Review

Is the gut microbiome of importance in fibromyalgia? A critical review of emerging evidence

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ABSTRACT

Fibromyalgia (FM) is a multifaceted chronic pain syndrome, predominantly affecting women, and characterised by a constellation of symptoms including diffuse musculoskeletal pain, fatigue, cognitive impairment and poor sleep quality. Its complex pathophysiology likely involves genetic, environmental and psychosocial factors. Recent studies have raised the possibility that the gut microbiome may influence FM symptoms via the gut-brain axis, although this hypothesis remains unconfirmed. This review aims to explore potential associations between gut microbiome alterations, nutrition, and FM, with particular attention to the limitations of current evidence. While certain studies have reported differences in the gut microbiota composition of patients with FM, these findings are preliminary and often derive from small, heterogeneous cohorts. Likewise, faecal microbiota transplantation studies in animals and limited human trials suggest a possible link to pain sensitivity, but further validation is needed.

Nutritional interventions, including prebiotics, probiotics and specific dietary strategies, have shown early promise in modulating gut microbiota and alleviating FM symptoms. Nutrients such as magnesium, selenium and omega-3 fatty acids, as well as antioxidant compounds, may influence pain and inflammation pathways, but definitive clinical recommendations are lacking. Given the emerging nature of this field, larger and better-controlled studies are required to clarify the role of the gut microbiome and nutrition in FM. A multidisciplinary management strategy, integrating nutritional approaches cautiously and based on individual profiles, may offer benefits, although no standard therapeutic guidelines currently exist.

Introduction

Fibromyalgia (FM) is a chronic condition characterised by widespread musculoskeletal pain, fatigue, cognitive disturbances, and significant sleep issues (1). This disorder, affecting approximately 2–8% of the global population, predominantly women, involves a complex interplay of genetic, environmental and psychosocial factors (2). With symptoms overlapping other chronic illnesses, it demands a multidimensional treatment approach (3). FM is considered one of the disorders associated with nociplastic pain, a mechanistic term used to describe pain that arises or is sustained by altered nociception despite the absence of tissue damage (4). Key symptoms are widespread pain, fatigue, cognitive issues, mood disorders, and gastrointestinal problems are common, making diagnosis and management complex (5). The gut microbiome has been hypothesised to play a role in FM and other nociplastic disorders. Altered microbiome composition in patients raises questions about dysbiosis' role in heightened pain sensitivity and inflammation (6). The gut-brain axis, involving bidirectional communication between the gut and nervous system, is implicated in the pathophysiology of FM, necessitating further exploration into the influence of the microbiome (7). Ongoing clinical trials focus on anti-inflammatory nutritional interventions, targeting the underlying inflammatory processes in FM (8, 9). Notably, faecal microbiota transplantation (FMT) from FM patients to germ-free mice has reported induced pain hypersensitivity, suggesting a direct link between gut microbiota and FM pain. A pilot study in humans showed reduced pain following FMT from healthy donors, highlighting the therapeutic potential of FMT (10).

One of the intriguing aspects of FM is the potential link between dietary choices and symptom severity. While there is no specific dietary therapy for FM, several studies have suggested that nutrition may play a significant role in influencing symptom presentation and overall quality of life for affected individuals (11). Researchers have explored how diet composition, food sensitivities, and micronutrient deficiencies may contribute to the manifestation and exacerbation of FM symptoms (12). Understanding these dietary factors and their impact on the condition is potentially relevant for tailoring effective treatment strategies. Dietary interventions such as prebiotics, probiotics, and personalised dietary plans show promise in modulating the gut microbiome and alleviating symptoms, suggesting a potential for personalised treatment strategies (13). The exact cause remains unclear, but emerging research suggests that the gut microbiome and nutritional status may play critical roles in modulating symptoms and influencing the disease's pathophysiology (14). The present review explores the ways in which interactions between the gut microbiome, dietary patterns, and FM can inform potential nutritional interventions for managing this multifaceted syndrome.

Gut microbiome and its role in the disease

Recent literature has increasingly illuminated the pivotal role of the gut microbiome in maintaining overall health and immune function (15). The human gut harbours trillions of microorganisms, including bacteria, viruses, fungi and other microbes, which collectively contribute to a complex and dynamic ecosystem essential for our well-being (16). Studies have shown that a diverse and balanced gut microbiome is potentially relevant for efficient digestion, nutrient absorption, and the production of vital metabolites such as short-chain fatty acids (17). These metabolites play a significant role in modulating immune responses and maintaining the integrity of the gut barrier, thus preventing pathogenic invasions and systemic inflammation (18). Moreover, emerging research has linked dysbiosis, or the imbalance of gut microbes, to various chronic diseases (19). Thus, alterations in the gut microbiome composition have been associated with metabolic disorders like obesity and type 2 diabetes (20), as well as autoimmune conditions such as inflammatory bowel disease (IBD) (21) and rheumatoid arthritis (22). The gut-brain axis, a bidirectional communication network between the gut and the brain, also underscores the microbiome's influence on mental health, with implications for conditions like depression and anxiety (23).

Interventions targeting the gut microbiome, including probiotics, prebiotics, dietary modifications, and faecal microbiota transplantation, are being explored as potential therapeutic strategies (12, 13, 18). As our understanding of the gut microbiome continues to evolve, it becomes increasingly clear that fostering a healthy microbial community is integral to preventing and managing a wide array of health issues, highlighting the gut microbiome's central role in human health (15).

Emerging research suggests a significant association between gut microbiome dysbiosis and the pathophysiology of chronic pain in general, and FM, in particular (23). Several studies have reported distinct alterations in the gut microbiome composition of individuals with FM compared to healthy controls (24, 25). A pioneering study by Minerbi *et al*. (25) found that the gut microbiota of FM patients exhibited a distinctive profile, with higher levels of bacteria such as *Flavonifractor plautii* and *Parabacteroides merdae*, and lower levels of beneficial species like *Faecalibacterium prausnitzii*. This altered microbiome composition was correlated with symptom severity, raising the hypothesis in the pathophysiology of FM. Further supporting this association, a 2021 study by Pimentel *et al*. examined the gut microbiome profiles of FM patients and reported similar findings of dysbiosis (26). They identified that these microbial imbalances were correlated with symptom severity, including pain levels, fatigue, and cognitive dysfunction, commonly referred to as "fibro fog." The study also suggested that gut dysbiosis might contribute to the low-grade inflammation observed in FM patients, which could exacerbate their symptoms.

Going beyond association, recent research has provided compelling evidence for a causal link between gut microbiome dysbiosis and FM. In groundbreaking studies further conducted by Minerbi *et al*. (25) as well as by Fang *et al*. (27), FMT from individuals with FM, but not from healthy controls, induced persistent pain hypersensitivity in germ-free mice. This pain hypersensitivity was accompanied by alterations in peripheral immune profiles, reduced intraepidermal nerve fibre density, and activation of spinal microglia, all of which contributed to the development of pain. Notably, the pain hypersensitivity resolved after FMT from healthy controls, further reinforcing the causal role of the gut microbiome in FM pain. A Mendelian randomisation study by Wang *et al*. (28) further strengthened the causal association between specific gut microbiota genera and FM risk. The study identified five genera with significant causal associations: Coprococcus, Eggerthella and Lactobacillus increased the risk of FM, while Family XIIIUCG001 and Olsenella reduced the risk. These findings provide genetic evidence for the causal role of gut microbiome dysbiosis in the pathogenesis of FM. These findings pave the way for further research into the underlying mechanisms and potential microbiome-based therapeutic interventions for this debilitating condition.

Gut microbiome and nutrition in the management of fibromyalgia

Gut microbiome plays a potentially relevant role in modulating the body's response to dietary nutrients, and this interaction can significantly impact the inflammatory and pain pathways associated with FM (19). The gut microbiome is responsible for metabolising various dietary components, including fibres, polyphenols, and other phytochemicals. This metabolic activity produces a wide range of bioactive metabolites, such as short-chain fatty acids (SCFAs), indoles, and phenolic

Table I. Concepts investigated regarding the role of the microbiome in chronic pain.

Concept	Details
Role of gut microbiome in health and disease	The gut microbiome maintains overall health and immune function. It harbours trillions of microorganisms that contribute to a dynamic ecosystem essential for well-being (15 16).
Dysbiosis and chronic diseases	Dysbiosis, or imbalance of gut microbes, is linked to chronic diseases such as obesity, type 2 diabetes, IBD and rheumatoid arthritis (19-22).
Gut-brain axis and mental health	The gut-brain axis highlights the microbiome's influence on mental health, affecting conditions like depression and anxiety (23).
Interventions targeting gut microbiome	Probiotics, prebiotics, dietary modifications and faecal microbiota transplantation are potential therapeutic strategies for gut microbiome health (12, 13, 18).
Gut microbiome and chronic pain	Research shows a significant association between gut microbiome dysbiosis and chronic pain, including fibromyalgia (23).
Gut microbiome and fibromyalgia	Studies reveal distinct alterations in the gut microbiome composition of fibromyalgia patients, with specific bacterial profiles correlated with symptom severity (24-26).
Impact of gut microbiome-derived metabolites	Gut microbiome-derived metabolites, such as SCFAs, indoles and neuroactive compounds, modulate inflammatory and pain pathways, influencing fibromyalgia management (16-18, 29-31).

compounds, which can exert profound effects on host physiology (16-18). Several studies have reported that the gut microbiome-derived metabolites can modulate inflammatory pathways relevant to FM. For instance, SCFAs like butyrate and propionate have been shown to exhibit anti-inflammatory properties by inhibiting the activation of nuclear factor-kappa B (NF-κB), a key transcription factor involved in the regulation of inflammatory responses (18, 19).

Additionally, certain gut bacteria can produce indole derivatives, such as indole-3-propionic acid (IPA), which has been found to attenuate inflammation by inhibiting the production of pro-inflammatory cytokines and promoting the differentiation of regulatory T cells (29). The gut microbiome-derived metabolites can also modulate pain pathways and exert neuroprotective effects, which are highly relevant in the context of FM. For example, SCFAs like butyrate have been shown to exhibit analgesic properties by modulating the expression of pain-related receptors and ion channels in sensory neurons (30). Furthermore, certain gut bacteria can produce neuroactive metabolites, such as gamma-aminobutyric acid (GABA) and serotonin, which can influence pain perception and modulate the activity of the central nervous system (31). Given the intricate relationship between the gut microbiome, dietary nutrients, and inflammatory and pain pathways, dietary interventions aimed at modulating the gut microbiome composition and function have emerged as a promising therapeutic approach for FM.

Strategies such as increasing the intake of prebiotic fibres, which selectively promote the growth of beneficial gut bacteria, or supplementing with specific probiotic strains known to produce anti-inflammatory metabolites, have shown promising results in reducing pain and improving quality of life in FM patients (32, 33) (Table I).

Nutritional status and fibromyalgia

FM patients often exhibit distinct dietary patterns that deviate from recommended nutritional guidelines. Several studies have identified common dietary trends and potential nutrient deficiencies or excesses in this population.

Reduced intake of nutrient-dense foods

Research indicates that individuals with FM tend to consume fewer nutrient-rich foods, such as dairy products, whole grains, fresh fruits and fish, compared to healthy controls and patients with other rheumatic diseases (34). A cross-sectional study by Arranz *et al*. (35) found that FM patients had significantly lower intakes of dairy products (OR=0.32), whole grains (OR=0.59), fresh fruits (OR=0.66), and fish (OR=0.64) compared to healthy controls (2). Similar reductions in these food groups were observed when comparing FM patients to those with rheumatoid arthritis. The reduced consumption of nutrient-dense foods in FM patients may contribute to deficiencies in various essential nutrients, including:

- Trace elements

Animal studies have shed light on the significant role that trace elements such as magnesium (Mg) and selenium (Se) play in managing symptoms related to FM, including muscle pain and weakness. Elevated levels of Mg intake have been associated with a reduction in these symptoms, highlighting its potential protective benefits (36). Similarly, Se deficiency has been linked to musculoskeletal pain, a common complaint in FM. Adequate Se intake, on the other hand, has shown preliminary promise in protecting against tissue damage from ischaemia and reperfusion, a process that can exacerbate pain (37). Mg deficiency not only contributes to low-grade chronic inflammation but may also elevate levels of substance P, a neurotransmitter closely associated with pain intensity in FM patients. This deficiency could lead to a slight increase in pro-inflammatory markers, like cytokines and C-reactive protein (CRP), potentially worsening FM symptoms (38). In veterinary medicine, the importance of Se for muscle strength is well-established, with conditions like white muscle disease in animals highlighting

the consequences of Se deficiency. This condition, prevalent in areas with low soil Se levels, underscores the protective role of Se supplementation, which has been beneficial in animal models for preventing ischemia-induced organ damage (39). Research into the role of trace elements like selenium, zinc, and magnesium in FM presents a mixed picture, with essential functions in cellular redox balance and ATP production at the centre of the debate (40). While some trace elements are potentially relevant for maintaining cellular health, studies on their levels in FM patients have yielded inconsistent results. For instance, Rosborg *et al*. and Sakarya *et al*. found no strong evidence linking trace element abnormalities with FM development, observing no significant correlation between magnesium levels and common FM assessment tools like Tender Points, Visual Analogue Scale, Fibromyalgia Impact Questionnaire, and Beck Depression Inventory (36, 37). Conversely, Sendur *et al*. have reported significantly lower serum levels of zinc and magnesium in FM patients, noting an association with tender points and fatigue, yet found selenium levels comparable to controls (38). Kim *et al*. also noted lower levels of certain trace elements, including magnesium, in the hair of FM patients compared to healthy controls (39). Meanwhile, Bazzichi *et al*. observed an increase in magnesium levels within platelet cells, suggesting that disruptions in calcium-magnesium homeostasis could be implicated in FM pathogenesis (40).

- Iron and vitamin B12

Iron and ferritin levels in FM patients have garnered attention due to the potentially relevant role of iron as a co-factor for enzymes in serotonin and dopamine synthesis, which could influence FM aetiology. Research presents a mixed view: Pamuk *et al*. (43) observed a higher FM prevalence in individuals with iron deficiency, anaemia and thalassaemia than in controls, suggesting a potential link. However, Mader *et al*. (44) countered this by reporting no significant differences in iron levels or iron store markers in FM patients, casting doubt on the benefits of iron supplementation for FM treatment. Adding another layer, Ortancil *et al*. (45) found that FM patients typically had lower ferritin levels than controls, with levels below 50 ng/ml significantly increasing FM risk. This divergence in findings highlights the complex nature of FM and the need for further research to clarify the role of iron in its pathophysiology and management.

Gharibpoor *et al*. (46) conducted a study examining the effects of vitamin B12 supplementation on FM patients. Administering a 1000 mcg daily dose of oral vitamin B12, they aimed to assess its impact on symptom severity and the psychological well-being of FM sufferers. Utilising the Revised Fibromyalgia Impact Questionnaire (FIQR), Hospital Anxiety and Depression Scale (HADS), the 12-item Short-Form Health Survey (SF-12), and the Pain Visual Analogue Scale (pain-VAS), the study documented patient conditions before and after B12 treatment. Remarkably, the results indicated significant improvements in FIQR scores across all domains, alongside a notable reduction in anxiety levels. However, there were no significant changes in depression, pain-VAS and SF-12 scores post-treatment. This study underscores the potential of vitamin B12, specifically in a sublingual 1000 mcg daily form, as a promising adjunct therapy for alleviating the severity of FM symptoms and anxiety, highlighting the nuanced role of nutritional supplementation in FM management.

- Calcium and vitamin D

Lower dairy intake can lead to inadequate calcium and vitamin D levels, which are potentially relevant for bone health and muscle function (47). The connection between vitamin D deficiency and chronic muscle pain has spurred significant research, although findings on the benefits of vitamin D supplementation in FM management remain mixed, calling for further investigation to clarify its role in FM treatment strategies (48, 49).

- Omega-3 fatty acids

Decreased fish consumption may result in insufficient intake of anti-inflammatory omega-3 fatty acids, which have been associated with pain reduction and improved quality of life in FM (50, 51).

- Amino acids

Studies indicate that patients with FM tend to have lower plasma concentrations of branched-chain amino acids (BCAAs), valine, leucine, and isoleucine and phenylalanine compared to healthy individuals (52). This difference suggests a potential connection between BCAA levels and FM, considering BCAAs are important for muscle energy and protein synthesis. Research by Bazzichi *et al*. (53) supports the finding of lower BCAA levels in FM patients and suggests this could be due to gut malabsorption or a diet low in essential amino acids, including BCAAs and sulphur-containing amino acids. Additionally, FM patients often show low levels of tryptophan (54), an amino acid related to serotonin production, which is consistent with the observed low serotonin levels in FM. These observations point to the relevance of monitoring amino acid levels in FM management, although the clinical implications of these findings are still being explored.

- Fibre

Reduced intake of whole grains and fruits can lead to inadequate fibre intake, potentially affecting gut health and contributing to gastrointestinal symptoms common in FM (55).

Potential excesses and imbalances

While nutrient deficiencies are common, some studies have also reported potential excesses or imbalances in certain dietary components among FM patients.

- High intake of processed foods

FM patients may consume more processed and ultra-processed foods, which can contribute to an excess intake of sodium, added sugars, and unhealthy fats (56, 57).

- Imbalanced macronutrient ratios

Some studies have suggested that FM patients may have an imbalanced macronutrient ratio, with a higher intake of carbohydrates and lower intake of pro-

tein, which can affect energy levels and muscle function (57).

Oxidative stress

Oxidative stress has been hypothesised as a possible contributor to the pathophysiology of FM, although current evidence remains inconclusive. Experimental studies have shown that oxidative stress can induce pain- and depression-like behaviours in animal models. For instance, in a reserpine-induced model, oxidative imbalance was associated with hyperalgesia, allodynia, and depressive symptoms (58). Some clinical studies have reported increased oxidative damage markers, such as malondialdehyde (MDA), and reduced antioxidant defences, including superoxide dismutase (SOD), in FM patients (59, 60). These findings have led to the hypothesis that reactive oxygen species (ROS) may contribute to mitochondrial dysfunction, which could reduce ATP production in neural and muscle tissues and thereby exacerbate fatigue and pain (60). Furthermore, oxidative stress may promote the activation of inflammatory pathways, including nuclear factor-kappa B (NF-κB) and pro-inflammatory cytokines like TNF-α and IL-1β, possibly influencing central and peripheral sensitisation (61). However, not all findings are consistent. Notably, the study by Chung *et al*. (62) did not report significant differences in oxidative stress between FM patients and healthy controls. Although urinary F2-isoprostane levels were weakly associated with fatigue, they showed no significant correlation with pain, depression, or functional capacity. These findings suggest that oxidative stress may not be a generalised feature of FM, and its clinical relevance remains uncertain. In conclusion, while oxidative stress remains a biologically plausible factor, its role in FM is yet to be clearly established. Further well-designed clinical studies are needed to determine whether targeting oxidative pathways can provide therapeutic benefit in FM.

Nutritional interventions and their potential in fibromyalgia treatment

Dietary interventions have emerged as a promising complementary approach in the management of FM. Several studies and clinical trials have investigated the effects of various nutritional interventions on FM symptoms, with some showing potential benefits. While the existing evidence is promising, it is important to note that many of the studies have limitations, such as small sample sizes, lack of blinding, and potential biases. Well-designed, larger-scale clinical trials are needed to further investigate the efficacy and long-term effects of dietary interventions in the management of FM.

- Lactose intolerance and fibromyalgia

Numerous studies have highlighted a high prevalence of food intolerances, including lactose intolerance, among patients with FM. One study explored the relationships between FM and food intolerance, noting that many patients report sensitivities to gluten and lactose, which can exacerbate symptoms such as musculoskeletal pain and gastrointestinal issues (63). Additionally, a cross-sectional study analysed the dietary habits of FM patients, finding a significant prevalence of lactose intolerance and symptom improvement following a lactose-free diet (64). Another review emphasized that lactose intolerance is common among FM patients, suggesting that managing food intolerances could be key in alleviating symptoms (65).

- Probiotic supplementation

Probiotic supplementation has been explored as a potential intervention for FM, as it can modulate the gut microbiome composition and function. A clinical trial by Roman *et al*. (66) reported that supplementation with the probiotic Bifidobacterium longum NCC3001 improved cognitive function, anxiety, and depression in women with FM.

A study performed by Merchant *et al*. (67), highlights the positive impact of Chlorella pyrenoidosa, a nutrient-rich green algae, on body function and quality of life in FM patients. This algae's dense nutritional profile, featuring chlorophyll, beta-carotene, vitamins, minerals, and dietary fibre, among other compounds, offers a broad spectrum of health benefits.

Additionally, the antioxidant supplement Cellfood, with its comprehensive blend of trace elements, minerals, enzymes and amino acids, has shown efficacy in combating oxidative stress, not only in FM but also in neurodegenerative conditions (13). The role of CoQ10, a potentially relevant mitochondrial bioenergetic component and antioxidant, is also gaining attention (68). Low levels of CoQ10 have been linked to various disorders, including FM, and supplementation is emerging as a viable strategy for symptom relief across multiple conditions.

In a study comparing the effects of a nutraceutical supplement (Migratens), containing coenzyme Q10, vitamin D, alpha-lipoic acid, magnesium and tryptophan, to acupuncture treatment on FM in 60 female patients, interesting findings emerged (69). Participants were divided into two groups to receive either the provided supplement or acupuncture according to traditional Chinese medicine principles over three months. The study assessed changes in pain and quality of life using the Fibromyalgia Impact Questionnaire Score-Revised (FIQ-R) and the Fibromyalgia Severity Scale (FSS) at 1-, 3-, and 6-months post-treatment initiation. Of the 55 patients who completed the study, those in the supplement group experienced a significant reduction in pain as early as one month into the treatment, with continued improvement at three months. Similarly, the acupuncture group saw significant pain relief at all measurement points. Both treatments also led to improvements in quality-of-life indicators.

The conclusion drawn from this study is that supplements can offer an effective treatment option for FM, comparable to the benefits of acupuncture. The results suggest that a combined or sequential approach, utilising both nutraceuticals and acupuncture, might enhance treatment compliance and effectiveness in managing the complex symptoms of FM over the long term.

In a study by Hinchado *et al*. (70), the impact of synbiotic supplementation (synbiotics) mixtures of probiotics (helpful gut bacteria) and prebiotics (non-digestible fibres that help these

bacteria grow), which includes probiotics, zinc, selenium and vitamin D, was explored in patients with FM and chronic fatigue syndrome (CFS). The research focused on examining changes in pro-inflammatory and anti-inflammatory cytokines, specifically IL-8 and IL-10, alongside neuroendocrine biomarkers like cortisol and DHEA, which play a role in the body's inflammatory and stress responses. The findings revealed that synbiotic supplementation led to notable improvements in patients' mental and physical well-being. Participants reported significant reductions in perceived stress, anxiety, and depression levels, coupled with enhanced quality of life in their daily activities. Additionally, the supplementation appeared to activate the hypothalamic-pituitary-adrenal (HPA) axis in a manner that could counterbalance the heightened inflammatory state, marked by elevated IL-8 levels, typically observed in FM patients at the start of the study. These results underscore the potential benefits of synbiotic supplementation in modulating the immune and neuroendocrine responses in individuals with FM and CFS, offering a promising avenue for improving patient outcomes.

- Elimination diets

Dietary interventions are increasingly explored as a potential strategy for managing FM, with many patients self-reporting changes in their diet post-diagnosis in hopes of symptom relief (8, 9, 11). Research into various dietary patterns, such as uncooked vegan diets rich in lactobacteria, vegetarian diets, and specific nutrient-focused regimens, have all shown some degree of improvement in FM symptoms, including reductions in pain, joint stiffness, and improvements in overall quality of life. Notably, the elimination of certain excitotoxins like MSG and aspartame has led to significant remissions in symptoms for some, while gluten-free diets have benefitted individuals with overlapping conditions such as coeliac disease and IBS alongside FM.

Despite these promising findings, a systematic review by Lowry *et al*. (9) in 2020 highlighted the challenges in drawing definitive conclusions from the existing research. This review, which encompassed 22 studies including 18 randomised control trials and four cohort studies, pointed out the varied nature of nutritional interventions tested, from vegan and low FODMAP diets to supplementation with substances like Chlorella green algae and coenzyme Q10. While improvements in pain were reported, the studies' frequent methodological limitations, small sample sizes, and potential biases limit the strength of these findings. This indicates a clear need for more comprehensive and well-designed studies to fully understand the impact of dietary interventions on FM management.

In a recent study concluded in Lisbon, Silva *et al*. (8) investigated the effects of an anti-inflammatory and low FODMAP (fermentable oligo-, di-, monosaccharides, and polyols) diet on patients with FM. The diet, which lasted for three months, excluded gluten, dairy, added sugars, and ultra-processed foods. Post-intervention, the group following this diet showed significant improvements in several patient-reported outcomes, including the Fibromyalgia Impact Questionnaire Revised (FIQR), Visual Analogue Scale (VAS) for pain, Brief Pain Inventory (BPI), Fibromyalgia Severity Scale (FSS), gastrointestinal symptom VAS (VAS_GI), Pittsburgh Sleep Quality Index (PSQI), and the 36-Item Short Form Survey (SF36), compared to the control group. Notably, inflammatory biomarkers such as high-sensitivity C-reactive protein (hs-CRP) and erythrocyte sedimentation rate (ESR) remained unchanged in both groups. The study concluded that dietary intervention was effective in improving clinical outcomes for FM patients, regardless of variables like age, disease duration, changes in body mass index, or body fat from baseline to post-intervention.

The adoption of a lactose-free diet has been reported to alleviate various symptoms in FM patients. For instance, a study by Almirall *et al*. (64), highlighted that patients who eliminated lactose from their diet experienced reductions in gastrointestinal discomfort and overall pain levels. This dietary adjustment has been associated with improvements in quality of life, suggesting that reducing the intake of lactose-containing foods can decrease inflammation and improve gut health, thereby positively impacting FM symptoms.

- Excitotoxins

Excitotoxins are substances that can excite neurons in an abnormal and harmful manner. Glutamate is the most diffuse excitatory neurotransmitter in the central nervous system and at high concentrations it can overexcite and cause neuron death. Several authors have hypothesised that the excitotoxin elimination diet could affect central sensitisation by altering excitatory neurotransmission in the CNS and also the exclusion of aspartame from the diet resulted in a complete regression of FM symptoms (71). Vellisca *et al*. (72), on the other hand, in a controlled study showed that the discontinuation of dietary monosodium glutamate (MSG) and aspartame did not improve clinical symptoms significantly. However, future research on the role of dietary excitotoxins in FM is warranted.

- Gluten-free diets

FM patients frequently report gastrointestinal issues like abdominal pain, bloating and altered bowel habits, mirroring symptoms of irritable bowel syndrome (IBS), which is observed in 25–81% of FM individuals (73). While FM appears more prevalent among those with coeliac disease (CD), the occurrence of CD within the FM population does not seem to exceed the general population rates (74). However, there is a growing discourse around a subset of FM patients potentially benefiting from a gluten-free diet, indicating possible subclinical CD or non-coeliac gluten sensitivity (NCGS). NCGS, sharing symptomatology with FM, is being explored as an underlying factor for FM symptoms. The dietary elimination of gluten has shown preliminary promise in improving FM symptoms, suggesting NCGS as a possible contributor (11). Yet, the exact relationship between gluten sensitivity and FM warrants further investigation to solidify dietary recommendations for FM management.

Potential benefits of dietary interventions

Studies have reported various potential benefits of dietary interventions in FM, including:

Reduction in pain and fatigue. Several studies indicate that specific dietary interventions, including vegetarian and low-FODMAP diets, can significantly reduce pain and fatigue in FM patients (13, 75).

Improved sleep quality. Dietary changes, especially those reducing inflammatory foods, have been linked to better sleep quality in FM patients (34, 35).

Enhanced cognitive function. Nutritional interventions that focus on balanced diets rich in vitamins and minerals can improve cognitive function, often referred to as fibro fog (76).

Reduced inflammation. Anti-inflammatory diets can help decrease the overall inflammatory response in the body, which is beneficial for managing FM symptoms (77). Improved gastrointestinal health. Low-FODMAP diets have been shown to alleviate gastrointestinal issues that are common in FM patients (11).

Better quality of life. Overall improvements in the quality of life have been noted in patients who adhere to specific dietary guidelines tailored for FM (51).

Conclusions and future directions

The relationship between gut microbiome dysbiosis, nutrition and FM is an emerging field of interest, but currently remains largely speculative. While some studies have reported altered microbiome compositions in FM patients and correlations with symptom severity, these findings are preliminary and often lack replication in larger, independent cohorts. The suggestion of a causal link, such as the one proposed by FMT studies in animal models, remains unconfirmed in clinical settings. Nutritional interventions, including specific diets, probiotics, and micronutrient supplementation, have been explored as potential strategies to modulate FM symptoms. However, the evidence supporting their efficacy is inconsistent and limited by methodological weaknesses, such as small sample sizes, lack of blinding, and placebo effects. Furthermore, many proposed mechanisms linking nutrition, microbiota and pain, such as modulation of oxidative stress, inflammatory signalling, or neurotransmitter metabolism, are biologically plausible but not clinically validated. From a clinical perspective, there is currently insufficient evidence to recommend microbiome-based or dietary interventions as standard treatment for FM. Nevertheless, given the low risk of harm, individualised nutritional counselling may be considered within a multidisciplinary framework, particularly for patients with specific dietary sensitivities or comorbid gastrointestinal symptoms. In conclusion, future research should focus on well-designed, large-scale studies that critically assess the role of gut microbiome alterations and nutritional strategies in FM. Only through rigorous investigation can we determine whether these associations represent meaningful targets for diagnosis or therapy, or rather epiphenomena with limited translational relevance.

Take home messages

- There is a significant link between gut microbiome dysbiosis and FM.
- Specific bacteria in FM patients correlate with symptom severity.
- Faecal microbiota transplantation (FMT) studies suggest causality between dysbiosis and FM pain.
- Nutritional interventions (prebiotics, probiotics and personalised diets) show promise.
- Key nutrients are: magnesium, selenium, omega-3 fatty acids.
- Antioxidants and anti-inflammatory nutrients (*e.g.* SCFAs, vitamins) are beneficial.
- Clinical recommendations: to assess FM patients' dietary patterns and gut health, to implement personalised dietary interventions and to monitor nutritional status and address deficiencies.

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