients with mucopolysaccharidosis attending a national reference center in Portugal.

MATERIAL AND METHODS

This cross-sectional study consisted of twelve MPS patients with a positive diagnosis resulting from an enzyme assay followed at the Metabolic Diseases Unit of Centro Hospitalar de S. João, EPE/Faculty of Medicine, University of Porto and twelve healthy participants followed at the Faculty of Dental Medicine, University of Porto (control group). The age of participants was between five and twenty-eight years. The Ethics Committees of the Faculty of Dental Medicine and of the Centro Hospitalar de S. João approved the research project. All participants or their parents/legal guardians signed an informed, free and clear consent. Storage and processing of data guaranteed confidentiality of all information, thereby respecting the rules of conduct expressed in the Declaration of Helsinki.

The clinical oral evaluation was performed by a complete extra- and intra-oral examination to assess the presence of oral pathologies and occlusion status. Experienced examiners carried out dental caries examinations, using a mirror and explorer in accordance with World Health Organization criteria and methods. The total number of decayed, missing and filled primary (dmft) and permanent (DMFT) teeth was recorded for each included patient and control. The gingival index was made with a periodontal probe only to determine whether bleeding of dental surfaces occurred after 15 seconds of the sounding. Dental eruption delay was analyzed based on normal age of eruption of permanent teeth and on hospital medical records, when available.

Statistical analysis

Analyses were performed using the Statistical Package for Social Sciences (SPSS) 21.0 for MAC OS. The categorical variables were summarized as relative and absolute frequencies (%) and the continuous variables were described using mean and standard deviation. When appropriate, the chi-squared independence test was used to analyze hypotheses regarding the categorical variables; when expected counts were less then five, Fisher´s test was applied. Student's t-Test was used to evaluate differences between means of continuous variables. A level of 0.05 was considered significant.

RESULTS

MPS patients and controls presented similar age (16.5±7.5 vs. 14.4±6.3 years old, p=0.506) and sex distribution (50% males for MPS and 67% males for controls, p=0.637). The MPS group included one patient with MPS I, one patient with MPS II, one with MPS IIIC, one with MPS IV and eight patients with MPS VI.

Regarding oral hygiene all participants declared that they brush their teeth daily. The first dental appointment occurred before 4 years of age in 57% of the MPS children and in 43% of the controls (p = 0.629). Moreover, the percentage of participants attending dental appointments between 5 and 12 years old was also similar between groups (50% vs 50%, p > 0.99).

In comparison to the control group, MPS patients presented greater prevalence of hypoplasia, higher prevalence of delayed tooth eruption, and macroglossia, among other anomalies, as shown in Table 1.

Table 1 - Prevalence of oral and dental features in mucopolysaccharidosis (MPS) patients and healthy controls.

	MPS	Controls	p
Hypoplasia	75%	8%	0.003
Teeth morphological changes	75%	0%	<0.050
Teeth dimensional changes	75%	0	<0.050
Maxillary compression	83%	8%	0.001
Delayed teeth eruption	50%	0%	0.014
Macroglossia	67%	0%	0.001
Lingual interposition	83%	0%	<0.050
Diastematas	50%	8%	0.069

The presence of anterior open bite, posterior cross bite and limitation of mouth opening are shown in Table 2. MPS patients presented a very high prevalence of anterior open bite and a limitation of mouth opening vs. zero prevalence in controls.

Table 2 - Prevalence of occlusal characteristics in mucopolysaccharidosis (MPS) patients and healthy controls.

	MPS	Controls	p
Right posterior cross-bite	75%	17%	0.012
Left posterior cross-bite	58%	8%	0.027
Anterior open bite	92%	0%	<0.050
Limitation of mouth opening	92%	0%	<0.050

Although no differences were observed in the Decay-missing-filled-teeth (DMFT) index, MPS patients presented significantly greater prevalence of decayed teeth, but a lower, non-significant prevalence of filled teeth than the control group, as shown in table 3.

Finallly, we found a significantly higher prevalence of gingival bleeding in the MPS in comparison to controls as shown in Figure 1.

Table 3 - Decay-missing-filled-teeth (DMFT) index in mucopolysaccharidosis (MPS) patients and healthy controls.

	MPS	Controls	p
DMFT	100%	83%	0.478
Decayed teeth	100%	42%	0.037
Filled teeth	25%	67%	0.100
Missing teeth	33%	17%	0.640

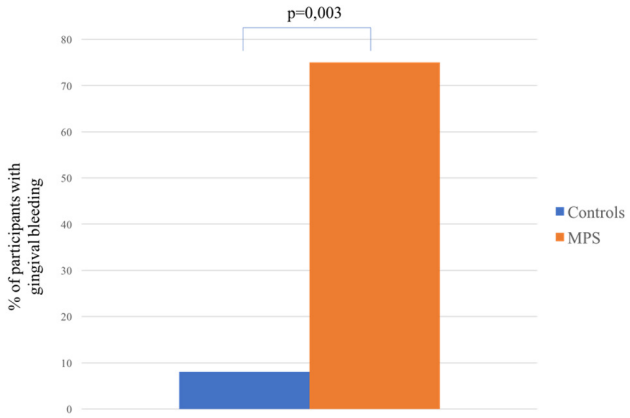

Figure 1- Gingival Bleeding Index in mucopolysaccharidosis (MPS) patients and healthy controls.

DISCUSSION

The accumulation of mucopolysaccharides impacts the stomatognathic system, causing changes in oral health and in the dentition of patients with this disease. The extent of the oral affections depends on the severity of the disease and the general state of health of the patient, and this will, in turn, impact upon oral care.[8,21,22] Our results showed a greater prevalence of macroglosia and lingual interposition in patients with mucopolysaccharidosis, which is corroborated in the literature by several authors.[7,9,13-15,20-24,26-29] The macroglossia is due to the deposition of glycosaminoglycans (GAG) in the tongue structure that usually results in an anterior open bite.[7,9,13,15,19-28,30,31] The higher prevalence of lingual interposition in patients with MPS may be due to the presence of macroglossia, anterior open bite and strong maxillary compression.[14] Similarly Turra et al[14] report the presence of lingual interposition in thirty-four participants of their study, being more frequent in the type VI.

MPS patients showed alteration of tooth shape and size, accompanied by hypoplastic teeth and delayed tooth eruption. McGovern et al[22] clinically detected the reduced size of permanent teeth in thirteen patients out of a total of seventeen, with an average of five affected teeth.

It has been suggested that enamel hypoplasia might be due to the random arrangement of materials, as a result of the irregular presence of glycosaminoglycans.[8,9,19,22,24,25]

Delayed tooth eruption can be explained by the presence of hyperplastic dental follicles due to excessive deposition of collagen and glycosaminoglycans around unerupted teeth[17,18,28,32] and also due to dentigerous cysts with smooth and clearly defined margins, as described by Alpôz et al.[28]

Through the evaluation of dental occlusion, we showed that MPS patients presented anterior open bite, right and left posterior cross-bites, limitation of mouth opening as well as maxillary compression in comparison to controls. Other studies corroborate these findings such as the study of Turra et al[14] that followed seventy-eight patients with MPS: 84.8% had anterior open bite, 37.9% had crossbite. Open bite and crossbite are explained by the presence of macroglossia and reverse swallowing.[7,9,14,19,22,24,27,30] Similar results were reported in the study by Antunes et al,[9] in which five participants in a total of twelve patients showed limitation of mouth opening. This limitation may be due to the presence of condylar defects.[7,9,14,19-22,24,25,27,28,30]

Our study found that 75% patients with MPS had a higher incidence of bleeding gums in over 30% of the tooth surfaces, corroborating the marginal gingivitis previously described in MPS patients associated with a poor oral hygiene and limited manual dexterity.[7-9,13,19,21-24] These findings are possibly related with tissue changes that occur in mucopolysaccharidosis, but also with other factors including difficulty in maintaining oral hygiene, lack of brushing techniques, poor attendance to dentist and lack of collaboration. In MPS patients a greater involvement of dentists is required, in order to arrive at better diagnostics and preventive protocols to improve oral health of these patients.[8,9,13,15,20,21,27,33,34]

SUMMARY

Patients with mucopolysaccharidosis have a high prevalence of eruption delay, teeth morphology alterations, occlusal problems, dental caries and bleeding gums, highlighting the need of oral health care providers to improve diagnostics and preventive protocols to overcome the factors that limit the oral health of these patients and promote together with parent/caregiver efficient oral care strategies.

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CONFLICT OF INTEREST

The authors declare no conflict of interest relative to this project.

AUTHOR CONTRIBUTION

All the authors reviewed the literature and conceived the study. Ponciano was involved in patient selection, monitoring and data collection at S. João-Porto Hospital. Ponciano and Areias were involved in patient selection, monitoring and data collection at Faculty of Dental Medicine. All the authors performed the statistical analysis, wrote and revised the manuscript.

MANIFESTAÇÕES ORAIS DE MUCOPOLISSACARIDOSE EM CRIANÇAS

INFORMAÇÕES GERAIS: Os pacientes com mucopolissacaridose apresentam diversas alterações do complexo estomatognático, representando um desafio para os médicos dentistas.

OBJETIVO: O estudo pretendeu avaliar e caracterizar a saúde oral em pacientes com mucopolissacaridose num centro de referência em Portugal.

MÉTODO: A amostra foi constituída por doze pacientes com mucopolissacaridose (MPS) seguidos na Unidade de Doenças Metabólicas do Centro Hospitalar de São João e doze participantes saudáveis seguidos na Faculdade de Medicina Dentária da Universidade do Porto. A avaliação clínica oral consistiu num completo exame extra-oral e intra-oral para avaliação de patologias orais, índice gengival e perfil oclusal.

RESULTADOS: Pacientes com MPS e controlos apresentaram médias similares de idade e de distribuição de género. Em comparação com os controlos, crianças com mucopolissacaridose apresentam maior prevalência de dentes cariados, sangramento gengival, macroglossia, hipoplasia dentária, interposição lingual, erupção dentária atrasada, mordida aberta anterior, mordida cruzada posterior direita e esquerda, limitação da abertura da boca, alteração do tamanho e forma dentária, diastemas e compressão maxilar.

CONCLUSÃO: Pacientes com mucopolissacaridose apresentam maior prevalência de erupção dentária atrasada, alterações morfológicas dentárias, problemas oclusais, cáries dentárias e gengivas inflamadas, reforçando a necessidade de prestadores de saúde oral para melhorar diagnósticos e protocolos preventivos para ultrapassar os fatores que limitam a saúde oral destes pacientes e promover em conjunto com pais/ cuidadores estratégias de saúde oral eficientes.

PALAVRAS-CHAVE: Mucopolissacaridose; saúde oral, pediatria, manifestações dentárias.

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