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Body Composition of Individuals with Mucopolysaccharidosis

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Abstract

Objective: To describe body composition of individuals with mucopolysaccharidosis (MPS).

Methods: A cross-sectional study was carried on with a convenience sample of MPS individuals of both sexes, five years of age or older. Exclusion criteria: physical deformity, neurological problems or other associated syndrome, precluding full measure's accomplishment. Body composition was estimated by anthropometric method, according to international standards. Accomplished measurements of skinfold, body girth, bone diameters, total body mass and stature were made. Body mass index (BMI), body fat percent (BF%) and body mass were calculated. Body composition was also evaluated through Dual-energy X-ray Absorptiometry (DXA). **Results:** Twenty-three individuals were identified; three were excluded (cognitive deficit) and five losses occurred. Fifteen individuals were evaluated (average age = 12.1 ± 7.7 years); three MPS I, five MPS II, one MPS IV and six MPS VI. For DXA, eight were included (average age = 14.1 ± 9.8 years), six common to the anthropometric assessment. BMI average: 19.8 ± 3.8 kg/m²; BF% average: 13.9 ± 5.1%. Short stature was present in 76.9%, obesity in 25.0%, macrocephaly in 26.6%; osteoporosis in 25.0%. Perimeters' measures increased with the increasing of age. Bone lengths were not always shortened and there was no pattern related to age and MPS type. No significant differences were observed between anthropometry and DXA. The results varied in the same type of MPS and in the same age group. **Conclusions:** Physical parameters were in agreement with literature, as short stature and macrocephaly. Measurements' variations between different MPS types and among individuals of the same type strengthen the heterogeneity of this disease.

Keywords: Mucopolysaccharidosis; Anthropometry; Body composition; Children and adolescents

Introduction

Mucopolysaccharidosis (MPS) is a rare and heterogeneous genetic disease, caused by deficiency or absence of lysosomal enzymes involved in the degradation of glycosaminoglycans. Abnormal and progressive accumulation occurs in many tissues, giving a multisystemic characteristic of this disease [1]. The main clinical manifestations are hepatosplenomegaly; join stiffness; cardiopathy by valvular and coronary artery impairment; respiratory, eye, ear and central nervous system impairment. Neurological involvement is associated with more severe forms of the disease and may not occur in almost all types [2]. However, phenotypic heterogeneity, variability and severity of clinical manifestations can be distinguished from MPS within and among types [3]. The incidence of MPS varies from 1.9 to 4.5 in 100,000 live births [4,5]. In Brazil, a study conducted in the state of Pará identified the incidence of MPS I as 1:1.440,000 live births [6]. MPS Brazil Network [*Rede MPS Brasil*] initiative that enhances the diagnosis and treatment of MPS in Brazil, identified 1,000 patients with MPS until December, 2012 [7].

Anthropometry aims to investigate the way physical performance can be altered by growth and development, with regard to body shape, proportion and composition [8]. Anthropometric evaluation includes variable measurements according to international protocols, which can be obtained also by Dual-energy X-ray Absorptiometry (DXA), gold standard health examination for body mass estimation in humans [9].

By obtaining data from body fat percent (BF%) and body masses, health professionals can analyze and classify the growth and global status of these individuals.

This study will allow body composition characterization of individuals with MPS. The results present a great scientific and clinical relevance, as several unpublished variables are studied and other hitherto little explored in this group. The aim of this study was to describe the body composition of individuals with MPS and, on the exploratory level, to verify the agreement between the methods for assessing body composition.

Materials and Methods

A cross-sectional study was undertaken in three medical genetics services in Rio de Janeiro, references in monitoring and treatment of patients with MPS. A convenience sample of individuals with MPS, of both sexes, who were regularly followed-up in those services, was selected; all individuals who were followed-up and met the inclusion criteria were invited (23 individuals). The study included individuals with biochemical diagnosis of MPS, five years of age or older, followed-up by medical staff between the years 2009 and 2010, and whose caregivers or patients themselves, when older than 18 years, had signed the Informed Consent (IC). The age of eligibility was due to the protocols used for the tests. Individuals with MPS who had any physical deformity (joint or muscle) that would prevent the full realization of the proposed

measures were excluded, besides the presence of associated syndrome or other status that might also prevent the action of the study protocol. If the patient (or his guardian) agreed to participate in the study, the IC was signed and implemented, as well as an anamnesis with information relating to the patient and study. After the clinical history, anthropometric measurements began, so as to characterize the body composition of the study group. The measurements were performed twice in succession and always by the same investigator (skilled in the art) to decrease the chance of measurement errors. Within availability of the exam, attendance for performing DXA was scheduled. The study was approved by the Research Ethics Committees of the institutions involved.

Body Composition

Body composition was assessed by anthropometric method and by DXA.

Anthropometric Assessment

The International Standards for Anthropometric Assessment, published by the International Society for Advancement of Kinanthropometry (ISAK) were adopted [10]. A skinfold caliper (Cescorf/Top Tec - 0.1 mm precision) was used to measure skinfold thickness at three anatomical sites (triceps, subscapular and leg). For measurements of body circumferences an anthropometric tape (Cardiomed/WCS – 1 mm precision) was used, considering the following perimeters: head, neck, relaxed arm, waist, hip and leg. Height measures were also registered using a stadiometer (Cardiomed/WCS – 1 mm precision), total body mass using a scale (Welmy/W110H – 100 g precision), length of limbs and bone diameters using a segment caliper (Cardiomed/WCS - 1mm precision), considering the following lengths and diameters, respectively: arm, forearm, thigh and leg; biestiloid, biepicondilian of humerus and biepicondilian of femur. Body Fat Percentage (BF%; %), Body Mass Index (BMI, kg/m²), Fat Body Mass (FBM; Kg), Bone Body Mass (BBM; kg), Residual Body Mass (RBM; kg), Muscle Body Mass (MBM; kg) and Lean Body Mass (LBM; kg) were obtained from measurements [11].

DXA

The equipment used was the DXA Prodigy Advance Lunar / GE, which measures the attenuation of x-rays beams emission between 70 and 140 kilovolts synchronized with the line frequency for each pixel of the image taken by the body scanner. The values obtained in DXA were: Bone Mineral Content (BMC; g) obtained for trunk, legs, arms, android, gynoid and total; Bone Mineral Density (BMD; g/cm²); Body Fat Percentage (BF%; %) obtained for trunk, legs, arms, android, gynoid and total; Total Body Mass (TBM; kg); Fat Body Mass (FBM; g) obtained for trunk, legs, arms, android, gynoid and total; Lean Body Mass (LBM; g) obtained for trunk, legs, arms, android, gynoid and total; Z-score.

Clinical and Demographic Characteristics

The ones responsible for the individuals or the individuals themselves, when they were 18 years old, answered an anamnesis containing the following information: age, sex, type of MPS, school routine and physical activity routine.

Statistical treatment

Analysis was performed using the Statistical Package for the Social Sciences / SPSS 17.0 for Windows. The descriptive analysis of data addressed frequency distribution, measures of central tendency (median) and dispersion (minimum and maximum values and percentiles). The intraclass correlation coefficient (ICC) was also calculated [12].

Results

Twenty-three individuals who met the inclusion criteria for study

participation were identified. Three individuals were excluded for cognitive impairment that prevented measurements proposals. There were five losses (5/20; 25%): four individuals who did not attend the proposed schedule for evaluation and one who died during the study period. Fifteen individuals (median = 10 [5 – 34] years) were evaluated: three with MPS I, five MPS II with, one with MPS IV, and six with MPS VI. Of the total sample, only four individuals were female, one with MPS I: one with MPS IV and two with the diagnosis of MPS VI. For the DXA examination, due to the difficulty of scheduling availability and suitability of participants, only eight were included in this part of the study (median = 10 [5 – 34] years), six in common for anthropometric assessment. Of this total, two had MPS I (one of each sex), two had MPS II (male), one had MPS IV (female) and three had MPS VI (male). This group showed similar clinical characteristics, comparing to the total of individuals.

It was found that 40.0% (n = 6) of individuals practiced some kind of regular physical activity, and almost the whole of that number (83.3%) in school physical education. As to the school routine, it was found that 66.7% (n = 10) of individuals studied regularly and among these only one in special class, while two had completed high school.

Table 1 shows the general characteristics of the individuals who participated in the study. Participants with MPS II (n = 5) had a median age of 14 years [5 – 34] years, with two adults in the group, and MPS VI participants had a median age of nine years [5 – 19] years, with an adult in the group. The two participants with MPS I were less than 18 years. The average height of the group was 1.12 [0.94 - 1.35] m. Individuals with MPS II had higher median value (median = 1.25 [1.16 - 1.35] m compared with MPS VI individuals (median = 1.03; 0.96 - 1.08 m). Short stature (below the third percentile) was observed in 10 participants (76.9%).

The median body mass in the group was 23.5 [15.4 - 41.2] kg. Individuals with MPS II had higher median value (median = 37.4; 24.8 - 41.2 kg) compared with MPS I (median = 22.6 [15.9 - 29.2] kg and MPS VI individuals (median = 21.2 [15.4 - 28.5] kg. The percentile ranking of

	MPS	Sex	Age (years)	Height (m)	TBM (Kg)	BMI (Kg/m²)	BMI Percentile	HC (cm)
1	I	M	5	1.08	15.9	13.6	3	49.5
2	I	M	15	1.28	29.2	17.8	25	53.0
A	I	F	9	1.12	21.3	17.0	50	#
3	II	M	34	1.25	39.6	25.3	*	57.4
4	II	M	20	1.27	41.2	25.5	85	59.3
5	II	M	10	1.22	24.8	16.7	75	52.3
6	II	M	5	1.16	26.0	19.3	97	60.7
7	II	M	14	1.35	37.4	20.5	75	58.0
B	IV	F	10	0.98	20.9	21.7	95	#
8	VI	F	19	1.09	28.5	24.0	75	54.0
9	VI	M	12	1.18	23.5	16.9	50	53.7
10	VI	M	5	0.94	15.4	17.4	95	52.2
11	VI	M	10	1.00	22.8	22.8	97	56.5
12	VI	M	8	0.95	19.6	21.7	97	53.9
13	VI	F	6	1.06	18.2	16.2	75	51.6
median minimum value maximum value			10.0 5.0 34.0	1.12 0.94 1.35	23.5 15.4 41.2	19.3 13.6 25.5		53.9 49.5 60.7

Note: MPS = Mucopolysaccharidosis; TBM = Total Body Mass; BMI = Body Mass Index; HC =Head Circumference; m = meters; cm = centimeters; kg = kilograms; kg/m² = kilograms persquare meter; M = Male; F = Female; * = individual > 20 years old; A and B = individuals who have made only DXA; # = individuals do not have anthropometric measurements.

Table 1: General characteristics of individuals with MPS who participated in the study

individuals up to 20 years old [13], which corresponds to 92.3% of the sample (n = 12) indicated that these, 8.3% (n = 1) were underweight, 50.0% (n = 6) with normal weight, 16.7% (n = 2) were overweight, and 25.0% (n = 3) had obesity.

When comparing the classifications obtained by BMI and FBM data, we obtained the following indices and mean BMI and FBM, respectively: low weight = 1.9 kg (n = 1), normal weight = 3.4 kg (n = 6), overweight = 3.5 kg (n = 2), and obese = 4.7 kg (n = 3). This demonstrates that the mean values of FBM had a tendency to increase linearly with the changes within each group classified by BMI. Mean skinfold values in the three anatomic sites were similar.

The BF% obtained by anthropometric method can classify individuals over seven years of age [14,15] (69.2% of the sample; n = 9); of these, 22.2% (n = 2) were classified with excessively low BF%; 22.2% (n = 2) were classified with low BF%; 33.3% (n = 3) with appropriate BF%; and 22.2% (n = 2) with moderately high BF%.

Eight individuals were identified with head circumference above the 50th percentile (8/13; 61.5%), and among these, four had macrocephaly (above the 98th percentile) [16]. No individual had microcephaly.

We found that bone lengths do not follow a pattern in relation to age and type of MPS. The length increases with increasing age, but without the same uniformity observed in perimeters' measurements (Figures 1 and 2).

With the completion of DXA we could analyze the correlation between this test and the anthropometric method for the following measurements: TBM, BF%, FBM and MBM (Table 2). We calculated the ICC and the

Figure 1: Distribution of body circumferences in relation to age

Figure 2: Distribution of the lengths of limbs in relation to age

obtained values for FBM and for MBM were 0.89 and 0.99 respectively, both with statistical significance.

Through the Z-scores obtained in DXA we observed that two individuals (2/8; 25%) were classified with osteoporosis and none with osteopenia.

Discussion

The knowledge of variables related to the growth and development of children and adolescents, such as height, body mass, body fat and muscle mass, is extremely important as these, among others, are health indicators of such populations. Several factors are directly related to the growth and development of children and adolescents, especially genetics, physical activity level, dietary patterns, access to health services and the presence of certain diseases [17].

Stature is a major indicator of the growth of a population and, therefore, is recommended for systematic monitoring. MPS is a disease associated with short stature due to dysostosis multiplex that affects, among other body segments, the spine, long bones and the bones of the hands and feet [18]. In this study, findings of short stature compared with that predicted for age group and sex, observed in 76.9% of the study individuals, corroborate other findings in the literature. The degree of impairment of linear growth also appears to be influenced by the type and severity of MPS [19]. In our study, individuals with MPS II had higher height values, probably because they have minor clinical impairment, beside the fact that MPS VI has greater osteoarticular involvement, which could also lead to greater height reduction. In other studies, the effect of enzyme replacement therapy also showed positive height trends, not only by the capacity for growth, but also as the increased range of motion in lower limbs [19,20].

A study conducted in mice with lysosomal storage diseases (MPS I, MPS IIIB, MPS VII, Niemann-Pick types A and B, and child neuronal ceroid lipofuscinosis) observed decrease of adiposity [21]. However, not only low weight and low height were found in our sample; 25.0% of the samples were classified as obese according to BMI, and according to BF%, 22.2%, a moderately high rate. Two types of analysis, quantitative and qualitative, may have shown increased caloric intake, with or without decrease in energy expenditure. Although in practice we observe the presence of obesity, we found no reports of its frequency in individuals with MPS. It has been observed that the increasing prevalence of overweight and obesity, particularly in children and adolescents, appears to be directly linked to a lack of motor experience and participation in physical exercise programs, as well as inadequate eating habits [22].

Most individuals (61.5%) had head circumference above the 50th percentile, and among these, four individuals had macrocephaly, which is an observed finding in MPS [23].

We found a 25% frequency of osteoporosis in this study, and it is expected that this disease occurs in individuals with MPS [24]. The Z-scores obtained in DXA present lower values in older individuals, which may result from the disease progression, as changes occur in the bones due to bone dysostosis and decreased joint motion. This is a characteristic highly prevalent in all types of MPS [3,18] which can cause the decrease of bone mass along with the physical decrease [25]. Our results are in accordance with other study [26], which used DXA to assess 13 children with MPS I, II, IV and VI, aged from five to 13 years: except for MPS I and II, all had bone mineral density below the expected for their age group in the spine region L1-L4.

A little reported fact is the frequency of school activities and physical activity among MPS individuals. In our study there was a very small percentage of attendance to physical activities (40.0%), which may be explained by the clinical manifestations of MPS, such as the
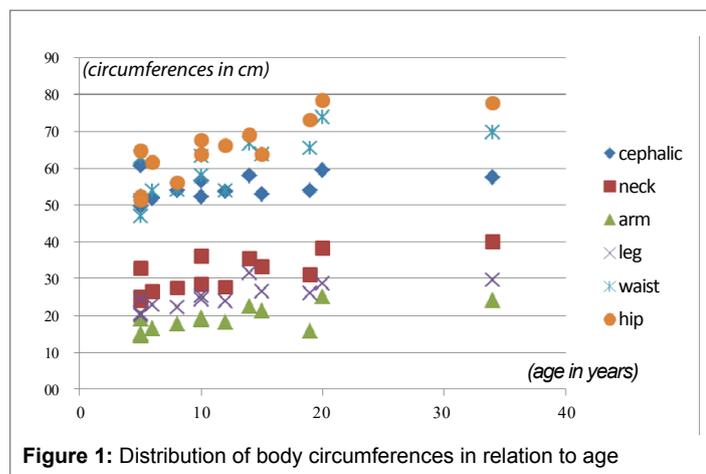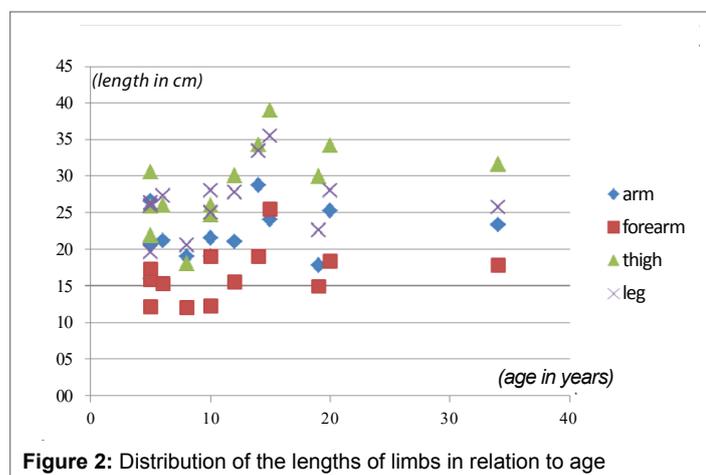
	MPS	Sex	Age (years)	DXA TBM (Kg)	ANTH TBM (Kg)	DXA BF% (%)	ANTH BF% (%)	DXA FBM (Kg)	ANTH FBM (Kg)	DXA MBM (Kg)	ANTH MBM (Kg)
1	I	M	5	14.6	15.9	12.3	12.1	1.7	1.9	12.9	14.0
3	II	M	34	38.4	39.6	9.4	7.0	3.4	2.8	34.9	36.8
4	II	M	20	40.2	41.2	13.2	13.3	5.1	5.5	35.0	35.7
8	VI	F	19	30.3	28.5	23.3	17.6	6.9	5.0	23.4	23.5
9	VI	M	12	24.2	23.5	8.6	9.5	2.0	2.2	22.2	21.3
10	VI	M	5	15.5	15.4	5.9	9.7	0.9	1.5	14.7	13.9
Median			15.5	27.3	26.0	10.9	10.9	2.7	2.5	22.8	22.4
Minimum value			5	14.6	15.4	5.9	7.0	0.9	1.5	12.9	13.9
Maximum value			34	40.2	41.2	23.3	17.6	6.9	5.5	35.0	36.8

Note: MPS = Mucopolysaccharidosis; DXA = Dual energy X-Ray Absorptiometry; ANTH = Anthropometry; TBM = Total Body Mass, BF% = body fat percent; FBM = Fat Body Mass, LBM = Lean Body Mass; M = Male; F = Female; The numbers of individuals were kept for further identification; The six individuals who appear in this table were common between DXA and ANTH

Table 2: Comparison of body composition values obtained by DXA and anthropometry

musculoskeletal limitation that makes them less mobile and ultimately leads to muscle atrophy [27]. School attendance was also considered low (66.7%) among the participants, and may also be a reflection of the aforementioned clinical manifestations and especially the neurologic involvement associated with more severe forms of the disease [2].

No significant differences between anthropometry and DXA concerning variables related to body composition were observed. Regarding the ICC, statistical significance was found for FBM and MBM. We suggest that anthropometry can be used without loss of accuracy for these data [12]. In anthropometry, the acceptable technical error of inter-evaluators measurement for skinfold for beginners is 10%, and experienced evaluators is 7.5%, while for other measures it is 2% and 1.5%, respectively.10 DXA provides more accurate data, as these are directly obtained [9]. It must be emphasized that the accessibility of the anthropometric method is much larger than the DXA, lower cost and valid for this type of individual. It would be of great value training evaluators for this method as compared to the purchase of large equipment.

Increased neck perimeter can be correlated to increased levels of adiposity, including BMI [28]. It has been suggested checking the neck perimeter as an indicator of cardiovascular risk in different populations [29]. In this study, only one individual (MPS VI) presented the perimeter above expectations, showing BF% rated "moderately high" and BMI classified as "normal weight".

Bone lengths are not always reduced, not following a pattern in relation to age and type of MPS. Length increases with increasing age, but without the same uniformity observed in perimeters' measures, and this may reflect the heterogeneous aspect and duration of the disease.

The current treatment approach in MPS is booming and is complex, which has allowed some reduction in the severity of complications and increased survival of individuals affected by the disease, but early diagnosis and treatment seem to be fundamental. However, given the great complexity of the MPS and the wide phenotypic variability within and between types, knowledge of the characteristics of the disease should be further explored for the effective management of these individuals [30].

The number of individuals included in this study (13 for anthropometry, and eight for DXA) reflects the rarity of the disease and was a limitation of this study, together with the lack of normality curves for some parameters, leading to difficulties in comparing with the general population.

Conclusion

The study aimed to describe the body composition of individuals with MPS and altered physical parameters were found, as described in the literature. Some important changes were found in the sample, with heterogeneity of results among different types of MPS and among individuals of the same type. This may reflect the heterogeneity of the disease stage. Short stature, head circumference above the 50th percentile and macrocephaly were found and described. The importance of a multidisciplinary approach to these individuals, who demand interaction between the various health professionals, must be highlighted. The goals of treatment are better understanding the disease and giving special attention to each individual with MPS, respecting their own characteristics and desires.

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