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Oral health-related quality of life of young people with mucopolysaccharidosis: a paired cross-sectional study

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Abstract: The purpose of the present study was to compare the perceptions of the parents/ caregivers of young people with and without Mucopolysaccharidosis (MPS) with regards to their oral health-related quality of life (OHRQoL). A cross-sectional study was conducted with 29 individuals with MPS and 29 normotypic individuals aged three to 21 years and their parents/caregivers. All parents/caregivers of young people with MPS in follow-up at two reference hospitals in the city of Belo Horizonte, southeastern Brazil, were invited to participate in the study. Individuals without MPS were recruited from the pediatric clinics of both hospitals. Parents/caregivers answered a structured questionnaire addressing the sociodemographic characteristics, behavioral habits and medical and dental history of the children as well as the Brazilian short-form version of the Parental-Caregiver (P-CPQ). The individuals with and without MPS were examined for malocclusion, dental caries and oral hygiene by an examiner who had undergone training and calibration exercises. Mean age of the subjects was 12.1 years (± 4.2). Comparing total P-CPQ scores and scores on the oral symptoms, functional limitations and wellbeing domains, the parents/caregivers individuos with MPS reported a statistically significant greater negative impact on OS domain than their counterparts. Regarding the clinical variables, malocclusion was also associated a greater negative impact on OHRQoL of young people with MPS when compared to those of young people without MPS. Our findings show the great negative impact caused by the malocclusion of young people with MPS.

Keywords: Mucopolysaccharidosis; Rare Diseases; Quality of Life; Oral Health; Dental Care for Disabled.

Introduction

Mucopolysaccharidoses (MPS) are a group of rare genetic diseases caused by an enzyme inadequacy in the lysosomes of the organism. The absence or malfunctioning of these enzymes causes the non-degradation of glycosaminoglycans (GAG) and their consequent deposition within the lysosomes. The accumulation of GAG in the cell promotes progressive clinical manifestations that affect several organs.[1,2,3]

MPS is a musculoskeletal disease, the classification of which is based on enzyme deficiency. The absence or malfunctioning of 11 enzymes is responsible for seven different types of the disease (MPS I, II, III, IV, VI, VII and IX). The overall incidence of MPS is estimated to range from 1:25,000 to 1:52,000 live births.[1,2,3] In Brazil, 1069 individuals with MPS were identified between 2004 and 2013.[3,4]

Some signs and symptoms are characteristic and common to different types of MPS, such as typical facies, excessive body hair growth, short stature, visual impairment, cardiopathy, sleep apnea, neurological problems, skeletal distention, corneal opacification, inguinal and abdominal hernias, enlarged liver and spleen, hearing impairment, respiratory problems, progressive joint limitation, enlarged tongue and abnormalities in the number and shape of the teeth.[1,2,5,6]

The main oral problems described in individuals with MPS are abnormalities in the number and anatomy of the primary and permanent teeth, enamel defects (primary and permanent teeth), delayed eruption of permanent teeth, impacted teeth, diastema, malocclusion (especially anterior open bite and crossbite), protruding tongue, a lack of lip seal, mouth breathing, limited mouth opening, bruxism and dental caries.[7,8,9,10,11] Oral health plays a fundamental role in the lives of individuals with MPS, as oral diseases may result in infection as well as nutritional, respiratory, chewing and speech problems, compounding their already severely weakened state of general health.[5,11,12,13,14]

Oral health-related quality of life (OHRQoL) regards the impact of oral problems on aspects of daily living.[15] The magnitude of impact in terms of frequency, severity or duration can affect an individual's perception of his or her life in general. The presence of oral problems can negatively affect the OHRQoL of MPS patients. Many of problems can also impair the performance of their daily activities. This happens because these conditions are often associated with pain, discomfort and aesthetic change.[10,16]

Radiological and oral changes are very common in individuals with MPS. These changes in individual with MPS may impair mouth opening, chewing and eating. These changes can negatively impact the quality of life of these individuals. Regular follow-up, preventive applications and dental treatments must be included in the approach of the multidisciplinary team of patients with MPS. These actions can provide better oral health.[10]

To the best of our knowledge, there are no previous reports addressing the impact of the nature and severity of MPS on OHRQoL. As individuals with MPS have systemic characteristics of motor and neurological impairment, it is important to know how these characteristics affect quality of life.[5,13,15,16,17,18]

To fill this gap in knowledge, the aim of the present study was to compare the perceptions of parents/caregivers regarding the OHRQoL of young people with and without MPS.

Methods

Study design and sample characteristics

A paired cross-sectional study was carried out with 58 individuals divided into two groups (29 with MPS and 29 without MPS) and their respective parents/caregivers. The individuals with MPS was recruited from two public hospitals in the city of Belo Horizonte, southeastern Brazil. Both hospitals are reference centers for the disease. The diagnosis of MPS was recorded on medical records made available for the present study. All parents and caregivers of these individuals were contacted either in person or by telephone, received clarifications regarding the objectives of the study and were invited to participate. Individuals without MPS were recruited from among patients awaiting routine appointments at the pediatric outpatient clinics of the same hospitals. These individuals had no chronic diseases or physical or mental disabilities.

The OpenEpi® statistical software (Dean, Sullivan and Soe; OpenEpi: Open Source Epidemiological Statistics for Public Health, http://www.OpenEpi.com) was used to calculate the test power for the sample of 29 individuals with MPS. For such, a significance level of 0.05 and test power of 0.80 were considered. Moreover, prevalence values of occlusal problems were obtained from the pilot study (68.0% among individuals with MPS and 32.0% among those without MPS).

Non-clinical data collection

Parents/caregivers who agreed to participate in the study with their children provided written informed consent. This study received approval from the Human Research Ethics Committee of the 255.475.

The parents/caregivers answered a pre-structured questionnaire addressing the sociodemographic characteristics (sex, age, economic status, parent's/caregiver's age and parent's/caregiver's schooling). The economic status of the family and educational level (years of study) of the parents/caregivers were evaluated using the Brazilian line Economic Classification,[19] grouping the participants into higher (classes A and B), middle (class C) and lower (classes D and E) economic classes.

The parents/caregivers were answered using the short form of the Parental-Caregiver Perceptions Questionnaire (P-CPQ)[15,20] for the determination of OHRQoL in the individuals with and without MPS. This proxy-report instrument was selected because the majority of the participants with MPS had mental disabilities and could have had difficulty answering the questions.

The P-CPQ is used to evaluate the perceptions of parents/caregivers regarding the OHRQoL of children in the previous three months and has 13 questions distributed among three domains: oral symptoms (three items), functional limitations (four items) and wellbeing (six items). The questions follow a scale from 0 to 4 points. Each item has five response options: never=0; once or twice = 1; sometimes = 2; often = 3; every day or almost every day = 4. The total score ranges from zero to 52 points, with higher scores indicating a greater negative impact on OHRQoL. A "do not know" response option is also included on all items. This response option scored 0 point.[15,20]

Clinical data collection

The examination of the oral cavity of each participant (young person with or without MPS) was performed after the administration of the questionnaire to the parents/caregivers. The participants were examined under artificial light in a dental chair, on a cot or in a wheelchair. The team was composed of an examiner and assistant (scorer/organizer). The examinations were performed with the aid of a mouth mirror (PRISMA®, São Paulo, Brazil) and Community Periodontal Probe (WHO-621; Trinity, Campo Mourão, Brazil).

Dental caries experience was recorded based on the diagnostic criteria of the World Health Organization (WHO). The DMFT (permanent dentition) and dmft (deciduous dentition) indices were used to identify the number of decayed (D/d), missing or indicated for extraction (M/m) and filled (F/f) teeth (T/t).[21]

Oral hygiene was analyzed using the Simplified Oral Hygiene Index (OHI-S), for which six dental surfaces are used to represent the entire buccal cavity. Each surface receives a code ranging from zero to three based on the amount of calculus and bacterial plaque.[22,23]

Malocclusion was recorded based on Oliveira et al.[24] and the WHO criteria:[21] horizontal overjet (increased/diminished, negative/anterior crossbite), vertical overjet/overbite (increased/deep bite, diminished, negative, top-to-top) and posterior crossbite. When at least one condition was diagnosed, the subject was classified as having an occlusal problem resulting from an abnormal vertical or transverse occlusion. No child or adolescent selected for the study had a history of orthodontic treatment.

Training and calibration process

The first step was a thorough reading of the clinical diagnostic criteria used. The theoretical training was performed using images and slides analyzed on two separate occasions separated by a 10-day interval for the determination of intra-examiner diagnostic variability. The next step was the practical calibration of the examiner. Inter-examiner agreement was determined by comparing the results to those of an experienced specialist with a doctoral degree in pediatric dentistry on two separate occasions separated by an eight-day interval. Due to the limited number of individuals with MPS, children and adolescents without MPS were examined during the calibration exercise (n = 20). The students from a public school in Belo Horizonte participated in this stage. Kappa values ranged from 0.76 to 0.98 for the conditions investigated (dental caries = 0.83; oral hygiene = 0.76 and malocclusion

= 0.93). The participants in the calibration exercise were not included in the main study.

Pilot study

Five individuals with MPS and five without MPS from one of the previously selected hospitals participated in this phase along with their parents/caregivers. The results of the pilot study revealed no need for any change to the methods. The participants in this phase were included in the final sample of the study.

Data analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS for Windows, version 22.0, IBM Inc., Armonk, USA). First, the Shapiro-Wilk test was performed to verify the sample distribution. There was a non-normal distribution, and non-parametric tests were performed. After the descriptive analysis, bivariate analysis was performed with the chi-square, Student's t, Mann-Whitney and Wilcoxon tests ($p < 0.05$).

Results

Among the 34 individuals recruited with MPS, five were not included in the study (refusal, death, transportation difficulty and advanced disease conditions). Thus, the final sample consisted of 29 individuals with MPS and 29 individuals without MPS and their parents/caregivers.

The age of the young people ranged from three to 21 years (mean: 12.1 ± 4.2 years; median: 14.5 years). Most were in the favored economic class (56.5%). The age of the parents/caregivers ranged from 23 to 59 years (mean: 40.9 ± 9.0 years; median: 40.0 years). No significant difference between the two groups were found regarding sex, age, economic status, parent's/caregiver's age or parent's/caregiver's schooling ($p > 0.05$) (Table 1).

The distribution of individuals according to the type of MPS is displayed in Figure. MPS I: 24,2%; MPS II: 20,6%; MPS III: 10,3%; MPS IV: 3,4%; MPS VI: 34,6% and two patients with MPS did not have a defined diagnosis at the time of the data collection (6,9%).

Table 1. Distribution of independent variables according to presence/absence of MPS (n = 58).

Variable	Group		Total	p-value*	Odds ratio
	With MPS	Without MPS			
	n (%)	n (%)	n (100.0%)	value	(95%CI)**
Sex					
Male	17 (50.0)	17 (50.0)	34	1.000	1.00 (0.35-2.84)
Female	12 (50.0)	12 (50.0)	34		1
Age (years)					
3–12	13 (50.0)	13 (50.0)	26	1.000	1.00 (0.35-2.81)
13–21	16 (50.0)	16 (50.0)	32		1
Economic status					
High	13 (56.5)	10 (43.5)	23	0.421	1.54 (0.53-4.45)
Low	16 (45.7)	19 (54.3)	35		1
Parent's/Caregiver's					
Age (years)					
23–39	12 (42.9)	16 (57.1)	28	0.293	0.57 (0.20-1.62)
40–59	17 (56.7)	13 (43.3)	30		1
Parent's/Caregiver's Schooling (years)					
< 8	14 (58.3)	10 (41.7)	24	0.286	1.77 (0.61-5.10)
> 8	15 (44.1)	19 (55.9)	34		1

MPS; mucopolysccharidosis; *X2 Test (5% significance level); **95%CI: confidence interval.

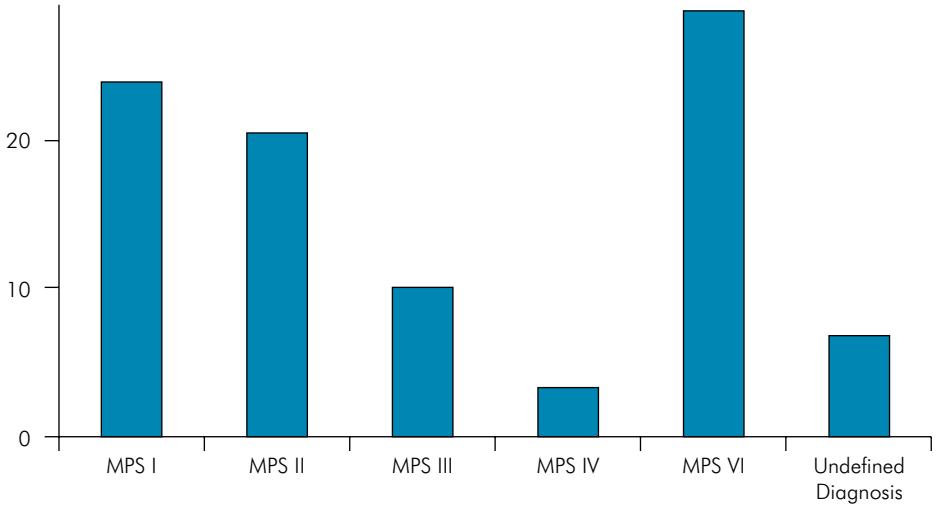

Figure 1. Distribution of individuals with MPS by type (n = 29).

Table 2. Mean total P-CPQ score and domain scores (n = 58).

P-CPQ	GROUP				p-value
	With MPS		Without MPS		
Domain	Mean (SD)	95% CI	Mean (SD)	95% CI	
Oral Symptoms	2.8 (± 2.1)	1.9–3.6	1.3 (± 1.8)	0.6–2.0	< 0.001*
Functional limitations	5.4 (± 2.8)	4.3–6.5	1.4 (± 1.8)	0.7–2.1	< 0.001*
Wellbeing	3.2 (± 1.4)	2.7–3.2	1.4 (± 2.1)	0.6–2.2	< 0.001*
Total Score	11.5 (± 5.0)	9.6–13.4	4.1 (± 3.3)	2.9–5.4	< 0.001**

MPS: mucopolysccharidosis; P-CPQ: Parental-Caregiver Perceptions Questionnaire; SD: standard deviation; CI: confidence interval; *Wilcoxon test (5% significance level); **Student's t-test (5% significance level).

Table 2 displays the total P-CPQ scores as well as the scores on the oral symptoms, functional limitations and wellbeing domains for the groups with and without MPS. Statistically significant differences were found for the total score and all domain scores ($p < 0.001$). The parents/caregivers of the young people with MPS had more negative perceptions of the impact of oral conditions on quality of life compared to those of the young people without MPS.

Table 3 displays the associations between the P-CPQ scores and the clinical variables investigated. According to the parents/caregivers, the occurrence of malocclusion was correlated with more negative impact on the OHRQoL of the individuals with MPS, as demonstrated by the total P-CPQ score and scores on the oral symptoms, functional limitations and wellbeing domains ($p < 0.05$).

Discussion

In the present study, the young people with MPS had greater negative impacts on OHRQoL compared to those without MPS, as demonstrated by the total P-CPQ and domain scores. Thus, the inherent health problems of individuals with MPS may have detrimental effects on OHRQoL. Living with a rare disease and disability exerts a negative influence on the lives of affected individuals and their families due mainly to the medical care and rehabilitation that most of these individuals need on day-to-day basis. This routine is associated with financial expenses that greatly affect the family's economic situation, priorities and quality of life.[13,17,18,25]

Despite the low values found in the total score for groups with MPS and without MPS. Parents and

Table 3. P-CPQ scores among individuals with and without MPS according to independent variables (n = 58).

Independent variable	Group			
	With MPS		Without MPS	
	Mean (SD)	p-value*	Mean (SD)	p-value*
Oral symptoms				
Malocclusion				
Present	3.17 (± 2.16)	0.029	1.00 (± 1.31)	0.576*
Absent	1.33 (± 1.50)		1.57 (± 2.24)	
Oral hygiene				
Inadequate	3.82 (± 2.52)	0.097	2.17 (± 2.99)	0.389*
Adequate	2.17 (± 1.68)		1.04 (± 1.36)	
Dental caries				
> 1	3.32 (± 2.26)	0.063	0.95 (± 1.35)	0.212*
0	1.80 (± 1.62)		1.90 (± 2.42)	
Functional limitations				
Malocclusion				
Present	6.00 (± 2.82)	0.006	0.93 (± 1.53)	0.169*
Absent	3.00 (± 1.55)		1.93 (± 2.09)	
Oral hygiene				
Inadequate	5.91 (± 2.80)	0.281	0.33 (± 0.82)	0.102*
Adequate	5.06 (± 2.94)		1.70 (± 1.96)	
Dental caries				
> 1	5.00 (± 2.58)	0.336**	1.57 (± 2.04)	0.630*
0	6.10 (± 3.38)		1.10 (± 1.52)	
Wellbeing				
Malocclusion				
Present	3.52 (± 1.34)	0.010	1.80 (± 2.39)	0.499*
Absent	2.00 (± 1.26)		1.07 (± 1.83)	
Oral hygiene				
Inadequate	3.55 (± 0.69)	0.543	1.67 (± 2.65)	0.951*
Adequate	3.00 (± 1.74)		1.39 (± 2.04)	
Dental caries				
> 1	3.37 (± 0.83)	0.418**	1.95 (± 2.39)	0.092*
0	2.90 (± 2.23)		0.50 (± 1.10)	
Total P-CPQ				
Malocclusion				
Present	12.87 (± 4.61)	0.003**	3.73 (± 2.81)	0.512**
Absent	6.33 (± 2.73)		4.13 (± 3.51)	
Oral hygiene				
Inadequate	13.64 (± 4.78)	0.076**	4.17 (± 2.99)	0.765*
Adequate	10.22 (± 4.85)		4.13 (± 3.51)	
Dental caries				
> 1	11.89 (± 4.67)	0.587**	4.47 (± 3.55)	0.562*
0	10.80 (± 5.84)		3.50 (± 3.03)	

MPS: mucopolysccharidosis; P-CPQ: Parental-Caregiver Perceptions Questionnaire; SD: standard deviation; *Mann-Whitney test (5% significance level); **Student's t-test (5% significance level).

caregivers of individuals with MPS perceive the impact of oral conditions on OHRQoL more than the group without MPS. Parents and caregivers of individuals with MPS perceive this impact on OHRQoL, because the oral conditions of individuals with MPS are worse (hygiene, greater presence of malocclusion, greater experience with caries) than individuals without MPS.[7,14]

According to the literature, GAGs progressively accumulate in bones, cartilage, muscles and ligaments, generating an inflammatory process and tissue damage that result in functional limitations and pain.[13,16,17, 8] A study conducted in Norway involving 209 parents of children and adolescents (six to 18 years) with rare congenital disorders showed that health-related quality of life was lower among the children with rare disorders than children from the general population; the greatest reduction in quality of life was found for physical functioning, whereas the smallest was found for emotional functioning.[25]

Cognitive impairment can also exert a negative impact on OHRQoL by limiting one's independence with regards to oral hygiene, which, when neglected, can lead to consequences such as periodontal disease and dental caries.[11,13,14,15,16,17,23] In the present study, only malocclusion exerted a significant negative impact on the OHRQoL of the individuals with MPS, as evidenced by the total P-CPQ score and scores on the oral symptoms, functional limitations and wellbeing domains. Malocclusion may be due to the skeletal and joint abnormalities these individuals have due to the deposition of GAGs in the head and neck region. Occlusal problems, such as dental crowding, open bite and tooth impaction, can lead to functional, respiratory and esthetic problems, which can exert a negative impact on OHRQoL.[8,9,10]

Individuals with MPS have a smaller nasopharyngeal space, which causes mouth breathing and may lead to open bite. Open bite can have a negative effect on phonation, which makes communication difficult and affects quality of life.[6,10] This situation may result in less participation in school, at work and in one's social life.[8,12,13,14,17,26] Moreover, such individuals may have difficulty chewing food properly due to open bite and deficient molar occlusion. Consequently, chewing and swallowing occur less effectively, which could lead to asphyxia and choking episodes.[5]

Occlusal problems can also compromise the esthetics of one's facial appearance, generating low self-esteem and psychological conditions, such as anxiety and depression.[10,14,16,26] According to the literature, patients acquire good occlusion and chewing function after an orthodontic intervention. The negative impact that malocclusion can have on quality of life is mitigated when the diagnosis is made early and dental care is available.[8,9,12,14,18]

The major limitation of this study was the use of a convenience sample, which restricts the ability to generalize the results to other groups of patients with MPS. Despite the small sample size, it can be considered representative of individuals with MPS in the state of Minas Gerais, as this is a rare disease and the vast majority of affected individuals registered in the state participated in the study (90.0%). However, one of the strengths of this study is the matching of the groups for sex and age. This made the intergroup comparisons of clinical, socioeconomic and behavioral variables more reliable by eliminating possible confounding factors and bias.

The results of the present study can serve as a source of knowledge and assist in disseminating information on the disease to health professionals, because no previous study was found in the literature evaluating the perceptions of parents/caregivers regarding OHRQoL. Such information is of extreme importance to an early diagnosis and the treatment of the disease, resulting in improvements in signs and symptoms and, consequently, the quality of life of affected individuals.

It is evident that the path to improving the quality of life of individuals with MPS is multidisciplinary care and good communication among health professionals. This is the starting point for the promotion of oral health, more effective multidisciplinary care and a more democratic policy directed at this population. The importance of the participation of a dentist on the multidisciplinary team that provides care and follow-up for individuals with MPS is evident. Dentists can provide such

individuals with a better oral health status. The early identification of signs and symptoms can lead to the timely establishment of appropriate therapy and have a positive influence on both OHRQoL as well as general quality of life.[5,11,14,27]

Conclusions

Parents/caregivers of young people with MPS reported a greater negative impact on OHRQoL when compared to those of young people without MPS. Malocclusion in individuals with MPS was also associated with poorer quality of life.

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