DOI: 10.12957/demetra.2017.27833

Nutritional recommendations for the treatment of fibromyalgia

Recomendações nutricionais para o tratamento da fibromialgia

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Abstract

Fibromyalgia is a clinical syndrome characterized by chronic pain, fatigue, sleep disturbances, anxiety, depression, among other symptoms. The objective of this review was to update dietetic knowledge about fibromyalgia. An integrative review was carried out, in which the databases Science Direct, Medline Pubmed and Scientific Electronic Library Online (Scielo) were consulted from July to September 2016, with fibromyalgia and nutrition descriptors, searching originaland reviewed articles, guidelines and consensus of national and international recommendations published from 2003 to 2016. Fibromyalgia occurs most often in women aged 35 to 60 years, commonly overweight or obese. There are few original studies on nutrients or nutritional therapy for fibromyalgia, and there are no specific dietary recommendations. There is an important relationship with oxidative stress, wherein there are may be mitochondrial dysfunction, which would make beneficial therapy with antioxidant nutrients, such as vitamins C, E and β-carotene. There are reports of vitamin E reduction in individuals with fatigue and depression. Some topics addressed in studies were oxidative stress and supplementation with coenzyme Q10 (coQ10), the relationship between body composition and symptoms of fibromyalgia and vitamin D deficiency. Fatigue can be aggravated in individuals with non-celiac gluten sensitivity, however, studies that further investigate this relationship are still needed. Although there are no specific nutritional recommendations, these individuals can benefit from diet based on the principles of healthy nutrition, rich in antioxidants and weight reduction, when indicated.

Keywords: Fibromyalgia. Diet Therapy. Nutrients. Dietary Supplements. Recommended Dietary Allowances.

Resumo

A fibromialgia é uma síndrome clínica caracterizada pela presença de dor crônica, fadiga, alterações de sono, ansiedade e depressão. O objetivo desta revisão foi atualizar os conhecimentos dietoterápicos acerca da fibromialgia. Realizou-se uma revisão integrativa, na qual foram consultadas as bases de dados *Science Direct*, *Medline Pubmed* e *Scientific Electronic Library Online* (Scielo) no período de julho a setembro de 2016, com os descritores *fibromyalgia* e *nutrition*, buscando artigos originais, de revisão, guias e consensos de recomendações nacionais e internacionais publicados de 2003 a 2016. A fibromialgia ocorre com maior frequência em mulheres com 35 a 60 anos, comumente com sobrepeso ou obesidade. Existem poucos estudos originais sobre nutrientes ou terapia nutricional para fibromialgia, não há recomendações nutricionais específicas. Existe relação importante com o estresse oxidativo, em que possivelmente há disfunção mitocondrial, o que tornaria benéfica a terapia com nutrientes antioxidantes, como as vitaminas C, E o β-caroteno. Há relatos da redução da vitamina E em indivíduos com fadiga e depressão. Alguns temas abordados em estudos foram o estresse oxidativo e a suplementação com coenzima Q10 (coQ10), a relação entre a composição corporal e sintomas da fibromialgia e a deficiência de vitamina D. A fadiga pode ser agravada em indivíduos com sensibilidade ao glúten não celíaca, contudo, ainda são necessários estudos que investiguem melhor essa relação. Embora não existam recomendações nutricionais específicas, esses enfermos podem beneficiar-se com dieta baseada nos princípios da nutrição saudável, rica em antioxidantes, e da redução de peso, quando houver indicação.

Palavras-chave: Fibromialgia. Dietoterapia. Nutrientes. Suplementos Nutricionais. Recomendações Nutricionais.

Introduction

Fibromyalgia has an unknown etiology. It is characterized by generalized chronic pain in the locomotor system, in addition to intense fatigue, sleep disorders, paresthesia in the extremities, depression, anxiety, joint stiffness, headache and a feeling of swelling in the hands.[1-3]

There are no laboratory tests to confirm the diagnosis, which is based on the presence of body pain for at least three months, with fatigue, sleep disorders, cognitive changes, mood disorders and other variable-grade somatic symptoms that cannot be explained by the presence of other

diseases.[2,4] Generalized pain is defined as the presence of pain in the left and right quadrants of the body, above and below the waist, in addition to axial pain, in which there is involvement of the cervical, thoracic or lumbar spine. For the diagnosis, digital palpation is performed at 18 *tender points* and it is considered positive when there is pain in at least 11 of these points.[5]

Patients with fibromyalgia may present other associated diagnoses, such as irritable bowel syndrome[6] and hypothyroidism.[7]

The prevalence of fibromyalgia assessed according to the American College of Rheumatology (ACR) criteria for 1990 ranges from 0.66% to 4.4%, and it is more common in women aged 35-60 years.[8] In Brazil, a prevalence of 2.5% of fibromyalgia was found.[9] Although the disease is more common in middle-aged people, it also affects children, adolescents and the elderly.[10]

Among the treatments that can be employed, complementary and alternative medicine comprises the use of natural products, vitamins, minerals, probiotics and other dietary supplements.[11]

The science of nutrition presented many advances during the twentieth century, highlighting the discovery of vitamins to bioactive substances in food. Currently, issues such as nutrigenomics and individualized nutritional recommendations are discussed. It is speculated that in the future there may be dietary recommendations for the bioactive substances present in foods considered functional.[12] It is also important to note that considerable advances have been made in enteral and parenteral nutrition therapy, making it possible to support patients for long periods of time.[13,14]

However, there are still many challenges related to nutritional therapy in various diseases, including fibromyalgia. This review aims to find the scientific evidence related to nutrition in fibromyalgia, through an integrative literature review,[15] which is considered a subdivision of the systematic review, along with meta-analysis, systematic review and qualitative review.[16]

Methodology

The databases *Science Direct*, *Medline Pubmed*, *Medline Bireme* and *Scientific Electronic Library Online* (Scielo) were consulted in the period from July to September 2016. The descriptors *fibromyalgia* and *nutrition* were used, searching for original reviewed articles, as well as guides and consensuses of national and international societies available in their own electronic addresses, considering pharmacological and non-pharmacological treatment, that have been published from 2003 to 2016. In addition to the bases mentioned above, as a search strategy, the Google Scholar site was also used and the list of references of the most recent publications was checked.

As inclusion criterion, articles in Portuguese, Spanish and / or English were selected to provide evidence on the nutritional recommendations for the treatment of fibromyalgia. The steps for the

research design are shown in Figure 1. The initial screening of articles consisted in the evaluation of titles and abstracts, seeking to answer the nutritional recommendations for fibromyalgia. Afterwards, a critical reading of the selected articles was carried out to determine which ones met the criteria to be included in the review.

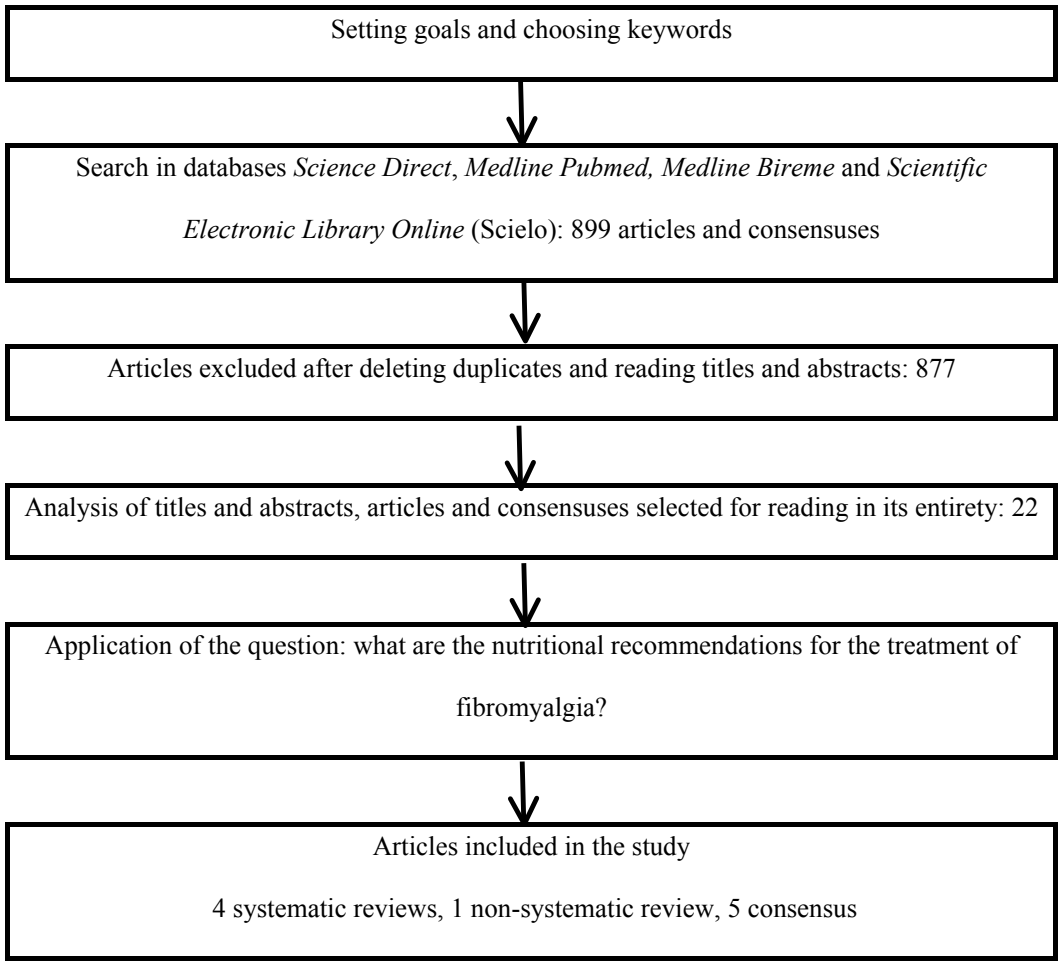

Figure 1. Flowchart of the research on nutritional evidence in the treatment of fibromyalgia.

Results

Twenty two scientific articles were selected and five of which were included in the analysis. Four of which were systematic reviews of the literature and one classified as a non-systematic review, in addition to five consensuses of fibromyalgia treatment (Table 1). It is important to note that most of the studies on nutrition related to fibromyalgia contain small numbers of individuals, are not randomized and therefore are not conclusive, and that the systematic reviews selected group the majority of these studies. Thus, articles that were read in full and not included in the critical analysis, because they did not meet the inclusion criteria, were often cited in the discussion. The topics addressed in these articles were oxidative stress and supplementation with coenzyme Q10 (coQ10),[25,27-30,32] body composition and symptoms of fibromyalgia[35,37,39] and vitamin D deficiency and its influence on fibromyalgia.[41-43]

Table 1. Nutritional recommendations for the treatment of fibromyalgia

Author	Year	Methodology	Main goal	Main results
Arranz, Canela and Rafecas[17]	2010	Systematic Review from 1998 to 2008	Relating nutrition and fibromyalgia	Presence of overweight or obesity; micronutrient deficiency.
Holdcraft, Assefi and Buhwald[18]	2003	Systematic Review from 1975 to 2002	To find evidence regarding the use of complementary and alternative medicine in the treatment of fibromyalgia	Moderate evidence for magnesium supplementation, strong for SAM-e supplementation and limited for *Chlorella pyrenoidosa supplementation*.
Holton, Kindler and Jones[19]	2009	Systematic Review from 1986 to 2008	To investigate the effects of vegetarian diet, elimination and / or weight loss in fibromyalgia	There is no evidence for dietary restrictions in fibromyalgia.

to be continued

Author	Year	Methodology	Main goal	Main results
Li and Micheletti[20]	2011	Review	To investigate the effects of vegetarian diet, elimination and / or weight loss in fibromyalgia	There is an increase in pain related to glutamate and aspartame ingestion; there are no dietary recommendations for the treatment of fibromyalgia.
Terhorst et al.[11]	2011	Systematic Review from 1950 to 2010	To find evidence regarding the use of complementary and alternative medicine in the treatment of fibromyalgia	Favorable results for micronutrient supplementation, SAM-e, *Chlorella pyrenoidosa* and soybean.
Carruthers and Sande[21]	2003	Canadian Consensus	Recommendations for the treatment of fibromyalgia	Indicated balanced and nutritious diet; authors discuss the role of nutrients.
Fitzcharles et al.[4]	2013	Canadian Consensus	Recommendations for the treatment of fibromyalgia	It does not contemplate nutritional treatment.
Hassett and Gevirtz[23]	2009	Review	Recommendations for non-pharmacological treatment of fibromyalgia: use of complementary and alternative medicine	To look for individual factors to define better forms of supplementation.
Heymann et al.[22]	2010	Brazilian Consensus	Recommendations for the treatment of fibromyalgia	It does not contemplate nutritional treatment.
Rivera et al.[2]	2006	Spanish Consensus	Recommendations for the treatment of fibromyalgia	To seek patient self-efficacy in treatment.

In the systematic review by Arranz et al.,[17] the authors reviewed articles on vegetarian diets, rich in antioxidants, although there are few studies and a small number of individuals. As for nutritional status, patients are generally overweight and / or obese, and have micronutrient deficiencies such as selenium, zinc and magnesium, and low levels of branched chain amino acids (BCAA), although it has not been possible to determine if these deficiencies are due to changes in ingestion and influence the etiopathogenesis of fibromyalgia. The authors conclude that a healthy diet for weight maintenance and nutritional supplements is recommended for the best nutritional status, although more studies are needed to understand the potential benefits of nutrition.

On the use of complementary and alternative medicine and nutritional supplementation in the treatment of fibromyalgia, the studies present small samples, are not randomized, and lack placebo or double blind control, most of them presenting limited or insufficient evidence. To date, there is moderate evidence for the use of magnesium, which is essential for ATP synthesis, strong evidence for S-adenosyl-L-methionine (SAM-e) supplementation and limited to *Chlorella pyrenoidosa,* while anthocyanidins and vegetarian diet have limited evidence.[18]

There is questioning whether the removal of some foods, additives or increased nutrient levels influence the treatment of fibromyalgia, or whether results are due to weight loss caused by restrictive diets. It is hypothesized that monosodium glutamate may contribute to increased obesity but it has not yet been tested in humans. Although the evidence for dietary modifications is restricted, the authors consider that these changes are safer and less expensive than pharmacological therapies and are under the control of the patient, noting that less restrictive diets may achieve greater adherence.[19]

According to Li and Micheletti,[20] most of the studies that relate diet and fibromyalgia are observational and descriptive, which results in low statistical power for vegetarian diets, lack of controls in studies with weight loss and difficult evidence of effects for elimination diets. Although there are reports of patients believing in a relationship between fibromyalgia and diet, more rigorous studies are needed to determine the function of the diet in fibromyalgia or specific dietary recommendations for treatment.

In the systematic review on the use of dietary supplements, such as micronutrients, SAM-e, *Chlorella pyrenoidosa* and soybeans, favorable results were obtained for these nutritional interventions, although most studies are preliminary or exploratory, and with small samples.[11]

Regarding recommendations for nutritional treatment, the Canadian Consensus[21] proposes that patients should be encouraged to eat balanced and nutritious meals at regular times, maintain good hydration, take multienzyme along with meals when associated with irritable bowel syndrome (IBS), use supplements when needed for treatment. Specific recommendations involve the elimination of those non-tolerated foods in patients with IBS and low-glycemic diet in case of hypoglycemia.

Still according to Canadian recommendations, vitamins are often cofactors that help enzymes in the use of nutrients. The recommended intake is based on the estimated sums required to prevent symptoms of deficiencies and not at optimal levels for chronic diseases. The balanced vitamin profile is helpful. Vitamins C and E (α-tocopherol) and β-carotene are antioxidants and stimulate the immune system. Vitamins of the B complex reduce stress; folic acid can help in lowering cholesterol. Calcium is involved in hundreds of enzymatic reactions and has increased absorption by vitamin D. Magnesium maleate can reduce fatigue and prevent muscle cramps, patients with fibromyalgia may require extra magnesium maleate compared to the usual ratio of 2:1 of calcium to magnesium. Zinc improves the function of nerve and muscle tissues and is involved in the formation of collagen.[21]

As for the use of supplements, essential fatty acids (EFA) are required for cell membrane integrity and prostaglandin synthesis. Ingestion of foods such as ice water fish, salmon oil and primrose oil may influence blood flow and nerve impulse transmission. Lecithin has function in the nervous and muscular tissues, in the brain and in the circulation; methylsulfonylmethane (MSM) can strengthen connective tissue and reduce joint pain; glucosamine sulfate can reduce pain and improve mobility of joints; glutamine can improve muscle function and promote growth hormone production; procyanidolic oligomer (PCO) can protect muscles and help prevent arthritis and bursitis.[21]

In 2013, the *Canadian Guide for the diagnosis and treatment of fibromyalgia* was published, which discusses the lack of evidence based on scientific studies, leading to the exclusion of nutritional recommendations from the protocols. Thus, nutritional treatment is not contemplated in the Canadian guide,[4] just as it is not contemplated in the *Brazilian Consensus on the Treatment of Fibromyalgia*.[22]

Hassett and Gevirtz,[23] in their work on the non-pharmacological treatment of fibromyalgia and the use of complementary and alternative medicine, argue that studies with nutritional supplements should explore individual factors to identify which subgroups of patients may respond better to each type of treatment.

The use of non-pharmacological strategies for the treatment of fibromyalgia is based on the stimulus to patient independence, social support and lifestyle that promote health, psychological assessment and counseling, and the practice of moderate physical activity.[2,4]

Discussion

The most recent literature has presented discussion about the oxidative stress present in fibromyalgia and the use of antioxidants, the issue of excess body weight and micronutrient deficiency.

Patients with fibromyalgia produce 3.2 times more reactive oxygen species (ROS) than controls, comparable results to patients with rheumatoid arthritis, systemic lupus erythematosus, systemic vasculitis and systemic sclerosis, diseases with inflammatory profile.[24] Oxidative stress in fibromyalgia is an accepted fact, but its role in the disease, from a physiological point of view, is unclear, and the mechanism by which it may have an effect on worsening symptoms is still unknown.[25]

The use of antioxidant therapy or stress reduction with administration of antioxidant drugs and control of risk factors, such as smoking cessation, physical activity and diet, can be effective therapy for fatigue. It is possible that oxidative stress is an important mediator in the vicious cycle, aggravating chronic fatigue, if not the primary cause of fatigue.[6]

CoQ10 is present in cell membranes and has the function of transferring electrons from complexes I and II to complex III in the mitochondrial respiratory chain. It presents a critical role in the production of ATP, contains important role in cellular metabolism and limits the production of reactive oxygen species (ROS). It is suggested that CoQ10 is a marker of mitochondrial function.[26]

CoQ10 supplementation induced increased mitochondrial biogenesis and protein expression levels, with increased mitochondrial DNA copy numbers. These results suggest the function of CoQ10 and mitochondrial dysfunction in the pathogenesis of fibromyalgia. Treatment with CoQ10 can be used as an alternative therapy in fibromyalgia and its beneficial effects can be monitored at the cellular level. However, more research is needed to clarify precise mechanisms by which CoQ10 can contribute to pathological and therapeutic processes.[27]

Coenzyme Q10 (CoQ10) supplementation improved sleep and mental alertness, reduced joint pain, headache episodes and intensity, *tender points* numbers and lipid peroxidation, as well as improving fatigue symptoms , depression and anxiety.[28-30] Mitochondrial dysfunction may be involved in several symptoms observed in fibromyalgia.[31] Studies with CoQ10 involve a small number of individuals and their results cannot be generalized.

In addition to the symptoms of the disease, it is necessary to administer the side effects of drug therapy. Amitriptyline causes increased ROS and reduction in CoQ10 levels, increased lipid peroxidation, and a reduction in mitochondrial mass, suggesting that the treatment aggravated mitochondrial dysfunction in these patients. ATP levels were also decreased, probably because CoQ10 is an essential component of mitochondrial electron transport and is directly involved in ATP biosynthesis. CoQ10 supplementation may prevent or reduce the effects of amitriptyline.[32]

Other effects related to drug treatment may be cited, such as weight gain, edema, constipation and nausea.[33] Increased body mass index (BMI) influences sleep quality, hyperalgesia and quality of life, which may complicate the clinical picture, insofar as physical strength and flexibility are

affected, in addition to pain sensitivity, especially in the lower part of the body.[34] Individuals who were overweight or obese presented higher levels of pain, fatigue and stiffness, as well as lower vitality.[35] The establishment of correlations between body composition and variables, such as emotional function, pain, vitality and physical capacity, was not possible.[36] Although fibromyalgia was more common in premenopausal women, the relationship between percentage of body fat and eating disorders was observed in adolescents.[37]

Regarding nutritional status, there is a prevalence of overweight and obesity, which may involve up to 70% of patients with fibromyalgia.[33] Excess weight may increase serum concentrations of C-reactive protein (CRP), which can be reduced with exercise. Serum CRP concentrations, an important indicator of inflammation, are not affected by diet or sleep.[38]

Reduction in BMI improves symptoms of fibromyalgia, such as pain and body dissatisfaction. Weight loss may be responsible for reducing joint pressure, reducing energy demands for tasks, reducing fatigue, and increasing willingness to perform tasks.[39]

Among the major changes in fibromyalgia are the presence of chronic fatigue and depression. In both, the studies demonstrated low serum concentrations of α-tocopherol, which may indicate the presence of oxidative stress.[6,40]

In a control case study with premenopausal women, it was observed that vitamin D deficiency is not more common in fibromyalgia than in controls. However, there was an association between low concentrations of vitamin D and pain in the patients group, indicating that hypovitaminosis D may have an impact on pain intensity.[41]

As for vitamin D supplementation, there was reduction of pain in the treatment group, with no difference with controls in somatization, depression and anxiety nor in physical or mental health. The authors conclude that the lack of improvement in some fibromyalgia symptoms may be related to both the small sample size and the complexities of the symptoms, which are not related only to vitamin D deficiency.[42]

Women with premenopausal fibromyalgia presented lower concentrations of vitamin D than controls, and also had lower bone mineral density (BMD) in the lumbar region. In patients with severe vitamin D deficiency, there was loss of short-term memory, confusion, mood disorders, sleep disorders, and palpitations. Vitamin D concentrations were inversely related to the visual pain scale, Beck score of depression and bone mineral density (BMD) in the lumbar region. This study concludes that there is a prevalence of vitamin D deficiency among fibromyalgia patients, who will benefit from vitamin D and calcium supplementation, as well as physical activity, along with medical treatment to prevent the development of osteoporosis.[43]

The chronic fatigue syndrome present in fibromyalgia may be aggravated by the sensitivity to non-celiac gluten, recently considered comorbidity of both conditions. In this syndrome, there is the presence of intense fatigue and unexplained cognitive, autonomic and neuroendocrine symptoms, in the last six months, with the possible presence of gastrointestinal symptoms as diagnostic criteria.[44] Sensitivity to non-celiac gluten presents clinical manifestations that overlap with those of fibromyalgia, chronic fatigue and irritable bowel syndrome.[45] Thus, some symptoms of fibromyalgia, such as fatigue, headache and gastrointestinal discomfort, are also common symptoms in individuals with gluten sensitivity.[46] In individuals with fibromyalgia with non-celiac gluten sensitivity, the exclusion of gluten from the diet was related to the remission of the pain criteria, return to work and discontinuation of opioid use, as well as improvement of symptoms such as fatigue, gastrointestinal symptoms, migraine and depression.[47] Similarly, there was reduction of intestinal frequency in individuals with irritable bowel syndrome and dominant diarrhea after exclusion of gluten from the diet.[48]

The exclusion of gluten should be followed by a balanced diet, with the ingestion of whole grains, increase of vegetables and reduction of the energy density of foods,[46] seeking adequate nutrition and dietary balance according to the symptoms, more than the simple exclusion of gluten from the diet.[44] Because of this gluten sensitivity issue potentially having relevant effects on the symptoms of fibromyalgia, the protocol of the first randomized controlled trial was recently published to evaluate the effects of gluten exclusion among fibromyalgia-sensitive patients.[49]

Final considerations

The science of nutrition has made great advances in the last 100 years, although nutrition is considered complementary therapy in the treatment of various diseases. There are no specific nutritional recommendations for the treatment of fibromyalgia. This group of patients should adopt the principles of healthy eating. Reduction of obesity may contribute to decrease pain and improve functional capacity, as well as to reduce inflammatory markers and improve quality of life.

Contributors

Da Silva AF participated in the design of the article, the bibliographical survey and the preparation of the manuscript. Schieferdecker MEM participated in the design of the article, the preparation of the manuscript and the final revision of the article.

Conflict of interests: The authors declare no conflict of interest.

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Received: March 06, 2017
Reviewed: August 06, 2017
Accepted: August 21, 2017