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Fibromyalgia and nutrition: Therapeutic possibilities?

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ABSTRACT

Fibromyalgia (FM) is a complex chronic condition of unknown etiology, characterized by deep and widespread pain, sleep problems, cognitive impairment, fatigue, and other well-known functional symptoms. Recently, it has been proposed that an imbalance of nutritive components, including essential metal ions and vitamins, might play a critical role in the development of FM. Muscle pain has been associated with deficiencies in amino acids, magnesium, selenium, vitamins B and D, as well as with the harmful effects of heavy metals, such as mercury, cadmium, and lead. Research indicates that patients deficient in certain essential nutrients may develop dysfunction of pain inhibitory mechanisms together with fatigue and other FM symptoms. Additionally, mercury and other toxic elements may interfere with the bioavailability of essential nutrients. This review examines the many effects of metals and vitamins in pain evaluation of FM patients. Dietary guidance is therefore critical for FM patients to help them in correcting a suboptimal or deficient intake of essential nutrients. When optimal levels of nutrition are achieved, pain levels are usually lowered. Additional research is recommended in the field of FM and nutrition to disclose further possible relationships.

1. Introduction

Fibromyalgia (FM) is a complex, painful syndrome of non-articular origin characterized by diffuse fatigue and other functional symptoms in combination with pain and tenderness in at least in 11 of 18 tender point sites [1]. Additionally, sleep problems, musculoskeletal pain, cold fingers and toes, cognitive impairment, depression, tingling in the limbs, gastrointestinal disorders, and morning stiffness are commonly experienced symptoms of the disease [2–5]. FM often overlaps with a high frequency of non-musculoskeletal symptoms such as chronic fatigue syndrome (CFS), affective disorders, tension headaches, migraine, and irritable bowel syndrome [6–9].

Reports from animal studies indicate that the levels of magnesium (Mg) are critical in inducing muscle pains, leg weakness, and related symptoms, with a protective effect of elevated Mg intake [10]. Furthermore, selenium (Se) deficiency is a possible cause of musculoskeletal pain associated with FM. In multiple animal experiments, an adequate intake of Se has been demonstrated to play a protective role against damage induced by ischemia and subsequent reperfusion [11–14]. Similar protection has been reported in different animal studies with other antioxidant nutrients such as carnosine and taurine and the hormone melatonin. These agents may induce expression of different antioxidant enzymes, including superoxide dismutase (SOD), glutathione peroxidase (GPX), as well as glutathione reductase (GR) [15–17]. Moreover, it has been suggested that an elevated total burden of toxic metals, such as cadmium (Cd) and mercury (Hg) [14,18,19], may induce worsening of diverse muscle pains with different etiologies in humans [20–22].

According to recent studies, the prevalence of FM is between 0.2 and 6.6% in the general population, between 0.7 and 11.4% in urban areas, between 2.4 and 6.8% in women, and up to 15% in subjects previously affected by serious trauma [4,23–26]. It is well documented that FM has both social and economic effects, with sufferers often unable to work. In the present article, we aim to evaluate the possible relationship between nutrition and FM. We also review the main studies carried out on nutrient imbalances and dietary interventions. We have explored current data related to FM and some dietary supplementations and highlighted the major concerns or issues about the current information regarding the relationship between FM and nutritional intake.

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2. The nutritional context of fibromyalgia

The relationship between FM and nutrition has been recently thoroughly reviewed [4,27]. Dietary habits in female subjects with FM may fundamentally affect the clinical course of this disease [28,29], although it is difficult to associate FM with a specific dietary imbalance or impairment in metabolism [30]. However, the metabolic syndrome [31] characterized by arterial hypertension and obesity and increased risk of stroke may exacerbate FM-related pain [31,32]. A number of articles indicate the benefits of adequate nutritive advice to FM patients. Thus, after following a diet rich in anti-oxidant nutrients, clinical improvement in FM symptoms was reported [27]. Multiple antioxidant-rich nutritive therapies targeting muscle cells appear to represent a promising approach. A combination of various antioxidant and anti-ischemic protective substances, including Se, GSH precursor amino acids, taurine, carnosine, and melatonin [33,34], as well as plant-derived substances, such as flavonoids, which can enhance the expression of thioredoxin reductase, for example isothiocyanates, such as sulforaphane, erucin, and iberin [10,35] has been proposed.

Both nutrition and exercise based protocols have been suggested in the treatment of FM. Antinociceptive therapy targeting the C-fibres, with antioxidant nutrients for reducing prostaglandin production and minimizing oxidant stress activation of protein kinase C (PKC) activation in the C-fibres [36,37], combined with low dietary omega-6/omega-3 polyunsaturated fatty acid (PUFA) ratio in order to reduce prostaglandin production [38], represent possibilities to improve FM via a nutritional approach. Physical exercise, in form of both endurance [39] and resistance [40–43] training in order to train the mitochondria [39] of the skeletal muscle cells, induce respiratory and perhaps antioxidant defense enzymes in the muscle cells [40,43], and may stimulate the transfer of “healthy mitochondria” from satellite cells to muscle cells [41,44–47]. These might all represent good nutritional and exercise based suggestions to reduce FM incidence and treat mood disorders.

3. Fibromyalgia, metabolism, and muscle pain

FM is characterized by persistent and diffuse musculoskeletal pain, usually associated with sleep, mood, and cognitive impairments [48,49]. Fig. 1 shows the major areas of the widespread musculoskeletal pain associated with FM. Exacerbating causes for the typical musculoskeletal pain associated with FM are mainly related to obesity and carbohydrate-rich diets [50,51]. It is well known that an altered metabolic status has been reported in FM-affected patients [52]. Some authors have tried to explore the possible relationship between impaired glucose metabolism in migraine and FM, particularly in the dysregulation of lactate, which could cause muscle pain, but to date, no significant association has been found [53,54]. However, FM affected females are much more sensitive than controls to the suppressive effect of nitric oxide (NO) on oxidative phosphorylation, causing an excess of glycolysis by-products during a muscular exercise [55]. This may suggest that foods triggering inducible nitric oxide synthase (iNOS) and the content of NO may exacerbate FM-related pain. Conversely, plant-enriched diets containing foods able to boost NO to its normal levels, e.g., pomegranate, citrus fruit, walnuts, rocket, lettuce, spinach, L-citrulline containing watermelon, can help in reducing FM-related pain. Some fruits and vegetables, rich in chemical acids, such as tomatoes or citrus fruits, are felt (or, believed, by sufferers) to contribute to FM-related pain [56,57]. Creatine supplementation seems to be efficacious in reducing FM-associated musculoskeletal pain [31,57]. Creatine reduces the glycolytic-derived lactate, and in this sense, it lowers FM-associated muscle fatigue and pain [57]. Additionally, foods containing histamine may also contribute to FM pain. Together with further inflammatory mediators, such as substance P, bradykinin, TNF-α, interleukins, and prostaglandins, also histamine triggers inflammation-related pain [58,59]. The inhibition of H1 receptors increases analgesia [60]. Therefore, in the metabolic-related exacerbation and pathogenesis of FM-related musculoskeletal pain, both immune (also allergic) and dysmetabolic factors work together.

Moreover, deficiency of fundamental nutritional components may elicit or exacerbate FM-related musculoskeletal pain. Aside from Se, FM subjects have lower levels of serum magnesium (Mg) and zinc (Zn) [61]. It is well known in murine studies that Zn deficiency negatively affects recovery from muscle injury [62]. Mg deficiency affects muscle function, as Mg is physiologically related to muscle tension. Mg supplementation resulted in the reduction of headaches associated with muscle tension [63]. A deficiency in myoadenylate deaminase is a leading cause of painful metabolic-derived myopathies, including FM-related musculoskeletal pain [64]. As well as the vitamin deficiencies associated with FM, such as folic acid or vitamin B_{12} deficiency, it seems that decreased ferritin levels are associated with FM and its related muscle pain [64,65]. Possibly, iron (Fe) as a cofactor in serotonin and dopamine production may have a role in the etiology of FM.

4. Fibromyalgia, overweight, and protein malnutrition

Obesity and overweight are common co-morbidities in patients with FM [66]. It has also been suggested that increased body mass index correlates with the severity of FM symptoms [67]. However, available reports are unable to determine whether obesity is a cause or a consequence of FM. Among the mechanisms proposed to explain the link are reduced physical activity, sleep disturbances, and depression [68]. In this field, further research is important. Obese individuals with FM often have a low intake of protein-rich food and vegetables. It has been reported that FM patients with severe muscle pain, have significantly lower plasma concentrations of the three branched amino acids, valine, leucine, and isoleucine, which supply energy for muscle function and strength [27]. Furthermore, it has been claimed that leucine has an anabolic effect on muscular tissue [69]. Intake of aromatic amino acids may also be low, involving a relative deficiency of tyrosine and tryptophan, which are important for the adequate synthesis of neurotransmitters [70].

Tryptophan deficiency falls within the field of the protein malnutrition spectrum. A possible cause of FM-related pain is a deficient tryptophan-serotonin metabolism, which can arise if the tryptophan-kynurenine pathway is stressed by inflammatory conditions. Patients suffering from FM also appear to have an atypical or protracted response to infection [71]. Recent research has suggested that FM is in part a neuroinflammatory condition with stressed kynurenine pathways involving both the central and the peripheral nervous system [72,73]. FM may be associated with mood disorders such as depression and bipolar spectrum disorder, in turn, these behavioral disorders are associated with dysfunctional dietary habits [74]. Recent, successful attempts to change dietary regimens in subjects with FM have been reported. For example, a diet enriched in low fermentable oligo-di-monosaccharides, with polyols (called FODMAP), should contribute to preventing overweight and obesity, promoting weight loss and ameliorating FM symptoms [75].

5. Vitamins and fibromyalgia

Some FM patients might have B vitamin deficiencies, especially B_{12} [76,77]. The positive effects of B_{12}/folic acid supplementation for FM patients have been reported [76]. In this study of FM patients who reported themselves as “much improved” subjects had been given higher, more frequent doses for a longer period. Furthermore, increased levels of homocysteine in the cerebrospinal fluid and low levels of B12 in the brain of FM subjects were described and further associated with FM-related musculoskeletal pain [76,78–80]. In many of these cases, FM patients may benefit from B vitamin supplements [81–83].

In some FM patients, problems may be associated with low vitamin D levels, which also interferes with the absorption of Mg [84]. One