Journal of the Neurological Sciences 381 (2017) 169–175

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Body composition and adipokines plasma levels in patients with myasthenia gravis treated with high cumulative glucocorticoid dose

Nayara Felicidade Tomaz Braz[a], Natalia Pessoa Rocha[a], Érica Leandro Marciano Vieira[a], Rodrigo Santiago Gomez[b], Adriana Maria Kakehasi[c], Antonio Lucio Teixeira[a,b,*,1]

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

ARTICLE INFO

Keywords:
Myasthenia gravis
Obesity
Adipokines
Body composition
Dual-energy X-ray absorptiometry

ABSTRACT

This study aimed to evaluate changes in body composition, *i.e.* overweight, obesity, fat accumulation and low lean body mass and plasma levels of adipokines in patients with MG. The study enrolled 80 patients with MG, and 62 controls. Body fat mass and body lean mass was analyzed by dual-energy X-ray absorptiometry technique (DXA). Plasma levels of leptin were analyzed by Luminex® and adiponectin and resistin were analyzed by ELISA. The mean age of patients with MG was 41.9 years, with 13.5 years of length of illness, and mean cumulative dose of glucocorticoids 38,123 mg. Our results showed that the frequency of obesity is higher in MG patients than in controls, and patients with MG presented higher body fat mass, android body adiposity and total body fat than controls. MG patients presented lower levels of resistin and higher levels of leptin in comparison with controls. There were no differences in the plasma levels of adiponectin. Higher total body fat and lower body lean mass were associated with increased severity of MG symptoms. This result points to the relevance of estimation of body composition in planning long-term care of MG patients.

1. Introduction

Myasthenia gravis (MG) is a neuromuscular disease characterized by muscle weakness that improves with rest. The most common form of MG is caused by antibodies against the postsynaptic membrane at the neuromuscular junction [1]. Patients with MG experience fluctuating and fatigable skeletal muscle weakness that often affects selected muscle groups. Usually, patients note weakness fluctuations from day to day or even from hour to hour. The most common manifestations include ptosis, diplopia, dysarthria, dysphagia, dyspnea, facial weakness, or fatigable limb or axial weakness [2].

The current management of MG includes the use of anticholinesterase drugs for temporary improvement of neuromuscular transmission, use of nonspecific immunosuppressant or immunomodulatory drugs and thymectomy [3]. The use of glucocorticoids (GCs) is the first-choice immunosuppressive therapy for generalized MG and has extensively been used in MG treatment mainly because of the rapid response onset [4]. Nevertheless, chronic use of GCs is limited by the numerous and frequent side effects. These side effects include but are not limited to osteoporosis, obesity, lipodystrophy, muscle atrophy, steroid myopathy, hypertension, impaired glucose tolerance, sodium/fluid retention, potassium loss, cataract, glaucoma, peptic ulcer and suppression of growth (children) [5–7].

Oral GCs use is particularly associated with obesogenic effects, such as body weight gain, altered energy expenditure and increased appetite [5,8–11]. In addition, long-term GCs use results in changes in body fat composition known as GCs-induced lipodystrophy (GIL), featured by fat accumulation in facial ('moon face'), dorsocervical ('buffalo hump', supraclavicular fat pads) and abdominal regions. GIL has been reported in subjects with inflammatory conditions that were subjected to long-term glucocorticotherapy, such as rheumatoid arthritis and systemic lupus erythematosus [12–15]. Patients under GCs consider weight gain one of the most distressing adverse events induced by these drugs, that impacts negatively in treatment adherence [5,10]. It is worth mentioning that GIL is not only an aesthetic issue, but it has been associated with severe metabolic abnormalities including insulin resistance, dyslipidemia and glucose intolerance [16].

The pathophysiology of GIL is complex and involves changes in the

* Corresponding author at: Interdisciplinary Laboratory for Medical Research, Faculty of Medicine, Federal University of Minas Gerais (UFMG), Avenue Alfredo Balena, 190, room 281, Santa Efigenia, 30130-100 Belo Horizonte, MG, Brazil.
E-mail address: Antonio.L.Teixeira@uth.tmc.edu (A.L. Teixeira).
[1] Current address: Neuropsychiatry Program, Department of Psychiatry and Behavioral Sciences, McGovern Medical School, University of Texas Health Science Center at Houston, 1941 East Road, Houston, TX 77054, BBSB Room 3140.

http://dx.doi.org/10.1016/j.jns.2017.08.3250
Received 9 May 2017; Received in revised form 22 August 2017; Accepted 23 August 2017
Available online 24 August 2017
0022-510X/ © 2017 Elsevier B.V. All rights reserved.

expression of adipokines [17–19]. Adipokines are adipose tissue-derived peptides that contribute to the regulation of appetite and satiety, fat distribution, insulin secretion and sensitivity and energy expenditure [20]. Previous studies showed that GCs induce changes in plasma levels of adipokines [18,19,21]. For instance, one week of GCs use was associated with increase of leptin and adiponectin levels in physically fit women [21].

Because of long-term treatment with GCs, patients with MG may be predisposed toward unfavorable body composition characteristics and changes in circulating levels of adipokines. To the best of our knowledge, no previous studies addressed these issues in the context of MG. Therefore, this study was designed to investigate changes in body composition, *i.e.* overweight, obesity, fat accumulation and low lean body mass and plasma levels of adipokines in patients with MG. We hypothesize that patients with MG present changes in body composition and in the plasma levels of adipokines in comparison with controls.

2. Methods

2.1. Subjects

This cross-sectional study was approved by the Research Ethics Committee of the *Universidade Federal de Minas Gerais*, Brazil (Permit number: 501.655) and all subjects provided written informed consent before admission to the study. This study included 80 patients with MG followed at the Neuromuscular Disease Outpatient Clinic, University Hospital, *Universidade Federal de Minas Gerais*, Belo Horizonte, Brazil. Patients were diagnosed based on the Myasthenia Gravis Foundation of America (MGFA) criteria [22]. Briefly, MG diagnosis was established considering clinical findings (fluctuating symptoms with easy fatigability and recovery after rest) along with amelioration of symptoms after use of acetylcholinesterase inhibitor, decremental muscle response to a train of low frequency repetitive nerve stimuli, or the presence of autoantibody against skeletal muscle acetylcholine receptors [22]. Exclusion criteria were pregnancy and previous osteoporosis treatment. In addition, this study included a control group comprising 62 age- and gender- matched subjects recruited from the community. Exclusion criteria for control group were the presence of risk factors for osteoporosis, pregnancy, presence of chronic inflammatory diseases, cancer, HIV infection, current use of GCs, insulin, statins, growth hormone, anabolic agents and hormone replacement therapy.

2.2. Clinical evaluation

Clinical status and severity of MG were determined according to the recommendations of the MGFA [22]. Muscle strength was evaluated by the MG Composite scale [23]. Participants were evaluated by a single trained researcher (NB) who also collected sociodemographic, clinical and anthropometric data. Body mass index (BMI) was calculated as body weight in kilograms divided by height in meters squared (kg/m^2). Individuals were classified based on the criteria recommended by Bray [24] according to age, sex and fat body percentage (determined with DXA). Accordingly, individuals with BMI $< 18.5\ kg/m^2$ are considered underweight; between 18.5 and 24.9 as normal; between 25 and 29.9 as overweight; and values > 30.0 indicate obesity [24]. The waist-to-hip ratio was calculated dividing waist circumference by hip circumference. Waist circumference was measured as the horizontal distance around the abdomen at the level of the umbilicus, and hip circumference was measured as the largest circumference between the waist and thighs.

The cumulative dose of prednisone - *i.e.* the total dose of prednisone used by the patient throughout the course of her/his illness - was based on data obtained from medical records. All medications taken by the patient at the time of evaluation were registered.

2.3. Body composition assessment

Whole body composition was measured by dual-energy X-ray absorptiometry (DXA) using the Discovery W equipment (Hologic, Bedford, MA, USA), software version 3.3. Measurements were performed in the supine position after removing all metal fittings. Scan images were analyzed using manufacturer specifications and normative data. All scans were performed by a single certified clinical densitometrist (AK). Daily calibration and quality control tests were performed according to the manufacturer's recommendations and different regions of interest were manually checked for maximal reliability. The DXA provides body characteristics accurately, including whole body fat and lean and mineral composition in various body compartments. DXA may be the preferred method to evaluate body composition as the whole body may be easily scanned, radiation exposure is low, and it is likely to be more accessible and more economical to obtain than computed tomography or magnetic resonance imaging [25,26].

Using the DXA results, we evaluated body fat mass (kg); body fat percentage (%); fat mass distribution (% fat trunk/% fat legs); android body adiposity (%); body lean mass (kg); appendicular skeletal muscle mass (ASM, kg); skeletal muscle mass index (SMI, calculated as lean mass / $height^2$) and sarcopenic index (appendicular lean + BMC / $height^2$).

Based on DXA data, sarcopenia is defined as appendicular skeletal muscle mass less than two standard deviations below the mean of a young reference group [27]. Accordingly, the cutoff values of 5.45 kg/m^2 for women and 7.26 kg/m^2 for men were applied in this study [27].

2.4. Biochemical measurements

Eight milliliters of peripheral blood samples were drawn by venipuncture in vacuum tubes containing heparin at the same day of the clinical assessment (between 8 and 11 AM). Blood was immediately centrifuged at 1800*g* for 10 min, 4 °C. Plasma was collected and stored at − 70 °C until assayed.

Plasma levels of leptin were measured by the Luminex® technique using the Analyst 5.1 software for analysis (Merck Millipore, Darmstadt, Germany). Adiponectin and resistin levels were assessed by enzyme-linked immunosorbent assay (ELISA) following the manufacturer's instructions (DuoSet R & D Systems, Minneapolis, MN, USA). All results were expressed as ng/mL.

2.5. Statistical analysis

All variables were tested for Gaussian distribution by the Kolmogorov-Smirnov normality test. Two groups (patients *vs.* controls) 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 plasma levels of adipokines. All statistical tests were two-tailed and were performed using a significance level of $p = 0.05$. Data were analyzed using the Statistical Package for the Social Sciences® version 22.0 (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, including 60 women, were enrolled in this study. Demographic and clinical features of patients with MG and controls are shown in Table 1. Over the course of the disease, 53 (66.3%) patients with a mean age of 35 years (± 15.50) 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). Medical comorbidities in the

Download English Version:

https://daneshyari.com/en/article/5502512

Download Persian Version:

https://daneshyari.com/article/5502512

Daneshyari.com