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Clinical commentary

Muscle strength and psychiatric symptoms influence health-related quality of life in patients with myasthenia gravis

Nayara Felicidade Tomaz Braz [a,*], Natalia Pessoa Rocha [a], Érica Leandro Marciano Vieira [a], Izabela Guimarães Barbosa [a], Rodrigo Santiago Gomez [b], Adriana Maria Kakehasi [c], Antonio Lucio Teixeira [a,b]

[a] Neuroscience Branch, Interdisciplinary Laboratory of Medical Investigation, School of Medicine, UFMG, Belo Horizonte, Brazil
[b] Neuromuscular Disease Center, University Hospital, UFMG, Belo Horizonte, Brazil
[c] Locomotor System Department, School of Medicine, UFMG, Belo Horizonte, Brazil

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ABSTRACT

Myasthenia gravis (MG) is a neuromuscular autoimmune disease characterized by skeletal muscle weakness which can impact motor function and, furthermore, produce negative impact on the health-related quality of life (HRQOL). *Objective:* To evaluate the predictors for HRQOL in patients with MG. *Methods:* Eighty patients were evaluated with the MG Foundation of America classification and the MG Composite scale. HRQOL was estimated by the MGQOL15, while anxious and depressive symptoms were evaluated with the Hospital Anxiety and Depression Scale (HAD). *Results:* The mean age of patients was 41.9 years with mean illness duration of 13.5 years. Almost half of the patients (43.75%) had significant anxiety and more than a quarter (27.50%) had depressive symptoms. Factors that influenced the HRQOL in MG were skeletal muscle weakness and anxiety and depressive symptoms ($p < .001$ in logistic regression model). *Conclusion:* Anxiety and depressive symptoms, besides motor symptoms, influence HRQOL in MG. Mental health must be a clinical focus in addition to the treatment of somatic symptoms during the course of MG.

1. Introduction

Myasthenia gravis (MG) is an autoimmune disease caused by antibodies directed to the postsynaptic membrane at the neuromuscular junction. In approximately 80% of all cases, MG is associated with antibodies against AChR [1].

Symptoms of MG range from only ocular symptoms such as diplopia and ptosis (ocular MG) to more generalized symptoms, including dysarthria, dysphagia, chewing and breathing difficulty, and limb weakness (generalized MG). Such symptoms influence social functioning of the patients, impacting negatively on their health-related quality of life (HRQOL) [2–5]. Other factors may influence HRQOL in MG such as the number and severity of myasthenic crisis and drug treatment [6]. Furthermore, psychiatric symptoms such as anxiety and depression have been associated with poor self-reported HRQOL [6–8].

There are only few studies that investigated the determinants of HRQOL in Brazilian patients with MG [6,7]. Hence, the objective of this study was to determine the factors associated with HRQOL in a Brazilian sample of subjects with MG.

2. Methods

2.1. Subjects

This study comprised 80 patients with MG followed at the Neuromuscular Disease Outpatient Clinic, University Hospital, Federal University of Minas Gerais, Belo Horizonte, Brazil. Patients were diagnosed based on the Myasthenia Gravis Foundation of America (MGFA) criteria [9]. Exclusion criteria included pregnancy, and presence of cancer. This study was approved by the Research Ethics Committee of the Federal University of Minas Gerais, Brazil (Protocol number: CAAE-19045413.0.0000.5149). All subjects provided written informed consent.

* Corresponding author at: Interdisciplinary Laboratory for Medical Research, School of Medicine, Federal University of Minas Gerais (UFMG), Avenue Alfredo Balena, 190, Room 281, Santa Efigênia, 30130-100 Belo Horizonte, Minas Gerais State, Brazil.
E-mail address: nayaraftbraz@hotmail.com (N.F.T. Braz).

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2.2. Clinical assessment

Clinical status and severity of MG were determined following the recommendations of the MGFA [9]. Skeletal muscle strength was evaluated with the Myasthenia Gravis Composite (MG Composite) scale that measures the degree of muscle weakness and comprises 10 items evaluating ocular (3 items), bulbar (3 items), respiratory (1 item), neck (1 item), and limb (2 items) signs and symptoms [10]. Participants were evaluated by a single previously trained researcher who collected socio demographic, clinical and anthropometric dates.

A total dose of glucocorticoids used by the patient throughout the course of his disease, so called, cumulative dose, was calculated. All medications taken by the patient were recorded.

The HRQOL was assessed with the Brazilian version of the Questionnaire of Life Quality Specific for Myasthenia Gravis – 15 Items (MGQOL15) [2,6]. Each item is scored from zero to four according to its frequency, scoring a maximum of 60, with the higher the score, the worse the perceived HRQOL.

Table 1
Clinical and demographic features of myasthenia gravis patients.

Characteristics	MG (n = 80) ± SD	(%)
Gender		
Female	60	75
Male	20	25
Age (years)	41.89[#] (±14.171)	–
Education (years)	9.288[#] (±3.728)	–
Age at onset (years)	29.10[#] (±13.483)	–
Length of disease (years)	13.53[#] (±10.053)	–
Cumulative glucocorticoid dose (mg)	38123.477[#] (±41895.659)	–
Age at thymectomy (years)	32.50 (±11.829)	–
Mean MG composite	4.96[#] (±5.021)	–
MGFA		
I	10[*]	12.5
IIA	9[*]	11.3
IIB	7[*]	8.8
IIIA	15[*]	18.8
IIIB	4[*]	5.0
IVA	6[*]	7.5
IVB	5[*]	6.3
V	22[*]	27.5
HAD anxiety subscale score	7.68[#] (±4.453)	–
Mild	13[*]	16.3
Moderate	15[*]	18.8
Severe	7[*]	8.8
HAD depression subscale score	6.52[#] (±4.686)	–
Mild	8[*]	10
Moderate	7[*]	8.8
Severe	7[*]	8.8
MGQoL15	16.23[#] (±12.858)	–

MGFA: Myasthenia Gravis Foundation of America Clinical Classification; HAD: Hospital Anxiety and Depression Scale; MGQoL15: Myasthenia Gravis Quality-of-Life Questionnaire; SD: standard deviation.
[#] Value average.
[*] Absolute value.

Symptoms of anxiety and depression were evaluated with the Hospital Anxiety and Depression Scale (HAD). The HAD comprises 14 items, seven to assess anxiety and seven depression [11]. The authors recommend as cutoff for both subscales $\geq$9, being less than nine classified as without clinically significant symptoms, between 9 and 10 mild form of anxiety/depression, 11 and 14 moderate form and, more than 14 severe form [12].

2.3. Statistical analysis

The Kolmogorov-Smirnov test was used to analyze the normality of the data. The patients with anxiety and depressive symptoms were compared by Mann–Whitney or Student's t tests when non-normally or normally distributed, respectively. Association between dichotomous variables was assessed with the chi-square test. Spearman's correlation analyses were performed to examine the relationship between clinical variables and quality of life.

We performed linear regression analyses testing possible associations between HRQOL in patients with MG and selected parameters: age, gender, years of education, age at onset, MG composite, number of myasthenic crises, cumulative glucocorticoids dose and total HAD scores. Variables with a univariate correlation with a p-value <0.20 were tested in the final model.

All statistical tests were two-tailed and were performed using a significance level of $\alpha = 0.05$. Data were analyzed using the Statistical Package for the Social Sciences® version 20.0 (SPSS; Chicago, IL, USA) and GraphPad Prism® version 5.0 (GraphPad Software, La Jolla, CA, USA).

3. Results

3.1. Clinical and demographic features of MG patients

Eighty patients with MG were evaluated (60 women and 20 men). Sociodemographic and clinical features are shown in Table 1. The patients had a mean age of 29.10 years at disease onset. Sixty-four (80%) patients were classified as early onset MG subtype (<40 years of age) and were more frequently female (52 females and 12 males), whereas patients with late onset MG (>40 years of age) were 8 females and 8 males. The most common initial symptoms were hip flexor muscle weakness, diplopia and ptosis. The frequency of all items composing the MG Composite is described in Table 2.

Over the course of the disease, 53 (66,3%) patients had at least one myasthenic crisis (45 patients had only one crisis, 3 had two crisis, 2 had three crisis and 3 had four crisis) with a mean age of 35 years (±15.50). Comorbidities were present: obesity (67.5%), hypertension (33.8%), hypercholesterolemia (27.5%), osteoporosis (14%), type 2 diabetes mellitus (13.8%), hyperthyroidism (11.3%), cataract (11.3%), glaucoma (7.5%). Four patients reported the

Table 2
Frequency of symptoms and severity of muscle weakness according to MG Composite Scale.

Grade	0	1	2	3	4
Ptosis, upward gaze (physician examination)	49 (61.3%)	14 (17.5%)	2 (2.5%)	11 (13.8%)	–
Double vision on lateral gaze, left or right (physician examination)	46 (57.5%)	15 (18.8%)	1 (1.3%)	7 (8.8%)	7 (8.8%)
Eye closure (physician examination)	52 (65%)	22 (27.5%)	2 (2.5%)	–	–
Talking (patient history)	64 (80%)	12 (15%)	–	–	–
Chewing (patient history)	67 (83.8%)	9 (11.3%)	–	–	–
Swallowing (patient history)	59 (73.8%)	1 (1.3%)	16 (20%)	–	–
Breathing (thought to be caused by MG)	61 (76.3%)	15 (18.8%)	–	–	–
Neck flexion or extension (weakest) (physician examination)	57 (71.3%)	15 (18.8%)	1 (1.3%)	3 (3.8%)	–
Shoulder abduction (physician examination)	63 (78.8%)	1 (1.3%)	10 (12.5%)	1 (1.3%)	1 (1.3%)
Hip flexion (physician examination)	44 (55%)	2 (2.5%)	22 (27.5%)	6 (7.5%)	2 (2.5%)