ENERGY EXPENDITURE DURING GAIT IN PATIENTS WITH MUCOPOLYSACCHARIDOSIS

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ABSTRACT

Objective: The aim of this study is to evaluate energy expenditure in gait by mucopolysaccharidosis affected patients by means of a simple and adequate to the clinical environment methodology. Methods: A cross-sectional study was carried out comparing energy expenditure during gait in 19 patients suffering from mucopolysaccharidosis (MPS Group) with 19 asymptomatic control individuals (Control Group). Energy expenditure was measured in calories (cal) using a Polar telemetric watch (model FT7) during a 50 meter walk. Variables such as age, weight, height, body mass index (BMI), initial hart rate, final hart rate, and walking time, were recorded. Results: MPS Group showed a mean energy expenditure during gait of 2.84 cal (±1,01), *versus* 1.42 cal (±0,51), 100% higher than the Control Group; MPS also presented increased initial hart rate (22% higher), final hart rate (13% higher) and walking time (13% higher). Conclusions: Energy expenditure during gait in MPS patients was two times higher than control individuals; the methodology used showed to be a promising alternative, also adequate to the standard clinical environment. ***Level of Evidence III, Cross-sectional Comparative Study.***

Keywords: Mucopolysaccharidosis I. Evaluation. Gait.

INTRODUCTION

Mucopolysaccharidosis (MPS) are an heterogeneous group of lysosomal storage diseases characterized by intracellular accumulation of glycosaminoglycans (GAG), causing damage and dysfunction of various degrees in multiple organs and systems, progressive and letally.[1]

The involvement of the musculoskeletal system or "dysostosis multiplex" is a common point in all MPS.[1, 2] This involvement is characterized by osteoarticular deformities (kyphosis, scoliosis, knee valgus, equinus foot), stiff joints with loss of range of motion (MR) and upper motor neuron involvement (myelopathy, hypertonia and spasticity).[1,2]

The progression of motor manifestations such as walking ability and deambulation, sedestation, and functional independence for daily life activities, has a direct relationship with the overall clinical severity of the disease.[1-3]

Energy expenditure during gait obtained by indirect calorimetry is the gold standard for evaluating the locomotor system efficiency and could be used to assess the degree of impairment of the musculoskeletal system of patients with MPS, however, due to its characteristics, it can only be done in metabolism testing laboratories.[4] Therefore, simpler alternative methodologies have been proposed to provide estimates of energy expenditure, and the most widespread are based on the cardiac rate.[5-7] The measurement of estimated energy expenditure during gait, being an objective and simple methodology, and applicable to the clinical environment can provide a reliable indicator for the assessment of walking ability, the motor system impairment and hence the clinical severity in individuals with MPS. The aim of this study is to assess energy expenditure during gait in patients with mucopolysaccharidosis, using a simple methodology applicable to the clinical environment.

PATIENTS AND METHODS

We conducted cross-sectional study comparing the energy expenditure during gait in patients with mucopolysaccharidosis compared to asymptomatic individuals in the community. The study was approved by the institutional Research Ethics Committee; all patients or their responsible were informed of the risks and benefits of the study and signed Free Informed

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Consents. The MPS group was composed of 19 patients with mucopolysaccharidosis from the Medical Genetics Service of University Hospital Professor Edgar Santos; Faculdade de Medicina da Universidade Federal da Bahia (HUPES-UFBa). Because it is a rare disease, all patients under treatment in the Medical Genetic Unit were enrolled in the study without sample size calculation. Another 19 individuals originating from the community (from the Evangelical Church Community at Platforma neighborhood - Salvador/BA), with ages similar to MPS patients, who were evaluated by health questionnaire and considered healthy, were selected to form the Control Group. On both groups socio-demographic data were collected in a standardized way, which consisted of the following parameters: age, gender, weight, height and body mass index (BMI). In the MPS patients group data about the disease, such as clinical type of MPS, capability to daily living and walking activities, and current clinical status were also collected.

The energy consumption during gait was evaluated while conducting a 50 meters walk. This type of method is commonly recommended to evaluate the caloric cost in activities known as submaximal, in which the task performed is similar to or lower than the required tasks in daily life activities.[4,8]

All subjects in both groups were initially instructed about the test and performed a previous simulation to ensure that there was complete understanding of the task. After that, each subject was instructed to sit, rest for at least five minutes prior to the actual test. After the resting period, each subject was asked to walk 50 meters on a flat surface, at his own and most comfortable pace and speed, not being allowed to run.

In order to calculate energy expenditure during gait, the following parameters were recorded: initial heart rate (immediately after rest), heart rate at the end of the walk, and total time of the gait. These data were collected by the Polar brand telemetric digital watch (FT7 model). The estimated energy expenditure (in calories) during gait was also provided by telemetric FT7 watch, according to the parameters established by the software manufacturer, based on heart rate and anthropometric parameters.[9-11]

The data obtained from both groups were tabulated by frequency for categorical variables or mean and standard deviation for continuous variables. The comparison between groups was performed by Student's t test for continuous variables, and chi-square test when the variables were discrete. The level of 0.05 was adopted as the criterion for statistical significance in all tests.

RESULTS

All individuals in both groups understood the directions and were able to perform both the pre-test simulation and the actual test with no difficulties. Even in patients with MPS there was not any trouble for walking spontaneously at a comfortable speed. The 50 meters walk test designed to obtain energy expenditure proved to be easy to perform and efficient on the way it has been done. Thus, the data were collected without difficulties and the test performed optimally. The data referring to the MPS Group are shown in Table 1, the data for the control group are presented in Table 2; Table 3 presents the comparisons between means and standard deviations for both groups, with corresponding p values. The data obtained show that the two groups were similar according to their average age, gender and BMI: this fact validates the control group for

the study. In all other variables the two groups were statistically different. In relation to the Control Group, the MPS Group had energetic expenditure during gait 100% higher, initial heart rate 22% higher heart rate and final heart rate 13% higher, and walking time 25% higher.

Table 1. Distribution of variables in patients with mucopolysaccharidosis (MPS Group).

Patient	Age (years)	Weight (Kg)	Height (m)	BMI	Initial HR (bpm)	Final HR (bpm)	Test Time (s)	Energy Expenditure (cal)
1	19	41	1.33	23.18	75	108	50	2
2	22	33	1.15	24.95	76	135	52	3
3	21	56	1.53	23.92	78	90	65	2
4	16	32.5	1.33	18.37	116	118	56	3
5	15	31	1.37	16.52	108	113	55	4
6	13	43	1.35	23.59	82	100	49	2
7	10	24.4	1.22	16.39	115	123	38	2
8	14	16.7	1.01	16.37	110	128	60	2
9	11	15	0.91	18.11	119	139	56	4
10	15	38.5	1.37	20.51	94	114	55	2
11	12	21.3	0.96	23.11	109	149	79	3
12	10	23	1.06	20.47	104	127	75	2
13	2	15	0.97	15.94	156	163	63	5
14	7	28	1.18	20.11	90	122	58	3
15	3	15	0.92	17.72	118	125	63	2
16	4	14	0.9	17.28	140	164	98	5
17	3	14	0.94	15.84	118	134	62	3
18	9	30	1.3	17.75	115	127	83	3
19	9	18	1.11	14.61	120	128	58	2

BMI: Body Mass Index. HR: heart rate; bpm – heart beats per minute. cal: calories.

DISCUSSION

In this study, patients with mucopolysaccharidosis presented energy expenditure during gait of 2.84 cal. while the control group spent 1.42 cal. This spending account for significantly higher energy consumption and more than twice the spending of control subjects to perform the same task. The MPS patients did not differ significantly from control subjects regarding age. gender and BMI. although they differed as to height and weight. During the march, MPS patients had initial and final heart rate higher than controls and also required a longer time to perform the 50 meters walk. compared to controls. These data indicate that the heart rate of MPS patients is even greater at baseline, which influenced performance and also increased gait time. reveals that these individuals have greater difficulty in performing the task.

Table 2. Distribution of variables in healthy patients (Control Group).

Patient	Age (years)	Weight (Kg)	Height (m)	BMI	Initial HR (bpm)	Final HR (bpm)	Test Time (s)	Energy Expenditure (cal)
1	11	50	1.53	21.36	93	117	50	1
2	19	70	1.72	23.66	72	89	49	1
3	9	48	1.1	39.67	89	125	46	2
4	8	52	1.42	25.79	83	122	52	2
5	10	39	1.35	21.40	83	122	49	2
6	16	45	1.6	17.58	83	103	51	1
7	12	39	1.52	16.88	96	112	43	1
8	7	32	0.9	39.51	94	107	51	2
9	10	32	1.47	14.81	98	125	55	1
10	18	66	1.68	23.38	75	88	49	1
11	10	27	1.4	13.78	92	116	48	2
12	11	40	1.4	20.41	88	118	51	2
13	8	33	1.29	19.83	92	119	47	1
14	9	40	1.28	24.41	90	119	49	1
15	11	45	1.52	19.48	90	103	48	1
16	12	47	1.55	19.56	83	112	51	2
17	11	36	1.48	16.44	88	113	52	1
18	10	33	1.42	16.37	99	116	50	2
19	17	65	1.66	23.59	82	96	49	1

BMI: Body Mass Index. HR: heart rate; bpm – heartbeats per minute. cal: calories.

Table 3. Variable distribution on individuals from both MPS and Control Groups.

Variables	MPS Group	Control Grupo	P
Age (years)	11.32(5.95)	11.53(3.47)	0.895
Gender			0.313
Male	10	14	
Female	9	5	
Weight (Kg)	26.81(11.85)	44.16(12.23)	0.000
Height (m)	1.15(0.20)	1.44(0.20)	0.000
BMI	19.20(3.21)	21.99(7.05)	0.125
Initial HR (bpm)	107.53(21.32)	87.89(7.26)	0.000
Final HR (bpm)	126.68(18.79)	111.68(11.25)	0.005
Test time (s)	61.84(13.74)	49.47(2.57)	0.000
Energy Expenditure (cal)	2.84(1.01)	1.42(0.51)	0.000

BMI: Body Mass Index. HR: heart rate. bpm – heartbeats per minute. cal: calories.

Being a multisystemic disease, MPS presents both locomotor and cardiopulmonary impairment. These patients, therefore, have ambulation difficulties associated with decreased vital and functional capacity. The higher baseline heart rate clearly reflects the decreased cardiopulmonary (vital) capacity. while the longer gait time reflects the limited motor skills.

The relationship of energy expenditure during walking with the integrity of the locomotor system, with the overall functional capacity and efficiency to perform activities of daily living are defined in literature.[8] Studies involving energy expenditure during gait have been used by several authors with the purpose of measuring the severity of clinical manifestations and responses to treatment. especially in diseases that affect the cardiorespiratory system.[5]

MPS patients present a musculoskeletal profile characterized by stiffness and joint deformities that incapacitate and prevent normal gait. This fact alone would already be able to justify higher caloric expenditure during gait.[1,2] However, beyond the osteoarticular deformities. MPS patients present important clinical systemic complications such as upper airway obstruction, hepatosplenomegaly, cardiopulmonary disease, hydrocephalus and medular compression.[12,13] These comorbidities decrease vital capacity, further increasing the energy consumption baseline and subsequent caloric expenditure in physical activities of daily life.[14] The energy expended during walking, therefore, represents an indicator of overall physiological and clinical motor efficiency in these patients.

This hypothesis is supported by results from clinical trials that evaluated improvement in MPS treatment with enzyme replacement therapy. In these studies the motor and functional ability of the patients was assessed by six or 12 minutes walking tests to evaluate the distance the patient is able to walk in these times respectively. Based on this test, it was confirmed that the performance of patients with mucopolysaccharidosis was directly related to the severity of the impairment and that the treatment was able to improve the performance on the tests as the clinical profile improved.[12,15]

Although the 12 (or six) minutes' walk test 12 is a good method for evaluating the cardiopulmonary system and show good correlation (r = 0.73) with oxygen consumption in patients with

pulmonary disease[16] this test has some limitations for patients with mucopolysaccharidosis. The performing is difficult for patients and examiners; also many patients do not support an exercise burden for a period equal to or greater than 6 minutes.[14] the test can potentially trigger cardiopulmonary disorders during its execution, especially in patients with resting heart rate higher that 120bpm[17]; there is also lack of standard reference values for different ages and genders. which makes it difficult to compare the values obtained in clinical tests.[18]

The estimated energy expenditure using Polar telemetric based on heart rate and anthropometric data has been used with satisfactory results.[10,11,19] This method has also been shown to have good correlation with measurements of indirect calorimetry (oxygen consumption) in low and moderate intensity activities ($r = 0.80$ and $r = 0.95$).[19] The assessment of energy expenditure during gait measured by Polar® monitor showed to be simple, safe and applicable to the clinical environment.

CONCLUSIONS

The present study was able to show that the energy expenditure during gait in patients with mucopolysaccharidosis is higher compared to asymptomatic individuals, being twice as high. This result is probably related to the clinical status of patients who produces increased physiological expenditure baseline. The used methodology besides being unique for MPS, has shown to be efficient and can, therefore, be used in common clinical environments as an indicator of the severity of functional and motor impairment in this patient group.

REFERENCES

1. Neufeld EF, Muenzer J. The mucoplysaccharidoses. In: Scriver CR, Beaudet AL, Sly WS, Valle D, Childs B, Kinzler KW, Vogelstein B, editors. The metabolic and molecular bases of inherited disease. 8th ed. New York: McGraw-Hill; 2001. p. 3421–52.
2. Valayannopoulos V, Nicely H, Harmatz P, Turbeville S. Mucopolysaccharidosis VI. Orphanet J Rare Dis. 2010;5:5.
3. Wraith JE, Scarpa M, Beck M, Bodamer OA, De Meirleir L, Guffon N, et al. Mucopolysaccharidosis type II (Hunter syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr. 2008;167(3):267-77.
4. Boyd R, Fatone S, Rodda J, Olesch C, Starr R, Cullis E, et al. High- or low-technology measurements of energy expenditure in clinical gait analysis? Dev Med Child Neurol. 1999;41(10):676-82.
5. Fredrickson E, Ruff RL, Daly JJ. Physiological Cost Index as a proxy measure for the oxygen cost of gait in stroke patients. Neurorehabil Neural Repair. 2007;21(5):429-34
6. Bailey MJ, Ratcliffe CM. Reliability of physiological cost index measurements in walking normal subjects using steady-state, nonsteady state, and post-exercise heart rate recording. Physiotherapy. 1995;81:618-23.
7. Mossberg KA. Reliability of a timed walk test in persons with acquired brain injury. Am J Phys Med Rehabil. 2003;82(5):385-90.
8. Cunha IT, Lim PA, Henson H, Monga T, Qureshy H, Protas EJ. Performance-based gait tests for acute stroke patients. Am J Phys Med Rehabil. 2002;81(11):848-56.
9. Electro Polar S410™/S210™ Heart Rate Monitor User's Manual. Woodbury, NY: Polar Electro, Inc.; 2002. p. 63–70.
10. Crouter SE, Albright C, Bassett DR Jr. Accuracy of polar S410 heart rate monitor to estimate energy cost of exercise. Med Sci Sports Exerc. 2004;36(8):1433-9.
11. Erdogan A, Cetin C, Karatosun H, Baydar LM. Accuracy of the Polar S810i heart rate monitor and the Sensewear Pro Armband to estimate energy expenditure of indoor rowing exercise in overweight and obese individuals. J Sports Sci Med. 2010; 9:508-16.
12. Harmatz P, Ketteridge D, Giugliani R, Guffon N, Teles EL, Miranda MC, et al. Direct comparison of measures of endurance, mobility, and joint function during enzyme-replacement therapy of mucopolysaccharidosis VI (Maroteaux--Lamy syndrome): results after 48 weeks in a phase 2 open-label clinical study of recombinant human N-acetylgalactosamine 4-sulfatase. Pediatrics. 2005;115(6):e681-9.
13. Giugliani R, Harmatz P, Wraith JE. Management guidelines for mucopolysaccharidosis VI. Pediatrics. 2007;120(2):405-18.
14. Reybrouck T. Clinical usefulness and limitations of the 6-minute walk test in patients with cardiovascular or pulmonary disease. Chest. 2003;123(2):325-7.
15. Muenzer J, Wraith JE, Beck M, Giugliani R, Harmatz P, Eng CM, et al. A phase II/III clinical study of enzyme replacement therapy with idursulfase in mucopolysaccharidosis II (Hunter syndrome). Genet Med. 2006;8(8):465-73.
16. Cahalin L, Pappagianopoulos P, Prevost S, Wain J, Ginns L. The relationship of the 6-min walk test to maximal oxygen consumption in transplant candidates with end-stage lung disease. Chest. 1995;108(2):452-9.
17. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111-7.
18. Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. Phys Ther. 2002;82(2):128-37.
19. Cole PJ, LeMura LM, Klinger TA, Strohecker K, McConnell TR. Measuring energy expenditure in cardiac patients using the Body Media Armband versus indirect calorimetry. A validation study. J Sports Med Phys Fitness. 2004;44(3):262-71.