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THE POSSIBLE ROLE OF KETOGENIC DIET IN FIBROMYALGIA TREATMENT

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Abstract

The aim of this review is to highlight some of the possible pathogenic mechanisms of fibromyalgia and some possible alternative ways of treating this syndrome.

Fibromyalgia syndrome (FM) is a common chronic pain condition that affects at least 5% of the adult population worldwide, in particular women. Chronic, widespread pain is the defining feature of FM, but patients may also exhibit a range of other symptoms, including sleep disturbance, fatigue, irritable bowel syndrome, headache, and mood disorders. Although the aetiology of FM is not completely understood, the syndrome is thought to arise from influencing factors such as stress, intestinal dysbiosis, medical illness, and a variety of pain conditions in some, but not all patients, in conjunction with a variety of neurotransmitter and neuroendocrine disturbances. These include reduced levels of biogenic amines, increased concentrations of excitatory neurotransmitters, including substance P, and dysregulation of the hypothalamic-pituitary-adrenal axis. A unifying hypothesis is that FM results from sensitization of the central nervous system. Establishing diagnosis and evaluating effects of therapy in patients with FM may be difficult because of the multifaceted nature of the syndrome and overlap with other chronically painful conditions. A range of medical treatments, including antidepressants, opioids, nonsteroidal antiinflammatory drugs, sedatives, muscle relaxants, and antiepileptics, have been used to treat FM. Nonpharmaceutical treatment modalities, including exercise, physical therapy, massage, acupuncture, and specific diets, can be helpful. The multifaceted nature of FM suggests that multimodal individualized treatment programs may be necessary to achieve optimal outcomes in patients with this syndrome.

Keywords: *Fibromyalgia, Fibromyalgia syndrome, Ketogenic diet.*

Introduction

Fibromyalgia or as it is better defined fibromyalgia syndrome, involves widespread musculoskeletal pain and debilitating form of fatigue, asthenia called generically, the estimation of the people who are affected is about 1.5 - 2 million Italians.

One of the difficulties of diagnosis of Fibromyalgia is that does not involve alterations found through laboratory tests, there are no active antibodies to detect or specific blood tests to diagnose it; in fact the diagnosis mainly depends on the symptoms that the patient reports.

Those affected often considered a hypochondriac, because of the impossibility of finding signs and evidence through diagnostic tools, disorders are often attributed to the autonomic sphere, so that especially in the past, ended up cataloging people suffering as a sick imagination. The normal current Protocol provides for the rheumatologist according to the case, prescribe medication to relieve the pain, but this symptomatic therapy does not solve the disease, we only control its effects.

Fortunately, medicine has been able to develop studies in the last 10 years that led to establish guidelines for the diagnosis of fibromyalgia, it has been demonstrated that some symptoms, such as the widespread musculoskeletal pain and the presence of specific algogenic areas to acupressure, or areas that if touched determine pain, tender calls points are present in the patients with fibromyalgia syndrome unlike healthy people or patients with other painful rheumatic diseases.

The diagnosis is usually made by a rheumatologist.

Characteristic symptoms present in most patients with Fibromyalgia:

- sleep disorders (shallow nocturnal sleep and non-restorative)
- tension-type or migraine headache
- tiredness (fatigue)
- morning stiffness (especially neck and shoulder)
- colon irritable (constipation and / or diarrhea)
- paresthesia (tingling and consist of sensations similar to stings)
- burning with urination
- feeling of swelling of the hands
- chest pain
- memory loss
- difficulty concentrating

In more recent times has made its way the hypothesis that food can have a significant effect on the disease itself.

This because the intestinal microflora and intestinal hyperpermeability are believed to be contributing factors to the develop of all this symptoms since intestine acts as an important immunologic protection barrier [1].

Results

The application of ketogenic diets in the neurological field is widely accepted at an international scientific level thanks to the demonstrated regulatory effects exerted by this type of diet on the Central Nervous System (CNS) [2-3-4-5].

Specifically, ketone bodies have shown to be able to reduce excitability, inflammatory state and neuronal oxidative stress and to improve energy dysregulation, all factors underlying multiple CNS diseases and dysfunctions. During the ketogenic diet, very low in carbohydrates and at the same time the parent of ketone bodies, each energy molecule produces an "amplifying" effect leading to an increase in the overall energy yield and reducing oxidative stress. Ketogenic diets thus become candidates for the treatment of many CNS diseases and dysfunctions, especially when the metabolic treatment is started in a pre-clinical phase of the disease [6].

The hypothesis that many neurological conditions are pathophysiologically linked to energy dysregulation could provide a common platform for research and therapeutic experimentation, so the course of different neurological diseases could be favorably influenced by the same dietary treatment [3].

It is in this context that the possibility of evaluating the adjuvant treatment of fibromyalgia by means of the ketogenic diet therapy is placed.

Fibromyalgia is a known clinical condition that has only recently received a scientific definition and a formal recognition. Although the international scientific interest and public attention have increased exponentially over the last few decades, at a national level the fibromyalgia syndrome is not included in the list of chronic diseases for which there is an exemption from sharing in healthcare costs and it is not defined and shared a specific care path.

Fibromyalgia is characterized by chronic and widespread musculoskeletal pain, often associated with asthenia, sleep disorders, cognitive problems (eg attention, memory), mental problems (eg anxiety, depression) and a wide range of somatic symptoms and neurovegetative that make the patient live in a condition of profound discomfort and disability. According to the Superior Health Council (2015) the prevalence of the syndrome is equal to 1.5-2% of the general population (about 900 thousand people), is more frequent in women than men and can develop at any age.

The aetiology of fibromyalgia has not yet been fully understood and uncertainty exists regarding the pathophysiological picture. The etiopathogenetic hypotheses formulated and most accredited concern [7]:

- Dysregulation of pain control mechanisms (probably also due to a dysregulation of gut-brain axis which affects the nervous transmission of the whole organism) by the CNS responsible for its amplification. Dysregulation also appears to be responsible for the other symptoms of the disease (memory disorders, fatigue and depression).

- Reduction of pain modulation capacity through the serotonergic-noradrenergic descending pathways.

- Activation of glial cells by stimulation by pro-inflammatory cytokines (TNF, IL-6, IL-8) and opioids, not through opioid receptors, but through the activation of TLR-4 recently discovered as a competing element to chronic pain.

- Increased levels of glutamate and gamma aminobutyric acid (GABA) decreased at the level of cerebrospinal fluid. It is assumed that the release of inhibitory neurotransmitters such as GABA in the anterior cingulate cortex can reduce the excitability of neurons in this region, which are responsible for the descending modulation of pain.

- Temporal summation of pain (or "windup") supported by the repetitive stimulation of nociceptive fibers.

- Perfusion abnormalities with elevated activity in the somatosensory cortex and reduced in the frontal cortex, cingulum, temporal and cerebellar cortex.

The etiopathology of the syndrome therefore seems to find a contributing cause between the alteration of pain pathways in the CNS and the inflammation of small peripheral fibers with simultaneous absence of tissue inflammation or other rheumatic or systemic pathology (primary form), as well as greater frequency of manifestation in patients who have suffered head trauma (form associated with other conditions).

Discussion

Recent studies show that the monophosphate kinase (AMPK) protein is involved in the control of peripheral nociceptor sensitization and inflammatory nociception since it is involved in the regulation of the NFLP3 inflammasome responsible for the activation of innate immune defenses through the maturation of proinflammatory cytokines (interleukins IL- 18 and IL-1β). The NLRP3 inflammasome was therefore correlated with some pain conditions, such as the neuropathic one, fibromyalgia and the complex regional pain syndrome [8-9].

Further studies have also shown the direct anti-inflammatory action of beta-hydroxybutyrate on the NLRP3 inflammasome of human monocytes with consequent reduction of the levels of interleukins IL-1β and IL-18 and of the related inflammation [10-11].

On the basis of these scientific evidences, interventions able to positively interfere with the physiopathological fibromyalgic mechanisms, and of nociception in general, could represent new therapeutic targets in the treatment of fibromyalgia and pain syndromes.

It is in this experimental context that the strong biochemical bases of the ketogenic diet could be made available as a valid aid in the treatment of acute and chronic pain states. Indeed, the ability of the ketogenic diet to modulate the down-regulation of the NLRP3 inflammasome through AMPK activation and by direct action of beta-hydroxybutyrate is demonstrated, thus contributing to decrease peripheral nociceptor sensitization and inflammatory nociception [12-13 -14].

The ketogenic diet is also able to bring about changes in the levels of some neurotransmitters as a result of altered synthesis and / or synaptic clearance. In particular, an alteration of excitatory glutamate metabolism was seen, in response to ketosis, with consequent increase in GABA levels and increased inhibitory neurotransmission [15].

In a recent study altered microbiome composition in individuals with fibromyalgia was observed, when comparing 77 women with FM with 79 unrelated controls, in FM patients using differential abundance analysis, were revealed significant differences in several bacterial taxa [16].

In this contest the positive effect of the ketogenic diet is probably due to the modulation of gut microbiota by inhibiting pathogenic strains proliferation responsible of most of above intestinal and extra-intestinal symptoms.

Currently rheumatologists and many other specialists agree in recommending that the initial management of fibromyalgia patients be carried out by the family doctor and within a multi-professional and interdisciplinary team, where they can find wide-ranging also the non-pharmacological treatments of nutritional, ketogenic and classic type, which are recommended given the demonstrated correlation between the fibromyalgic and ketogenic molecular mechanisms and the strong link between high BMI and increased sensitivity to pain, worsening of fatigue, quality of sleep and tone of mood in fibromyalgia [7-16].

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