Sight-dependent quality of life and ophthalmic findings in a group of Brazilian patients with multiple sclerosis

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ABSTRACT

Objective: To assess the visual quality of life in patients with multiple sclerosis (MS), and to observe whether this parameter could be correlated to the findings of the ophthalmologic examination. **Method:** The translated and validated 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25) was used to assess the visual quality of life. Clinical data on MS, visual acuity, visual fields, optic coherence tomography (OCT) and disc cupping were used for assessing correlation with VFQ-25. **Results:** The mean VFQ-25 value was 78.6±18.2% in 27 patients. VFQ-25 did not correlate with patients' ages, with disability (EDSS), disease duration or medication use. Visual acuity showed a relatively poor (<60%) correlation to VFQ-25, while no correlation could be established between visual fields, OCT and disc cupping with VFQ-25. **Conclusion:** MS patients present several alterations in their eyes and sight that cannot be assessed by isolated measures. Ophthalmological examination of these patients must include many parameters not usually used in standard ophthalmologic consultations.

Key words: multiple sclerosis, ophthalmology, visual acuity, visual fields, optic coherence tomography, quality of life.

Qualidade de vida visual e achados oftálmicos em um grupo de pacientes brasileiros com esclerose múltipla

RESUMO

Objetivo: Avaliar a qualidade de vida visual de pacientes com esclerose múltipla (EM) e observar se este parâmetro pode ser relacionado aos achados do exame oftalmológico. **Método:** O questionário traduzido e validado *25-Item National Eye Institute Visual Function Questionnaire* (VFQ-25) foi utilizado para avaliar a qualidade de vida visual. Dados clínicos da EM, acuidade visual, campo visual, tomografia de coerência óptica (OCT) e escavação do disco foram utilizados para correlação com VFQ-25. **Resultados:** A média do VFQ-25 foi 78,6±18,2% em 27 pacientes. VFQ-25 não se correlacionou com a idade dos pacientes, com a incapacidade (EDSS), duração da doença ou medicação em uso. A acuidade visual mostrou uma correlação relativamente pobre (<60%) com VFQ-25, enquanto não foi observada nenhuma correlação entre campo visual, OCT e escavação de disco com VFQ-25. **Conclusão:** Pacientes com EM apresentam diversas alterações oculares e na visão que não podem ser avaliadas por medidas isoladas. O exame oftalmológico destes pacientes deve incluir parâmetros que não são habitualmente utilizados em consultas oftalmológicas padronizadas.

Palavras-Chave: esclerose múltipla, oftalmologia, acuidade visual, campo visual, tomografia de coerência óptica, qualidade de vida.

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Patients with multiple sclerosis (MS) may develop a variety of disabilities over decades of central nervous system inflammation and degeneration. Nearly 50% of all MS patients will develop at least one episode of acute demyelinating optic neuritis[1]. Although severe vision loss is uncommon in MS[2], even a slight visual impairment may be critical in patients who already have motor, sensory and coordination disabilities. The optic neuropathy that affects MS patients may progress in a silent, subclinical manner, or may have acute demyelinating stages that translate as acute optical neuritis[3]. Although axonal and neuronal degeneration of the optic nerve might be expected in eyes with a known history of acute optic neuritis, unaffected eyes also have been shown to have the same alterations[3].

Routine ophthalmic examinations on MS patients often show no significant abnormalities, unless the patient is experiencing an acute demyelinating episode or already has severe visual impairment. However, when assessed using the 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25)[4], MS patients have been found to present a high degree of self-reported visual dysfunction that is not entirely expressed in terms of visual acuity[5]. These abnormalities were independent of patients' ages or disabilities due to MS[6], and often are not exclusively found in patients with previous histories of optic neuritis.

The axonal distribution within the retinal nerve fiber layer (RNFL), as measured by optical coherence tomography (OCT), correlates with overall axonal viability and integrity. A panel of experts has concluded that OCT may evolve into an important primary or secondary outcome parameter for MS clinical trials and for patient care[7]. The retina is highly enriched in axons but has no myelin. Therefore, it is an ideal structure for representing disease progress. It has been consistently reported that the RNFL is affected in patients with MS, regardless of clinical episodes of optical neuritis[8-10].

The aim of the present work was to assess sight-related quality of life among MS patients using the VFQ-25 questionnaire[4], which has recently been validated for Brazilian Portuguese[11]. The VFQ-25 was developed and described as being a measure that provides reproducible and valid data when used across multiple ophthalmological conditions of varying severity. This instrument provides information on several domains of sight and quality of life, including those related to daily tasks and well being of the subjects.

METHOD

The present study was approved by the UNIMES Ethics Committee. All participants signed an informed consent prior to entering the study.

The inclusion criteria for evaluation were that subjects needed to be 18 years of age or over, and to have had their MS diagnosis for at least one year, according to the McDonald criteria[12]. The degree of disability was assessed using the expanded disability status scale (EDSS)[13]. The clinical presentation of MS at the time of this study was classified according to Lublin and Reingold[14] as either relapse-remitting or secondary progressive. Patients were excluded if they had presented a clinical MS relapse during the three months preceding the examination. Patients with severe psychiatric symptoms and signs were also excluded. Patients with other diseases affecting the eyes or with MS-related conditions that could affect the ophthalmological evaluation were equally excluded.

All patients were completely assessed on a single day. The assessment included MS parameters, history of optic neuritis, medication use, VFQ-25 score (using 100% as the maximum VFQ result, meaning perfect visual quality of life), visual acuity using the Snellen scale (20/20=1.0), and visual fields (assessed in terms of area (mm^2) and degree of impairment by standard achromatic perimetry) with the Humphrey Field Analyser - model 7501 (Carl Zeiss, Germany) apparatus. The degree of visual field alteration is, however, subject to the comprehension and collaboration of the subject undergoing the examination. The 25 questions are divided into 12 classes, and 11 of them assess vision[15]. OCT (Stratus - OCT Carl Zeiss, Germany) was used to evaluate RNFL thickness around the papilla (severity assessed as the area affected and the degree of impairment).Fundus pictures of both eyes were taken (non-midriatic Zeiss Visucan NM-AS, Carl Zeiss, Germany) to assess optic disc cupping. All examinations were performed in the right eye (RE), left eye (LE) and, if applicable, in both eyes. Normal range values were considered to be those of historical populations from the literature.

Mean values and standard deviations (SD) were used for continuous variables. The t test was used to assess the significance of differences, and p≤0.05 was considered to be a statistically significant value. The degree of linear agreement between parameters was calculated using the Pearson correlation coefficient. All statistical analyses were performed blindly, by an independent author (AF), using SPSS v 13.0.

RESULTS

Fifty-four eyes from 27 patients (6 M and 21F) were assessed. Clinical and demographic characteristics of the patients are presented in Table 1. The mean age of these patients was 40.3±12.3 years (range 19 to 60 years). Two patients presented the secondary progressive form of MS, while the remaining 25 patients presented the

Table 1. Clinical characteristics of 27 patients with multiple sclerosis (MS).

MS patients (n=27)	
Gender	6 males, 21 females
Age (years)	40.3±12.3 (19 to 60)
Disability (EDSS)	2.3±1.5 (zero to 7.0)
Clinical presentation	RRMS (n=24), SPMS (n=2)
Disease duration (years)	8.5±7.4 (1 to 30 years)
Medication in use for MS	Beta interferon (n=9)
	Glatiramer acetate (n=13)
	No medication (n=5)
Previous episodes of optical neuritis	17 patients (who reported 1 to 10 episodes)

EDSS: expanded disability status scale[13], clinical presentation according to Lublin and Reingold[14] as either relapse-remitting (RRMS) or secondary progressive (SPMS).

Table 2. Correlation of visual-related quality of life assessed by visual function questionnaire (VFQ-25) with clinical data and ophthalmological parameters in 27 multiple sclerosis patients (54 eyes).

VFQ-25 (average ± SD; range)	Non-significant correlation with the following parameters	Mild significant correlation with
78.6 ± 18.2 % (35.4% to 97.9%)	Age (−0.06)	RE (0.59)
	EDSS (−0.20)	LE (0.60)
	Disease duration (0.02)	Both eyes (0.59)
	Medication in use (0.04)	
	Previous optical neuritis (−0.41)	
	Visual fields	
	RE (0.50), LE (0.44), both eyes (0.48)	
	Optic disc cupping	
	RE (0.24), LE (0.09), both eyes (0.24)	
	Visual acuity	

SD: standard deviation; RE: right eye, LE: left eye.

relapse-remitting form of MS. The mean time elapsed since their MS diagnosis was 8.5±7.4 years (range one to 30 years). Their disability according to EDSS was, on average, 2.3±1.5 (range zero to 7.0). Nine patients were regularly using beta-interferon and 13 patients were using glatiramer acetate, while five patients were not using any immunomodulatory drugs.

Although two patients with severe visual impairment presented abnormalities in all the assessed parameters (and in their VFQ-25), VFQ-25 was not specifically related to any given clinical or ophthalmological parameter in the other patients. Even excluding the two most severely visual impaired patients, VFQ-25 was not correlated to any clinical or ophthalmic assessed parameter. The correlation results are summarized in Table 2.

The mean VFQ-25 value was 78.6±18.2% (ranging from 35.4% in a patient with ten previous episodes of optic neuritis, to 97.9% in a patient with no previous optic neuritis, no visual complaints and no abnormalities in any of the ophthalmological parameters assessed). VFQ-25

did not correlate with patients' ages (−0.06), EDSS (−0.20), disease duration (0.02) or medication use (0.04). Ninety-two percent of all eyes that had been affected at least once by optic neuritis showed thinning of the RNFL.

Previous episodes of optic neuritis were reported by 17 patients, ranging from one to ten episodes. Ten patients denied having had any sign or symptom that could be suggestive of optic neuritis. There was no correlation between previous history of optic neuritis and VFQ-25 (−0.41). The average quality of vision assessed by VFQ-25 was 74.6% for patients who had at least one episode of optic neuritis and 80.7% for patients who never had optic neuritis. Although no statistical significant differences were observed in these populations, it is necessary to observe the small size of the sample.

Visual acuity was, on average, 0.7 for the RE and 0.7 for LE (ranging from 0.1 to 1.0). Although the correlation of VFQ-25 and visual acuity presented the highest values for correlations (OD=0.59; OS=0.60; both eyes=0.59), it barely reached 60%.

Visual fields were severely compromised in those two patients with several episodes of optical neuritis and very low visual acuity. In fifteen patients the visual fields were considered to be normal, in eight patients there were areas of visual loss, while in two patients the results were inconclusive. There was no correlation between visual fields and VFQ-25 for the RE (0.50), LE (0.44) or both eyes (0.48). Twelve patients presented normal optic disc cupping and fifteen patients had variable amounts of abnormalities in excavation. Optic disc cupping did not correlate with VFQ-25 in the RE (0.24), LE (0.09) or both eyes (0.24).

DISCUSSION

VFQ-25 is a useful tool for the assessment of MS patients. Only a modest correlation between VFQ-25 and clinical parameters in MS patients was shown by Noble et al.[16]. The same authors showed that the quality of vision in MS patients was comparable to those with glaucoma and cataracts. The results from the present work showed a weak correlation of quality of vision with clinical parameters, and a discreet correlation with optical neuritis, visual filed and visual acuity. The patients sample is not particularly large and great care should be taken into consideration regarding the interpretation of results. The findings from the present study were similar to those of Nobel et al., who showed that the effect on visual quality of life in MS could not be specifically correlated with any of the neurological or ophthalmological parameters, except in patients with several episodes of optic neuritis. In all the other patients, with or without previous optic neuritis, the visual quality of life was not related to any specific finding. Only a modest correlation (<60%) could be established between VFQ-25 and visual acuity in the present study. Visual fields, usually routinely investigated in MS patients, showed a poor correlation with VFQ-25 and the highest level of normal results among these patients. Again, the small size of the sample may have influenced this finding.

The design of the present study did not envision the use of visual evoked potentials (VEP) or MRI in the assessments for correlations. VEP would provide data on the visual pathway and MRI would provide parameters relating to brain lesions and/or atrophy. These parameters, although very important, were not taken into consideration in the present study, which focused purely on the ophthalmic examination.

OCT is being increasingly used for MS studies[3]. As shown by several authors over the last few years, and summarized by Pula and Reder[17], OCT is becoming a means for assessing neurodegeneration in MS. A recent study[9] on OCT measurements showed good correlation between RNFL thickness and MS duration in 50 patients.

RNFL thinning in eyes with a history of optic neuritis has been reported in 74% of MS patients[18]. The present study showed that 92% of all eyes that had been affected at least once by optic neuritis showed thinning of the RNFL. When eyes that had never been affected by optic neuritis were assessed in the present study, 21% of them presented thinning of the RNFL. Similar findings have also been reported by other authors, as reviewed by Kallenbach and Frederiksen[19].

As expected, patients with severely compromised eyes showed significant impairment in all ophthalmological parameters in the present study. However, MS patients with unaffected or mildly affected eyes frequently reported inadequate quality of vision in the present study. Other authors have attempted to correlate visual findings in MS and, except for patients with clearly affected eyes, no important correlation has been described[20-23]. In fact, the common conclusion is that MS patients have more visual complaints and a variety of ophthalmological abnormalities that warrant comprehensive examination. As reported by Sisto et al.[24], no single ophthalmic test would be able to detect all the subclinical abnormalities present in MS eyes. The recent work of Mowry et al.[25] also points towards the use of different and meaningful ophthalmological measures in order to better interpret the visual impairment and visual-related quality of life in MS. The assessment of the optic disc, visual acuity and/ or visual fields alone, as often happens during routine examinations on these patients, is not sufficient to establish the degree of visual impairment and their visual quality of life. The ophthalmological methodology used in the present study focused on the optical nerve integrity. Other factors, such as deviations from the visual axis might be important in the study of vision in MS. The present work did not take this possibility into consideration, but further work should expand this investigation.

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