A Pilot Trial Evaluating the Effect of an Inflammatory-Modulating Medical Food in Patients with Fibromyalgia

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Abstract

Fibromyalgia (FM) is a complex syndrome characterized by reproducible tenderness on palpation at specific anatomical sites, generalized stiffness and aching, and a variety of other systemic complaints. It is a common syndrome in the United States and one of the most common reasons for rheumatological referrals. Its etiology and pathogenesis are controversial. A variety of approaches have been used with a lack of consistent results. We present data suggesting that an approach using a complex medical food designed for clinical management of inflammatory conditions may also have a beneficial effect for FM patients. With this medical food, we observed a significant improvement in mental functioning ($p<0.05$) as assessed by the SF-36 questionnaire, a significant decrease in Tender Point Index (TPI; $p<0.05$), and a substantial improvement in grip strength and physical symptoms. Although the mechanism(s) underlying these observations is not understood, we propose that a number of activities may act synergistically to produce the noted improvements in FM patients treated with this Inflammatory-Modulating Medical Food.

Introduction

The latter half of the twentieth century has been characterized by an increasing prevalence of chronic disorders. Indeed, seven of the ten leading causes of death in the United States are chronic in nature, accounting for 72 percent of the deaths from all causes.[1] Certain chronic conditions such as chronic fatigue syndrome (CFS), multiple chemical sensitivity (MCS), and fibromyalgia (FM), while generally not life-threatening, significantly impact the quality of life of a sizeable proportion of the population. Research on these conditions is complicated, however, by the fact that these patients rarely have consistent clinical presentations, making comparison of improvement difficult between subject groups in clinical trials. Moreover, studies have shown a variety of biological markers routinely used in clinical practice have an inconsistent relationship to symptoms in these chronic health conditions.[2] In fact, some reports suggest that 30 to 80 percent of patients may have conditions for which no physiological or organic cause can be found during routine investigation.[3]

FM is a chronic condition that exemplifies the complexity of diagnosis and treatment. FM patients commonly report morning stiffness, fatigue, sleep disturbances, and widespread pain, which they often suffer over many years without a diagnosable or definable disease. No biological markers have been shown to differentiate this condition; therefore FM is generally diagnosed by exclusion and often overlooked. As an example, one study reported that patients see an average of three to four doctors and present with the same complaints before being diagnosed with FM.[4] Overall, FM patients average 39.7 doctor visits per year.[5] FM primarily afflicts women in their mid-forties; it is estimated that 3.4 percent of U.S. women suffer from FM.[6,7] FM is significantly debilitating, and it is not uncommon for FM patients to report they are unable to work.[8] In spite of the serious and pervasive disruption in a patient's life, and the difficulty found in correlating FM symptoms to organic etiologies and underlying mechanisms, many continue to consider this an entirely psychosomatic illness.

FM is clinically differentiated by the relatively

objective evaluation of pain at specific sites, which are called tender points.[9] These tender points are located bilaterally in nine distinct areas of the body, including the base of the skull, above and between the shoulder blades, below the elbows, the lower back, lateral hips, buttock, posterior knee, and lateral chest. The American College of Rheumatology (ACR) has specifically defined FM as widespread pain and the presence of tenderness in 11 or more of the 18 defined tender points.[10] A patient presenting with FM may report peripheral arthralgias as well, which can be confused with rheumatoid arthritis.[11] However, FM is commonly believed to be pain that is not associated with inflammation or joint dysfunction, whereas arthralgias are considered inflammatory and associated with joint dysfunction.

While there are many theories regarding the etiology of FM, few therapies have resulted in demonstrable, predictable improvement. Without laboratory or biological correlation, a patient's response to therapy is often monitored by the number of tender points reported over the time course of the therapeutic intervention. Although widespread pain and tenderness at specific anatomical sites is the accepted criterion for diagnosing FM, some researchers have questioned whether overall improvement can be determined by monitoring tender points. Simms et al. compared a variety of parameters designed to assess clinical outcome in FM patients, including sleep patterns, tender points, and a global assessment of physical functioning.[12] Their results suggest that, despite the clinical importance of pain as a cardinal feature of FM, improvement in pain alone did not discriminate as well as did a combination of outcome measures. This suggests that questionnaires evaluating different aspects of fatigue and functioning should be included with tender point analysis when assessing response to therapy for FM. The Medical Outcomes Survey Short Form-36 (SF-36) questionnaire is an instrument particularly suited to this type of analysis, since it has been widely used in clinical trials and in clinical practice to assess physical and mental health outcome.[13,14,15] The Medical Symptoms Questionnaire© (MSQ) has also been used as a tool for general evaluation of symptoms and functioning in clinical studies and in research trials with patients experiencing fatigue.[16,17,18]

While it has been shown that FM has none of the common inflammatory characteristics associated with other rheumatological conditions such as Rheumatoid Arthritis and Systemic Lupus Erythematosus, some recent literature suggests that the pathophysiology of FM may be associated with more subtle signs of inflammation and immune dysregulation.[19] Consistent with this notion, we have obtained favorable anecdotal reports on the use of a recently developed Inflammatory-Modulating Medical Food in clinical management of FM patients. These observations led us to undertake a preliminary assessment of the efficacy of this medical rice-based food designed for inflammatory conditions, on the clinical management of FM.

Methods

Subjects

Twenty-one subjects were selected for this trial on the basis of past diagnosis of FM, musculoskeletal pain lasting longer than six months, and complaints of unrestorative or disturbed sleep as assessed by a symptoms questionnaire. Subjects were females in the 29 to 65 years age range, with an average age of 47 years. Prior to initiating the study, subjects were evaluated with blood chemistry tests, medical history, and physician examination. Subjects who had been diagnosed with a serious debilitating condition such as Acquired Immune Deficiency Syndrome (AIDS), cancer, congestive heart failure, liver disease, chronic obstructive pulmonary disease, or advanced diabetes, were excluded from the study. Each subject signed an informed consent prior to participation in the study.

Study Design and Dietary Intervention

The medical food used in this study was originally designed for nutritional support of conditions associated with chronic inflammation of the lungs, joints, and intestinal tract. The nutrient profile of this Inflammatory-Modulating Medical Food (UltraInflamX™, UltraBalance Inc., Gig Harbor, WA) is shown in Table 1. Specifically, this medical food was designed as a low-allergy-potential, rice-based product fortified with the following components: antioxidant vitamins and minerals to reduce free radical generation from oxidative stress;[20,21] phytonutrients, such as rosemary and limonene, and sulfate-containing compounds such as N-acetylcysteine and sodium sulfate, to support

Table 1.

COMPOSITION OF INFLAMMATORY-MODULATING MEDICAL FOOD

Macronutrients	*Amount per Day*
Protein	30 g
Fiber	8 g
Carbohydrates	48 g
Fat	10 g
Micronutrients	Amount per Day
Vitamin A/Mixed Carotenoids	10,000 IU
Vitamin C	360 mg
Calcium	550 mg
Iron	2 mg
Vitamin D	200 IU
Vitamin E	200 IU
Thiamin (B1)	4 mg
Riboflavin (B2)	4 mg
Niacin (B3)	70 mg
Vitamin B6	10 mg
Folic Acid	160 mcg
Vitamin B12	6 mcg
Biotin	300 mcg
Pantothenic Acid	10 mg
Phosphorous	400 mg
Magnesium	560 mg
Zinc	20 mg
Selenium	150 mcg
Copper	2 mg
Manganese	4 mg
Chromium	120 mcg
N-acetylcysteine	200 mg
Sodium sulfate	100 mg
Molybdenum	76 mcg
L-glutamine	1500 mg
L-threonine	68 mg
L-lysine HCl	1540 mg
Citrulline	200 mg
Hesperidin	400 mg
Quercetin	400 mg
Curcumin	400 mg
Rosemary Extract	200 mg
D-limonene	200 mg
Rutin	400 mg
Ginger	200 mg

detoxification processes[22,23,24,25,26]; anti-inflammatory phytonutrients such as curcumin and rosemary to nutritionally support clinical management of inflammation symptoms;[27,28] and enhanced levels of vitamins and minerals, such as C, B3, B6, zinc, and magnesium, which are involved in fatty acid synthesis and promote balance in production of pro- and anti-inflammatory cytokines and prostaglandins.[29,30,31]

Dietary changes consisted of a modified elimination diet, which is described as a diet free of substances likely to produce allergenic responses. Foods eliminated on this diet include dairy, eggs, gluten, corn, pork, and yeast.

Subjects were assigned to one of two protocols by date of initial appointment at the research clinic. Protocol A included the Inflammatory-Modulating Medical Food nutritional supplement daily with no other dietary changes, and Protocol B included the Inflammatory-Modulating Medical Food nutritional supplement daily with dietary changes. The medical food was provided as a powdered drink mix supplement to be prepared by each subject at the time of use by mixing the recommended amount of powder – 52 grams – in either water or a juice of the subject's choosing. Taken alone with water twice a day, the drink provided a total of 400 daily calories.

Both protocols were followed for a 6-week period. Subjects were instructed to make no changes during the course of the study – other than those noted above – in their supplementation, medication, or exercise routine. Compliance to the respective protocol was documented at each office visit by the technologist responsible for the study, at which time exercise and medication use were also documented.

Clinical Assessment

Subjects were evaluated initially, after 3 weeks, and after 6 weeks by questionnaires, documentation of tender points, and grip strength. Questionnaire evaluation included: the SF-36 questionnaire, a well-validated general quality of life instrument; a written inventory to evaluate history of illness, medication use, sleep patterns, perceived pain, and compliance to the protocol; and the Medical Symptoms Questionnaire (MSQ), which evaluates general physical symptoms.

Tender points were assessed by the subjects at each visit and were reported as the Tender Point Index (TPI). Subjects were presented with a diagram that identified the 9 specific bilateral points and asked to circle areas in which they felt pain. The number of tender points circled was summed to determine the

TPI; the maximum possible value for TPI was 18.

Grip strength was assessed as the static grip force in kilograms with an adjustable handgrip dynomometer (Asimow Engineering Co., Santa Monica, CA). The grip strength test was performed with the subject in a standing position and the arms in a neutral position. Subjects were asked to squeeze the handgrip dynomometer as hard as possible without moving the arm. Grip strength measurements for the left and right hand were performed at each office visit.

Data were analyzed by standard statistical methods using the Wilcoxon Matched Pairs analysis for determination of significance. Calculations were performed on Microsoft® Excel software program. Percent change in MSQ was determined as follows: Percent MSQ Change = [(initial MSQ score – final MSQ score)/ initial MSQ score] x 100.

Results

Twenty-one subjects were selected for the trial. An initial questionnaire was completed to provide information on the history and onset of each subject's illness. As shown in Table 2, the majority of subjects reported having been diagnosed with fibromyalgia over 3 years ago, and all responding subjects reported experiencing symptoms for at least 1-2 years. Ten of the subjects indicated that their symptoms had a gradual onset, whereas 9 reported a rapid onset of symptoms; 2 subjects did not respond to the question. Twelve of the subjects indicated their illness affected their ability to perform work on either a part-time or full-time basis, while 9 subjects indicated they were able to work in spite of their illness.

Fourteen of the subjects completed the entire trial, and 7 subjects chose to withdraw from the trial prior to its completion, as indicated in Figure 1. In total, 1 subject on Protocol A and 2 subjects on Protocol B withdrew for reasons of "feeling poorly" on the respective protocol, whereas 2 subjects on Protocol A and 2 subjects on Protocol B withdrew for reasons unrelated to the protocol. One subject was moved from Protocol A and added to Protocol B at the time of the 3-week visit, since it was determined that this subject had been following the diet instructions outlined for Protocol B (rather than the ones for Protocol A, which required no dietary changes).

Table 2.

Summary of initial presentation and history of illness for all subjects accepted for the clinical trial.

What is your ethnic background?
- 17 subjects indicated Caucasian
- 2 subjects indicated Northern European
- 1 subject indicated Asian
- 1 subject indicated Northern European and Native American

How many years since you were diagnosed with fibromyalgia?
- 5 subjects indicated diagnosis from 1 to 2 years ago
- 6 subjects indicated diagnosis from 3 to 5 years ago
- 8 subjects indicated diagnosis over 5 years ago
- 2 subjects provided no response

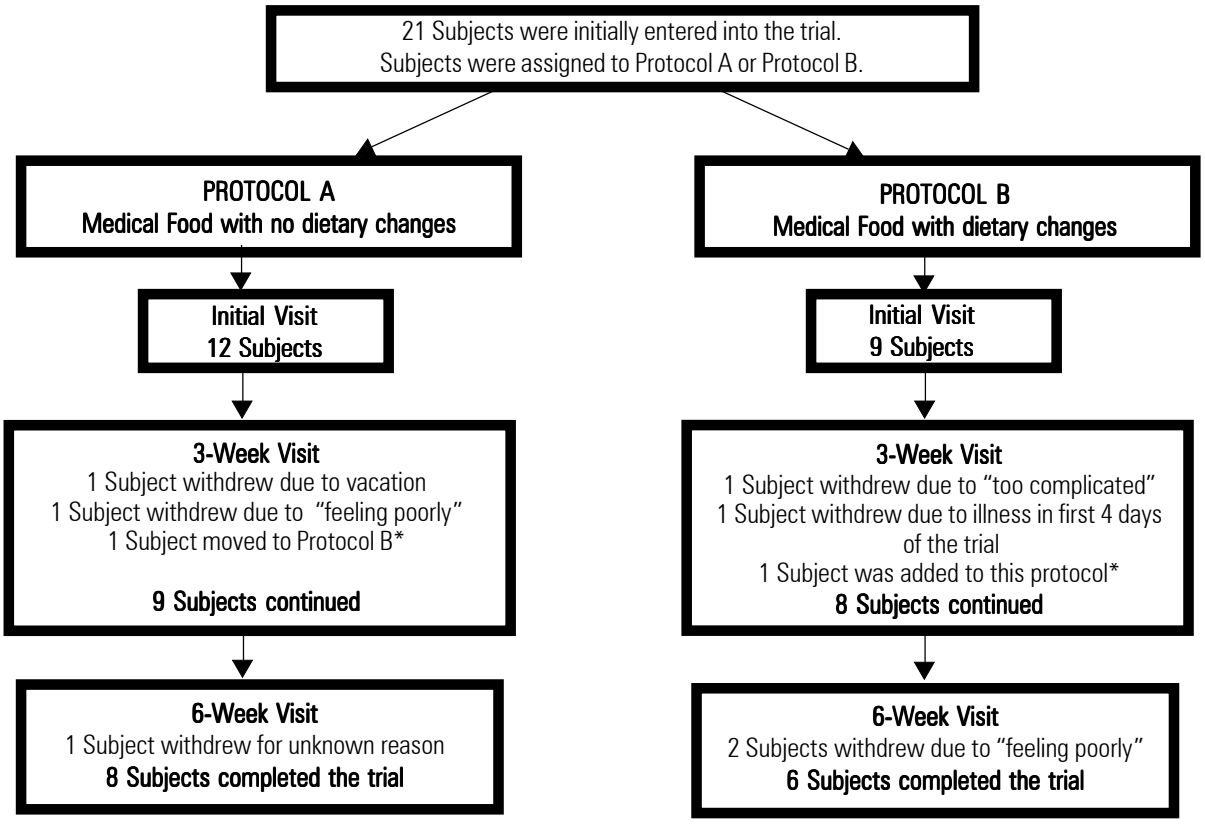
How many doctors have you seen for fibromyalgia?
- 5 subjects responded 1 doctor only
- 6 subjects responded 2-3 doctors
- 2 subjects responded 4-5 doctors
- 3 subjects responded 9-10 doctors
- 1 subject responded "several"
- 1 subject responded "too many"
- 2 subjects provided no response

How did symptoms come on?
- 10 subjects indicated gradual onset
- 9 subjects indicated quick onset
- 2 subjects provided no response

Has your illness affected your ability to perform work?
- 9 subjects were able to work in spite of their illness
- 5 subjects were only able to work part-time due to their illness
- 7 subjects were unable to work due to their illness

The SF-36 is a 36-item questionnaire that summarizes health outcome in two reliable, reproducible scores: the *Physical Component Summary*

Figure 1. Summary of subjects completing and withdrawing from the trial.



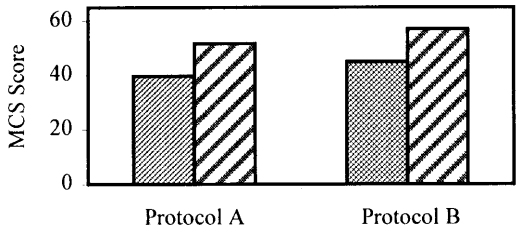
* 1 subject was moved from Protocol A to Protocol B at the 3-week visit since she had misunderstood instructions and had been following the diet anyway.

(PCS) and the *Mental Component Summary* (MCS). These scores are converted to a scale of 0 to 100, in which 50 is the mean for the United States (US) population. Low scores on the MCS indicate frequent psychological distress, compromised social and role disability due to emotional problems, and/or generally poor health, whereas high scores indicate frequent positive affect, and absence of psychological distress and limitations in usual social and role activities. Similarly, low scores on the PCS indicate substantial limitations in self care, physical, social, and role activities, severe bodily pain, frequent tiredness, and health generally rated as poor, whereas high scores indicate no physical limitations, high energy level, and health generally rated as excellent.

As shown in Figure 2, the initial MCS scores were 40 ± 8.4 ($n=8$) and 45 ± 8.9 ($n=5$) for subjects on Protocol A and Protocol B, respectively, which was below the US average of 50. However, at the end of the 6-week study, the average MCS score had increased to the US average for subjects on both protocols, which was 51 ± 8.5 ($n=8$; $p=0.025$) and 57 ± 6.6 ($n=5$; $p=0.043$), for subjects on Protocol A and Protocol B, respectively. (One subject on Protocol B did not complete the questionnaire and, therefore, the data from this subject was not included in the analysis.) The improvement in mental well-being did not appear to be dependent on whether dietary changes accompanied the medical food, since both groups receiving the medical food, with and without dietary changes, showed significant improvement.

The PCS score from the SF-36 questionnaire, which provides an independent assessment of physical functioning, also showed improvement for subjects on Protocol A from 30 ± 6.8 initially to 38 ± 5.7 ($n=8$, $p=0.05$) after the intervention. Interestingly, no significant improvement was noted in PCS for the Protocol B group. However, this may have been due primarily to 1 subject, who reported an initial PCS score of 34 and a final score of 8.4. When the

Figure 2. SF-36 Mental Component Summary (MCS) scores before (initial) and after (final) intervention for FM subjects who completed Protocol A or B.



data from this subject was removed, the subjects on Protocol B showed modest improvement in PCS scores as well, from 25 ± 8.8 before the intervention to 31 ± 6.3 (n=5, p=0.080) after the intervention.

The Medical Symptoms Questionnaire (MSQ) is another clinical tool for the evaluation of general physical symptoms. Patients find it easy to fill out and can do so relatively quickly, while it is easy for the practitioner to score and evaluate. In contrast to the SF-36 questionnaire, in which a high score means high functioning and a low score means compromised functioning, a high score on the MSQ means a higher or more substantial amount of overall symptoms in terms of duration, frequency, and intensity. MSQ scores that total above 75 are generally associated with substantial symptomatology and disability. MSQ scores below 30 generally indicate few symptoms or symptoms of low intensity.

The MSQ values for each subject on Protocol A and Protocol B are indicated in Table 3 and Figures 3a and 3b. As seen in Table 3, 12 of the subjects reported MSQ scores above 75 before the intervention, whereas only 3 subjects reported MSQ scores above 75 after the intervention. The MSQ scores decreased on average by 53 percent and 32 percent for subjects on Protocol A and Protocol B, respectively, with an overall average decrease of 43 percent. Only 1 subject reported an increase in symptoms (Pt #12). *Note: one subject on Protocol A did not provide complete questionnaire data, therefore, data from this subject was not included in the analysis.*

As indicated in Table 4, improvement in grip strength was observed in subjects on both protocols as well. Right-hand grip strength improved from low average to mid-range average, and poor to mid-range average in the Protocol A and Protocol B groups, respectively. Left-hand grip strength improved from poor in both groups initially to within average range, however less difference was observed in the left-hand grip strength overall. Figure 4 shows the grip strength average of the right and left hand for each subject before intervention, after 3 weeks on the respective protocol, and after the 6-week intervention with Protocol A or Protocol B. Although improvement was observed in grip strength for both groups, the Protocol A subjects appeared to show improvement by the 3-week visit and sustain that improvement through the 6-week visit. In contrast, the Protocol B subjects showed no difference at the 3-week visit but did show improvement at the 6-week visit.

TPI also showed improvement after the intervention for subjects on both protocols, as

Figure 3. MSQ scores before intervention (week 0), at 3 weeks, and after intervention (week 6) for FM subjects who completed Protocol A or B.

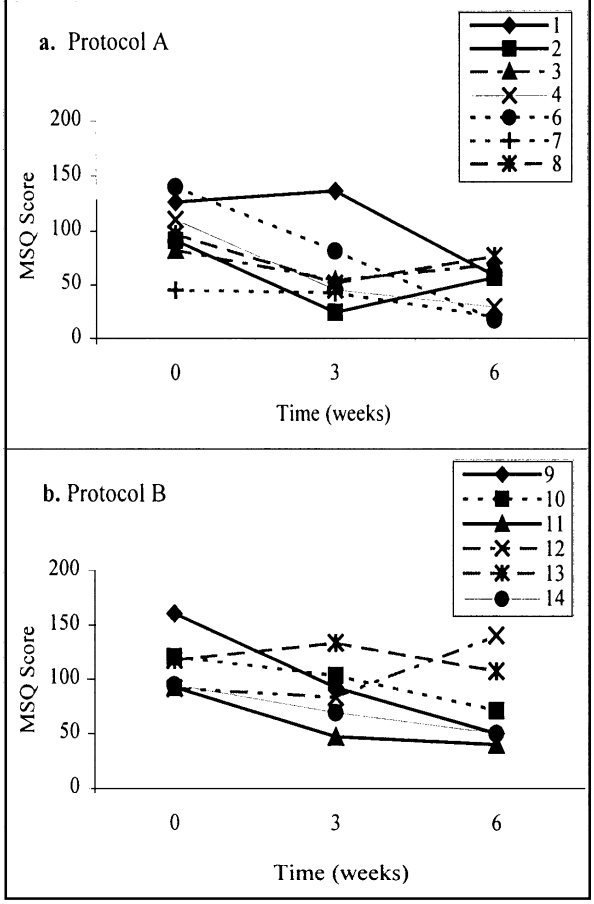


Table 3. Medical Symptoms Questionnaire (MSQ) values, before (initial) and after (final) intervention for fibromyalgia subjects on Protocol A or Protocol B. The average (±sd) changes in MSQ score observed with Protocol A and Protocol B are also represented.

	Pt #	MSQ Initial	MSQ Final	% Change in MSQ
Protocol A	*1*	*126*	*58*	*53.97*
	2	91	56	38.46
	3	82	68	17.07
	4	110	29	73.64
	5	n/a	n/a	n/a
	6	140	17	87.86
	7	45	20	55.56
	8	97	76	21.65
	Ave	**98.71**	**46.28**	**53.11**
	sd	**31.10**	**23.92**	**26.01**
Protocol B	9	161	51	68.32
	10	121	72	40.50
	11	93	41	55.91
	12	92	141	-53.26
	13	118	108	8.47
	14	95	51	46.32
	Ave	**113.33**	**77.33**	**31.76**
	sd	**26.67**	**39.32**	**44.45**

n/a = complete MSQ data not available for this subject

represented in Figure 5. However, the improvement in TPI was most evident with the subjects on Protocol A, in which the subjects reported a significant ($p=0.0425$) decrease in TPI from 13.3 ± 3.49 before intervention to 8.5 ± 4.77 after the intervention. The subjects on Protocol B reported a modest improvement in TPI from 11.2 ± 4.02 initially to 10.6 ± 4.72 after the intervention, which was not statistically significant.

Summary/Discussion

Fibromyalgia (FM) is a complex syndrome characterized by reproducible tenderness at specific anatomical sites and is one of the most common reasons for rheumatological referrals.[32] Its etiology and pathogenesis are controversial, and no clinical management approach has shown consistent results. We present data suggesting that an approach using an Inflammatory-Modulating Medical Food, which was designed to nutritionally support clinical management of chronic inflammatory conditions, may also provide benefit as nutritional support for patients with FM.

FM has not generally been assumed to be an inflammatory condition. However, we chose to investigate the Inflammatory-Modulating Medical Food product in patients with FM, since clinical observations suggested that patients presenting with FM concurrent with inflammation were showing favorable response to the medical food with respect to their symptoms. We observed that the use of this medical food resulted in a significant decrease in Tender Point Index (TPI; $p<0.05$), a significant improvement in the mental functioning section of the SF-36 ($p<0.05$), and a substantial improvement in grip strength and physical symptoms.

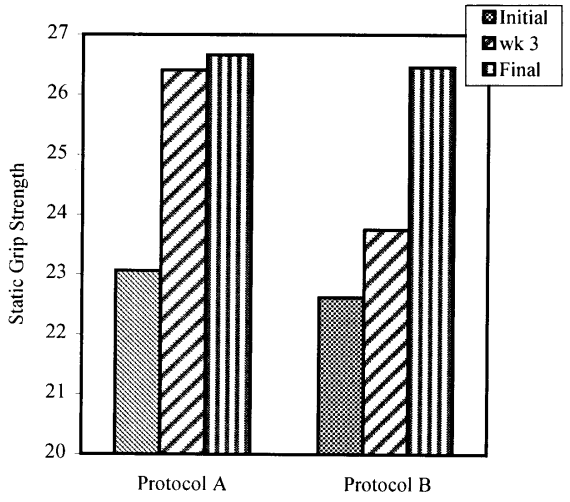
These preliminary favorable findings in FM patients raise interesting questions regarding the etiology and underlying mechanism(s) of FM. In general, anti-inflammatory pharmaceutical approaches, such as non-steroidal anti-inflammatories, have shown minimal positive response in clinical trials on FM, and generally result in no significant improvement above placebo effects.[33] In contrast, some evidence has been reported to support an inflammatory component in FM. For example, Maes et al. investigated biological markers of the inflammatory system in 21 FM patients and 33 non-FM controls.[34] These researchers reported an alteration in the expression of some markers of the inflammatory response system in FM patients,

Table 4. Grip Strength Test: Number of subjects who rated in each category are shown. Ratings were determined by comparing the average of the left- and right-hand grip strength with the same average determined as normal values for women.*

Reference (kg)	*Protocol A*		*Protocol B*	
	Initial	*Final*	*Initial*	*Final*
Excellent >39	0	0	0	0
Good 36-38	0	0	0	0
Average 23.5-35	3	6	3	5
Poor 20–22.5	3	1	0	1
Very Poor <20	2	1	3	0

* Heyward V. Muscle Testing for Sports. In: Appenzeller O and Atkinson R eds. *Sports Medicine: Fitness, Training, Injuries.* Lippincott, Williams & Wilkins; 1988:352.

Figure 4. Static Grip Strength, as right and left hand averages for FM subjects at initial point, after 3 weeks and final point.

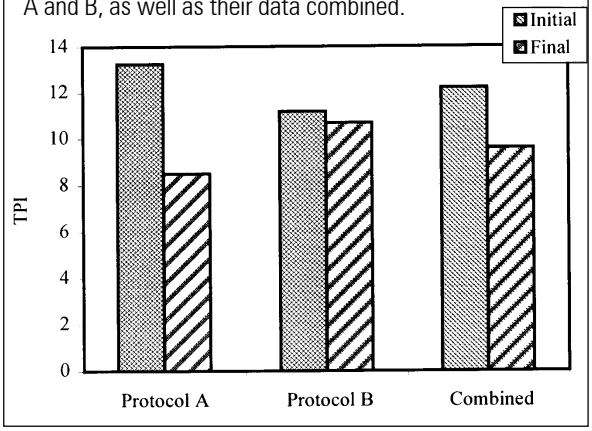


which suggested an activation of the inflammatory system in these patients. However, the clinical utility of this observation has not been explored. Taken together, the clinical consensus remains that a simple anti-inflammatory approach does not appear to be clinically effective for FM.

We believe that some subclinical inflammatory mechanisms may be part of the FM etiology, but these mechanisms have not been clearly elucidated. If this is the case, supplementing with phytochemicals and nutrients that have a modulating effect on subclinical inflammatory processes may be of benefit. For example, subclinical inflammation may be modulated through the application of phytonutrients, such as curcumin, which inhibit synthesis of interleukin-1 and tumor necrosis factor, and inhibit lipoxygenase and cyclooxygenase.[35,36] Ginger has shown efficacy in inflammation and may have a similar and/or complementary role as well.[37] Moreover, inflammation has been associated with oxidative stress resulting in excessive production of reactive oxygen species. FM has also been postulated to involve some degree of cellular hypoxia with mitochondrial uncoupling and concurrent generation of excessive reactive oxygen species.[38] Since the medical food contained a broad array of antioxidant support, we may have observed improvement due to protection against excessive damage and injury from oxidative stress.[39] Many phytonutrients, such as rutin and quercetin, appear to act synergistically with respect to their antioxidant activities, therefore, these may have provided additional support for the nutritional management of FM symptoms.[40,41]

Interestingly, the subjects on Protocol A who did not adhere to a specific diet regimen reported more improvement than did those subjects on Protocol B who were on a standard elimination diet in combination with the medical food. It has been our experience that many of the patients with chronic conditions, such as FM, respond with moderate improvement when put on a dietary program that eliminates common food allergens. However, this response has been variable, with a noticeable percentage of patients failing to respond to dietary changes alone. It was surprising in this context that while both groups showed improvement, the group without dietary changes showed the greater improvement. Since most subjects reported seeing several doctors over many years for their condition, it is possible that many of these patients had already attempted an allergen-free diet without success. Dietary changes are difficult to make, and if those changes do not appear to be working, the disappointment may be even more frustrating. Asking individuals to repeat a dietary therapy they have already found unsuccessful may be emotionally difficult and taxing. Therefore, the slightly decreased improvement on Protocol B, which included dietary changes, could be due to the added complication of this approach and the associated mental frustration. Certainly, dietary changes should be considered in those individuals who have not attempted such a therapy; however, this should be assessed carefully since dietary changes may not be effective.

Figure 5. Tender Point Index (TPI) before (initial) and after (final) intervention for subjects completing Protocol A and B, as well as their data combined.



Although extensive clinical trials are required to fully assess and document the success of this medical food with FM, it is the observations of the specific individual's response in the clinic that matter most to clinicians and patients. An interesting case experience from this trial is that of a 51-year-old white female who was diagnosed with FM over ten years prior to presentation. She was forced to quit her job and had been working on a part-time basis. She had consulted with ten doctors regarding her illness and had taken a variety of anti-inflammatory and antidepressant medications, but continued to have chronic myalgia pain, sore throats, headaches, and fatigue. She complained of sleep disturbances and stated that she woke up two or three times a night. She reported chronic pain in all standard trigger point areas, stating that she was almost never pain free. Her initial MSQ score was 140. She was assigned to Protocol A, receiving the Inflammatory-Modulating Medical Food with no dietary changes for six weeks.

At her three-week follow-up visit, the patient reported having some difficulty with the taste of the product and was, therefore, taking only half of the prescribed dose of the medical food. She was provided with more instructions for alternative blending recipes and was encouraged to increase to the full dose. At the six-week follow-up visit, she was taking the full dose successfully and reported that she could now awaken with no pain. Furthermore, she had noticed substantial improvement in sore throat, headache, and fatigue symptoms, and was also experiencing improved sleep, only waking on average one time per night. Perhaps most importantly, she reported that she was pain free over half of her waking hours, a significant improvement from the constant pain she experienced just six weeks earlier.

FM is a multifactorial syndrome that seriously compromises the quality of life of those it afflicts. For example, patients with FM have been reported to score lower on the quality-of-life instrument, the SF-36.[42] Moreover, there is strong co-morbidity between fibromyalgia and major depression, and an increased incidence of depressive symptoms in fibromyalgia patients.[43] A striking finding in the present study was the significant improvement in the mental functioning section of the SF-36 for FM patients after intervention with the Inflammation-Modulating Medical Food. The SF-36 has been shown to predict the course of depression over a two-year time course in clinical trials.[44] This observation, taken together with the substantial improvement observed in physical functioning in these patients, suggests that a complex medical food containing a variety of inflammatory-modulating pharmacological activities may be clinically efficacious with this chronic health problem. More studies are needed to verify this preliminary observation with FM. The complex nature and clinical challenge presented by an FM patient exemplifies the axiom that the whole is greater than the sum of its parts.

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