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Anti-inflammatory and antioxidant feeding and supplementation may serve as adjuvants in women with fibromyalgia

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HIGHLIGHTS

- Fibromyalgia syndrome is a chronic pain disorder with no markers to monitor progression and no cure.
- A turmeric-based supplement, a gluten-free, FODMAP and low histamine diet could be beneficial in women with fibromyalgia.
- No significant improvement was observed after one month of treatment as shown by CPGS, PCS, FSS, FIS and PSQI.
- Significant improvement was observed after one month of treatment for pain disturbances in work activities.
- Significant variations (p < 0.05) were observed in the intensity of symptoms, except for nausea and vomiting.

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ABSTRACT

Objectives: Fibromyalgia syndrome is a chronic pain disorder of unknown causation associated with debilitating fatigue, unrefreshing sleep, cognitive and affective symptoms. There are no markers to monitor fibromyalgia progression and no cure. We aimed to analyze the effects of a turmeric-based supplement and a gluten-free, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols and low histamine diet (*IGUBAC Diet*®), with antioxidant and anti-inflammatory characteristics, in women with fibromyalgia.

Methods: a randomized, controlled, clinical trial, with 13 women (51.46 ± 8.04 years) diagnosed with fibromyalgia were assessed using the Chronic Pain Grade Scale, the Pain Catastrophizing Scale, the Fatigue Severity and Impact Scale and the Pittsburgh Sleep Quality Index. Anthropometric parameters, antioxidant and anti-inflammatory analysis and symptoms progression were measured before and after one month of treatment with turmeric supplement and *IGUBAC Diet*®.

Results: No significant improvement was observed after one month of treatment as shown by Chronic Pain Grade-, Pain Catastrophizing-, Fatigue Severity- and Fatigue Impact Scales and Pittsburgh Sleep Quality Index, except for pain disturbances in work activities. Significant variations ($p < 0.05$) were observed in the intensity of symptoms, except for nausea and vomiting.

Conclusion: Additional research is necessary to further elucidate the effects of a turmeric-based supplement with *IGUBAC Diet*® in women with fibromyalgia. A multidisciplinary approach should be the goal of treatment for fibromyalgia.

1. Introduction

Fibromyalgia is a chronic generalized pain syndrome accompanied by other symptoms such as depression, anxiety, fatigue, or sleep disturbances. In Spain, 2.4% of the population over 20 years of age suffer from it, with a greater presence in women in a 21:1 ratio. Its etiology is unknown and there are no effective treatments [1]. The pathophysiological sign is a sensitized or hyperactive central nervous system that leads to greater gain in pain and sensory processing. In addition, other pathophysiological mechanisms such as mitochondrial dysfunction, oxidative stress, inflammatory component and neuroendocrine disorders must be taken into account [1].

High levels of oxidative stress have been associated with numerous pathologies such as rheumatoid arthritis, Parkinson's, Alzheimer's,

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atherosclerosis and cardiovascular diseases, diabetes mellitus. Oxidative stress is an imbalance between the production of reactive oxygen species and reactive nitrogen species and the mechanisms of antioxidant defense [2].

When considering nutritional therapy, there are currently no specific dietary recommendations for fibromyalgia; however, up to 30% of patients modify their diet after diagnosis [3]. Previous studies in Spain [4,5] have observed the remission of fibromyalgia symptoms following a gluten-free diet. It has also been shown that a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) is beneficial to reduce the symptomatology of this disease, especially those related to gastrointestinal problems (abdominal pain, dyspepsia and intestinal changes) [6]. Other studies have shown an improvement in the symptoms of this syndrome when a restrictive diet is performed on gluten, lactose and FODMAPs [7]. Due to the correlation between irritable bowel syndrome and fibromyalgia, some studies have based the application of a diet low in FODMAPs in fibromyalgia patients on previous studies performed in patients with irritable bowel syndrome [8].

Turmeric (*Curcuma longa*) is a widely used spice that has various biological effects [9]. Curcumin is the principle component of turmeric, which is used as treatment for a variety of chronic conditions like rheumatoid arthritis, inflammatory bowel disease, Alzheimer's and common malignancies like colon, stomach, lung, breast, and skin cancers [10]. Extracts of turmeric exhibit potent antioxidant activity and anti-inflammatory activity. These effects of *Curcuma longa* are at least partly attributable to bisacurone, a component of turmeric that has both antioxidant and anti-inflammatory activities [11]. This evidence suggests that turmeric could be a powerful ally against fibromyalgia.

Identifying changes in pain, fatigue or other symptoms persistently associated with fibromyalgia will help to effectively diagnose the disease, track its progression and, more importantly, control the effects of therapeutic approaches.

2. Hypothesis

Anti-inflammatory and antioxidant dietary products are adjuvants in the symptoms of fibromyalgia.

A controlled diet based on intestinal health could be adjuvant in female patients with fibromyalgia.

3. Objectives

1. Analyze the effects of a turmeric-based food supplement, with antioxidant and anti-inflammatory characteristics in women with fibromyalgia.
2. Evaluate the effects of a gluten-free, FODMAP and low histamine diet (anti-inflammatory and antioxidant diet) in women with fibromyalgia.

4. Material and methods

4.1. Study type

Randomized, controlled, prospective, clinical trial.

4.2. Study population

A sample of 13 participants, of the feminine sex, aged 30–60 years, was selected from Research Centers in Nutrition and Health, and Asociación de Fibromialgia de Madrid, in 2016.

Inclusion criteria were women aged 30–60 years, with fibromyalgia diagnosis, who agreed to participate voluntarily, following the *IGUBAC Diet*®, and filling in the informed consent. Criteria for diagnosis of fibromyalgia included generalized pain in at least 4 of 5 regions (left upper, right upper, left lower, right lower axial) and symptoms present at a similar level for at least 3 months, regardless of other clinically important illnesses [12]. Participants who did not meet inclusion criteria, had a severe psychiatric disorder, renal disease, cardiovascular disease, were pregnant or breastfeeding, allergic to turmeric or were under corticoids medication were excluded.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. The research project was evaluated and approved by the Research and Ethics Committee of Hospital Universitario Severo Ochoa, Madrid.

4.3. Study design

The study population consisted of 13 women (n = 6 in group 1 [G1] and n = 7 in group 2 [G2]), who were distributed by randomization, using randomization tables. G1 was the study group (turmeric-based food supplement) and G2 was the control group (no food supplement). The sample size was calculated by comparison of means. A 95% confidence interval and a statistical power of 90% were used.

The study group was supplemented during 1 month with a turmeric-based supplement of 500 mg, *AVECURM* by AVEDIAN, as turmeric is a natural analgesic and reduces inflammation and pain. They were also given the *IGUBAC Diet*® (Inflammatory Gut-Brain Axis Control Diet), a personalized diet evidence-based focus in the relationship between nutrition, inflammation and the gut-brain axis in 5 pillars: low FODMAP diet [13], gluten-free [4], low histamine and other amines or inflammatory molecular intermediaries [14], preservative free [15] and natural food [16]. The *IGUBAC Diet*® has been probed by CINUSA Clinic (Spain) in the treatment of rheumatic diseases, such as fibromyalgia or irritable bowel syndrome in adults, and autism or attention-deficit/hyperactivity disorder in children. Group 2 served as control sample for comparison, therefore none of the participants in this group ingested the food supplement.

4.4. Study factors

We conducted an anthropometric study to the subjects participating in the study, and analysed their eating habits with the PREDIMED questionnaire [17]. Antioxidant and anti-inflammatory parameters were analysed. Data on symptoms, pain, sleep and fatigue were also retrieved by validated questionnaires.

4.4.1. Anthropometric study

Anthropometric measurements included: height (cm), weight (kg), BMI (kg/m^2), fat mass (%), visceral fat (%), muscle mass (%), body water (%) and waist circumference (cm). Height was measured, according to the WHO [18] protocol, with the subjects standing barefoot using a SECA mobile stadiometer with a 1 mm accuracy. Weight, body fat mass, visceral fat, muscle mass and body water were measured with a digital bioimpedance analyser TANITA model BP-601, ranging from 0.1 to 150 kg. Quetelet index, based on weight and height, was used to calculate BMI [19]. Waist circumference was measured with a non-extensible tape measure (range 0–150 cm) around the midpoint between the lowest rib and the iliac crest. The anthropometric study was done by a single trained researcher, ensuring the homogeneity and standardisation of uniformity criteria and the methodology to follow.

4.4.2. Diet assessment

The PREDIMED questionnaire [17] was used to measure quality and adherence to the Mediterranean diet. The validated 14-point

Mediterranean Diet Adherence Screener (MEDAS) [20] consisted of 2 questions on food intake habits considered characteristic of the Spanish Mediterranean diet and 12 questions on food consumption frequency. Each question was scored 0 or 1. One point was given for the compliance of the recommendation. If the condition was not met, 0 points were recorded for the category. The final PREDIMED score ranged from 0 to 14. A score ≤ 9 means low adherence to the Mediterranean diet, from 9 to 12 improvable adherence and > 12 good adherence.

4.4.3. Pain

Chronic Pain Grade Scale (CPGS) [21] and Pain Catastrophizing Scale (PCS) [22] were used to assess pain.

- Chronic Pain Grade Scale: the severity of chronic pain can be graded based on its characteristics and its impact on a person's activities. The CPGS is a multidimensional measure that assesses 2 dimensions of overall chronic pain severity: pain intensity and pain-related disability. All 7-items are scored on an 11-point Likert scale, with responses ranging from 0 to 10. Scores are calculated for 3 subscales: the characteristic pain intensity score, which ranges from 0 to 100, is calculated as the mean intensity ratings for reported current, worst, and average pain; the disability score, which ranges from 0 to 100, is calculated as the mean rating for difficulty performing daily, social, and work activities; and the disability points score, which ranges from 0 to 3, is derived from a combination of ranked categories of number of disability days and disability score. The 3 subscale scores for pain intensity and disability are combined to calculate a chronic pain grade that enables classification of chronic pain patients into 5 hierarchical categories: grades 0 (no pain), I (low disability-low intensity), II (low disability-high intensity), III (high disability-moderately limiting) and IV (high disability-severely limiting).
- Pain Catastrophizing Scale: Pain catastrophizing is characterized by the tendency to magnify the threat value of a pain stimulus and to feel helpless in the presence of pain, as well as by a relative inability to prevent or inhibit pain-related thoughts in anticipation of, during, or following a painful event [23]. PCS was developed to help quantify an individual's pain experience, asking about how they feel and what they think about when they are in pain. People are asked to indicate the degree to which they experience each of 13 thoughts and feelings when they are experiencing pain using the 0 (not at all) to 4 (all the time) scale. A total score is yielded (ranging from 0 to 52), along with three subscale scores assessing rumination, magnification and helplessness. Research at the University Centre for Research on Pain and Disability indicates that a total PCS score of 30 represents clinically relevant level of catastrophizing. A total PCS score of 30 corresponds to the 75th percentile of the distribution of PCS scores in clinic samples of chronic pain patients. The 75th percentile cut-off scores for the three PCS subscales are 11 for rumination, 5 for magnification and 13 for helplessness [22].

4.4.4. Fatigue

Fatigue Severity Scale (FSS) [24] and Fatigue Impact Scale (FIS) [25] were performed to assess fatigue symptoms.

- Fatigue Severity Scale: FSS questionnaire contains nine statements that rate the severity of the fatigue symptoms. The items are scored on a 7 point scale, where a low value (e.g., 1) indicates strong disagreement with the statement, whereas a high value (e.g., 7) indicates strong agreement. Total score ranges from 9 to 63 points. A total score of less than 36 suggests that the subject may not be suffering from fatigue. A total score of 36 or more suggests that the subject may need further evaluation by a physician. Another way of scoring would be the mean of all scores with minimum score being 1 and maximum score being 7.
- Fatigue Impact Scale: this instrument provides an assessment of the effects of fatigue in terms of physical, cognitive, and psychosocial functioning. Participants rate on a 5-point Likert scale, with 0 = 'Never' to 4 = 'Almost always' their agreement with 8 statements. The 8 item version is scored 0–32. Higher numbers indicate greater fatigue.

4.4.5. Other symptoms

An ad hoc questionnaire was used to record the intensity of the following affections migraine, exhaustion, muscle pain, abdominal pain, dyspepsia, meteorism, swelling, heavy feeling, nausea and vomiting, acidity, reflux and itching was measured on an 11-point Likert scale, with responses ranging from 0 to 10. Higher numbers indicate higher intensity on the symptoms.

4.4.6. Sleep

Pittsburgh Sleep Quality Index (PSQI) to analyze sleep quality [26].

- Pittsburgh Sleep Quality Index: the PSQI contains 19 self-rated questions that are combined to form seven "component" scores, including (a) sleep duration, (b) sleep disturbance, (c) sleep latency, (d) daytime dysfunction due to sleepiness, (e) sleep efficiency, (f) overall sleep quality, and (g) sleep medication use. Each of the sleep components has a range of 0–3 points. In all cases, a score of 0 indicates no difficulty, while a score of 3 indicates severe difficulty. The seven component scores are then added to yield one global score, with a range of 0–21 points, with the higher total score (referred to as global score) indicating worse sleep quality. A global PSQI score > 5 is considered poor sleep quality.

4.5. Schedule

Visit 1: informed consent and supplement were delivery, questionnaires fulfilled and oxidation test carried out. Nutritional and anthropometric evaluation was also accomplished.

Visit 2: patients in group 1 received two follow-ups a month, one at day 15 with diet change and one at day 30. At the end of the study oxidation test, anthropometric assessment and surveys were re-conducted in both groups.

4.6. Statistical analysis

The statistical analysis entailed descriptive analyses, presenting the results in means, standard deviation and percentages. We used parametric statistical tests such as Student's t-test to analyze the differences between the means in two groups of quantitative variables and a Chi-square test for non-parametric qualitative variables. A value of $p < 0.05$ was considered a significant difference. Analysis of the data collected was processed with system SPSS® (version 21.0).

5. Results

We evaluated 13 participants of the feminine gender aged 30–60 years (mean age 51.46 ± 8.04). All participants were diagnosed of fibromyalgia. In addition, some presented cardiovascular disease (n = 5), thyroid disease (n = 3), arthritis (n = 2), depression (n = 2) and scleroderma (n = 1). The baseline characteristics of participants are summarized in Table 1. The groups did not differ significantly from each other in the beginning of the study in any parameter.

The percent of patients reporting Grade III (high disability) pain was highest for non supplemented patients (100%) and intermediate-high for supplemented patients (67%) at baseline. There were a significant proportion of patients who reported high pain intensity but who did not report significant pain-related activity limitation. Patients with appreciable pain not accompanied by significant disability, Grade II patients, were 33.3% of supplemented patients both at the beginning and at the end of the intervention. Only Grade III patients in G2 improved their

Table 1
Baseline characteristics of the participants according to study group.

	Supplement group		No supplement group		p-value
	Mean	SD[a]	Mean	SD[a]	
Age (years)	51.17	9.37	51.71	7.48	0.909
Height (m)	158.25	2.40	159.00	3.33	0.656
Weight (kg)	70.10	12.40	68.99	17.13	0.897
BMI (kg/m^2)	28.13	4.53	27.02	6.72	0.743
Fat mass (%)	38.72	4.65	37.45	9.51	0.792
Visceral fat (%)	7.60	2.70	8.17	3.92	0.791
Muscle mass (%)	38.86	5.28	38.93	5.73	0.983
Body water (%)	44.72	3.60	45.62	6.31	0.785
Waist circumference (cm)	95.33	16.71	89.86	11.80	0.504

[a] SD, standard deviation.

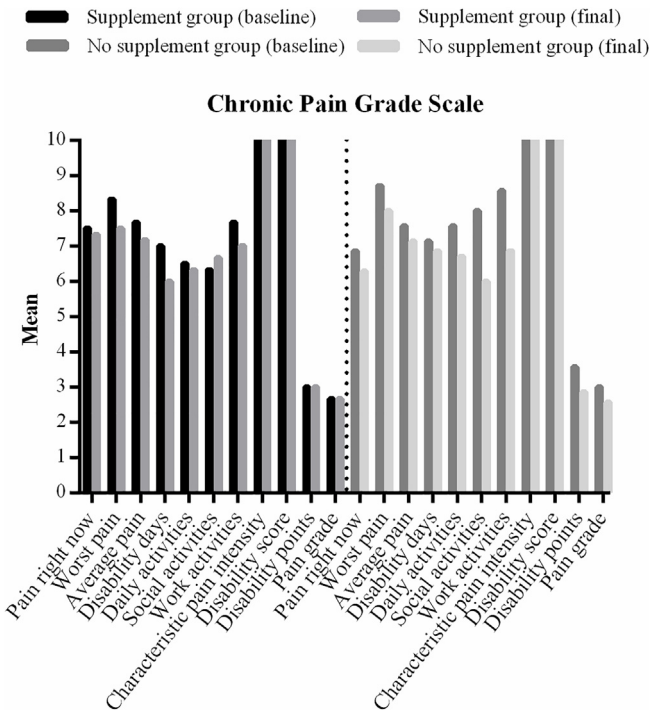

Fig. 1. Pain classification by Chronic Pain Grade Scale.

Chronic Pain Grade Scale (Figure 1).

There was a no significant group–time interaction for the total PCS score (P = 0.190), where the no supplement group demonstrated the greatest significant reduction in pain catastrophizing (P = 0.011) among the two study groups by month 1. There were no significant group– time interactions for the supplemented group scores (Table 2).

A positive correlation was found between total PCS scores [r = 0.7, p = 0.008] and the subscale scores (i.e. scores of rumination [r = 0.94, p < 0.001], magnification [r = 0.95, p < 0.001], and helplessness [r = 0.97, p < 0.001]) at the end of the intervention.

Moderate changes were found in both groups for FSS after the four-week intervention. There was a more pronounced decrease in the supplemented group (−0.77 vs. −0.23), although it was not statistically significant for either group (p > 0.05) (Table 3).

Fig. 2 provides statistics summarizing the symptoms characteristics of each of the 2 groups in terms of intensity. The typical supplemented patient rated the average intensity of pain as 7 (on a 0–10 scale) at baseline and as 3.9 at final count; while non-supplemented patients reported an average intensity of 6.9 at baseline and of 4.1 at final count. For all 2 groups, patients differed in pain intensity and persistence after intervention. All differences were statistically significant (p < 0.05) except for the intensity of nausea and vomiting.

The rate of reported poor sleep quality was found in 100% of supplemented patients and 85.7% of non-supplemented patients at baseline according to the PSQI global score (> 5) (Table 4). A total of 6 respondents (46.2%) reported using prescription sleep medications 3 or more times a week and the prevalence of sleep medication usage increased in G2 patients.

Spending 60 min falling asleep per night was observed in 3 (23.1%) patients and a total sleep time of less than 6 h/night was recorded in 4 (30.8%) patients.

A slight, non-significant progress was observed in the sleep efficiency and sleep disturbance after one month supplemented intervention. Similarly, no-significant changes were observed in overall sleep quality, sleep latency, sleep duration and daytime dysfunction due to sleepiness compared to sleep values obtained in basal conditions.

6. Discussion

The pathophysiological mechanisms of fibromyalgia are not well understood. The existence of different subtypes of fibromyalgia patients with different etiology, clinical characteristics and biological markers could help to understand the situation and therefore, to design more appropriate treatments for distinct subgroups [1].

The proposed grading system, the Chronic Pain Grade Scale, permits identifying factors that differentiate moderately disabled patients from non-disabled patients with high intensity pain, an interesting comparison. The CPGS has been used in epidemiologic studies and clinical trials to evaluate and compare pain severity across groups and in response to treatment effects, and in clinical practice to improve the prognostic judgments of physicians [27].

Studies carried out over the last 30 years reveal that psychological stress has a considerable impact on pain [28]. Pain catastrophizing consists of negative pain cognition induced by a response to the pain experience. Catastrophizers, by definition, negatively evaluate their ability to control pain [29]. Clinical studies indicate that catastrophizing correlates significantly with mood and personality variables, such as depression, fear of pain, coping strategies, mental state,

Table 2
Catastrophizing of pain classification by Pain Catastrophizing Scale.

	Supplement group			No supplement group			p-value
	Baseline	Final	p-value	Baseline	Final	p-value	
	M[a] ± SD[b]	M[a] ± SD[b]		M[a] ± SD[b]	M[a] ± SD[b]		
Total PCS score	30.3 ± 11.9	33.7 ± 13.3	0.536	27.4 ± 14.4	19.1 ± 13.2	0.011	0.190
Rumination	10.2 ± 3.3	11 ± 2.9	0.641	8.4 ± 4.3	7 ± 5.4	0.118	0.069
Magnification	5.3 ± 3.8	6.7 ± 3.3	0.479	6.3 ± 3.9	3.7 ± 3.3	0.028	0.568
Helplessness	14.8 ± 6.1	16.5 ± 6.7	0.368	12.7 ± 7.2	9 ± 6.5	0.051	0.142

[a] M, Mean;
[b] SD, Standard Deviation.

Table 3
Fatigue symptoms by Fatigue Severity Scale and Fatigue Impact Scale.

	Supplement group			No supplement group			p-value
	Baseline	Final	p-value	Baseline	Final	p-value	
	M[a] ± SD[b]	M[a] ± SD[b]		M[a] ± SD[b]	M[a] ± SD[b]		
Fatigue Severity Scale score (scoring 1)	51.2 ± 2.2	45 ± 9.8	0.129	51 ± 6.5	49.1 ± 9.5	0.687	0.608
Fatigue Severity Scale score (scoring 2)	6.40 ± 0.28	5.63 ± 1.22	0.130	6.38 ± 0.81	6.15 ± 1.19	0.687	0.597
Fatigue Impact Scale score	24.7 ± 5.2	24.5 ± 4.8	0.872	25.1 ± 3.4	28.4 ± 3.5	0.015	0.323

[a] M, Mean.
[b] SD, Standard Deviation.

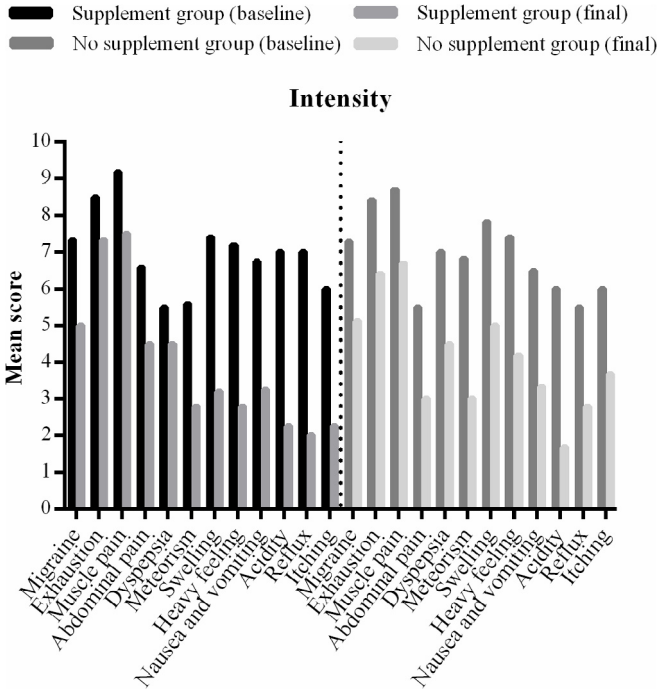

Fig. 2. Intensity of symptoms suffered by supplemented and non-supplemented patients, at the beginning and after intervention. P-values < 0.05 for all symptoms, except for intensity of nausea and vomiting.

personal traits, and anxiety [30]. The tendency of chronic pain patients to "catastrophize" has received considerable attention in recent years. Therefore, psychological assessment of patients suffering from pain would be helpful for long-term management of these patients.

The purpose of Heather et al. [31] study was to compare the effects of two different resistance exercise protocols on pain catastrophizing, and back pain symptoms in obese, older adults with low back pain. The Pain Catastrophizing Scale scores decreased in the total body resistance exercise intervention group compared with that in the control group by month 4 (64.3% vs 4.8%, $P < 0.05$). In our study, however, greater reductions in PCS due to fibromyalgia could be achieved with only the adapted diet compared with those achieved with the adapted diet supplemented with turmeric. Positive correlation was found between total PCS scores and subscale scores, in accordance with results obtained in Süren et al. [30] study. Similar to the data of the validation of the original scale, all 3 subscales of this study version (rumination, magnification, and helplessness), as well as the total of the scale, showed high internal consistency and similar correlation coefficients with the original scale.

Fatigue is a common and disturbing symptom in the patients with fibromyalgia. The most commonly used fatigue-specific measurement is the FSS. In the present study, the FSS scores of the G1 patients were similar to the scores of the G2 controls at baseline. Significant moderate changes were found for FSS after the three-week intervention in obese adults in Impellizzeri et al. [32] study. We also found moderate but no statistically significant reduction of the FSS score after intervention. The FSS has been proved to be valid and reliable to detect presence and severity of fatigue in fibromyalgia patients [33].

To our knowledge, there are few studies using FIS to assess for direct

Table 4
Pittsburgh Sleep Quality Index domain scores in fibromyalgia women.

	Supplement group			No supplement group			p-value
	Baseline	Final	p-value	Baseline	Final	p-value	
	M[a] ± SD[b]	M[a] ± SD[b]		M[a] ± SD[b]	M[a] ± SD[b]		
Global PSQI score	11.5 ± 4.1	10.7 ± 3.8	0.671	12.1 ± 5.3	12.3 ± 5.9	0.941	0.812
Components							
1. Overall sleep quality	1.7 ± 0.8	1.7 ± 0.8	1	1.9 ± 1.3	1.6 ± 1.1	0.522	0.549
2. Sleep latency	1.8 ± 1.0	1.8 ± 0.8	1	1.9 ± 0.7	1.6 ± 0.8	0.172	0.502
3. Sleep duration	1.3 ± 1.0	1.3 ± 1.2	1	1.3 ± 1.0	1.6 ± 1.0	0.172	0.613
4. Sleep efficiency	1.7 ± 1.5	1.2 ± 1.3	0.415	0.9 ± 1.1	1.3 ± 1.4	0.407	1
5. Sleep disturbance	2.2 ± 1.0	2.0 ± 0.6	0.695	2.1 ± 0.7	2.0 ± 1.0	0.604	0.502
6. Sleep medication use	1.0 ± 1.5	0.8 ± 1.3	0.363	1.9 ± 1.5	2.3 ± 1.1	0.555	0.687
7. Daytime dysfunction due to sleepiness	1.8 ± 0.8	1.8 ± 0.8	1	2.3 ± 0.8	2.0 ± 0.8	0.457	0.549
	% (n[c])	**% (n[c])**		**% (n[c])**	**% (n[c])**		
Poor sleep quality (PSQI > 5)	100 (6)	83.3 (5)	0.363	85.7 (6)	85.7 (6)	1	0.584
Good sleep quality (PSQI ≤5)	0 (0)	16.7 (1)		14.3 (1)	14.3 (1)		

[a] M, Mean.
[b] SD, Standard Deviation.
[c] n, sample.

comparisons of fatigue subdimensions in noninflammatory painful rheumatic diseases, such as fibromyalgia, in the literature. According to FIS, impact of fatigue on cognitive component was considerably high in patients with fibromyalgia. Physical component seemed to be less vulnerable to the negative impact of fatigue in patients with fibromyalgia [34].

Fibromyalgia is frequently accompanied by other symptoms, which are not comprised in classification criteria but may provoke a further increase of the patient's suffering and disability. Fibromyalgia patients report a frequent fluctuation in the presence and severity of symptoms, and unpredictable exacerbations [35]. As regards symptoms associated with pain of fibromyalgia, the frequencies of some symptoms observed in the present investigations are similar to the frequencies observed in other studies [36]. It is interesting to note that the intervention carried out in this study in both groups was efficient in improving the patients' symptoms.

O the other hand, sleep is an important factor influencing quality of life, performance, and productivity. An increase in sleep problems becomes more common and evident with age in both sexes [37], but especially fibromyalgia women seem to be more prone to them. In D'Aoust et al. study [38] of 76 women veterans there was a significant association of fibromyalgia with quality of life and sleep difficulty. Subjective sleep quality was also significantly lowest for patients with fibromyalgia syndrome in Yeung et al. study [39].

The treatment was composed by several different components and we do not know the importance and effects of the different components of the treatment in our group. Additional research is necessary to further elucidate this aspect.

It can be concluded that both the turmeric-based food supplement and the gluten-free, FODMAP and low histamine diet had beneficial effects on fibromyalgia symptoms at least in the short run. Further research is needed to elucidate whether chronic pain severity, pain catastrophizing, severity of the fatigue and sleep quality could also be improved by this treatment. The use of a multidisciplinary approach for fibromyalgia treatment is suggested.

7. Limitations

The major limitation of this study was the sample size, which limited us from being able to extrapolate the results to the Spanish population. Due to the higher costs of a more sophisticated analysis and a bigger cohort, we opted for a smaller humble research.

Conflict of interest

The authors declare that there is no conflict of interest.

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CRediT authorship contribution statement

Ismael San Mauro Martin: Conceptualization, Project administration. **Sara López Oliva:** Investigation, Data curation, Software, Validation. **Luis Collado Yurrita:** Methodology, Resources, Supervision. **Sara Sanz Rojo:** Investigation, Data curation, Software, Validation. **Elena Garicano Vilar:** Formal analysis, Writing – original draft, Writing – review & editing.

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