

Fatigue and Oropharyngeal Dysphagia in Patients with Multiple Sclerosis

Fadiga e Disfagia Orofaringea em Pacientes com Esclerose Múltipla

Fadiga y Disfagia Orofaringea en Pacientes con Esclerosis Múltiple

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Abstract

Multiple Sclerosis is a disease that affects the Central Nervous System, it is prevalent in women and its evolution and the severity of symptoms are variable, affecting each individual differently. Clinical manifestations depend on the location of the lesion and tissue injury and patients may present a series of symptoms, including fatigue and dysphagia. Fatigue in Multiple Sclerosis is multidimensional, and dysphagia is one of the symptoms that can be linked to fatigue. **Objective:** To identify and correlate symptoms of fatigue and risk of dysphagia in patients with Multiple Sclerosis. **Methods:** Descriptive cross-sectional study in which patients with a diagnosis of Multiple Sclerosis treated at the Neurology Department of a University Hospital were included. Patients were assessed using the MFIS-BR scale and the DYMUS-BR questionnaire related to fatigue and swallowing, respectively. **Results:** 74 patients were included. There was a prevalence of females (56.8%) and age over 60 years (95.9%). The most frequent form of Multiple Sclerosis was Relapsing-Remitting (81.1%), the risk of dysphagia was identified in 19 patients (25.7%) and the presence of fatigue symptoms in 32 patients (43.2%). There was a positive and weak correlation between fatigue symptoms and risk of dysphagia ($r < 0.5$). **Conclusion:** Although

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Authors' contributions:

AASL: data collection and study outline.

MFG and JAN: study outline and critical review.

EHMA: study design; methodology; study outline, critical review and guidance.

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weak, there was a positive correlation between fatigue symptoms and risk of dysphagia. The greater the degree of fatigue, the greater the risk of changes in swallowing.

Keywords: Multiple Sclerosis; Fatigue; Deglutition Disorders.

Resumo

A Esclerose Múltipla é uma doença que afeta o Sistema Nervoso Central, é prevalente em mulheres e tanto sua evolução como a gravidade dos sintomas são variáveis, acometendo de forma diferente cada indivíduo. As manifestações clínicas dependem da localização da lesão e da lesão tecidual e os pacientes podem apresentar uma série de sintomas, dentre eles destacam-se a fadiga e a disfagia. A fadiga na Esclerose Múltipla é de natureza multidimensional e a disfagia é um dos sintomas que pode estar ligado à fadiga. **Objetivo:** Identificar e correlacionar sintomas de fadiga e risco de disfagia em pacientes com Esclerose Múltipla. **Métodos:** Estudo do tipo transversal descritivo no qual foram incluídos pacientes com diagnóstico de Esclerose Múltipla atendidos no ambulatório de Neurologia de um Hospital Universitário. Os pacientes foram avaliados por meio da escala MFIS-BR e do questionário DYMUS-BR relacionados à fadiga e deglutição, respectivamente. **Resultados:** Foram incluídos 74 pacientes. Houve prevalência do sexo feminino (56,8%) e idade maior que 60 anos (95,9%). A forma da esclerose múltipla mais frequente foi a Remitente-recorrente (81,1%), o risco de disfagia foi identificado em 19 pacientes (25,7%) e a presença de sintomas de fadiga em 32 pacientes (43,2%). Houve correlação positiva fraca entre sintomas de fadiga e risco de disfagia ($r < 0,5$) **Conclusão:** Embora fraca, houve correlação positiva entre sintomas de fadiga e risco de disfagia. Quanto maior o grau da fadiga, tanto maior pode ser o risco de alterações da deglutição.

Palavras-chave: Esclerose Múltipla; Fadiga; Transtornos de Deglutição.

Resumen

La Esclerosis Múltiple es una enfermedad que afecta el sistema nervioso central, prevalece en las mujeres y tanto su evolución como la gravedad de los síntomas son variables y afectan a cada individuo de manera diferente. Las manifestaciones clínicas dependen de la ubicación de la lesión y la lesión del tejido y los pacientes pueden presentar una serie de síntomas, entre los que se destacan la fatiga y la disfagia. La fatiga en la Esclerosis Múltiple es de naturaleza multidimensional y la disfagia es uno de los síntomas que pueden estar relacionados con la fatiga. **Objetivo:** identificar y correlacionar síntomas de fatiga y riesgo de disfagia en pacientes con Esclerosis Múltiple. **Métodos:** estudio descriptivo de corte transversal en el que se incluyeron pacientes con diagnóstico de Esclerosis Múltiple tratados en la clínica ambulatoria de neurología de un hospital universitario. Los pacientes fueron evaluados utilizando la escala MFIS-BR y el cuestionario DYMUS-BR relacionados con la fatiga y la deglución, respectivamente. **Resultados:** se incluyeron 74 pacientes. Hubo una prevalencia de mujeres (56.8%) y mayores de 60 años (95.9%). La forma más frecuente de Esclerosis Múltiple fue la remisión recurrente (81.1%), el riesgo de disfagia se identificó en 19 pacientes (25.7%) y la presencia de síntomas de fatiga en 32 pacientes (43.2%). Hubo una correlación positiva débil entre los síntomas de fatiga y el riesgo de disfagia ($r < 0.5$). **Conclusión:** Aunque débil, hubo una correlación positiva entre los síntomas de fatiga y el riesgo de disfagia. Cuanto mayor es el grado de fatiga, mayor es el riesgo de cambios en la deglución.

Palabras clave: Esclerosis Múltiple; Fatiga; Trastornos de Deglución.

Introduction

Multiple sclerosis (MS) is a neuroinflammatory and neurodegenerative progressive disease that affects the Central Nervous System (CNS). MS is currently classified in the group of autoimmune diseases, in which the immune response is directed against antigens in the myelin sheath, leading to degradation¹⁻³.

About 2.3 million people worldwide have the disease according to the Multiple Sclerosis International Federation, with a prevalence twice as high in women than in men aged between 20 and 45 years old^{4,5}. The progression, severity and symptoms of the disease are variable and affect each individual differently. On the one hand, the progressive forms of MS may be more related to axonal destruction, but, on the other hand, the recurrent-relapsing (RRMS) forms may be more related to demyelination of the myelin sheath, leading to a variety of symptoms⁶. The recurrent-relapsing form is the most common, in which outbreaks last days or weeks, with remission of symptoms⁷.

Clinical manifestations depend on the location of the lesion and the extent of tissue destruction. Therefore, patients may experience pain, motor incoordination, optical changes, sensitivity disorders, bladder and intestinal control problems, depression, muscle weakness and fatigue. The latter two are the most frequent, in addition to dysarthrophonia in different degrees, characterized by respiratory, articulatory and laryngeal hypofunction, vestibular changes and dysphagia^{8,9}.

Fatigue in MS has a multidimensional nature, as it is related to primary mechanisms linked to the inflammatory process, dysfunction of the neuroendocrine axis, changes in the activation of the cerebral cortex and to secondary mechanisms such as sleep disorders, anxiety, depression, among others¹⁰. Fatigue patients have a higher burden of injury and gray and white matter atrophy when compared to those without fatigue. Axonal dysfunction is also directly linked to fatigue in MS¹¹.

Dysphagia is usually expressed when there is an involvement of the corticobulbar connections or tracts, cerebellum, brain stem and lower nerves^{12,13}. It reflects a varied symptomatology that is characterized by fatigue during feeding, presence of stasis, increased time of oral transit, penetration and/or aspiration (audible or silent), oral disorders, among others, and they can also be completely asymptom-

atic^{9,14}. The incidence of dysphagia in individuals with MS is estimated between 33 and 43%, and it is more frequent in those with the disease in a more advanced stage. However, dysphagia may also occur in patients with a lower level of impairment¹⁴.

Although the signs and symptoms of dysphagia are not always noticed by individuals with MS, the recognition helps in the early identification of the risk of dysphagia by health professionals, since it attenuates or eliminates its complications, such as dehydration, malnutrition and bronchoaspiration, pulmonary complications and death¹⁵.

Although impaired functions are not restored, much can be done so that patients can be independent and have a better quality of life. Therefore, it is essential to use reliable tools for screen and measure the risk of changes that may be related to MS^{16,17}. The presence of the fatigue as a symptom and its severity may be related to the disease progression and, hence, to changes in the swallowing biomechanics, although little studied in the literature. Thus, this study aimed to identify and correlate symptoms of dysphagia and fatigue in patients with MS.

Material and methods

This is a cross-sectional, descriptive study that was evaluated and approved by the Research Ethics Committee, of the institution, under the opinion no. 2.441.152 and CAAE no. 74967617.0.0000.5071. All participants signed the Free Prior Informed consent.

Data collection was conducted from December 2017 to September 2018, at the neurology outpatient clinic in a University Hospital. The study included patients diagnosed with MS, without gender or age restrictions, who were capable to respond to the protocols used and who were being followed up at the institution's neurology outpatient clinic. Patients with another concomitant neurological disease, with no interest or availability to participate in the study were excluded.

The patients' clinical and demographic data, as well as from their Kurtzke Expanded Disability Status Scale (EDSS) Total Score, were identified through medical records. Then, while waiting for medical assistance, the participants answered the MFIS-BR scale (Modified Fatigue Impact Scale)¹⁸ and the DYMUS-BR questionnaire (Questionnaire for the Assessment of Dysphagia in Multiple Sclerosis).

rosis)^{19,20}, which is validated at internal consistency and test-retest reliability of the DYMUS questionnaire (DYSphagia in MULTiple Sclerosis)²¹. Both instruments are specific to the disease and are related to fatigue and swallowing, respectively.

The MFIS-BR scale is validated, translated into Portuguese, and evaluates the impact of fatigue on patients through self-response, in which the individual describes and scores their own fatigue. As this symptom is frequent, it is considered to be subjective in character, and it may have a uni- or multidimensional focus. The MFIS-BR scale consists of 21 questions divided into three domains: physical (9 items), cognitive (10 items) and psychosocial (2 items). The format of the responses allows scores from 0 to 4 for each item, in a Likert type format, in which higher scores reflect greater impact of fatigue. The physical domain allows scores from 0 to 36, while the cognitive domain has scores from 0 to 40 and the psychosocial domain from 0 to 8. The total score of the MFIS-BR scale is calculated by adding the three domains and ranges from 0 to 84 points. Values below 38 in the total score indicate that there is no fatigue, while for values above this threshold, the higher the score, the greater is the degree of fatigue¹⁸.

The DYMUS is self-report questionnaire that detects the clinical signs of dysphagia and its main characteristics in patients with MS in order to identify the risk of dysphagia and allowing performing instrumental investigations and preventive measures in these patients. This questionnaire consists of 10 questions that assess two dimensions: risk of dysphagia to solids (seven items - questions 1, 3, 4, 5, 7, 8 or 10) and risk of dysphagia to liquids (three items - questions 2, 6 or 9). All responses are dichotomous and coded as 0 (no) or 1 (yes), depending on the absence or presence of risk of dysphagia. The total score is the sum of the two dimensions, ranging from 0 to 10 points, in which a score above 3 identifies the presence of risk of dysphagia^{19,20}.

Although the two instruments are designed as self-report questionnaires, due to the socio-economic conditions of the patients who attend the neurology outpatient clinic of the institution, the study chose to train the researcher, who was responsible for collecting data, and the questions were read and explained to each patient.

Statistical analyzes were performed using R (v.3.4.1) software. The Chi-Squared Test was performed to assess the association between the symptoms of dysphagia and fatigue. This test suggests that individuals with a MS and total score greater than 38 on the MFIS scale have fatigue, while individuals with a total score above 3 on the DYMUS-BR scale are at risk of dysphagia. The null hypothesis of the test indicates that there is no association between the two classifications. The Kendall rank correlation coefficient was used to correlate the scores of the domains included in the MFIS-BR and DYMUS-BR scales. The coefficient significance test was also performed, in addition to the correlation calculation. A significance level of 5% ($p < 0.05$) was adopted for all analyzes.

Results

80 MS patients were interviewed, of which 74 were included. Six patients were excluded due to concomitant neurological diseases. Most participants were female (56.8%, $n=42$), under 60 years old (95.9%, $n=71$), married (58.1%, $n=43$) and had completed high school (33.8%, $n=25$). The majority (75.7%, $n=56$) also had no previous or concomitant disease and half of the participants were diagnosed with MS at least 5 years ago. The recurrent-relapsing MS (81.1%, $n=60$) was the most frequent type of MS, while 85.1% ($n=63$) of the patients had total scores below 4 and 14.9% ($n=11$) had total scores above 4 in the EDSS.

Table 1. Clinical and Demographic Characteristics of Patients with Multiple Sclerosis (N=74)

Characteristic	N (%)
Gender	
Female	42 (56.8)
Male	32 (43.2)
Age	
≤ 60 years	71 (95.9)
> 60 years	3 (4.1)
Marital status	
Single	21 (28.4)
Married	43 (58.1)
Divorced	9 (12.2)
Widow/widower	1 (1.4)
Educational level	
Illiterate	1 (1.4)
Incomplete Primary School	5 (6.8)
Complete Primary School	6 (8.1)
Incomplete High School	12 (16.2)
Complete High School	25 (33.8)
Incomplete Higher Education	7 (9.5)
Complete Higher Education	18 (24.3)
Previous/concomitant disease	
No	56 (75.7)
Yes	18 (24.3)
Time since diagnosis of MS	
Up to 1 year	12 (16.2)
1-3 years	13 (17.6)
3-5 years	12 (16.2)
More than 5 years	37 (50.0)
Type of MS	
Recurrent-relapsing	60 (81.1)
Primary-progressive	4 (5.4)
Secondary-progressive	9 (12.2)
Relapsing-progressive	1 (1.4)
EDSS	
Total Score >4	11 (14.9)
Total Score <4	63 (85.1)

Legend: MS: Multiple Sclerosis; EDSS: Kurtzke Expanded Disability Status Scale.

The physical domain had the highest score in the MFIS-BR scale with 17.2. The mean total score was 35.3 points and 32 patients (43.2%) had a total

score above 38, which indicates the presence of symptoms of fatigue.

Table 2. Domain and Total Score of the Modified Fatigue Impact Scale (N=74).

Variables	Category	Measurements
Cognitive Domain	Min-Max	0-40
	Median	4,5
	Mean \pm SD	14.7 \pm 10.7
Physical Domain	Min-Max	0-36
	Median	17,5
	Mean \pm SD	17.2 \pm 11.1
Psychosocial Domain	Min-Max	0-8
	Median	3
	Mean \pm SD	3.3 \pm 2.6
Total Score	>38 points	32 (43.2%)
	<38 points	42 (56.8)

Legend: Min: Minimum; Max: Maximum; SD: Standard Deviation.

As for the DYMUS-BR questionnaire, respondents scored on average 1.6 in the liquid domain and 0.5 in the solid domain. Regardless the total score, 20 patients (27.0%) reported the at least one item of risk of dysphagia to liquids, and 43

patients (58.1%) reported at least one item of risk of dysphagia to solids. The mean total score was 2.1 points and 19 patients (25.7%) had a total score above 3, which indicates the presence of symptoms of dysphagia.

Table 3. Characterization of the Domains of the DYMUS-BR Questionnaire (N=74).

Domain	N (%)	Measurements	
Dysphagia to Liquids	20 (27.0)	Min-Max	0-7
		Median	1
		Mean \pm SD	1.6 \pm 1.8
Dysphagia to Solids	43 (58.1)	Min-Max	0-3
		Median	0
		Mean \pm SD	0.5 \pm 0.9
Total Score		Min-Max	0-8
		Median	1
		Mean \pm SD	2.1 \pm 2.4
>3	19 (25.7)		
<3	55 (74.3)		

Legend: Min: Minimum; Max: Maximum; SD: Standard Deviation.

Regarding swallowing solids, 16 patients (21.6%) reported difficulty swallowing solid food, 25 patients (33.8%) reported feeling of a lump in the throat, 16 patients (21.6%) reported feeling the food sticking to the throat, 19 patients (25.7%) reported the need to cut the food into small pieces before swallowing, 10 patients (13.5%) reported the need to swallow several times to completely swallow solid foods, 18 patients (24.3 %) reported feeling of suffocation after ingesting solids and 12 patients 16.2%) reported weight loss.

As for swallowing liquids, 15 patients (20.3%) reported difficulty swallowing liquids, 12 patients (16.2%) reported having a cough or a feeling of suffocation after drinking liquid and 11 patients (14.9%) reported to take several sips of liquid to swallow the liquid completely.

Thirteen (17.6%) patients showed a risk of dysphagia and also fatigue symptoms. There was an association between these parameters (p-value<0.05).

Table 4. Association between the Modified Fatigue Impact Scale and the Questionnaire for the Assessment of Dysphagia in Multiple Sclerosis.

Aspect	Risk of dysphagia	No risk of dysphagia	Total
Presence of fatigue	13	19	32
No fatigue	6	36	42
Total	19	45	74

*The result of the Chi-Squared Test was significant (p -value<0.05).

Despite all three domains of the MFIS-BR scale were statistically significant to solids, only the cognitive domain was statistically significant to liq-

uids (both p <0.05). However, all domains showed a poor positive correlation between symptoms of fatigue and risk of dysphagia.

Table 5. Correlation Coefficient of the Modified Fatigue Impact Scale and the Questionnaire for the Assessment of Dysphagia in Multiple Sclerosis.

MFIS-BR	Scales		Correlation coefficient (r)	p-value
		DYMUS		
Cognitive		Solid	0.27	0.002*
		Liquid	0.31	0.001*
Physical		Solid	0.24	0.005*
		Liquid	0.14	0,143
Psychosocial		Solid	0.26	0.004*
		Liquid	0.16	0,101

Statistically significant values (p -value<0.0).

Discussion

MS is a disease with a chronic evolution, which is characterized by outbreaks and remissions, and as the areas of demyelination are multifocal, there are different manifestations of symptoms. The socio-demographic data of this study, related to sex, age and type, are in line with those found in the literature, which indicates the prevalence of females, individuals under 60 years old and the recurrent-relapsing type²².

Fatigue is frequently and intensely expressed in patients with MS, as one of the first symptoms, even with small efforts, and it may be associated with a persistent degree of disability^{18,22,23}. Studies show a strong correlation of fatigue and brain damage in RRMS²³. Almost half of the patients (43.2%) in this study had symptoms of fatigue and there was a higher score for the physical domain of the scale. It is believed that the presence of the fatigue symptom may contribute to worsen the physical and functional symptoms¹⁸. In addition, fatigue is associated with the risk of dysphagia

in this population, and also a warning sign for a speech-language pathology evaluation.

Although fatigue is prevalent among patients diagnosed with MS, there are few studies that evaluate this symptom as an aggravating predictor of the disease. When compared to individuals without fatigue, individuals with MS and fatigue have increased brain atrophy, despite having similar levels of changes. Increased brain damage in individuals with fatigue may be associated with rapid disease progression²⁴.

Fatigue can trigger motor and cognitive changes, which further impairs the quality of life of these individuals¹¹. According to a study conducted at the Multiple Sclerosis Association of Goiás, Brazil, 60% of individuals with MS had cognitive alterations, including: memory, concentration, discernment and reasoning impairments²². The cognitive domain had the second highest average on the MFIS-BR scale in this study, being positively correlated with the 'Liquid' domain. Thus, it is expected that the greater the degree of fatigue, the greater is the risk of dysphagia.

It is important to know the pathophysiology of the disease to understand the signs and symptoms of sensory and motor capabilities in swallowing changes¹⁵. The risk of dysphagia was identified in 19 patients (25.7%) in this study. Although the frequency of swallowing disorders is relatively high in the population with MS, there are no studies that report the main symptoms that indicate risks for dysphagia in the disease¹⁴. The 'feeling of a lump in the throat' was one of the most reported characteristics in the DYMUS-BR questionnaire. According to the literature, this and other signs, such as cough, throat clearing, and choking during or after feeding are the most reported by patients.

The importance of acting at different levels of health care is emphasized, both in cases with symptoms that are clear, and perceived by patients with MS, already with some degree of disability; and also in cases, in which patients do not complain of swallowing changes, but have symptoms, and its potential influence on the result of the self-report questionnaire.

The onset of dysphagia is usually in individuals who have a mild degree on the Kurtzke Expanded Disability Status Scale (EDSS 2-3), with an increase in the symptom being observed when in moderate or severe degree (EDSS 8-9)⁸. According to the data in this study, about 14.9% of the participants had EDSS values above 4, which shows that a good part of them had an abnormal gait, thus increasing the risk of having other symptoms, such as fatigue and dysphagia. Nevertheless, as no records of the scores of the EDSS functional systems were found, it is not possible to infer the relationship of the specific functions altered with the changes caused in the dynamics of swallowing.

No studies were found in the literature associating or correlating the risk of dysphagia and the symptom of fatigue. There was an association between the risk of dysphagia and the presence of fatigue in this study. Thus, it is interesting to understand fatigue as a factor associated with dysphagia and to have it as a warning sign for early referral for a speech-language pathology evaluation. A poor positive correlation was evidenced between the symptoms of fatigue and dysphagia. Although the three domains of the MFIS-BR scale were significant for solid, only the cognitive domain was significant for liquids. Thus, it can be inferred that the greater the feeling of fatigue, the greater is the risk of dysphagia. This factor also corroborates the

findings in other studies on neurological disorders that are predictors for the risk of dysphagia²⁵.

The study had some limitations. Regardless of the duration of the last relapse, which can contribute to aggravate the permanent or temporary symptoms, the instruments were applied only once. As no data were found on patients' cognitive abilities in the medical records, only in the self-report of the cognitive domain of the MFIS-BR scale, it is impossible to know if any degree of cognitive alteration could have influenced the application of both questionnaires. The lack of cognitive and motor data prevented further correlations with the DYMUS-BR domains. In addition, the sample could have been larger and more detailed if all patients underwent regular treatment at the outpatient clinic.

The identification of individuals who have symptoms of fatigue and risk of dysphagia can assist in planning rehabilitation earlier and focused on avoiding complications, in addition to alert these individuals and the multidisciplinary team to a thorough follow-up of their symptoms. Thus, is essential to use instruments for screening and quantifying signs and symptoms through objective tests, making the results more reliable and maximizing the rehabilitation process^{17, 26}.

Conclusion

The present study showed a poor positive correlation between the risk of dysphagia and the symptom of fatigue in patients with MS. It could be notice that, the greater the degree of fatigue symptom in the studied population, the greater the risk of changes in the biomechanics of swallowing.

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