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Nutritional profile of multiple sclerosis

Perfil nutricional de la esclerosis múltiple

Laura Redondo Robles[1], Begoña Pintor de la Maza[2], Javier Tejada García[1], Juan José García Vieitez[3], María José Fernández Gómez[4], Inmaculada Barrera Mellado[4] and María Dolores Ballesteros Pomar[2]

Departments of [1]Neurology, [2]Endocrinology and Nutrition and [3]Biomedical Sciences. University Hospital of León. León, Spain. [4]Statistics Department. University of Salamanca. Salamanca, Spain

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Correspondence: Laura Redondo Robles. Departments of Neurology. University Hospital of León. Altos de Navas, s/n. 24071 León, Spain

e-mail: lredrob@saludcastillayleon.es

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ABSTRACT

Background: multiple sclerosis (MS) is an inflammatory, neurodegenerative disease of the central nervous system. Weight loss and malnutrition are prevalent in advanced stages of MS.

Objective: the aim of this study was to define the nutritional profile in moderate-advanced MS (especially by documenting malnutrition) and its evolution.

Methods: a case-control study was designed; cross-sectional observational study was complemented by a 12-month prospective longitudinal observational study of MS patients. Nutritional status was evaluated by collecting clinical, anthropometric, dietary and analytical data.

Results: one hundred and twenty-four patients with MS and 62 controls were recruited; 8% of the patients were malnourished or at risk of malnutrition. Only MS

patients with advanced disability needed nutritional support. During the follow-up, five patients died and four of them received nutritional support.

Conclusions: malnutrition was unusual in our sample of patients with moderate-advanced MS. The need for nutritional support is related to dysphagia in patients with advanced neurological disability. The nutritional status of patients with moderate-advanced MS is defined by a tendency to overweight and by the decrease in basal energy expenditure and handgrip strength test in relation to the loss of muscle mass. The deficient intake of polyunsaturated fatty acids, fiber and vitamin D is exacerbated in the evolution of the disease.

Key words: Multiple sclerosis. Nutritional status. Malnutrition. Vitamin D.

RESUMEN

Introducción: la esclerosis múltiple (EM) es una enfermedad inflamatoria y neurodegenerativa del sistema nervioso central. La pérdida de peso y la malnutrición son frecuentes en fases avanzadas de la EM.

Objetivo: el objetivo de este estudio fue definir el perfil nutricional en la EM en estadio moderado-avanzado (especialmente, documentando la malnutrición) y su evolución a 12 meses.

Métodos: se realizó un estudio de casos-controles; el estudio observacional transversal se complementó con un estudio observacional longitudinal prospectivo a 12 meses de los pacientes con EM. El estado nutricional se evaluó mediante la recogida de datos clínicos, antropométricos, dietéticos y analíticos.

Resultados: se incluyeron en el estudio 124 pacientes con EM y 62 controles. El 8% de los pacientes estaban desnutridos o en riesgo de desnutrición. Solo los pacientes con EM con discapacidad avanzada necesitaban soporte nutricional. Durante el seguimiento, cinco pacientes fallecieron y cuatro de ellos estaban recibiendo soporte nutricional.

Conclusiones: la desnutrición es infrecuente en nuestra muestra de pacientes con EM moderada-avanzada. La necesidad de apoyo nutricional está relacionada con la disfagia en pacientes con discapacidad neurológica avanzada. El estado nutricional de los pacientes con EM moderada-avanzada se define por una tendencia al sobrepeso y

por valores bajos en el gasto energético basal y en la dinamometría manual en relación con la pérdida de masa muscular. La ingesta deficiente de ácidos grasos poliinsaturados, fibra y vitamina D se acentúa en la evolución de la enfermedad.

Palabras clave: Esclerosis múltiple. Estado nutricional. Malnutrición. Vitamina D.

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory demyelinating chronic disease of the central nervous system (CNS). It is characterized by clinical relapses and progressive neurological disability (1). In fact, MS is the leading cause of neurological disability in young adults (2).

Malnutrition is usually present in inflammatory conditions. Weight loss and malnutrition are prevalent in advanced stages of MS associated with increased neurological disability (3). Malnutrition has a multifactorial etiology: decrease in nutritional intake determined by feeding difficulties and digestive symptoms (lack of appetite and nausea), increased energy and protein expenditure (especially during infections), increased losses associated with the underlying inflammatory state, decrease in muscle mass due to reduction in physical activity, cognitive impairment, pressure sores, pharmacological treatments (especially anticholinergics, cannabinoid derivates and amantadine), due to adverse digestive effects and their interaction with nutrients, and neurogenic dysphagia. Malnutrition is associated with a negative impact on the evolution of the disease, poor functional outcomes and an increase in health care costs. Malnutrition increases muscle weakness and decreases functional capacity, which leads to dysphagia and infection, prolonging the vicious circle of malnutrition. Finally, malnutrition is related to an increased morbidity and mortality (4-7).

It has been estimated that life expectancy in MS is shortened by approximately seven years when compared to the general population. Death is not directly related to the disease but occurs as a consequence of its complications, which are more prevalent at older age and at greater neurological disability. The main causes of mortality are infections (respiratory and urinary) and cardiovascular diseases (8,9). Malnutrition increases infection susceptibility and favors the formation of pressure sores.

The aim of this study was to define the nutritional status of moderate-advanced MS (by using clinical, anthropometric, dietary and analytical parameters) and to know its 12-month evolution.

MATERIAL AND METHODS

Study design

A case-control, cross-sectional observational study that was complemented by a 12-month prospective longitudinal observational study. Consecutive patients with MS admitted to the specialized MS clinics from February 2014 to July 2014 were included. The purpose of the selection of a control group was to define the nutritional characteristics of MS patients. To minimize confounding factors such as diet or socioeconomic status, the controls were healthy family volunteers of MS patients, matched by age and gender (10). It was necessary to count on the collaboration of other healthy volunteers not related to the patients in order to reach the estimated proportion of 2:1 (case:control).

All the patients had a definite diagnosis of MS according to McDonald's 2010 criteria (11); those patients with an Expanded Disability Status Scale (EDSS) score 3.5-9.5 were selected (12). None of the patients had a MS relapse or had received steroid treatment within the 30 days prior to the inclusion and none of them had other systemic diseases which could lead to a malnutrition state. The study and all the procedures were approved by the institutional ethics and research committee according to the Declaration of Helsinki and all the subjects signed an informed consent form.

Demographic data (age and sex) of case and controls and clinical variables (MS type, EDSS, duration of the disease) were collected at the beginning of the study. Subjective Global Assessment (SGA), significant weight loss, nutritional support, body composition, handgrip strength test, resting metabolic rate, 24-hour recall and blood sample were assessed at the baseline and after 12 months.

Questionnaires

Neurological impairment was measured by the EDSS. EDSS is a global scale developed to evaluate neurological disability in patients with MS. It has 20 available levels that describe progressive disability ranging from 0 (normal) to 10 (death due to MS) (12).

Nutritional status was evaluated by a registered dietitian (RD) collecting clinical, anthropometric, dietary and analytical data:

– Clinical nutritional status of patients was determined by SGA and by a significant weight loss (> 5% in the last six months). SGA takes into account the clinical history (weight loss, decreased dietary intake, gastrointestinal symptoms and functional capacity) and the physical examination (subcutaneous fat and muscle loss, edema and ascites) to classify a patient into three categories: well nourished (SGA A), moderately malnourished (SGA B) and severely malnourished (SGA C) (13).

– The body weight and height were measured and body mass index (BMI) was calculated. An electrical bioimpedance (BIA) was used to assess the body composition with a Tanita MC-780MA® multi-frequency analyzer with the Suite Biológica® 8.0 software. BIA is a non-invasive technique that allows estimating the total and segmental content of fat mass (FM) and fat-free mass (FFM). In analogy to the BMI and in order to obtain a nutritional advice regardless of height, fat mass index (FMI) and fat-free mass index (FFMI) were calculated (14).The normalized values of FFMI are 18.9 kg/m^2 in the male sex and 15.4 kg/m^2 in the female sex. The normalized values of FMI are 4 kg/m^2 in the male sex and 5.5 kg/m^2 in the female sex (15).

– Resting metabolic rate was measured by indirect calorimetry FIT-MATE RMR®. This technique is based on the determination of the oxygen and carbon dioxide volumes in exhaled air (16).

– A handgrip strength test was performed using a dynamometer (Mr. Smedley type, D-3611) selecting the mean value (kg) of three consecutive measurements on the non-dominant hand. The normalized value for the age range of 50-59 years in the male sex with the non-dominant hand is 39.6 kg and the normalized value for the age range of 50-59 years in the female sex with the non-dominant hand is 21.6 kg (17).

– A 24-hour recall was collected. The dietary information was analyzed by a RD using the software Dietowin® and the daily intake of energy, carbohydrates, proteins, fats, monounsaturated fatty acids, polyunsaturated fatty acids and fiber were obtained. Likewise, compliance with daily nutritional requirements was calculated by comparing the intake of our patients with the recommended daily dietary intakes of energy, carbohydrates, proteins, polyunsaturated fatty acids and fiber according to age and sex (18):

- Energy: energy requirement is estimated at 2,500 kilocalories (kcal) for the male sex and 2,000 kcal for the female sex.
- Carbohydrates: the carbohydrates requirements are 130 grams (g).
- Proteins: the protein requirements are 46 g/day (normalized value for the age range of 50-70 years in the female sex) and 56 g/day (normalized value for the age range of 50-70 years in the male sex).
- Polyunsaturated fatty acids: the polyunsaturated fatty acids requirements are 11 g/day (normalized value for the age range of 50-70 years in the female sex) and 14 g/day (normalized value for the age range of 50-70 years in the male sex).
- Fiber: the fiber requirements are 21 g/day (normalized value for the age range of 50-70 years in the female sex) and 30 g/day (normalized value for the age range of 50-70 years in the male sex).

– Blood samples were collected and the following parameters were analyzed: hemoglobin, lymphocytes, urea, creatinine, albumin and prealbumin, transferrin, vitamins B12, A, D and E, folic acid, calcium, magnesium and zinc, as well as lipid profile (total cholesterol, HDL-cholesterol [high density lipoprotein], LDL-cholesterol [low density lipoprotein], triglycerides), glucose and HbA1c (glycosylated hemoglobin), CRP (C-reactive protein) and liver profile (glutamic oxalacetic transaminase [GOT], glutamic-pyruvic transaminase [GPT], gamma-glutamyl-transpeptidase [GGT], alkaline phosphatase, total bilirubin).

Statistical analysis

The analysis of the categorical variables has been expressed by frequencies and percentages. The analysis of the continuous quantitative variables has been expressed by mean and standard deviation (SD) and the analysis of the discrete quantitative variables has been expressed by median and percentiles. The Chi-square test was used to analyze the relationship between qualitative variables (sex, MS type, SGA, weight loss, BMI < 20, nutritional support) for independent data and the McNemar test, for paired data. Regarding the quantitative variables (age, disease duration, anthropometric, dietary and analytical data), the Student's t test was used to compare quantitative variables with normal distribution and the U Mann-Whitney test was used to study the central tendency when the continuous quantitative variables were non-

normal and in case of discrete quantitative variables (EDSS). Data were analyzed using SPSS 23.0 for Windows software. The significance level used for all the statistical analyses was 5%.

RESULTS

Descriptive study

Five hundred patients who met all the inclusion criteria and no exclusion criteria were proposed to take part in the study and 15 patients refused to participate. Finally, 124 consecutive patients with MS were recruited.

Regarding the MS patients characteristics, the mean age was 53 ± 10.4 years, the mean disease duration was 17 ± 7.2 years, most patients were in the progressive secondary phase (secondary-progressive MS) (47.6%) and 66% presented a severe disability defined as EDSS ≥ 6 (19). The median EDSS score was 6 (median [p25-p75]: 6 [4.5-6.5]).

Clinical parameters

With regard to clinical parameters, 6.5% of patients were at risk of malnutrition (defined as SGA category B) and 1.6% were malnourished (defined as SGA category C). In addition, 12.1% of the patients reported a weight loss > 5% in the last six months and 13.7% had a BMI < 20. Regarding the nutritional support, three patients were fed by enteral nutrition (EN) and four patients received thickeners/oral supplements.

Anthropometric parameters

The mean BMI was 25.2 ± 4.9 kg/m². The mean FFMI was 17.5 kg/m^2 (median [p25-p75]: 17.7 [15.9-20.1]), which was between the normalized values of both genders. Thirty-seven per cent of patients had an FFMI below the normal range. The mean FMI was 7.1 kg/m^2 (median [p25-p75]: 7.1 [5.3-9.6]); it was higher than the normalized values of both genders.

Resting metabolic rate was 1,521.5 (1,223-1,767) kilocalories (kcal) (median [p25-p75]).

The mean value handgrip strength test in our patients was 22 kg (median [p25-p75]: 22.3 [17-28]); 74% of the patients were below the normal levels.

Dietary parameters

Once the 24-hour recalls were analyzed, a comparison was made with the recommended daily amount for the following macronutrients and energy, according to age and sex (18):

– Energy: only a small proportion of patients (25.2%) met the daily energy requirements.

– Carbohydrates: patients met daily carbohydrate nutritional requirements (210 ± 60.5 g).

– Proteins: patients met daily protein nutritional requirements (85 ± 22.4 g).

– Polyunsaturated fatty acids: only 12.9% of patients met the nutritional requirements of polyunsaturated fatty acids. The average value in our patients was 6.6 (4.9-9) g (median [p25-p75]).

– Fiber: only 12.1% of patients met the nutritional requirements of fiber. The average value in our patients was 17 ± 7.3 g.

Analytical parameters

All the analytical parameters were within the normal levels except for vitamin D, which was deficient (median [p25-p75]: 19 ng/ml [14-26]).

Analysis of the results of the case-control study

One hundred and twenty-four patients with MS and 62 controls were recruited. There were no statistically significant differences regarding age and sex between the two groups.

Clinical parameters

All patients of the control group had an adequate nutritional status defined by SGA (category A) and none of them had presented a significant weight loss in the last six months. In addition, a higher percentage of cases (13.7%) than controls (4.8%) had a BMI < 20, although this difference did not reach statistical significance (p = 0.06). Nobody in the control group received nutritional support against the seven patients with MS.

Anthropometric parameters

The two groups had similar characteristics in terms of weight, height, BMI and body composition; 39% of the patients compared to 6% of the controls had a low FFMI.

Statistical analysis (Table I) showed that patients with MS presented:

– Lower values in the handgrip strength test ($p < 0.01$): 74% *vs* 36% were below normal levels.

– Lower resting metabolic rate ($p < 0.01$).

Dietary parameters

Patients with MS had a lower intake of unsaturated fatty acids (both monounsaturated and polyunsaturated) ($p = 0.01$) than the control group. There were no statistically significant differences with respect to the rest of the macronutrients or energy intake.

No group covered the daily nutritional requirements established for energy, polyunsaturated fatty acids or fiber intake and both groups met the established requirements of proteins and carbohydrates (Table II).

Analytical parameters

Patients with MS showed a lower level of albumin ($p < 0.01$), vitamin D ($p < 0.01$), vitamin E ($p < 0.01$) and bilirubin ($p < 0.01$) compared to healthy volunteers and a higher alkaline phosphatase ($p < 0.01$) and magnesium ($p < 0.01$) levels (Table III).

Analysis of the results of the longitudinal study

Of the 124 patients included in the study, 20 were lost during follow-up: five patients died during the study, nine patients refused to continue in the study, four patients could not perform the second assessment due to logistical problems (unable to come to the hospital) and two patients changed their city of residence.

Clinical parameters

During the follow-up, five patients died and four of them received nutritional support. After, 12 months, a new patient required EN and a new patient required oral supplements during follow-up due to dysphagia.

No statistically significant differences were observed in the number of patients either malnourished or at risk of malnutrition between the two evaluations.

Anthropometric parameters

In the analysis of paired data, weight, height and BMI were analyzed in all patients. The analysis of the rest of the anthropometric parameters was conditioned by the clinical situation of the patients: 96 patients performed the calorimetry, 93 patients performed the handgrip strength test and 84 patients could undergo BIA.

No significant changes were observed in the 12 month follow-up except for an increase in the FFMI ($p = 0.02$) due to a decrease in the percentage of patients with FFMI below the normal range (36% of patients in the first visit *versus* 21.7% in the last visit).

Dietary parameters

Only 69 patients of the 104 patients who completed the study provided the 12-month 24-hour recall, which could bias the statistical results. The dietary analysis revealed that a large number of patients still did not meet the nutritional requirements established in terms of energy, polyunsaturated fatty acids and fiber (Table IV).

Analytical parameters

The statistical analysis of the analytical parameters between both evaluations showed a decrease in the protein values (creatinine [$p < 0.01$] and prealbumin [$p < 0.01$]), minerals (calcium [$p < 0.01$] and zinc [$p < 0.01$]), folic acid ($p < 0.01$) and vitamin D ($p < 0.01$). Likewise, an increase in GOT ($p < 0.01$), vitamin A ($p < 0.01$) and vitamin E ($p < 0.01$) was observed. Table V shows the analytical data in which statistically significant differences were observed.

Multivariate analysis regarding neurological disability

In order to know the impact that the neurological disability had on the nutritional status, a univariate analysis was performed with the initial EDSS value as the independent variable dividing the patients into two groups according to their grade of disability, considering those patients with an EDSS < 6 as moderate disability and those patients with an EDSS ≥ 6 as advanced disability (19).

Clinical parameters

There were no statistically significant differences between patients with moderate and advanced disability in relation to the clinical parameters of malnutrition. It is important to highlight that all the patients who needed nutritional support had an advanced disability.

Anthropometric parameters

The bioelectrical impedance analysis could not be carried out in those patients with inability to stand autonomously. For this reason, 99 patients were evaluated (42 patients from the group with an EDSS < 6 and 57 patients from the group with an EDSS ≥ 6). No statistically significant differences were found regarding the anthropometric characteristics according to the degree of neurological disability.

Dietary parameters

Patients with MS with advanced disability had a lower energy ($p = 0.01$) and fiber ($p < 0.01$) intake than patients with moderate disability (Table VI).

Analytical parameters

Patients with advanced disability had a lower level of albumin ($p = 0.03$), transferrin ($p < 0.01$) and folic acid ($p = 0.03$) and higher levels of CRP ($p < 0.01$). Table VII shows the analytical data in which statistically significant differences were observed.

DISCUSSION

Malnutrition was unusual in our sample of patients with moderate-advanced MS: 8% of patients were malnourished or at risk of malnutrition, although a slightly higher percentage reported significant weight loss (12%). Regarding the results of our study, the most useful clinical parameters to identify patients at risk of malnutrition are SGA and weight loss, however, BMI < 20 lacks diagnostic sensitivity (15,20). Nutritional support was exclusively of MS patients with advanced disability and dysphagia was the determining factor for the prescription. Regarding the anthropometric assessment, both the BMI and the FMI were higher than the normal range. Recent studies noted

that the percentage of FM correlates more rigorously with the metabolic syndrome/central obesity than the BMI (20,21). The fact that a large number of the patients could not be evaluated by BIA due to the impossibility to stand-up autonomously has been decisive to justify the absence of anthropometric characteristics that are associated with advanced MS. There was an increase in the FFMI and a decrease in the percentage of patients with a FFMI lower than normal, which could be justified by the fact that patients who have lost muscle mass have not been able to perform the BIA in the last evaluation (five patients). The type of BIA employed in the study required standing-up, so it has a limited utility in patients with decrease in muscle strength and imbalance. In addition, the fact that there are different devices has made it difficult to establish diagnostic cut-off points for malnutrition (22). However, the BIA is a non-invasive, safe and low cost test that should be incorporated into daily clinical practice to detect early malnutrition and cardiovascular risk, especially by detecting the loss of muscle mass. Body composition, along with the resting metabolic rate, would allow us to calculate the energy requirements of each patient and optimize their nutritional support (19). Handgrip strength test has proven to be a useful technique to identify patients at risk of malnutrition; our patients presented low values of handgrip strength test, which is related to the deterioration of the functional state secondary to the loss of muscle mass characteristic of malnutrition (6). However, we must be cautious because in our patients muscle weakness in the extremities is MS related. Finally, the patients showed a resting metabolic rate lower than healthy volunteers, which was even lower in patients with advanced disability. We consider that the main determinant is the lower proportion of muscle mass due to atrophy. This is an especially interesting fact because in another neurodegenerative disease in which there is also muscular atrophy, such as amyotrophic lateral sclerosis, the increase in resting metabolic rate has been related to hypermetabolism (7,23). It would be interesting to extend the knowledge of the metabolic situation in MS in future studies.

Regarding the dietary parameters, compliance with the nutritional requirements of our patients did not differ significantly with respect to the control population. The fact that both groups had an insufficient energy intake could be related to the underestimation of caloric intake in the completion of the 24-hour recall in both groups. It should be

noted that the lack of compliance with energy requirements was accentuated in the group with the greatest neurological disability. The sustained decrease of 50-75% of the recommended energy intake is considered as a parameter of moderate-severe malnutrition, respectively, so it would be very interesting to monitor this parameter (6). The consumption of polyunsaturated fatty acids and fiber was lower than recommended and, in particular, the fiber deficit was accentuated at the 12-month follow-up (24). It is important to emphasize the importance of maintaining an adequate consumption of fluids and fiber, since constipation is a common problem (25). Also, given that comorbidities influence the activity of the disease, disability, mortality and quality of life, the recommended guidelines for all patients should encourage to eliminate "pro-inflammatory" factors and favor "anti-inflammatory" factors such as: physical activity, giving up smoking, and an "anti-inflammatory diet" (a diet rich in essential fatty acids, especially omega 3 for its anti-inflammatory properties; unrefined carbohydrates; antioxidants; vitamins D and B12 as well as adequate supplements of zinc, fiber and liquids) (26-28).

All analytical parameters were within the reference ranges, as reflected in previous studies (29), with the exception of vitamin D. Vitamin D is essential in the etiopathogenesis and in the clinical course of MS. Vitamin D deficiency in MS has a multifactorial origin that is potentiated throughout the progression of the disease due to a decrease in sun exposure related to decreased ability to ambulate. Other factors such as treatment with glucocorticoids, some antiepileptic drugs and obesity intensify vitamin D deficit. As recommended by the guidelines, screening of the vitamin D serum level should be carried out on patients at risk of this deficiency (30). Sun exposure appears to reduce the risk of MS, but there is no reccomendation on what level of sun exposure is safe and adequate to increase the concentration of vitamin D (31,32). Recently, a study has concluded that it is almost impossible to obtain the recommended doses of vitamin D in winter in the countries of north latitude due to a lower body surface exposed and the low levels of UV radiation (33). Therefore, all patients with MS should be advised to eat foods fortified with vitamin D such as milk or cereals. Patients with low vitamin D levels should be supplemented with vitamin D. Vitamin D supplementation in adults should be based on the observed deficit (30,34). Obese patients or those who are treated with drugs that interfere in vitamin D

metabolism require a double or triple dose of that recommended. In addition, some authors recommend vitamin A supplementation to those patients that have a vitamin D deficiency, because vitamin A is required to bind vitamin D to its receptor so it can exert its anti-inflammatory effects (35).

Throughout the follow-up, a decrease in the serum level of creatinine, prealbumin and folic acid was observed. Albumin and prealbumin, which have traditionally been considered as markers of malnutrition, are currently thought to have greater importance as inflammatory markers, along with leukocytosis (6). Regardless of its clinical significance, it is necessary to periodically monitor the analytical protein parameters (creatinine, albumin, prealbumin, transferrin, PCR) and micronutrients (magnesium, zinc, folic acid) due to their importance of maintaining the integrity of the cell membrane and functioning of the nervous system.

The possible biases of this clinical study are those inherent to an open population-based case-control study, specially, the selection bias of cases/controls, as well as the information collected by participants in the 24-hour recall. The fact that MS is a disease with a slow neurological progression has conditioned the absence of nutritional changes after 12 months. Therefore, it would be interesting to know the evolution of their nutritional status with a longer follow-up period.

It should be emphasized that the fact that the deceased patients were those with malnutrition has conditioned the absence of that the number of patients with clinical malnutrition in the first and last assessments has hardly changed. At the same time, the comparison in the longitudinal study only of the patients who completed the study might have biased the statistical analysis, since those with worse nutritional situation and worse prognosis were excluded in the 12-month evaluation: deceased patients and patients who could not undergo the second anthropometric evaluation due to deterioration of its functional situation.

It can be concluded that the identification of MS patients that are malnourished or at risk of malnutrition would allow to implement prevention strategies that could avoid the complications arising from it (infections, death, pressure sores). Periodic monitoring of nutritional status and ensuring an adequate individualized nutritional support are key factors. As it has been reflected by the latest guidelines of the European Society of Clinical Nutrition and Metabolism, the detection and treatment of

the causes of malnutrition by a multidisciplinary team is highly recommended; likewise, they recommend nutritional counseling for prevention and improvement of the nutritional status in patients with MS (36).

Once the "patients at risk of malnutrition" are identified, it would be appropriate to carry out a comprehensive nutritional assessment that includes the evaluation of nutritional status, the estimation of nutritional and energy requirements, the detection of the main contributing factors for malnutrition (such as dysphagia) and the multidisciplinary information to ensure an adequate energy and protein intake (37).

CONCLUSIONS

Malnutrition is infrequent in patients with MS. The need for nutritional support is related to dysphagia in patients with advanced neurological disability. The nutritional status of patients with moderate-advanced MS is defined by a tendency to overweight and by the decrease in resting metabolic rate and handgrip strength that is related to the loss of muscle mass. Nutritional counseling is essential due to the deficient intake of polyunsaturated fatty acids and fiber. Vitamin D deficiency is prevalent and is exacerbated in the evolution of the disease; for this reason, daily sun exposure and foods enriched with vitamin D should be strongly recommended to all patients and, in the case of MS patients with vitamin D deficit, they should receive supplementation.

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Table I. Anthropometric parameters of the participants in the study

	MS patients	*Controls*	*p*
n	124	62	
Weight (kg)*	67.7 ± 14.3	69.7 ± 14.9	0.3
Height (m)*	1.63 ± 0.1	1.63 ± 0.9	0.6
BMI (kg/m²)*	25.2 ± 4.9	26 ± 4.2	0.2
Handgrip strength (kg)*	22 ± 9.2	28.1 ± 10.5	*< 0.01*
Resting metabolic rate (kcal)*	1,517.2 ± 435.6	1,717.2 ± 426.7	*< 0.01*
FFMI (FFM/m²)*	17.5 ± 3	18.3 ± 2.7	0.06
FMI (FM/m²)▪	7.1 (5.3-9.7)	6.8 (5.4-10.1)	0.5

BMI: body mass index; FFMI: fat-free mass index; FMI: fat mass index. *Normal distribution: mean ± SD. †Non-normal distribution: median (p25-p75).

Table II. Dietary parameters of the participants in the study

	MS patients	*Controls*	*p*
n	124	62	
Energy (kcal)*	1,902.1 ± 456.1	2,023 ± 389.3	0.08
Carbohydrates (g)*	210.7 ± 60.5	220.3 ± 53.8	0.3
Proteins (g)*	85.8 ± 22.4	88.1 ± 17.1	0.4
Fats (g)*	78.9 ± 23.9	84.5 ± 23.8	0.1
Saturated fatty acids (g)†	18.9 (15-25)	19.2 (15.7-25.6)	0.3
Monounsaturated fatty acids (g)*	30.6 ± 10	34.6 ± 10.8	*0.01*
Polyunsaturated fatty acids (g)†	6.6 (4.9-9)	7.8 (5.4-11.5)	*0.01*
Fiber (g)*	17.7 ± 7.3	18.3 ± 6.3	0.5
Nutritional requirements covered			
Energy, n (%)	31 (25.2)	20 (35.1)	0.1
Carbohydrates, n (%)	116 (94.3)	53 (93)	0.7
Proteins, n (%)	120 (97.6)	57 (100)	0.5
Polyunsaturated fatty acids, n (%)	15 (12.9)	12 (21.1)	0.1
Fiber, n (%)	14 (12.1)	12 (21.1)	0.1

*Normal distribution: mean ± SD. †Non-normal distribution: median (p25-p75).

Table III. Analytical parameters of the participants in the study

	MS patients	*Controls*	*Reference values*	*p*
n	124	62		
Magnesium (mg/dl)*	2.09 ± 0.1	2.01 ± 0.1	(1.6-2.6)	*< 0.01*
Alkaline phosphatase (U/l)*	73.4 ± 24.5	62.8 ± 23.4	(40-130)	*< 0.01*
Total bilirubin (mg/dl)†	0.4 (0.3-0.5)	0.4 (0.3-0.6)	(0.1-1.4)	*0.04*
Albumin (g/l)*	4.4 ± 0.2	4.5 ± 0.3	(3.5-5.2)	*< 0.01*
Vitamin D (ng/ml)†	19 (14-26)	28 (20.5-35.5)	(30-100)	*< 0.01*
Vitamin E (mcg/ml)†	1,446 (1,305-1,658)	1,703 (1,455-2,118)	(500-2,000)	*< 0.01*

*Normal distribution: mean ± SD. †Non-normal distribution: median (p25-p75).

Table IV. Dietary parameters of MS patients: initial evaluation and 12-month evaluation

	Initial evaluation	12 month-evaluation	p
n	124	104	
Dietary parameters (n = 69)			
Energy (kcal)*	1,973.4 ± 485.9	1,942.1 ± 867.2	0.7
Carbohydrates (g)*	2,16.94 ± 60.42	197.84 ± 66.22	*0.02*
Proteins (g)*	85.78 ± 23.96	83.78 ± 29.55	0.3
Fats (g)†	81.2 (65.3-96.4)	78.1 (66.3-94.7)	0.8
Saturated fatty acids (g)†	19.9 (16-25.3)	19.2 (15.2-24.6)	0.6
Monounsaturated fatty acids (g)†	30.6 (24.6-36.5)	32.5 (27.7-39.1)	0.1
Polyunsaturated fatty acids (g)†	6.7 (5-9.1)	7.3 (85.8-9.6)	0.1
Fiber (g)*	18.47 ± 7.56	16.12 ± 5.78	*< 0.01*
Nutritional requirements coverage			
Energy, n (%)	20 (29)	15 (21.7)	0.3
Carbohydrates, n (%)	66 (95.7)	65 (94.2)	1
Proteins, n (%)	67 (97.1)	67 (97.1)	1
Polyunsaturated fatty acids (g), n (%)	10 (14.7)	11 (16.2)	1
Fiber, n (%)	10 (14.5)	3 (4.3)	*0.03*

*Normal distribution: mean ± SD. †Non-normal distribution: median (p25-p75).

Table V. Analytical parameters of MS patients: initial evaluation and 12-month evaluation

	Initial evaluation	*12-month evaluation*	*Reference values*	*p*
n	124	106		
Calcium (mg/dl)*	9.52 ± 0.39	9.37 ± 0.36	(8.2-10.2)	*< 0.01*
Zinc (mcg/dl)†	87 (77-94.5)	80 (90-103)	(68-107)	*< 0.01*
GOT (U/l) †	18 (15-22)	20 (16-24)	(10-50)	*< 0.01*
Prealbumin (mg/dl)*	23.08 ± 5.01	21.41 ± 4.5	(10-40)	*< 0.01*
Creatinine (mg/dl)*	0.75 ± 0.17	0.72 ± 0.16	(0.7-1.2)	*< 0.01*
Folic acid (ng/ml)†	7.9 (5.9-11.1)	7.5 (5.7-10.3)	(4.2-19.9)	*< 0.01*
Vitamin D (ng/ml)†	19 (14-26.5)	18.5 (11.7-24)	(30-100)	*< 0.01*
Vitamin A (mg/l)†	54 (46-64)	67 (51-89)	(30-100)	*< 0.01*
Vitamin E (mcg/ml)*	1,530.54 ± 407.15	2,104.51 ± 641.3	(500-2,000)	*< 0.01*

*Normal distribution: mean ± SD. †Non-normal distribution: median (p25-p75).

Table VI. Dietary parameters of MS patients according to neurological disability

	EDSS < 6	EDSS ≥ 6	p
n	42	82	
Energy (kcal)*	2,028.9 ± 536.6	1,836.3 ± 396	*0.02*
Carbohydrates (g)*	221.5 ± 67.2	205 ± 56.2	0.1
Proteins (g)*	87.6 ± 24.8	85 ± 21.2	0.5
Fats (g)*	86.4 ± 28.4	75 ± 20.3	*0.02*
Saturated fatty acids (g)*	22.3 ± 9.8	19.1 ± 7.7	0.06
Monounsaturated fatty acids (g)*	31.1 ± 11.8	30.3 ± 8.8	0.6
Polyunsaturated fatty acids (g)†	6.8 (5-8.8)	6.3 (4.9-9)	0.4
Fiber (g)*	19.6 ± 9.2	16.6 ± 5.9	0.06
Nutritional requirements coverage			
Energy, n (%)	16 (38.1)	15 (18.5)	*0.01*
Carbohydrates, n (%)	39 (92.9)	77 (95.1)	0.6
Proteins, n (%)	41 (97.6)	79 (97.5)	0.7
Polyunsaturated fatty acids, n (%)	5 (11.9)	10 (13.5)	0.8
Fiber, n (%)	10 (23.8)	4 (5.4)	*< 0.01*

*Normal distribution: mean ± SD. †Non-normal distribution: median (p25-p75).

Table VII. Analytical parameters of MS patients according to neurological disability

	EDSS < 6	EDSS ≥ 6	Reference values	p
n	42	82		
Albumin (g/l)*	4.4 ± 0.2	4.3 ± 0.2	(3.5-5.2)	*0.03*
Transferrin (mg/dl)†	271.5 (252.5-314.5)	246.5 (219.7-276.5)	(200-360)	*0.02*
CRP (mg/l)†	1 (1-1.4)	1.5 (1-4.75)	(0-5)	*0.01*
Folic acid (ng/ml)†	10 (6.5-14.5)	7.6 (5.9-10.3)	(4.2-19.9)	*0.03*

CRP: C-reactive protein. Normal distribution: mean ± SD. †Non-normal distribution: median (p25-p75).