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Center of gravity oscillations in HTLV-1-associated myelopathy/tropical spastic paraparesis

Oscilações do centro de gravidade na mielopatia associada ao HTLV-1/ paraparesia espástica tropical

Oscilaciones del centro de gravedad en la mielopatía asociada al HTLV-1/paraparesia espástica tropical

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Abstract

Introduction: Postural control in individuals with HTLV-1-associated myelopathy or tropical spastic paraparesis (HAM/TSP) is usually compromised, which increases the risk of falls, makes it difficult to perform activities of daily living, and impairs the quality of life. The profile of the center of gravity oscillations in this population is unknown and may aid in clinical follow-up and research. **Objective:** To compare the stabilometric values between HAM/TSP and uninfected individuals and verify the existence of correlations between stabilometric variables and the Berg Balance Scale (BBS). **Method:** A cross-sectional observational study was performed with infected individuals, classified as defined and likely (WHO criteria), compared to accompanying persons

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and seronegative relatives. A baropodometry platform (Footwork®) was used to obtain the oscillation values of the body's center of gravity in total oscillation area (TOA), anterior-posterior oscillation (APO) and lateral oscillation (LO). Mean values were correlated with BBS by Spearman's Correlation (5% alpha). Approved by the ethical committee of Escola Bahiana de Medicina e Saúde Pública under Opinion 49634815.2.0000.5628. **Results:** An asymmetric distribution of all the stabilometric variables analyzed in the HAM/TSP population was found, different from the uninfected group (p < 0.05). It was also possible to verify strong to moderate and inverse correlations between the variables of center of gravity oscillation with the scores obtained in BBS, especially for TOA and LO. **Conclusion:** People with HAM/TSP presented higher values for the center of gravity oscillations and these were correlated with the BBS in the balance evaluation.

Keywords: Postural Balance. Automatic Control. Motor Activity. Paraparesis, Tropical Spastic. Human T-Lymphotropic Virus 1.

Resumo

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Introdução: o controle postural em indivíduos com mielopatia associada ao HTLV-1 ou paraparesia espástica tropical (HAM/TSP) é geralmente comprometido, o que aumenta o risco de quedas, dificulta a realização de atividades de vida diária e prejudica a qualidade de vida. O perfil das oscilações do centro de gravidade nesta população é desconhecido e pode auxiliar no acompanhamento clínico e na pesquisa. **Objetivo:** comparar os valores estabilométricos entre pessoas com HAM/TSP e não infectados, e verificar a existência de correlações entre variáveis estabilométricas e a Escala de Equilíbrio Berg (EEB). Método: foi realizado um estudo observacional transversal com indivíduos infectados, classificados como definidos e prováveis (critérios da OMS), comparados com acompanhantes e familiares soronegativos. Uma plataforma de baropodometria (Footwork®) foi utilizada para obter os valores de oscilação do centro de gravidade do corpo em área de oscilação total (AOT), oscilação anteroposterior (OAP) e oscilação laterolateral (OLL). Os valores médios foram correlacionados com a BBS pela Correlação de Spearman (alfa 5%). Aprovado pelo Comitê de Ética da Escola Bahiana de Medicina e Saúde Pública sob o CAAE 49634815.2.0000.5628. Resultados: encontrouse distribuição assimétrica de todas as variáveis estabilométricas analisadas na população com HAM/TSP, diferentes do grupo de não infectados (p < 0,05). Também foi possível verificar correlações de forte a moderada e inversas entre as variáveis de oscilação do centro de gravidade com os escores obtidos na EEB, especialmente para AOT e OLL. Conclusão: Pessoas com HAM/TSP apresentaram valores maiores para as oscilações do centro de gravidade e estas foram correlacionadas com a EEB na avaliação do equilíbrio.

Palavras-chave: Equilíbrio Postural. Controle Automático. Atividade Motora. Paraparesia Espástica Tropical. Vírus Linfotrópico T Humano 1.

Resumen

Introducción: El control postural en individuos con mielopatía asociada al HTLV-1 o paraparesia espástica tropical (HAM/TSP) suele estar comprometido, lo que aumenta el riesgo de caídas, les dificulta en las actividades de la vida diaria y perjudica su calidad de vida. Conocer el perfil de las oscilaciones del centro de gravedad en esta población puede ayudar en el seguimiento clínico y la investigación. **Objetivo:** Comparar los valores estabilométricos entre personas con HAM/TSP y personas no infectadas, y verificar la existencia de correlaciones entre las variables estabilométricas y la Escala de Equilibrio de Berg (BBS). Método: Se realizó un estudio observacional transversal con individuos infectados, clasificados como definidos y probables (criterios de la OMS), comparados a acompañantes y familiares seronegativos. Se utilizó una plataforma de baropodometría (Footwork®) para obtener los valores de oscilación del centro de gravedad del cuerpo en el área de oscilación total (AOT), oscilación antero-posterior (OAP) y oscilación lateral-lateral (OLL). Los valores medios se correlacionaron con la BBS por la correlación de Spearman (alfa 5%). Estudio aprobado por el Comité de Ética de la Escuela Bahiana de Medicina y Salud Pública bajo CAAE 49634815.2.0000.5628. Resultados: Se encontró una distribución asimétrica de todas las variables estabilométricas analizadas en la población HAM/TSP diferente en el grupo no infectado (p <0,05). También fue posible verificar correlaciones de fuertes a moderadas e inversas entre las variables de oscilación del centro de gravedad con las puntuaciones obtenidas en la BBS, especialmente para AOT y OLL. Conclusión: Las personas con HAM/TSP presentaron valores más altos en las oscilaciones del centro de gravedad, las cuales se correlacionaron con la BBS en la evaluación del equilibrio.

Palabras clave: Balance Postural. Control Automático. Actividad Motora. Paraparesia Espástica Tropical. Virus Linfotrópico T Tipo 1 Humano.

Introduction

The human T-cell lymphotropic virus (HTLV) infection is a sexually transmitted disease contracted by unprotected sex, breastfeeding, blood transfusion, and sharing of contaminated needles [1]. It is estimated that, in the world, approximately 5 to 10 million people are infected with the HTLV [2]. The virus infection does not have a uniform distribution, affecting mainly people in Japan, Caribbean, South and Central America, Equatorial Africa, Middle East and Melanesia [3]. In Brazil, the city of Salvador has the highest prevalence in the country, affecting 1.7% of population [4].

In most of the cases, infected persons remain asymptomatic. However, about 0.25% to 3% of infected individuals develop HTLV-1-associated myelopathy or tropical spastic paraparesis (HAM/TSP) [5]. This is described as a neurological condition that leads the spinal cord to progressive demyelination [6]. Among other symptoms, HAM/TSP causes motor and sensory dysfunction. This condition can result in the loss of proprioception and balance that directly impacts the performance of daily life activities (DLAs) [7] and increases the risk of falls [8].

It is recognized that HAM/TSP is associated with postural instability due to the spastic pattern affecting the lower limbs [5, 9]. The Berg Balance Scale (BBS) applied in people with HAM/TSP found values that were much lower than those found in elderly people with the Parkinson's disease and with sequelae of cerebrovascular accidents [10]. BBS is an examiner-dependent scale that takes an average of 30 minutes to be implemented; it is, therefore, difficult to standardize parameters to monitor and understand the balance profile in this population [11].

The baropodometry powder has been applied in people with HAM/TSP to evaluate the pattern of load and pressure on their feet [9]. Baropodometry can also be used to evaluate control and postural balance through the analysis of the area and trajectory of the gravity center (GC) in the standing posture [12]. This study aims to compare the stabilometric values between individuals with HAM/TSP and the ones that are uninfected; thus, allowing for a better understanding of the postural control in individuals with HAM/TSP and producing information for the longitudinal monitoring of this population.

Methods

This cross-sectional study was developed using data from the baseline of a randomized clinical trial that was held in a reference center of multidisciplinary assistance ambulatory in Salvador, Bahia, Brazil. Data were collected from April to October 2016 during the training time. The study followed the recommendations contained in Resolution 466/12 of Ministry of Health, and was approved by the Research Ethics Committee of the Catholic University of Salvador under the Opinion 49634815.2.0000.5628. Every participant signed the informed consent term according to Helsenki recommendations. To minimize the risk of leakage of confidential information from the research participants, data was saved in a computer stored in a room with restricted access to the researchers.

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Participants were recruited through a call in social networks and from the "HTLVida" patients association. They confirmed that they have had previous diagnosis of HAM/TSP presenting clinical reports from an expert neurologist. The participants were ranked as confirmed and probable to HAM/TSP according to the guidelines of the World Health Organization (WHO) [13], without any other neurologic diseases that could confuse the findings as diabetes neuropathy, vestibular syndromes, multiple sclerosis, stroke or Parkinson disease. According to these criteria, people classified as probable or confirmed for HAM/TSP present spasticity, Babinski signal, walking difficult, legs tangled, often falls, stiffness and numbness in the legs. They confirmed the diagnostic by Elisa, Western Blot tests, liquor with virus and magnetic resonance with lesions. The exclusion criteria were incomplete report, cognitive difficult to understand verbal commands and inability to stand for 20 seconds without auxiliary devices to the baropodometry. Participants were also recruited for a co-operative group, and matched by sex and age, family members, companions of the participants, seronegative volunteers and people with no neurologic disorders according to the expert neurologist responsible for clinical follow-up of patients and their families. Data collection was executed in a private environment.

Each participant was instructed to remain for 20 seconds in the bipedal support, breathing normally with a horizontal stare, without speaking or grinding

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their teeth on a Footwork[®] baropodometry platform [14]. The platform was connected to a computer with a special software or device that was installed to capture the beginning of commands and to complete

the evaluation. The analysis lasted for an average of 2 minutes and provided the values of total oscillation area (TOA), anterior-posterior oscillation (APO) and lateral oscillation (LO) for each person (Figure 1).



Figure 1 – Records of center of gravity of Footwork ® baropodometry platform. Source: Saran [15].

The baropodometry platform consists of a rigid base with dimensions of 465 mm × 520 mm × 25 mm, with 4,098 capacitive pressure sensors measuring 7.62 mm × 7.62 mm. The pressure sensors registered up to 120 N.cm of pressure each and are arranged in an area of 490 mm × 490 mm of active surface, which allows for an analysis of the pressure discharge in kilogram-force/cm² (kgf/cm²) and contact time of the foot with the soil (plantar surface in cm²) in the static standing position. This equipment consists of a 16-bit converter and a sampling frequency of 200 Hz.

Berg Balance Scale (BBS) was applied by the same examiner, followed by the recommended criteria of Miyamoto et al. and Fonseca et al. [11, 16]. This instrument consists of fourteen activities, for which scores are assigned from 0 to 4 per item and have a maximum value of 56 points. For the full realization of the activities, a digital timer was required as requested by items 2, 3 and 6. The score obtained by each participant was recorded on a standard plug. The application of all the topics of this scale was performed in 30 minutes per participant, being allowed the use of walking aids.

According to the sample calculation, performed with WinPepi software, which took as reference the

results obtained by Toosizadeh et al. [17] in a study with diabetic neuropathy peripheral blood pressure, assuming a standard deviation of 2.79 in group A and 0.76 in group B, difference to be detected equal to 3, significance equal to 5% and study power equivalent to 95%. Fourteen participants were necessary in each group.

Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0 for Windows. Numerical sociodemographic data was described in the mean and standard deviation in cases which the distribution was normal, and in the median and interquartile range, in which there was no normal distribution. The homogeneity between groups was verified by unpaired Student's t-test, accepting as homogeneous comparisons in which p > 0.05. The categorical variables were expressed in absolute numbers and percentages, and the homogeneity was verified for the sex variable through Fisher's exact test, assuming p > 0.05.

Stabilometric variables were expressed as mean and interquartile range because of their asymmetric distribution; the difference between the stabilometric variables between the groups was verified using the Mann-Whitney test. The Spearman Correlation test was used to verify the correlations between the stabilometric values and the BBS score. Data was considered statistically significant when p < 0.05.

Results

The homogeneous sample consisted of 28 participants, 14 with HAM/TSP and 14 without in comparison with the age of 51.43 ± 9.59 and 49.21 ± 9.12 , respectively (Table 1). The sample of

people with HAM/TSP was characterized by spasticity in lower limbs, posture presenting knee and hip flexion, difficulty with gait and using walking aids. 5

It was also possible to verify statistical difference between the stabilometric variables in two groups (Table 2).

Moderate to strong correlations were observed between the negative stabilometric measures and the BBS, in which the test group HAM/TSP presented average values of 38.86 ± 10.32 (Table 3).

Table 1 – Sociodemographic profile of HAM/TSP and uninfected individuals and homogeneity assessment between groups. Salvador-BA, Brazil, 2016 (n = 28)

Cosiedomographic veriebles	Individuals with HAM/TSP ($n = 14$)	Uninfected individuals ($n = 14$)	n valua	
Sociodemographic variables	Mean (± SD)	Mean (± SD)	p-value	
Age (years)	51.43 (± 9.59)	49.21 (± 9.12)	0.54 ¹	
Weight (kg)	62.81 (± 13.12)	69.41 (± 13.35)	0.20 ¹	
Height (m)	1.61 (± 0.07)	1.64 (± 0.09)	0.25 ¹	
Sex	Frequency (%)	Frequency (%)		
Female	9 (64.3)	11 (78.6)	0.68 ²	
Skin color ³				
Black	7 (50)	4 (28.6)		
Brown	6 (42.9)	7 (50)		
White	0 (0)	2 (14.3)		
Indigenous	0 (0)	1 (7.1)		
Yellow	1 (7.1)	0 (0)		

Note: ¹ Unpaired T-test; ² Fisher's exact test; ³ Skin color according to the Brazilian Institute of Geography and Statistics (IBGE); SD: standard deviation; kg: kilogram; m: meters.

Table 2 – Comparison of the stabilometric variables of individuals with and without HAM/TSP. Salvador-BA, Brazil, 2016 (n = 28)

Variables	Individuals with HAM/TSP ($n = 14$)	M/TSP (n = 14) Uninfected individuals (n = 14)	
	Median (IQI)	Median (IQI)	p-value
TCO-GC (cm ²)	4.15 (2.23-15.49)	0.99 (0.63-2.48)	0.004
APO-GC (cm)	2.83 (2.14-3.78)	1.65 (1.29-2.23)	0.022
LO-GC (cm)	1.77 (0.98-5.50)	0.77 (0.59-1.31)	0.002

Note: TCO-GC: Total center of oscillation gravity area; APO-GC: Anterior-posterior oscillation of the gravity center; LO-GC: Lateral oscillation of the gravity center. Mann-Whitney test (5% alpha).

Table 3 – Correlation of the Berg Balance Scale (BBS) with the stabilometric variables of individuals with HAM/TSP. Salvador-BA, Brazil, 2016 (n = 14)

Stabilometric variables	Berg Balance Scale (BBS) R	p-value
TCO-CG	-0.751	0.002
APO-CG	-0.599	0.024
LO-CG	-0.722	0.004

Note: TCO-CG: Total gravity center of oscillation area; APO-CG: Anterior-posterior oscillation of the gravity center; LO-CG: Lateral oscillation of the gravity center. Spearman Correlation test (5% alpha).

Discussion

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According to the results of this study, it was possible to verify a difference between all the values of the stabilometric variables presented by the HAM/TSP group and the uninfected individuals. The anterior-posterior, lateral, and total oscillations areas were significantly greater in individuals with HAM/TSP. Stabilometric variables were moderately to strong correlated with BBS.

The corticospinal tracts were the most affected by demyelination and axonal degeneration due to myelopathy [18-20]. They are the main responsible for voluntary motricity [19]. Recent studies [6, 21, 22] have pointed to the involvement of the spinal cord and the brain in the loss of postural control. The loss of postural control may have its origin in the suprasegmental system. Kandel [23] emphasizes the importance of the motor cortex-controlled anticipatory mechanisms for the maintenance of GC within the support polygon.

The maintenance of GC in the bipedal support position depends on the mechanisms of readjustment caused by counterbalancing movements to any unexpected motor stimulus [24]. The involvement of the spinocerebellar and gracilis tracts responsible for the regulation of proprioception [25] in persons with HAM/TSP may be another interference factor in the maintenance of GC in the limits of the support base.

Some of the results presented in this study point to an asymmetric distribution of stabilometric variables in HAM/TSP individuals. The lack of a specific pattern of body GC oscillation in this population may be related to the evolutionary pattern of HAM/TSP. The progression of the disease is not linear in the affected individuals and cannot be explained by the pro-viral load [6]. People with different degrees of evolution [20] may have different levels of oscillations [26]. However, even the comparative group of uninfected people did not present an oscillatory pattern for GC. It is likely that the sample size was insufficient to demonstrate patterns of a quantitative variable that was too susceptible to modifications.

TCO, APO and LO values presented about people with HAM/TSP are above those obtained in the uninfected population, and are lower when compared with individuals with multiple sclerosis (MS) [25-27], a neurodegenerative condition with similar characteristics to HAM/TSP. It is important to note that the values obtained in the two populations cannot be used to generalize the trend owing to few studies executed so far [23]. It is noted that the GC oscillation variables involving other populations showed, in similar studies, an asymmetric distribution, which is similar to the present data [11, 28]. The absence of a definite oscillatory pattern may lead to a conflict between different health conditions.

It was verified that LO has greater correlation strength with BBS compared to the APO. Considering the relationship between equilibrium strategies and stabilometric variables [29], we can suggest that the magnitude of GC oscillation in this population is superior to the body's ability to respond with the ankle strategy [16, 30, 31]. In this case, the hip is used for a better performance of activities that require balance.

Because of the reduced sample size, it was not possible to perform a regression model to identify which factors, including the level of integrity of the sensory system, have more influence on the values found in the stabilometry. Despite the collection of information regarding the occurrence or absence of falls in the participants, the results were heterogeneous, making it difficult to obtain a cutoff point between the stabilometric variables and the Berg scale for the outcome of risk of falls [16].

The results demonstrate that baropodometry is an instrument that can be applied both in clinical practice and in researches for the evaluation of GC oscillations. The instrument can be used to study the corporal balance with a shorter application time. In addition, it provides quantitative data that is more easily comparable in follow-up studies. Longitudinal studies may help to establish the cutoff point to assess the risk of falls by the baropodometry and BBS for the population. The higher the LO, the greater is the probability of utilizing the hip strategy, which is the desired result that may support the formulation of more specific therapeutic protocols for the balance deficit treatment in this population.

Conclusion

We conclude that HAM/TSP persons have different profiles in the stabilometric analysis and larger GC oscillations compared to the uninfected individuals. Inverse correlation was observed between the variables and stabilometric BBS score in the population, TCO and LO being the most correlated variables.

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