Description of Functioning in Children and Adolescents with Mucopolysaccharidosis – Case series

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Aline Mota Fleming[1], Carla Trevisan Ribeiro[1], Dafne Gandelman Horovitz[1], Luciana Castaneda Ribeiro[2], Ana Paula Carvalho Corrêa[1]

Abstract

Introduction: Rare health conditions as mucopolysaccharidoses (MPS) can directly influence functioning experiences. Mobility restriction, osteoarticular alterations, leads to delayed neuropsychomotor development are some of the negative impacts of MPS.

Aims: The purpose of this study is to evaluate the functioning of children with MPS, from the International Classification of Functioning, Disability, and Health (ICF) perspective.

Methodology: It is a case series study with a sample of 15 children and adolescents with MPS with a median age of 12 years, followed in a tertiary hospital in Rio de Janeiro, Brazil.

Results: The patients were assessed by the model ICF and results were as following: regarding body functions, most categories presented slight impairment. For mobility of joints and gait, the impairment was severe. Activity and participation with most significant limitations were "learning to read/write", "read/write", "listening" and "performing multiple tasks." In self-care, the main limitations were in "drinking", "taking care of body parts" and "taking care of one's health." Also, there were restrictions on "doing household tasks", "basic economic transactions", "community living" and "religion and spirituality".

Conclusion: MPS can have a significant impact in different body systems which act as limiting activities that require body mobility.

Keywords

Mucopolysaccharidosis; International Classification of Functioning, Disability and Health; Observational study.

Introduction

Mucopolysaccharidoses (MPS) are a group of rare diseases, being chronic and progressive conditions where the accumulation of glycosaminoglycans (GAGs) in tissues can lead to mobility restriction, osteoarticular alterations, hearing and language problems, which may lead to delayed neuropsychomotor development, besides neurological, cardiac and respiratory diseases[1–3]. Enzyme replacement therapy (ERT) produces statistically significant improvements in delaying symptoms in patients with MPS type I, II, IV-A and VI bringing benefits such as in Functioning experiences, by improving joint mobility, walking capacity, and pulmonary and respiratory functions[4–6]. However, changes in the functionality of these children still persist. MPS experiences in real life are affected in various manners according to individual progression.

According to the World Health Organization (WHO), Functioning refers to human experiences regarding Body Function, Body Structure, Activities, Participation and its interaction with Contextual Factors and Health Conditions[7,8]. According to the International Classification of Functioning, Disability, and Health (ICF), functioning and disability

[1] Fundação Oswaldo Cruz, Rio de Janeiro, RJ, Brasil
[2] Instituto Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brasil

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Corresponding Author:
Dafne Gandelman Horovitz. Fundação Oswaldo Cruz, Rio de Janeiro, RJ, Brasil..
Email: dafne.horovitz@iff.fiocruz.br

phenomena are supported by the Biopsychosocial Model. It, therefore, reflects the shift from an approach based only on health conditions consequences to a more inclusive and individual proposal that also incorporates activity and participation data and include contextual factors as part of functioning experiences. The ICF innovation as a universal and global health technology considers the environment - as a facilitator or as a barrier - and consequently brings enormous benefits to health care[9]. Thus, since 2001, it is possible to promote global and universal outcomes engaged in a more comprehensive point of view for rare diseases clinical assessment.

However, there are still few ICF health care initiatives to develope rare disease byopsicossocial assessment. The objective of this article is to outline the functional profile of children and adolescents with mucopolysaccharidosis from the ICF perspective in a public health service of reference in Rio de Janeiro, Brazil.

Methods

Study design, site and study population

An observational study of a case series was carried out in participants with a confirmed diagnosis of MPS, who were recruited from the medical genetics department and outpatient motor physiotherapy unit of a tertiary hospital and reference center for rare diseases in Rio de Janeiro - Brazil.

Inclusion and exclusion criteria

We selected children and adolescents with a confirmed diagnosis of MPS and who underwent enzyme replacement therapy. Those who abandoned treatment during the study or who presented conditions that modified the functioning not characteristic of MPS, like other associated syndromes verified in the physical examination, were excluded.

Outcomes

There is no validated functional assessment protocol for MPS. Since the ICF is an instrument for classifying functioning, it can be used in the description of a functional profile. The advantage is to use an instrument recognized by the WHO and bringing a universal language.

The following functioning outcomes obtained from the ICF perspective were selected: Functions and structures of the body (based on an evaluation roadmap); Activities, Participation and Environmental Factors (perception of those responsible) and Personal Factors (age, sex). Information was also collected on the type of MPS and enzyme replacement therapy (ERT).

In order to collect data on "Structure and Function of the body - related to movement", the evaluation considered in the following items: observation, inspection and palpation of bones, articulation, ligaments and fascia and muscles of body structures such as head and neck, shoulder, elbow, wrist and fingers, trunk, hip, knee, ankle and foot. Also, mobility, stability, strength and muscle tone, harmful reflexes and exteroceptive stimuli, voluntary movements such as going up and down stairs, take/put on a blouse, hairstyle, sit/stand up a chair, squat / stand up and walk were evaluated. Patients who were unable to assess muscle strength were classified in the ICF unspecified category. The assessment of ICF components by physical therapists classified patients with severe impairment (a problem present in more than 95% of the time, with an intensity that totally harms daily life), moderate (a problem present in more than 50% of the time, with an intensity that partially harms daily life), and mild (a problem that is present in less than 25% of the time, with an intensity that a person can tolerate), and no impairment or unspecified (the information is insufficient to specify the severity of the disability).

To collect data on "Activity, Participation and Environmental Factors" the perception of users and their responsibilities was used. Communication, mobility, self-care, domestic life, interpersonal relations and interactions, central areas of life, community life, social and civic life were the environmental factors that were considered as barriers or facilitators.

Data analysis and ethical aspects

Data were stored and analyzed in the Epiinfo 7.2 program, from absolute, median frequencies for quantitative variables and percentage frequencies for categorical variables. The Research Ethics Committee in Humans approved the present study under number 1827932.

Results

The whole sample of the present study was 15 patients with MPS, six females and nine males. The minimum age was 5 years and maximum of 17 years, with median age of 12 years. The median of age at diagnosis was 2 years. The most prevalent type of MPS was MPS VI (n = 6), followed by MPS IV-A (n = 4), MPS II (n = 3) and MPS I (n = 2). Regarding the duration of drug treatment, eight patients underwent enzyme replacement therapy for up to five years, and one participant has been on treatment for 10 years. Table 1 describes the study sample related to impairment on body structures. The majority presented slight impairment of body structures. Part of the participants presented moderate loss, more evident in lower limbs and spine.

Regarding Body Functions (Table 2), it should be noted that the majority did not show any impairment in motor reflex categories, involuntary motor reactions and involuntary movements. Only two users presented severe impairment in the category of mobility of the joints. The remainder was classified as mild impairment or without impairment to this function. Also the loss found in the gait pattern was quite diverse. The vast majority were classified as mild impairment, but three participants presented severe impairment and complete loss.

Table 1. Absolute frequency of children and adolescents with MPS in the Body Structures category according to the ICF (n = 15).

Body Structures	Without Injury	Mild Injury	Moderate Injury	Severe Injury	Complete Injury
Head and neck part	–	12	3	–	–
Shoulder part	2	10	3	–	–
Upper limb	3	10	2	–	–
Arm	3	10	2	–	–
Forearm	2	12	1	–	–
Hand	2	11	2	–	–
Pelvis	3	11	1	–	–
Lower member	2	9	4	–	–
Thigh	4	8	3	–	–
Leg	4	10	1	_	–
Ankle and Foot	3	8	3	1	–
Trunk	6	7	2	–	–
Spine	2	9	4	–	–
Trunk muscles	6	9	–	–	–

Table 2. Absolute frequency of children and adolescent with MPS in the Body Functions Category according to the ICF (n = 15).

Body Functions	Without Injury	Mild Injury	Moderate Injury	Severe Injury	Complete Injury
Mobility of joints	2	10	1	2	–
Stability of joints	4	9	2	–	–
Mobility of bones	3	10	2	–	–
Muscle strenght	4	10	–	–	–
Muscle tone	5	9	1	–	–
Muscle endurance	6	9	–	–	–
Motor reflexes	9	5	1	–	–
Involuntary motor reactions	12	3	–	–	–
Control of voluntary movement	6	7	2	–	–
Involuntary movement	12	2	1	–	–
Walking pattern	2	9	-	3	1
Sensations related to muscles and functions of movement	10	3	1	1	–

In the component "Activity and Participation" learning and application of knowledge in the "learn to read/write", "to hear" and "read/write" categories were the main limitations/restrictions. In the domain of general tasks and demands, the category with the most limitation/restriction was "performing multiple tasks". Overall, the communication domain was slightly affected (Table 3).

The categories that presented the greatest limitation/restriction were: "Taking care of body parts", "drinking" and "taking care of one's health". In addition, restrictions/limitations on "doing household tasks", "basic economic transactions", "community life" and "religion and spirituality" were also present. Environmental factors can act as barriers and facilitators. The facilitating factors found were family, caregivers, use of cane, walker, wheelchair and orthoses (Table 4). The terrain was the main barrier for displacement (n = 10). The physical barrier of the terrain was subdivided in presence of stairs, hill and lack of asphalt. However, lack of access to adapted transportation, incentive to activity and difficulty in seeing were also pointed as barriers to social activities and participation. Other barriers found were exclusion and / or stigma in places such as the school and in the community where they live and difficulty in accessing comprehensive health care, especially in specialized medical appointments and rehabilitation (Table 4).

Table 3. Main changes in the components Activity and Participation of children and adolescents with MPS.

Domains	Categories	Affected (n)	Not affected (n)	Not evaluated (n)
Learning and Application of knowledge	To hear	5	10	0
	Learn to read	6	9	0
	Read	6	8	1
	Learn to write	4	11	0
	Write	4	11	0
	Learn to calculate	3	11	1
	Calculate	3	11	1
	Acquire competencies	4	11	0
Tasks and general demands	Performing one task	2	13	0
	Performing multiple tasks	6	9	0
Comunication	Communicate and receive oral messages	3	12	0
	Speak	4	11	0
	Conversation	4	11	0
Mobility	Changing the basic position of the body	2	–	–
	Crouch down	3	13	0
	Sit down	2	12	0
	Maintaining body position	5	13	0
	Lifting and transporting objects	2	10	0
	Use fine hand movements	1	13	0
	Walking short distances	4	14	0
	Walking long distances	7	11	0
	Up/down	5	8	0
	Running	5	10	0
	Jumping	7	10	0
Self care	Wash up	5	10	0
	Taking care of body parts	6	9	0
	Care related to the excretion process	9	6	0
	Dress up	8	7	0
	Eating	4	11	0
	Drinking	4	11	0
	Taking care of one's health	10	5	0
Domestic life	Doing household tasks	9	6	0
Relationships and interpersonal interactions	Informal social relationships	1	14	0
	Relationships	1	5	9
Major areas of life	Schooling	1	14	0
	Basic economic transactions	15	0	0
Community, social and civic life	Community life	10	5	0
	Recreation and lesure	7	8	0
	Religion and spirituality	9	6	0

Table 4. Description of **Environmental Factors** of children and adolescents with MPS.

Barriers	Ground (hill, stairs, lack of paving), lack of adequate transportation, vision, lack of access to health services and exclusion/stigma of the disease.
Facilitators	Family, AFO*, walking stick, walker, wheelchair, caregivers, eyeglasses.

Note: AFO – ankle-foot orthosis

Discussion

The results of this study point out to the diversity of categories that presented losses, limitations, restrictions and barriers according to the model and language of the ICF. The prominent impairment in body structures with moderate to severe impairment was in the spine and lower limb structures, as already reported in the studies of Oussoren et al., Schmidt et al., Noh & Lee and Alden et al.[10–13]. Many features of multiple dysostosis, such as thoracolumbar kyphosis, scoliosis, broad oar ribs, shortened long bones, valga thigh, dysplastic femoral heads, valgus knee, and bullet-shaped phalanges are due in part to abnormal endochondral ossification[12–14], and may affect functionality primarily related to mobility. The most compromised body function was gait pattern, followed by impairment of joint mobility. The literature indicates that the gait of children with MPS is impaired by the lack of joint mobility associated with the presence of bone deformities, loss of cardiorespiratory resistance, short stature and high body weight, causing many individuals to use wheelchairs as a means of displacement[14]. The participants on this research were on ERT treatment, and one of the characteristics of this treatment is the improvement in joint mobility, which may justify the lower severity of the injuries found. However, ERT is not a curative treatment, but rather a palliative treatment with the attenuation of symptoms, slowing but not preventing disease progression[7,15–17].

Regarding the Activity and Participation components, limitations and restrictions were also observed in the domain of "learning" and "application of knowledge". In the study by Cross & Hare[18], some patients with MPS presented behavioral disorders, and the first signs were developmental delay, speech and hearing problems, trouble sleeping and fear[18]. In addition, children with MPS may present visual and / or auditory deficiencies due to the accumulation of glycosaminoglycans (GAGs) in the systems[19–21]. The involvement of self-care categories should be highlighted. Individuals with MPS have movement limitations and flexural contractures of the joints affecting especially knees, hips, elbows, wrists and fingers of the hands, leading to self-care activities impairments[22]. Rocha and colleagues emphasize in their study that the loss of muscle strength, especially in the flexor and extensor muscles of the fingers and forearm pronators and supinators, also hinders manual skills and, consequently, self-care[22].

It draws our attentions the low restriction found in the "relationships and interpersonal interactions". Despite of the limitations and restrictions, individuals with MPS in the case series studied can maintain friendly relationship with people that surround them, as already highlighted in Cross & Hare study[18]. Although in the work of Martins et al.[23] the domain religiosity/ spirituality / personal beliefs is understood as one of the coping resources for chronic disease that the adolescent uses, as well as a way to signify the disease and to confront it, being an important strategy to face the barriers and stigmata imposed by the disease. The research sample also showed participation restriction in the domain "community life" and "religion and spirituality".

Another significant finding was the constraints on "performing household chores" and "basic economic transactions" in part of the sample. This data seems to have an interplay with the works of Moreira et al.[24] and Castro & Piccinini[25] on chronic diseases in childhood. According to these authors, there seems to be an overprotection of the caretakers, who believe that their children do not have to worry about domestic or economic tasks, because they already live in a complex health situation, with treatment routines, selflessness of life situations that would be natural for a child[24,25].

Environmental factors are also an important part of the information needed to be understood in the context and the interrelationship with the presented commitments[26]. Architectural barriers in public places constitute obstacles for people with chronic diseases with mobility limitations[27], aspects consistent with MPS. However, the family is a preponderant environmental factor in the population with chronic disease's life [28,29], however it acted also as a facilitator in our results. Stigma is widely reported in children with chronic and rare diseases. Mello & Moreira[27] points out that children and adolescents with chronic diseases sense the school as a place of discrimination.

Finally, the difficulties of access to specialized medical and rehabilitation consultations also appear as barriers and are verified in the studies of Llerena Jr.[30] and Horovitz et al.[31,32]. These authors emphasize that children with genetic and rare diseases have problems such as: inadequate amount of specialized consultations available; concentration of services in large urban centers; difficulties in accessing specialized services; difficulties in being referred and counter-referred; and very few medical genetics services in the public health system.

On the relevance of ICF in the clinical evaluation scenario, although it is also a classification system, in our perspective it was used as a guiding model for the biopsychosocial evaluation of Functioning[33]. By presenting an integrative approach, it has become a global framework for rehabilitation practices and medical evoluation[34,35]. It can be used for decision making at the macro, meso and micro levels of the health sector. It is noticed that there is an imminent need of incorporating information about functionality, aiming to surpass only the oriented look to the Components of Functions and Structures of the Body. Context aspects that are still little valued in the clinical environment play a fundamental role in the context of rare diseases.

The evaluation of children with MPS was a dependent evaluator, based on their vision and knowledge/assessment of patients, which may be a limitation of the study. Thus, caution is recommended in the extrapolation of the findings and it is suggested that analytical studies, with paired evaluation to reduce the observation bias may be done.

In addition, the small sample size makes it difficult to generalize the results. However, this is an intrinsic limitation to the field of clinical study of rare diseases. Nevertheless, the operationalization of the biopsychosocial evaluation is undoubtedly a strong point of the present study that can subsidize protocols for evaluation of Functionality outcomes.

Conclusion

Individuals with MPS, even during treatment with ERT, present impairment especially in the structure of the spine and lower limbs, negatively affecting the performance of tasks such as displacement. Functioning evaluation showed that aspects acting as barriers were decisive in understanding the context of vulnerability that children and adolescents with MPS experience in low- and middle-income countries. In a scenario of rehabilitation and clinical care that is able to identify the real needs of patients with chronic and rare diseases, ICF becomes a tool capable of provoking changes in the health care culture oriented to the Biopsychosocial model.

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