



The role of nutrition in patients with fibromyalgia: Is there an impact on disease parameters?

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Date submitted:

11.04.2020

Date accepted:

05.06.2020

Online publication date:

15.09.2020

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Keywords: Fibromyalgia, nutrition, biochemical parameters

ABSTRACT

Aims: The aim of our study is to assess the associations between dietary intake and biochemical parameters, clinical assessments of pain, sleep quality and current health status of patients who were diagnosed with fibromyalgia.

Methods: This is a prospective study on patients with fibromyalgia. In patients' routine controls, data were recorded about their nutrition by using food consumption recording form. Also, the biochemical parameters were recorded. Clinical symptoms were evaluated by using Short form of MacGill Pain Questionnaire (SFMPQ), Fibromyalgia Impact Questionnaire (FIQ) and Pittsburg Sleep Quality Index (PSQI).

Results: Eighty-one patients with a disease duration of minimum 12 months were included. The mean age was 48.9 years and 90.1% of patients were female. The correlation analysis between serum vitamin B₁₂ and clinical symptoms showed a weak negative correlation with FIQ ($r=-0.257$, $p=0.021$), sleep duration ($r=-0.317$, $p=0.004$), sleep disturbance ($r=-0.279$, $p=0.012$), sleep quality ($r=-0.235$, $p=0.035$), and PSQI total score ($r=-0.316$, $p=0.004$). Percentage of energy from dietary carbohydrate showed a moderate positive correlation with FIQ ($r=0.383$, $p<0.001$). Dietary fat showed a moderate negative correlation with FIQ ($r=-0.29$, $p=0.007$). While dietary saturated fat showed a moderate positive correlation with FIQ ($r=0.361$, $p<0.001$), dietary unsaturated fat displayed a weak negative correlation with FIQ ($r=-0.228$, $p=0.041$). Dietary fiber had a moderate negative correlation with FIQ ($r=-0.357$, $p<0.001$), SFMPQ-present pain intensity ($r=-0.357$, $p<0.001$), and SFMPQ-visual analogue scale ($r=-0.419$, $p<0.001$) subscores.

Conclusions: The current study results suggest that a healthy diet habit consisting of low saturated fat, carbohydrates and higher fiber, vitamins and minerals may provide improvement in fibromyalgia symptoms. Dietary assessment and intervention should be a part of the management of patients with fibromyalgia.

Introduction

Fibromyalgia is a chronic disease characterized by general pain in the body with particular tender points, fatigue, depression, anxiety, non-restorative sleep, morning stiffness, headaches, cognitive impairment, paresthesia, affective disorders, irritable bowel and bladder syndrome. Fibromyalgia symptoms can be associated with several factors such as dysfunction of hypothalamic axis and increase of cortisol, changes in the central nervous system, oxidative stress, mitochondrial dysfunction, and also changes in the intestinal microbiota (1,2). As the etiology

is multifactorial, a multidimensional management which consists of a combination of pharmacological and non-pharmacological treatments is necessary for fibromyalgia'. Nutrients and nutritional supplements are also effective factors for fibromyalgia patients (3,4). There is a linkage between dietary patterns and fibromyalgia symptoms (5,6). However, according to the literature, the effects of different dietary approaches are not clear yet. A low fermentable oligo, di and monosaccharides, alcohols and polyols (FODMAPS) diet, a raw vegetarian diet and a hypocaloric diet may relieve pain and improve functional parameters in fibromyalgia patients. A

nutritionally balanced diet contributing to weight loss can reduce the severity of fibromyalgia symptoms (7).

Fibromyalgia is a chronic disease caused by some neurologic, genetic, psychological conditions or mineral-vitamin deficient status. However, to date, there are few studies linking biochemical parameters and fibromyalgia. A deficit of nutritive elements including necessary metal ions and vitamins might have an important effect in the occurrence of fibromyalgia. Patients with deficiencies of some fundamental nutrients may develop dysfunction of pain pathways together with fibromyalgia symptoms (8).

In the treatment of fibromyalgia, some minerals and vitamins have beneficial effects. Sufficient intake of vitamin D, vitamin B₁₂ and magnesium is important. Deficiency of certain essential elements may cause dysfunction of pain inhibitory mechanisms. Insufficient levels of magnesium and selenium cause muscle pains. Deficiency of magnesium can cause chronic systemic inflammation, increase substance P levels and induce an increase in pro-inflammatory cytokines and C-reactive protein (CRP). Selenium has a protective role against ischemia (8).

Iron is necessary for enzymes in neurotransmitter production. Investigation of cerebrospinal fluid in fibromyalgia syndrome has shown a decrease in the concentration of serotonin, dopamine and norepinephrine (8). Moreover, as iron is a cofactor in dopamine and serotonin synthesis, it may have an effect in the etiopathogenesis of fibromyalgia (8,9). Therefore, the management of diet is very important for fibromyalgia patients in order to ameliorate inadequate intake of essential nutrients. When optimal nutrition is obtained, pain levels are usually decreased. Also, by consuming antioxidant-rich foods, it is possible to relieve fibromyalgia symptoms.

Researches about nutrition are necessary to reveal relationships between nutrition and fibromyalgia. The aim of our study is to assess the associations between dietary intake and biochemical parameters, clinical assessments of pain, sleep quality and current health status of patients who were diagnosed with fibromyalgia.

Methods

This was a prospective study conducted between April 2019 and September 2019 on patients with fibromyalgia (diagnosed with American College of Rheumatology 2010 Criteria), who were admitted to the physical medicine and rehabilitation clinics. Eighty-one patients with a disease duration of minimum 12 months aged between 18 and 65 years were included. The patients were selected according to the use of similar medical treatment and having similar exercise habits. Exclusion criteria included the presence of any disease which could affect biochemical parameters and clinical symptoms. The study protocol was approved by the bioethics and Gülhane Training and Research Hospital Research Committee with the number of

19/156 on April 30th of 2019, and all procedures were performed in compliance with the Helsinki Declaration. All patients were informed about the study and written informed consent was obtained. In patients' routine controls, data were recorded about their nutrition by using food consumption recording form, biochemical parameters including serum hemoglobin, ferritin, vitamin B₁₂, thyroid stimulating hormone, calcium, magnesium, folic acid, vitamin D, total protein, albumin, sedimentation, CRP levels. Twenty-four hours dietary recall was taken by investigator to determine daily nutrient intake of patients. Portion sizes and volumes were estimated with a portion size picture book including 120 photographs of foods, each with 3-5 different portion sizes (10). The BeBiS software version 7.2 was used to calculate daily intake of energy, macro and micronutrients (11). Dietary intakes of patients were assessed according to the Turkey-Specific Nutrition Guide (12). Clinical symptoms were evaluated by using the Short form of MacGill Pain Questionnaire (SFMPQ), Fibromyalgia Impact Questionnaire (FIQ) and Pittsburg Sleep Quality Index (PSQI).

Statistical Analysis

Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 22.0 for Mac (SPSS Inc., Chicago, IL). Continuous variables were presented as mean \pm standard deviation. Qualitative variables were presented as number and percentage. The Kolmogorov-Smirnov test was used to determine the normality of data distribution. Correlation analyses were done with the Pearson test. A value of $p < 0.05$ was considered to be statistically significant.

Results

Main characteristics of the patients are given in Table 1. Most of the patients were female (90.1%) and most of them were married (82.7%). Education duration was generally low (1-5 years in 49.4% of the patients). Laboratory findings are given in Table 2. All parameters except 25-OH D were in normal range. The mean 25-OH D level was 22.8 ± 14.1 ng/mL.

FIQ total, SFMPQ, and PSQI scores of the patients are given in Table 3. FIQ total score was 48.7 ± 23.5 , SFMPQ total pain rating index was 12.9 ± 8.6 , and PSQI-total was 9.7 ± 4.5 .

The correlation analysis between serum vitamin B₁₂ and clinical symptoms showed a weak negative correlation with FIQ ($r = -0.257$, $p = 0.021$), sleep duration ($r = -0.317$, $p = 0.004$), sleep disturbance ($r = -0.279$, $p = 0.012$), sleep quality ($r = -0.235$, $p = 0.035$), and PSQI total score ($r = -0.316$, $p = 0.004$). There was no correlation between other biochemical parameters and clinical symptoms.

The mean intakes of energy, carbohydrate, protein and fat were 1919.5 ± 618.8 kcal, 212.2 ± 94.7 g, 71.9 ± 21.2 g, and 84.0 ± 31.9 g, respectively. When daily energy percentage from carbohydrate, protein and fat were assessed according

to the Turkey-Specific Nutrition Guide, energy percentage from carbohydrate was over reference values in five (6.17%) patients, energy percentage from protein was over reference values in 10 (12.3%) patients and energy percentage from fat was over reference values in 60 (74.1%) patients. In addition, the contribution of saturated fat to energy was determined above the recommended level in 69 (85.2%) individuals. The correlation between FIQ, SFMPQ, macronutrients, and some micronutrients (which were significantly correlated) were shown in Table 4. Dietary energy, carbohydrate, protein, and percentage of energy from dietary protein were not correlated with FIQ and SFMPQ. The percentage of energy from dietary carbohydrate showed a moderate positive correlation with FIQ ($r=0.383$, $p<0.001$). Dietary fat showed moderate negative correlation with FIQ ($r=-0.29$, $p=0.007$). While dietary saturated fat had a

moderate positive correlation with FIQ ($r=0.361$, $p<0.001$), dietary unsaturated fat had a weak negative correlation with FIQ ($r=-0.228$, $p=0.041$). Percentage of energy from dietary fat showed a negative moderate correlation with FIQ ($r=-0.411$, $p<0.001$) and a weak negative correlation with SFMPQ-visual analogue scale (VAS) subscore ($r=-0.225$, $p=0.044$). Dietary fiber displayed a moderate negative correlation with FIQ ($r=-0.357$, $p<0.001$), SFMPQ-present pain intensity (PPI) ($r=-0.357$, $p<0.001$), and SFMPQ-VAS ($r=-0.419$, $p<0.001$) subscores. In addition to dietary energy and above mentioned macronutrients, some vitamins and minerals (folic acid, calcium, phosphor, vitamin B₁, vitamin B₂, biotin, iron, zinc, and magnesium) showed a weak to moderate negative correlations with FIQ, SFMPQ-PPI, and SFMPQ-VAS subscores (as presented in Table 4).

Discussion

In this study of 81 patients who were diagnosed with fibromyalgia, results have shown some associations between biochemical parameters, dietary intake and clinical assessments of pain, sleep quality and current health status. The mean vitamin B₁₂ level was in normal range and vitamin B₁₂ levels showed a negative correlation with clinical scores such as FIQ and sleep scores. Although low vitamin B₁₂ levels were reported with pain related pathologies before (13), studies including patients with fibromyalgia demonstrated no link between serum vitamin B₁₂ levels and fibromyalgia (14,15). In a study by Regland et al. (16), cerebrospinal fluid vitamin B₁₂ levels were correlated with fatigue and psychological ratings. This result was similar to the result in the current study notwithstanding sample differences. We suppose that more studies are necessary to firmly report a vitamin B₁₂ effect on fibromyalgia symptoms.

Table 1. Main characteristics of patients

	Mean	SD
Age (years)	48.9	10.5
Gender	n	%
Female	73	90.1
Male	8	9.9
Education		
Illiterate	3	3.7
1-5 years	40	49.4
6-10 years	3	3.7
10-15 years	16	19.8
>15 years	19	23.5
Marital status		
Married	67	82.7
Single	14	17.3

SD: Standard deviation

Table 2. Laboratory findings of patients

Parameter	Mean	SD
Hemoglobin (g/dL)	13.2	1.1
ESR (mm/h)	15.7	10.6
CRP (mg/L)	3.4	4.4
Vitamin B ₁₂ (pg/dL)	327.8	205.7
Folic acid (ng/mL)	8.3	3.8
Ferritin (ng/mL)	31.7	30.1
Ca (mg/dL)	9.3	0.9
Mg (mg/dL)	2.1	0.7
25-OH D (ng/mL)	22.8	14.1
Total protein (mg/dL)	7.1	0.8
Albumin (mg/dL)	4.2	0.3
TSH (mU/L)	2.2	1.7

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, Ca: Calcium, Mg: Magnesium, SD: Standard deviation

Table 3. Fibromyalgia Impact Questionnaire total, Short form of McGill Pain Questionnaire, and Pittsburg Sleep Quality Index scores of the patients

	Mean	SD
FIQ total	48.7	23.5
McGill sensory	10.1	6.3
McGill affective	2.9	3.1
Total pain rating index	12.9	8.6
McGill present pain intensity	3.1	1.0
McGill VAS	5.2	2.3
PSQI		
Sleep duration	1.1	1.0
Sleep latency	1.8	1.0
Sleep disturbance	1.9	0.8
Habitual sleep efficiency	0.8	1.1
Sleep medication use	0.2	0.7
Daytime dysfunction	1.7	1.0
PSQI-total	9.7	4.5

FIQ: Fibromyalgia Impact Questionnaire, PSQI: Pittsburg Sleep Quality Index, VAS: Visual analogue scale, SD: Standard deviation

Table 4. Correlation between Fibromyalgia Impact Questionnaire, Short form of MacGill Pain Questionnaire, macronutrients and some micronutrients

	FIQ-total		McGill sensory		McGill affective		Total pain rating index		McGill present pain intensity		McGill VAS	
	r	p	r	p	r	p	r	p	r	p	r	p
Energy	-0.072	0.524	0.003	0.981	0.033	0.769	0.014	0.902	-0.026	0.815	-0.021	0.854
Cho	0.130	0.247	0.020	0.861	-0.043	0.704	-0.001	0.993	0.030	0.793	0.094	0.406
Cho %	0.383	<0.001	0.084	0.457	-0.103	0.358	0.054	0.829	0.123	0.276	0.203	0.070
Protein	-0.196	0.080	0.013	0.907	0.076	0.498	0.037	0.742	-0.045	0.692	-0.096	0.395
Protein %	-0.130	0.249	-0.042	0.710	0.034	0.766	-0.019	0.868	-0.012	0.918	-0.050	0.658
Fat	-0.29	0.007	-0.025	0.823	0.110	0.330	0.021	0.853	-0.106	0.345	-0.172	0.126
Fat %	-0.411	<0.001	-0.077	0.494	0.119	0.292	-0.014	0.902	-0.135	0.229	-0.225	0.044
Saturated fat	0.361	<0.001	0.105	0.350	-0.017	0.881	-0.083	0.460	-0.055	0.624	-0.123	0.274
Unsaturated fat	-0.228	0.041	0.015	0.891	0.158	0.158	0.068	0.545	-0.117	0.296	-0.173	0.123
Cholesterol	-0.213	0.056	-0.106	-0.344	0.013	0.907	-0.073	0.515	-0.018	0.871	-0.067	0.551
Fiber	-0.358	<0.001	0.111	0.325	0.116	0.302	0.123	0.274	-0.357	<0.001	-0.419	<0.001
Vitamin B1	-0.246	0.027	0.040	0.722	0.027	0.811	0.039	0.729	-0.274	0.013	-0.320	<0.001
Vitamin B2	-0.393	<0.001	-0.221	0.047	-0.083	0.464	-0.192	0.086	-0.265	0.017	-0.356	<0.001
Biotin	-0.262	0.018	-0.094	0.402	-0.053	0.641	-0.088	0.434	-0.315	0.004	-0.384	<0.001
Folic acid	-0.405	<0.001	0.003	0.979	0.100	0.374	0.038	0.735	-0.276	0.013	-0.498	<0.001
Vitamin C	-0.191	0.088	0.017	0.881	0.232	0.037	0.096	0.395	-0.118	0.293	-0.287	0.009
Calcium	-0.473	<0.001	-0.237	0.034	-0.124	0.269	-0.218	0.05	-0.274	0.013	-0.418	<0.001
Magnesium	-0.259	0.020	0.022	0.847	0.044	0.694	0.032	0.777	-0.227	0.042	-0.335	0.002
Phosphor	-0.435	<0.001	-0.122	0.277	-0.023	0.840	-0.098	0.385	-0.263	0.018	-0.364	0.001
Iron	-0.323	0.003	0.081	0.472	0.084	0.453	0.090	0.425	-0.271	0.014	-0.390	<0.001
Zinc	-0.273	0.014	-0.030	0.791	0.036	0.752	-0.009	0.935	-0.184	0.099	-0.245	0.028

SFMPQ: Short form of MacGill Pain Questionnaire, FIQ: Fibromyalgia Impact Questionnaire, VAS: Visual analogue scale, Cho: Carbohydrate

Vitamin D is also important in both inflammatory and pain pathways. We know an association between vitamin D deficiency and fibromyalgia, but in fact, little is known about its mechanism in fibromyalgia. A recent review showed that patients with fibromyalgia had low levels of vitamin D according to healthy controls (17). Literature shows contradictory results about the effect of vitamin D on pain or symptom control, with no clear results indicating the role of supplementation in the management of fibromyalgia. Although there are studies that found negative correlation between pain or tender points count and vitamin D levels, the remaining studies could not describe a correlation (18). In a study it was found that fibromyalgia patients with vitamin D levels ≤ 20 ng/mL to be more likely to have humor disruption, confusion, memory deterioration, sleep problems, palpitations and restless-leg syndrome (19). In addition, vitamin D supplements are reported to improve disease symptoms in patients with fibromyalgia (20,21). In the current study, the mean vitamin D level was 22.8 ± 14.1 ng/mL and thirty patients showed vitamin D insufficiency. However, there was no correlation between serum vitamin D levels and clinical symptoms.

The hypothesis about connection between dietary patterns and fibromyalgia symptoms has directed clinicians to investigate the effects of different diets on fibromyalgia symptoms (8). Raw vegetarian diet, low FODMAPs diet, hypocaloric diet, monosodium glutamate- and aspartame-free diet are some of the dietary patterns which have been studied to date and results on pain, quality of life and sleep are contradictory. A study showed that a pure vegetarian, raw diet provided significant improvements in fibromyalgia symptoms (pain, physical performance, function and quality of life) (22,23). Another study reported that after a three-months vegan diet, there were significant improvements in pain scores, health assessment questionnaire scores, general health questionnaire, quality of sleep and morning stiffness (24). In a randomized controlled trial, it was shown that lacto-vegetarian diet combined with core stabilization exercises in patients with fibromyalgia who had low back pain provided pain reduction and body composition improvement (25). In another study, it was shown that a gluten-free diet improved all symptoms including pain, tender points, function, gastrointestinal complaints and fatigue (26). Despite the fact that there are studies in the literature about diet-

symptom association, few studies investigated macronutrient and micronutrient content of the diet. In the current study, we found dietary energy percent from carbohydrate, fat, and fiber association with FIQ and SFMPQ.

Fibromyalgia and obesity are very closely associated pathologies and obesity and carbohydrate-rich diets are potential factors that may affect the severity of symptoms, pain, and disease activity in fibromyalgia syndrome (27,28). We also found similar results in the current study. The percent of energy from carbohydrate showed a moderate positive correlation with FIQ. To date, some investigators tended to enlighten the possible relation between glucose metabolism and pain, but there is no significant result yet (29). In the current study, interestingly the percent of energy from fat showed a moderate negative correlation with FIQ and dietary fat showed a moderate negative correlation with FIQ. However, when we reanalyzed fat content considering saturated and unsaturated fat, saturated fat showed a moderate positive correlation while unsaturated fat showed a weak negative correlation with FIQ. We suggest that, according to this result, saturated fat content of diet may be the factor which worsens symptoms of the patient. Intake of saturated fat is increasing day by day due to processed food and fast food consumption. Diets containing excessive saturated fat are suspected to cause chronic diseases due to chronic low degree inflammation (30-33).

Plant-enriched diets are reported to increase nitric oxide levels which may help to relieve pain in fibromyalgia patients (8). In the current study, the amount of dietary fiber showed a moderate negative correlation with FIQ, SFMPQ-VAS and SFMPQ-PPI. Different from other dietary content, fiber showed a correlation with SFMPQ-VAS and SFMPQ-PPI and this gives a rise to the thought that increasing fiber content of diet may help relieving pain.

Redox balance changes in cells due to nutritional deficiencies like iron, magnesium, iodine, melatonin, zinc, selenium and branched chain amino acids can have a potential role in fibromyalgia symptoms (34). Although magnesium and selenium are suspected ions in physiopathology and symptom severity of fibromyalgia, a review showed that magnesium and malic acid use did not significantly change pain ratings or depressive symptoms in patients with fibromyalgia (35). While some authors reported that serum levels of selenium and magnesium were not significantly different from controls (36), another study showed a decrease in magnesium and zinc levels, but no significant difference in selenium levels. Also, serum magnesium and zinc levels were associated with clinical parameters, indicating a possible role of these two elements in fibromyalgia etiopathogenesis (37). However, this study did not investigate nutritional deficiency or low magnesium or zinc dietary intake. In the current study, we evaluated dietary intake of magnesium and found that dietary magnesium showed a

weak negative correlation with FIQ and SFMPQ-VAS. As it can be realized from the above mentioned results, cross-sectional or interventional studies show contradictory results.

In addition to study methodology, included patients in the current study were given nutrition advice according to dietary recalls. To the best of our knowledge, the current study is the first on the relationship between nutrition, biochemical parameters and clinical symptoms in fibromyalgia patients. The cross-sectional design can be interpreted as the limitation of this study. There are also strengths of the study. Large sample size and comprehensive assessment of patients with multiple questionnaires are the strengths of the study. Well-designed clinical trials about the effect of the dietary interventions on fibromyalgia patients are necessary in order to understand more details about the potential benefits from nutrition.

Conclusion

The current study results suggest that a healthy diet habit consisting of low saturated fat, carbohydrates and higher fiber, vitamins and minerals (folic acid, calcium, phosphor, vitamin B1, vitamin B2, vitamin B₁₂, biotin, iron, magnesium, zinc) may provide an improvement in fibromyalgia symptoms. We also suggest that dietary assessment and interventions should be a part of the management of patients with fibromyalgia.

Ethics

Ethics Committee Approval: The study protocol was approved by the bioethics and Gülhane Training and Research Hospital Research Committee with the number of 19/156 on April 30th of 2019, and all procedures were performed in compliance with the Helsinki Declaration.

Informed Consent: All patients were informed about the study and written informed consent was obtained.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.K., K.T.A., Concept: Ö.K., K.T.A., Design: Ö.K., K.T.A., Data Collection or Processing: Ö.K., K.T.A., Analysis or Interpretation: Ö.K., K.T.A., Literature Search: Ö.K., K.T.A., Writing: Ö.K., K.T.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support

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