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RESEARCH ARTICLE

FEEDING AND FIBROMYALGIA: A REVIEW AND POSSIBLE APPLICATIONS IN INTEGRATED MEDICINE

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ABSTRACT

Fibromyalgia (FM) is a chronic disease in which a generalized pain condition is usually accompanied by other symptoms such as fatigue, sleep disorders, mood disorders, headache, irritable colon syndrome, etc. Although FM has been known for many years, it has only recently been the subject of more thorough studies, although there are still many unknown issues about it.

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INTRODUCTION

In Italy, FM affects about 1.5 to 2 million people and it is prevalent among adult women (20-60 years). The exact cause of this syndrome has not yet been detected; it is increasingly evident that it has a multifactorial genesis and it is possibly triggered by different physical and psychological factors. There are many treatments proposed for it but the best approach for the management of fibromyalgia is nowadays multidisciplinary, pharmacological and not pharmacological. Within non-pharmacological therapies, nutrition is a promising tool, which is gaining more and more relevance. In the literature, remissions from fibromialgic conditions are described only after particular diets; usually, this does not occur after pharmacological treatments. Why does nutrition play this important role?. Many studies correlate FM and its aggravation to overweight and to an alteration of metabolic parameters (in particular cholesterolaemia and insulinemia). Other studies confirm the presence of high oxidative stress and reduced antioxidant capacity in fibromyalgic patients; this is also associated with low levels of some fundamental micronutrients such as vitamins and trace elements. The theory that oxidative stress may be implicated in the physiopathology of FM is taking more and more foot, but it is not clear yet if it is a cause or a consequence of the fibromyalgic syndrome. Surely, a change of diet with a greater intake of antioxidants is necessary, because it is able to counteract free radicals, cause of oxidative stress. In these patients, the carential states of many minerals have been highlighted (especially iron, selenium, zinc and magnesium), of some vitamins(in particular vitamin D and B12), of fatty acids (Omega 3) and of Coenzyme Q10. Furthermore, there's also a significant reduction of plasma's concentration of BCAAs (branched amino acids: valine, leucine and isoleucine) and phenylalanine. BCAAs provide energy to the muscles and regulate muscle protein synthesis. All these deficiencies may depend on insufficient food intake or intestinal malabsorption, due to dysbiosis. The supplementation of amino acids, Omega 3, coenzyme Q10, vitamins and minerals could certainly be useful in patients with fibromyalgia, but mainly it is necessary to intervene with a proper diet, which will provide all the nutrients that the body needs, aimed at the return to a correct intestinal function, which allows the absorption of the eaten or integrated nutrients. In the end, fibromyalgia is often associated with allergies or food intolerances and these problems too are connected toa not proper bowel's function, that must be managed also by a correct diet. Changes in the diet are often safer and much cheaper than drugs and supplements; they also are under the control and responsibility of the patient. Clinical trials have been carried out with the aim

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of studying the effects of particular diets on FM symptoms. The various diets proposed in the literature are:

Diet rich in antioxidants: it aims at reducing free radicals generally by a vegan or vegetarian diet. Patients following this kind of diet use to describe its benefits.

Slimming diet: it aims at resetting the metabolic framework. Overweight and obesity are two common comorbidities in FMand BMI causes the fibromyalgic symptoms aggravation, the alteration of the metabolic balance (dyslipidemia and insulin resistance) and a reduction of the quality of life. It is still unclear whether overweight and obesity are the cause or the consequence of FM. Surely, weight loss determines a proven improvement.

Diet excluding excitotoxins (glutamate and aspartame): it aims at eliminate substances that are able to abnormally and dangerously excite neurons. In particular, glutamate is the most widespread neurotransmitter of the central nervous system; its excessive concentration could overexcite neurons and bring them to death. Cases of complete regression of fibromyalgic symptoms have been reported following the implementation of this type of diet. Disturbing foods are stock cubes, canned foods, cold cuts, frozen and freeze-dried products, cheeses, soy products, ready meals (containing E620 and E625 additives), sweeteners with aspartame, light drinks, confectionery «without sugar », etc ...Moreover, in a review, 4 foods able to increase pain are examined: monosodium glutamate, aspartame, caffeine and arachidonic acid. Reducing or eliminating these foods and nutrients from the diet could be useful in the treatment of chronic pain and FM too.

Gluten-free diet: gastrointestinal problems, irregular brow and abdominal pain are often concomitant with FM. Some cases, with subclinical celiac disease or non-celiac gluten sensitivity, benefited from a gluten-free diet. It has also been hypothesized that gluten sensitivity may be a cause of FM also because this is a condition often present in these patients. In the end there are many scientific evidences of correlations between FMand eating disorders. Psychiatric problems (especially anxiety and mood disorders) are associated with chronic pain; bulimia and anorexia are often present in fibromyalgic patients; binge eating disorder (current or previous, nighttime too) is present in obese or overweight subjects. Neurotransmitters in fibromyalgic condition have been studied and dysfunctions in their production have been evidenced; deficiencies or excesses of these molecules lead to neurological problems such as those described. In particular, the role of serotonin, often lacking in these patients, has been examined, and another proposed nutritional intervention is the integration of its precursor, the tryptophan, an amino acid. In a recent study, it has been suggested that the presence of non-absorbed molecules in the intestine, especially fructose, may reduce the absorption of tryptophan. A low absorption of tryptophan leads to a reduced synthesis of serotonin which triggers the fibromyalgic symptoms. In addition, the unabsorbed sugars may also cause an alteration of the intestinal microbiota which could be no longer able to absorbethe fructose and tryptophan in the intestine, entering a vicious circle. The therapeutic idea is about supporting the serotonin' ssinthesis allowing the proper absorption of tryptophan. The core of the curative treatment is the exclusion from the diet of some carbohydrates (fructose) and the substantial reduction of some others. In conclusion, we can state that with a correct diet it is possible to control and prevent malnutrition (excess or inadequate), reduce excess of fat mass or avoid loss of lean mass, improve response to therapies, improve the immune system response , reduce inflammation and improve the quality of life. It is fundamental, however, to choose the nutrients useful to the patient and manage the income correctly; it is also necessary to educate the patient to a correct diet. Supplementation is recommended, but must be managed by a competent professional, as well as the choice of specific and targeted diets. The do-it-yourself is absolutely not recommended because of the risk of malnutrition or nutrient overload.

Fibromyalgia must be treated with a multidisciplinary approach, in which nutrition is increasingly taking on a leading role

Gut and Fibromyalgia: a brief introduction: Fibromyalgia is counted among idiopathic pathologies, without a specific cause, or direct etiology, but the result of a set of direct and indirect causes. For this reason it is difficult to diagnose and turns out to be a real "brain-teaser" in treatment and prognosis. Lately it has been highlighted how the "intestine-brain axis" is at the center of numerous psycho-physical or psycho-neuro-endocrine-immunological discomforts. These dysfunctions are often partly ignored because they do not have a real symptomatology, without causing an acute but very often low-grade inflammation; they are therefore not treated in a serious and resolutive manner, leading then, if neglected, into diseases much more serious and often irreversible or at least disabling. The SIBO (Small Intestine Bacterial Overgrowth) and the LGS (Leaky Gut Syndrome) are two of the most interesting "modern" affections of the enteric tract, often the result of both pharmacological abuses (antibiotics, anti-inflammatories, proton pump inhibitors, etc.), both of real excesses perpetrated in food time; all this combined with psycho-physical stress.

The metabolic syndrome or "X Syndrome" is related to poor eating habits (junk food, non-respect of the correct food associations and the chrono-biology, excess perpetrated over time of refined foods, lack of dietary introduction of seasonal fruit and vegetables, ultra-cooked of food, almost non-existent mastication, total absence of foods with antioxidant properties due to previous refining pretreatments and methods of transformation in the production chain, etc.) is a set of disorders concerning the metabolism of macronutrients accompanied by an inflammatory component and a genetic predisposition. There is no doubt therefore that the coexistence and the intimate link between inflammation and excess leads to a "silence discomfort" at the beginning (insomnia, anxiety, irritability, little joint problems, exhaustion, asthenia, apathy, etc.) or in any case, it is not such that a pharmacological intervention is necessary (often out of place as we tend to treat its symptoms without going back to the root). As for Fibromyalgia, the tendency is to use anti-inflammatories and / or painkillers, with very poor or partial results, obtaining only a temporary "relief" in the disappearance of the symptoms that, however, reappear (in some situations even more strongest). Some studies have found for example that: - 73% of fibromyalgia patients reported gastrointestinal symptoms, compared to 37% of those with osteoarthritis. - Irritable Bowel Syndrome (IBS) is present in 30-70% of fibromyalgia patients. - 33% of patients with IBS meet the diagnostic criteria for fibromyalgia, compared to only 4% of control subjects. - Up to 50% of fibromyalgia patients have functional dyspepsia, which is a fancy term for "indigestion" without known cause.

Dyspepsia is often the "upstream" cause of inefficiency of gastric digestion and therefore downstream of in expression and therefore not finalization of enteric digestion, often leading to a “fertile soil" for SIBO and therefore consequently to LGS. Furthermore, as fibromyalgia, IBS and functional dyspepsia are simply symptom-based diagnoses, so these articles have not shed light on what could actually cause fibromyalgia and IBS / indigestion. One of the cornerstones of functional medicine is to find the underlying mechanism or cause. Tackling the underlying problem will lead to the most effective and lasting treatment and therefore more EFFICIENT.

A study in 2008 highlighted a relationship between alterations of the intestinal microbiota (ie "intestinal flora") and fibromyalgia. Researchers at Cedars-Sinai Medical Center in Los Angeles found that 100% (42/42) of fibromyalgia patients studied had excessive intestinal bacterial growth (SIBO). This is stunning!. A study of 40 patients with fibromyalgia, 28 (70%) had intestinal permeability (LGS). It is important to note that 12 of the 28 patients with a leaky gut did not have intestinal symptoms. I think this is one of the reasons why the intestine is often overlooked as a potential cause of fibromyalgia. A group of fibromyalgia patients who were positive for SIBO were divided into two groups. One group received antibiotics to treat SIBO and the other group received a placebo. A significant improvement in fibromyalgia symptoms was observed in patients who achieved SIBO eradication with antibiotics, while no improvement was observed in patients who took placebo or who tested positive for SIBO after antibiotics. This suggests that SIBO plays a crucial role in Fibromyalgia, at least for such of them. While LGS is often a consequence of SIBO (between 50% and 70% of the cases observed), SIBO is a consequence of: - Dyspepsia - Achlorhydria - Poor intestinal motility - Excess of proton pump inhibitors - Anatomical dysfunctions

MGP Gold®: Papaya has always been used by indigenous peoples in the tropical and subtropical regions of our wonderful planet. Not surprisingly, because in those countries there is the lowest incidence of diseases and / or diseases of the gastro-enteric tract. Papaya contains a plethora of substances both of high nutritional value and with a notable physiological-functional action, as well as all the fruits with pulp or "tinte" peel (red, orange, yellow). Among the peculiarities of this extraordinary plant there is one that makes it unique and characteristic of its kind, that is the presence of proteolytic enzymes with a very wide spectrum of action: papain and chymopapain. These enzymes are "cysteine" type proteases, with 3 disulfide bridges that give it heat stability and a certain mechanical resistance. They are active at both acidic and alkaline pH. But these purified and clarified enzymes could generate skin irritability even at the mucosal level. It is therefore important to have a product that reveals the enzymatic properties but is not limiting in terms of intake. The proteolysis is of fundamental importance in the digestive process, especially dyspeptic or that however they use antacids (which strongly limit the finalization of the digestive process especially in case of indiscriminate abuse). In fact, the "soil" for the cultivation of bacteria, above all gram- (very often what are called pathogens) consists of undigested proteins that linger for a long time in the small intestine and form a substrate suitable for SIBO. Another peculiarity of this fruit is the presence of "gel-forming" Pectins. Characteristics of these Pectins is the "comb" structure, with a central skeleton made up of Omogalatturonans (HG) and of the lateral ramifications made up of Rhamnogalatturonans and Arabinogalatturonans respectively of class I and II. This type of Pectine was very interesting on several aspects involving both the tropism of the gastro-enteric tract and its functionalty. In fact, it has been observed that not only do they work on the mucosa mechanically, relying on intestinal motility (peristalsis), thus avoiding stagnation of organic material often due to putrefactive and / or fermentative phenomena, but it also acts on the restoration of microvillary function often compromised by drug abuse (as outlined above) or insults due to invasive pharmacological therapies (eg chemotherapy) or radiotherapy. Nonetheless, pectins were found to be fundamental as a PREBIOTIC source for their ability to produce a certain amount of SCFA (Short-Chain Fatty acids) following the demolition by the autochthonous microbial flora or integrative probiotics. The latter play a role of primary importance both in on-site eubiosis and in communication - the brain-intestinal axis and in the precarious and very delicate as fundamental immunomodulation that oversees the balance between the intestinal (external) and submucosa (internal) lumen. Let's not forget that in the deep layers of the small intestine there are "follicular" areas, such as access doors, in the bottom of which there is an important part of the immune system. Here, as everything returns: digestion, intestine, immune system, microbial flora, intestine-brain communication. From here we understand the importance in the early diagnosis of SIBO and LGS. MGP Gold is a cleverly prepared preparation that therefore has both a natural source of papain (in this case within the pectinic mesh of cold processed fruit) and partially hydrolysedPectins rich in AG and RG. To obtain a perfect balance between enzymatic activity and Pectine at the right degree of methylation and presence in AG I / II and / or RG I / II, the cultivar and the residence time after harvesting and before processing are fundamental (Papaya in fact it is a climacteric fruit).

Kluyveromyces marxianus B0399: As highlighted above, intestinal eubiosis is fundamental in maintaining the integrity and cellular function of the intestinal alve. A valid help can certainly come from the integration of valid probiotics, which not only provide a specific and characteristic support, but also contribute to the improvement of the autochthonous bacterial balance by interacting with Bifidobacteria and / or Lattobacilli, increasing their number and activity and thus counteracting the activity of pathogens.

Kluyveromyces marxianus represents the prototype of PROBIOTIC, as it is a PROBIOTIC LACTIC YEAST OMOFERMENTATIVE; this means that it is a eukaryotic cell, produces 2 molecules of ATP instead of 1, produces SCFA, is gastro-resistant and resistant to bile salts and is resistant to the most common antibiotics (but does not transfer its antibiotic-resistance to other microorganisms being free of plasmids and antibiotic resistance is intrinsic to yeast). Among the peculiarities of this microorganism there is also a marked production of Beta-galactosidase and a marked anti-inflammatory and immunomodulatory activity. Finally, it has been seen that it acts in concert that the other intestinal saprophytic bacterial populations, also increasing the activity of Bifidobacteria, thus resulting in an excellent SIMBIONTE.

Turmeric: As far as inflammation is concerned, it is often present both as a cause in the onset of fibromyalgia (associated with other events, such as for example chronic inflammation of

the chronic type or IBS) or as a perceptive effect of pain associated with neuropathies. the use of Curcuminoids, active ingredients contained in the rhizome of Curcuma (plant native to India and Southeast Asia). Curcumin acts actively on the whole inflammatory sphere (local and systemic) and this has been amply demonstrated by more than 12,000 publications to date. Particular importance is its action at the level of intestinal inflammation (or IBS) determining both in vitro and in vivo a marked improvement in symptoms, acting on both interleukins responsible for acute inflammation and first response (IL-6, Il-1beta , TNF-alpha), but also on different transcription factors responsible for the production of other pro-inflammatory signals (NF-kb, STAT3, PKC, etc.). The only limitation to the use of Curcumin that respects the extraordinary results obtained *in vitro* or *in vivo* laboratory tests is the poor absorption, at the intestinal level, the degradation rate of the absorbed active principles, the acidic pH and the bile salts in the gastro-enteric tract and the formation of true insoluble crystals once Curcumin comes into contact with a liquid whose solvent is strongly polar (eg blood). Recently a new preparation has been developed that combines two types of Turmeric with characteristics very different from one another in a gelling matrix and together with other substances that allow a more than adequate absorption at the level of the oral cavity (HGC-C® gel complex). This allows an almost immediate response as an anti-inflammatory action.

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