

Complementary and alternative medicine in fibromyalgia: a practical clinical debate of agreements and contrasts

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ABSTRACT

Fibromyalgia (FM) is currently classified as a chronic pain syndrome. Its main features are chronic widespread pain in the presence of tender points (TPs) upon physical examination, sleep disturbances and fatigue, although patients also report a variety of other complaints.

Many therapies have been proposed over recent years with mixed results, including various pharmacological therapies for the treatment of symptoms; but there is still no effective drug treatment for the syndrome itself.

Non-pharmacological therapies are an important part of the treatment, and there is evidence supporting a number of interventions, including aerobic exercise, strength and stretching training, cognitive-behavioural therapy, and patient education. Complementary and alternative medicine (CAM) techniques have not yet been fully acknowledged by scientific medicine because little is known about their mechanisms of action and usefulness.

The aim of this wide-ranging review of the literature is to analyse the types of CAM techniques used to treat FM and their effectiveness, highlighting the disagreements among the authors of more specialised reviews.

Introduction

Fibromyalgia (FM), which is currently classified as a chronic pain syndrome, is a frequently observed disorder (particularly among women) whose prevalence in the general population seems to be about 2%. Its cardinal features are chronic widespread pain in the presence of multiple tender points (TPs) upon physical examination, sleep disturbances and fatigue, although patients also report a variety of other complaints (1).

Treating FM is a considerable challenge because the effects of the various treatments are often poor and the patients are frequently unsatisfied. Many therapies have been proposed over last decades with mixed results (2). These include various pharmacological therapies for the treatment of symptoms, but there is still no effective drug treatment for the syndrome itself. Furthermore, the many and very different non-pharmacological treatments suggested make any evaluation very complicated. In an attempt to suggest the best treatment for patients, a task force of the European League Against Rheumatism (EULAR) provided evidence-based recommendations for the management of FM (3) on the basis of expert opinion and some experimental data. Underlining the fact that optimal treatment requires a multidisciplinary approach, it recommended combining a number of non-pharmacological therapies with tailored drug treatments chosen in relation to pain intensity, functional status and associated conditions. The same concept was expressed by the American Pain Society in 2005 (4) and the German Association of Medical Scientific Societies in 2008 (5).

Given the lack of any treatment that is always effective, it is not surprising that non-pharmacological treatments, particularly those belonging to the fields of complementary and alternative medicine (CAM), are frequently suggested for the management of FM. Patients perceive them as being more natural, and both physicians and patients consider that they have fewer adverse effects.

Complementary Techniques (CTs) and Alternative Medicine (AM) are Unconventional Medicine and refer to therapeutic interventions that are still not fully acknowledged by scientific medi-

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Table I. National Center for Complementary and Alternative Medicine (NCCAM) classification of complementary and alternative medicine therapies (6).

- 1) *Alternative Medical Systems*
Alternative medical systems are built upon complete systems of theory and practice. Often, these systems have evolved apart from and earlier than the conventional medical approach used in the United States.
- 2) *Mind-Body Interventions*
Mind-body medicine uses a variety of techniques designed to enhance the mind's capacity to affect bodily function and symptoms.
- 3) *Biologically-Based Therapies*
Biologically based therapies in complementary and alternative medicine use substances found in nature, such as herbs, foods, and vitamins.
- 4) *Manipulative and Body-Based Methods*
Manipulative and body-based methods in complementary and alternative medicine are based on manipulation and/or movement of one or more parts of the body.
- 5) *Energy Therapies*
Energy therapies involve the use of energy fields. They are of two types: 1) biofield therapies are intended to affect energy fields that purportedly surround and penetrate the human body; 2) bioelectromagnetic-based therapies involve the unconventional use of electromagnetic fields.

cine because little is known about their mechanisms of action and usefulness (Table I). CTs are empiric in origin but are usually studied using the methods of scientific research and practised on the basis of the nosological and physiopathological principles of scientific medicine. They are not "alternatives" because they are totally different from the holistic and vitalist conception of AM. CTs most widely used cannot replace pharmacological or surgical therapies, but work together with them, except in very limited circumstances (6). AM is often used in conjunction with conventional medicine (7), and it has been said that there is some high-quality evidence of the safety and effectiveness of this integrative (or integrated) approach (6). According to Weil, the principles of integrative medicine include the appropriate use of conventional medicine and CAM, patient participation, the promotion of health as well as the treatment of disease, and a preference for natural and minimally invasive methods (8).

Wahner-Roedler *et al.* (9) investigated the frequency and patterns of CAM in 289 patients referred for FM treatment (263 females and 26 males), who completed an 85-item questionnaire concerning the previous six months. The results showed that 98% of the patients had made use of CAM, and that the ten most frequently used treatments were exercise for a specific medical problem (48%), spiritual healing (45%), mas-

sage therapy (44%), chiropractic (37%), vitamin C (35%), vitamin E (31%), magnesium (29%), vitamin B complex (25%), green tea (24%), and weight-loss programmes (20%); 83% of the patients used at least one vitamin and 52% at least one dietary supplement.

An Internet survey asked 2,596 people with FM in the USA to select the interventions they used in their management strategies from a predefined list that included many complementary and alternative treatments, of which the most frequently used were nutritional supplements (68%), stretching (62%), prayer (57%), relaxation/meditation (47%), massage/reflexology (43%), aerobic exercise (32%), chiropractic manipulation (30%), and non-aerobic exercise (24%) (10).

The aim of this paper is to offer a general overview of some CAM treatments for FM (we have not considered physical exercise, rehabilitation programmes, physiotherapy, educational approaches or cognitive-behavioural therapy), and purpose some considerations about the different ways to analyse and evaluate the available literature. This different clinical approach would be functional for the everyday practice (Table II).

Acupuncture and electro-acupuncture

The ancient Chinese practice of acupuncture (AP) is one of the oldest forms of therapy and is widely used throughout the world. Since it was in-

troduced into modern medicine, some newer forms have been developed, and researchers have provided some evidence-based data concerning its use in various clinical conditions. Basic scientific research suggests a number of possible explanations concerning the mechanisms underlying its physiological effects (11), and the term "Western AP" is now often used for this form of CT (12).

More than ten years ago, Berman *et al.* (13) considered seven studies involving FM patients, and concluded that AP has a more positive effect on symptoms than placebo. However, some mild but unpleasant discomfort and bruising were reported.

Sprott *et al.* (14) studied 29 FM patients who underwent AP during 6 weekly sessions, monitoring pain by means of a visual analogue scale (VAS) and tender point count (TPC), and analysing plasma-derived substance P and plasma and platelet serotonin levels. The VAS scores and TPC decreased, and platelet serotonin levels halved. Subsequently, the same author *et al.* (15) verified an improvement of TPC and an enhancement in the pain threshold, temperature and blood flow response over the tender site in an open study of 20 FM patients. The data concerning micro-circulatory changes after acupunctural stimulation have been confirmed (16).

Clarke used a combined programme of AP and lifestyle counselling in a group of 20 FM patients, 17 of whom gained some benefit. The patients underwent 12 weeks of AP combined with moxibustion treatment, three 4-week cycles of twice weekly, with a 1-2 week interval between cycles. During the 30-minute AP sessions they received counselling about nutrition, lifestyle, sleep, stress management, pacing, breathing and relaxation exercises, mind-body strategies, and cognitive therapy. All of the patients were advised to stop smoking, drinking coffee and alcohol, and gradually increase exercise levels (17). Some recent randomised controlled trials (RCTs) need to be mentioned. Harris *et al.* (18) treated 114 FM patients randomly allocated to one of four groups who underwent different types of AP in 18 sessions of different

duration and frequency: 25-35% experienced a decrease in pain. The authors pointed out that correct needle location and stimulation were not a factor suggesting the possibility for a strong placebo response. The use of thrice-weekly sessions provided more analgesia. Assefi *et al.* (19) studied 100 subjects (divided into one interventional group and three sham AP control groups: AP for an unrelated condition, needle insertion at non-acupoint locations, or non-insertive simulated AP) who were treated twice a week for twelve weeks and followed up to six months. They did not find any difference in outcome measures between the AP group and a pooled control with sham AP, AP for another syndrome and needle insertion away from acupoints group. It must be pointed out that the controls were not a placebo but an active treatment group in this trial; therefore, they should probably be considered as effective as the AP treatment group.

Targino *et al.* (20) randomly allocated 58 women to receive AP combined with tricyclic antidepressants and exercise, or tricyclic antidepressants and exercise alone. Pain was rated by means of VAS and the mean pressure pain threshold of TPs, and the quality of life was evaluated using the Short Form Health Survey (SF-36). At the end of 20 sessions, all of the measures were significantly better in the patients who underwent AP for up to six months, but there was no significant difference after one and two years.

Many years ago, Cassisi *et al.* performed an RCT (using a blinded evaluator) in 42 patients divided into three groups treated with AP, mianserin (a tetracyclic antidepressant), or AP plus mianserin (21). Standardised AP and individual acupoints were used once a week for ten weeks and the patients were followed up for six months. The outcome measures were VAS, the Italian version of the McGill Pain Questionnaire (MGPO), the mean pressure pain threshold of TPs, and the cutaneous pain threshold after electrical stimulation; the level of depression was also evaluated. There was a significant improvement in pain and depression in all three groups (although it was less in

Table II. Therapies analysed in this review.

ACUPUNCTURE	DIETOTHERAPY
ELECTRO-ACUPUNCTURE	DIETARY SUPPLEMENTS
HYDROTHERAPY	<ul style="list-style-type: none"> • S-adenosylmethionine • Magnesium • Soy • 5-hydroxytryptophan • Melatonin • Anthocyanidins • Deutrosulfazyme • L-acetyl-carnitine • Chlorella pyrenoidosa
<ul style="list-style-type: none"> • Balneotherapy • Thalassotherapy • Hydro-electric therapy 	HOMOEOPATHY
THERMOTHERAPY	MISCELLANEA
<ul style="list-style-type: none"> • Mud-bath treatment • Infra-red hyperthermia 	<ul style="list-style-type: none"> • Aromatherapy • Music therapy and vibration • Religiosity and spirituality • Hypnotherapy • Cannabis • Capsaicin • Vitamin D
BIOFEEDBACK	
MANUAL THERAPY	
<ul style="list-style-type: none"> • Massage therapy • Chiropractic manipulation • Osteopathy 	
BODY-MIND TECHNIQUE	
<ul style="list-style-type: none"> • Meditation • Guided imagery • Autogenic training • Body awareness technique • Group therapy 	
MAGNETIC FIELD TREATMENT	
ENERGY AND MOVEMENT THERAPY	
<ul style="list-style-type: none"> • Qigong • Tai Chi • Reiki • Therapeutic touch • Yoga • Biodanza • Pilates 	

the group treated with mianserin alone for pain), which was maintained in the AP group during the six-month follow-up period.

Iannucelli *et al.* (22) recently combined somatic and abdominal AP in 30 consecutive female FM patients to evaluate the reduction in pain and well-being state. All patients maintained drug consistent therapy for at least three months and were treated with weekly AP sessions for ten weeks. The results of this open study showed a statistically significant decrease of TPC and pain, FIQ, HAQ, Fibromyalgia Assessment Status, disease activity VAS, Zung self-rating anxiety and depression scale at the end of the treatment, suggesting that the combination of two types of AP could be useful to control pain and to improve associated symptoms and quality of life. No follow-up was done.

Electro-acupuncture (EAP) is a modern adaptation of AP. Electric stimulation is widely diffuse, most of all to treat acute and chronic pain. In an old RCT, Deluze *et al.* (23) evaluated 70 patients randomly assigned to standardised AP with individual acupoints for three weeks or a non-acupoint

needling group (sham AP), and found a significant improvement in most of the outcome variables (particularly the main variable of the pain threshold) in the former. There was no follow-up.

Martin *et al.* (24) more recently treated 50 patients, randomised to six standardised AP sessions (twice a week for three weeks) or to a non-insertion control group (mock AP). The patients were followed up for seven months, and the Fibromyalgia Impact Questionnaire (FIQ) and Multidimensional Pain Inventory (MPI) were used as outcome measures. There was a significant improvement in both the FIQ and MPI scores (particularly pain, fatigue and anxiety) after one month in the AP group.

Ceccherelli *et al.* recently carried out an open study of 52 FM patients who underwent EAP three times a week for two weeks followed by twice a week for five weeks, and received low-dose amitriptyline (AMT) daily. A comprehensive integrated programme was also suggested (physical exercise, stretching, educational or group therapy) as well as dietary supplements (magnesium, S-adenosyl methionine, L-acetyl-carnitine) for different periods. At the end of the EAP

treatment, and three and six months later, the pain measured using MGPQ and VAS was significantly less (25).

Over the last few years, the many reviews of AP and EAP have reached different conclusions. On the one hand, Hassett *et al.* (26) evaluated AP treatment quite favourably, Porter *et al.* (27) systematically reviewed RCTs and non-RCTs and concluded that AP may be effective, and systematic qualitative reviews of RCTs by Baranowski *et al.* (28) and Terhorst *et al.* (29) indicated a positive trend in favour of AP; on the other, systematic reviews and meta-analyses of RCTs by Mayhew *et al.* (30), Langhorst *et al.* (31), and Martin-Sanchez *et al.* (32) found no evidence of the effectiveness of AP treatment, although Langhorst *et al.* (33) have very recently stated that AP can be considered as a treatment for FM patients.

Hydrotherapy

Various FM treatments make use of water under different names: balneotherapy (BT), aquatherapy, pool therapy, water therapy, Spa therapy, thalassotherapy, swimming and hydrogalvanic therapy. BT uses natural mineral water, whereas hydrotherapy (HT) uses ordinary water; electric current application is used by hydrogalvanic bath therapy; Spa treatment consists of a range of different treatments.

Buskila *et al.* (34) evaluated the effectiveness of BT at the Dead Sea in 48 patients randomly assigned to sulphur bath treatment at 37° or a control group. All of the participants stayed at a Spa for 10 days, and their physical functioning, FM-related symptoms, TPC and dolorimetry were assessed before their arrival, after 10 days of BT, and one and three months after the treatment. The severity of pain, fatigue, stiffness and anxiety, and the frequency of headache, sleeping problems and subjective joint swelling, decreased in both groups, but the effects lasted longer in the treatment group.

Dönmez *et al.* (35) compared 16 FM patients with 14 controls receiving usual care who stayed at a Spa center and underwent 12 sessions (six times a week) of thermal poolbath at 37° associated with a pressure shower or mas-

sage. There was a significant improvement in pain and FIQ scores in the treatment group for up to six months.

Zijlstra *et al.* (36) conducted an RCT in which thalassotherapy (ThT) with supervised exercise and group education was used to treat 58 Dutch FM patients for two weeks at a Tunisian Spa resort and the results were compared with those of usual care in 76 controls. There was a significant improvement in the treatment group that lasted up to three months.

In another Turkish RCT, Evcik *et al.* (37) found that the effect of BT (a 20-minute bathing session once a day, five times a week for three weeks) in 42 FM patients randomly assigned to 2 groups was significantly superior to that of usual care, and the improvement in TPC and VAS and FIQ scores lasted for six months.

De Andrade *et al.* (38) compared the effectiveness of a 12-week programme of aerobic exercise in a heated swimming pool (HT) with that of aerobic exercise in the sea at a similar temperature (ThT) in 46 randomised female FM patients. He found that the seawater exercises had more advantages, although the differences between the two groups were not significant.

Altan *et al.* (39) obtained significant within-group improvements in various outcome measures when they randomised 50 FM patients to thrice weekly 35-minute sessions of BT with or without pool-based exercises for 12 weeks, but there were no significant between-group differences.

An old study of hydroelectric (hydrogalvanic) therapy compared to relaxation training by Guenther *et al.* (40) found that they had similar effects on various outcome measures, thus suggesting that this type of HT is as useful as the control therapy. More recently, Eksioglu *et al.* (41) compared the use of a Stanger hydroelectric bath plus AMT with AMT alone in 50 randomised FM patients, and found a significant improvement in FIQ values in the treatment group.

In recent systematic qualitative reviews of RCTs, Terhorst *et al.* (29) stated that the overall effects in the treatment group signified that BT was

more effective than the control method, and Baranowsky *et al.* (28) concluded that FM patients can benefit from various kinds of water therapy, and that this benefit can be maintained during a follow-up period. Furthermore, in a very complete, systematic review of RCTs, McVeigh *et al.* (42) examined the effectiveness of all kinds of HT in ten studies of sufficient quality, and concluded that they had positive effects on pain, health status and TPC, and that there was strong evidence supporting their use in the management of FM. However, in a previous meta-analysis, Langhorst *et al.* (43) found moderate evidence of improved pain only in the case of Spa therapy and Porter *et al.* (27) stated in their review that, although there is some evidence to suggest the effectiveness of BT, it is still not possible to draw any firm conclusions.

The differences in these opinions can probably be explained by the difficulty in interpreting the results of such multi-component therapies, the different outcome measures used, and the frequently poor methodological quality of the trials.

Thermotherapy

Thermal water is often used in BT, and this should probably be taken into account when evaluating the positive results of the therapy.

Fioravanti *et al.* (44) performed an RCT to evaluate the effects and tolerability of mud-bath treatment in FM patients in 40 patients who underwent a cycle of 12 mud packs and thermal baths, and 40 controls who received usual treatment. The patients were evaluated using the FIQ, TPC, VAS, the Abnormal Involuntary Movement Scale (AIMS1) and the Health Assessment Questionnaire (HAQ) at baseline, after thermal treatment, and 16 weeks later. The mud packs, which were well tolerated and led to no drop-outs, significantly improved the overall parameters at both post-treatment assessments.

Brockow *et al.* (45) tested near-infrared whole-body hyperthermia in a comparatively large group of 139 patients in a rehabilitation setting, and found a significant improvement in pain, FIQ scores and depression in comparison

with the randomised controls. The patients received standard medical rehabilitation (as in the controls), mild, whole-body hyperthermia twice weekly at up to 38°C for three weeks, and were followed up for six months. The significant post-treatment benefit disappeared at the follow-up, but all the intergroup differences maintained.

Biofeedback

Biofeedback (BFB) is a form of behavioural CT that enables subjects to learn how to change their physiological activity for the purpose of improving health and performance. Precise techniques (electrocardiography, electro-encephalography, electromyography [EMG], etc.) are used to measure physiological activity such as brainwaves, heart function, breathing, muscle activity, and skin temperature. These instruments rapidly and accurately “feed-back” information to the user that can be useful to support the desired physiological changes, which can be maintained without the continuing use of instrumental measurements (46).

Many years ago, Ferraccioli *et al.* (47) gave EMG-BFB training sessions to 15 FM patients with some benefit. Subsequently, 12 patients were alternatively allocated to “true” or “false” EMG-BFB treatment (in a blinded fashion). After 15 sessions given twice weekly, the former showed a significant improvement in pain intensity, TPC and morning pain at the end of the treatment and after six months of follow-up.

Buckelew *et al.* (48) randomly assigned 119 subjects to one of four treatments: BFB/relaxation training, exercise training, a combination treatment, or an educational/attention control programme. The interventions involved a 6-week individual training phase and a 2-year group maintenance phase. All three treatment groups experienced improvements in function in comparison with the controls, particularly in terms of TP index scores. The combination group best maintained the benefits during the 2-year period.

Different results were obtained in an RCT conducted by Van Santen *et al.* (49). One hundred and forty-three female FM patients were randomised to

undergo: a fitness programme (58 patients), or BFB training (56 patients), or usual treatments (29 patients). Analysis of the subgroups showed no improvement and, after 24 weeks, the data showed that neither fitness nor BFB training had any clear beneficial effect. Babu *et al.* (50) carried out an RCT involving two groups of 15 FM patients, one undergoing real surface EMG/BFB and the other sham BFB. After six successive days of treatment, VAS scores and TPC were significantly better in the real BFB group, whereas the patients in both groups experienced subjective improvements in the physical and psychological domains.

In order to manipulate suboptimal heart rate variability in FM, Hassett *et al.* (51) planned an open label trial of heart rate variability BFB, in 12 women, for 10 weekly sessions during which they were taught to breathe at their resonant frequency and asked to practice twice daily. There was a clinically significant decrease in depression and pain, and improvement in functioning that lasted until the 3-month follow-up period, although with poor clinical relevance.

The authors of the only systematic review of the use of BFB to treat FM (27) stated that, although the outcomes were generally positive, it was impossible to draw any firm conclusions because of the small number of studies, their poor methodological quality, and differences in diagnostic approaches and criteria.

Manual therapy

The term manual therapy (also known as manipulative therapy or manual manipulation) describes the physical treatments used by some physicians, physiotherapists, chiropractors, and osteopaths to treat musculoskeletal pain and disability. It most frequently involves massage therapy, joint mobilisation and joint manipulation (52) and it may be defined as a clinical approach utilizing skilled, specific hands-on techniques to diagnose and treat soft tissues and joint structures mainly in order to modulate pain, increase range of motion, and improve function.

Massage (MG) therapy manipulates the muscle system and is widely used in FM patients because it leads to the

highest levels of patient satisfaction (53, 54). A number of studies of various muscle manipulation techniques have been published. Brattberg *et al.* (56) evaluated 48 randomised FM patients treated with regular sessions of connective tissue MG for 10 weeks using a waiting list (50%) and education (50%) control group. There was a significant improvement in FIQ and pain scores in the first group, but the effects dissipated over a 6-month follow-up period. Connective tissue MG has recently been compared with manual lymph drainage therapy by Ekici *et al.* (56) in an RCT involving 50 FM women. The treatments were given for five weeks and led to significant improvement in both groups, but the FIQ scores indicated that manual lymph drainage therapy was more effective. Other RCTs have achieved similar beneficial effects and improvements in symptoms (57, 58), and only one randomised study of 37 FM patients found no positive effects of Swedish massage in comparison with no treatment group (59).

These trials indicate that MG treatment may have an effect on FM, although the results do not seem to last over the long term. However, a systematic review by Terhorst *et al.* (29) disbelieves these results pointing out that the composite effect are not successful.

Chiropractic (CP) medicine is aimed at treating vertebral misalignments that deregulate the central nervous system, and is also very popular among FM patients (54). However, only two relatively small RCTs have been published. Blunt *et al.* (60) conducted a pilot study of 21 subjects randomised to undergo four weeks of spinal manipulation, soft tissue therapy and passive stretching (at the chiropractor’s discretion) or the continuation of their previously prescribed medication. There was statistically significant between-group difference between the two groups, although there was some improvement in pain and range of motion. One CP study (61) used a multimodal technique and randomly assigned 21 women to resistance training (RES) consisting of ten exercises twice a week for 16 weeks, or RES combined with CP. Both treatments led to improved FIQ and myal-

gic scores, and TPC, with the addition of CP facilitating greater improvements in the functional domains. Finally, a review by Porter *et al.* (27) suggested that CP manipulation may offer some benefit to FM patients, and a recent systematic review has provided some limited evidence in favour of spinal manipulation (62).

Osteopathy is a non-invasive form of manual medicine aimed at strengthening the musculoskeletal framework. Gamber *et al.* (63) randomly assigned 24 female patients to one of four treatment groups for six months: weekly manipulation, weekly manipulation and teaching, moist heat and current medication alone (controls), and found an increase in the TP pain threshold in the first two groups, as well as improvements in daily living activities, perceived pain and ability. However, these findings are clearly not sufficient to recommend osteopathy in the treatment of FM.

Body-mind techniques

It is very difficult to define the various fields of mind-body medicine, as there is no agreement concerning which therapeutic approaches can be unquestionably include. Relaxation and awareness techniques are generally considered behavioural interventions, and many forms are similar to cognitive-behavioural therapy (CBT), which is not analysed in this review. Relaxation techniques include progressive muscle relaxation (PMR), autogenic training (AT), guided imagery (GI) and meditation (MT). BFB (see above) has some similarities with these approaches, and some authors include Qigong and Tai Chi (27, 28) and consider MT a traditional Buddhist practice (27). Furthermore, hypnosis has also sometimes been included (27, 29).

As pointed out in two recent reviews (27, 28), the published results of MT are quite positive but to some extent equivocal. In an early study of 77 FM patients (64), Kaplan *et al.* used a 10-week MT-based stress reduction programme and found that 51% of the completers showed moderate to marked improvements. More recently, Sephton *et al.* (65) carried out an RCT in which 51 women were assigned to an 8-week

mindfulness MT programme and 40 to a waiting list control group. The patients were subsequently followed up for two months, and showed a significant improvement in depressive symptoms; no pain measures were performed.

An RCT conducted by Astin *et al.* (66) compared an 8-week programme of combined Qigong and MT training in 128 FM patients with a control group of patients receiving educational support, and found an improvement in the FIQ, total myalgic, pain and depression scores, with no significant differences between the groups.

No RCT has evaluated PMR alone in FM patients, and none has demonstrated the superiority of AT over any other treatment, although Keel *et al.* and Rucco *et al.* noted some clinical improvement (67, 68). However, Erickson's techniques significantly improved all parameters in comparison with AT in the study of Rucco *et al.* Allen *et al.* (69) included PMR and AT as central aspects of a CBT protocol for somatisation disorders (including FM), and observed a greater decrease in symptom severity in comparison with standard medical care plus a psychiatric consultation intervention.

Two RCTs respectively involving 55 women (70) and 48 men and women with FM (71) used GI for muscle relaxation and distraction from pain. In comparison with the controls, the first demonstrated less pain after GI treatment, and the second improved functional status and a greater sense of self-efficacy for managing pain.

The available RCTs provide little or no evidence concerning the body awareness technique (BAT). Mannerkorpi *et al.* (72) compared combined BAT and Qigong with usual care, and found no improvement in the FIQ or functional test scores. Kendall *et al.* (73) carried out a pilot study comparing BAT with the Mensendieck system, and found that the latter was more efficacious.

In a recent RCT, Hsu *et al.* (74) randomised 45 female FM patients to a manualised affective self-awareness intervention (n=24) or a waiting list (n=21). The treatment significantly improved pain severity, physical function and TP threshold after six months, by

which time 45.8% of the members of the intervention group experienced a plus than 30% reduction in pain severity.

Many years ago, Bennett *et al.* (75) pioneered group therapy in a non-randomised controlled trial involving 170 FM patients for four years. One hundred and four patients completed the 6-month programme of weekly 90-minute group sessions (15–25 patients) based on formal lectures, behavioural modifications, stress reduction techniques and strategies for improving fitness and flexibility, together with support sessions for spouses/significant others. The TPC of 70% of the patients decreased (<11) and FIQ scores improved by 25%. Thirty-three patients continued to show an improvement after two years. There was no significant improvement in the control group.

Keel *et al.* (67) compared once-weekly integrated group therapy sessions based on information, instructions in self-control strategies, gymnastics, relaxation and discussion for 15 weeks with AT, and followed up the patients for three months. Average pain intensity was significantly higher in the AT group.

Finally, in two recent reviews, Hasset *et al.* (26) provided some evidence in favour of relaxation techniques as an adjunctive treatment for FM, and Terhorst *et al.* (29) highlighted the potential benefit of GI, MT and self-awareness. However, Porter *et al.* (27) pointed out the methodological limitation of the lack of an appropriate and easily administered placebo or sham treatment in which participant blinding is often not possible.

Magnetic field treatment

Magnet therapy involves applying the magnetic field of an electromagnetic device or permanent static magnets to the body because of its purported health benefits. The products are popular among patients, who usually apply them themselves.

Colbert *et al.* (76) carried out a randomised, double-blind pilot study of 25 female FM patients who slept on an experimental magnetised or non-magnetised sham mattress pad for 16 weeks. The subjects sleeping on the magnetised pad experienced a signifi-

cant decrease in pain, fatigue, total myalgic scores, and in FIQ reported sleep and physical functioning. The sham mattress offered no benefit.

In a similar 6-month RCT with two control groups (sham pad and usual treatment), Alfano *et al.* (77) did not find any significant between-group difference in the overall FIQ scores of the 56 patients, but pain intensity was significantly lower in the magnetic pad group.

Shupak *et al.* (78) carried out a double-blind, sham-controlled study of 13 female patients with rheumatoid arthritis (RA) and 18 FM patients in order to investigate the effects of acute 30-minute pulsed electromagnetic field (PEMF) exposure on pain and anxiety. The McGill Pain Questionnaire and VAS scores indicated similar benefits for the RA and FM patients in the treatment group, but no significant reduction in VAS anxiety ratings.

Thomas *et al.* (79) exposed patients with chronic generalised pain due to FM or chronic localised musculoskeletal or inflammatory pain to a specific PEMF (a portable device fitted to their heads during twice-daily 40-minute treatment sessions over seven days) in a randomised, double-blind, sham-controlled trial. Only the patients with FM showed a statistically significant differential effect of the active treatment, despite their small number (n=17).

More recently, Sutbeyaz *et al.* (80) carried out a double-blind, sham-controlled RCT to evaluate the clinical effectiveness of twice-daily, 30-minute sessions of low-frequency PEMF therapy for three weeks in 56 women with FM who were subsequently followed up for 12 weeks. The PEMF group showed significant improvements in FIQ, VAS pain, Beck's Depression Inventory, and SF-36 scores at the end of therapy and during the follow-up. The sham group also showed a slight improvement.

The authors of two recent reviews (27, 28) conclude that there seems to be a trend towards improved of symptoms in FM patients treated by means of magnetic pads

Energy and movement therapies

Energy therapy, one of the five domains of CAM, is based on the belief

that a healer can channel healing energy into other people in various ways. Therapeutic touch and Reiki, but often Qigong and Tai Chi, are considered as falling into this category.

As an internal martial art, Qigong involves aligning breathing, movements and awareness for the purposes of exercise, healing or meditation (movement therapy); in the case of external Qigong, a master projects or emits his own Qi to serve or heal another. Tai Chi also started primarily as an external exercise, but it has become an increasingly internal means of exercising bodily organs and the mind, as well as the musculoskeletal system. Reiki, Yoga, transcendental MT and Biodanza can reasonably be considered western equivalents of Chinese internal Qigong, whereas pranotherapy or therapeutic touch resembles external Qigong. In addition, Pilates can be considered a movement therapy; it is a physical fitness system developed by Joseph Pilates, in which a body conditioning routine may help build flexibility, muscle strength, and endurance. Astin *et al.* (66) carried out an RCT involving 128 FM patients who were assigned to eight weeks of MT plus Qigong group or educational support. There were significant improvements in FIQ, total myalgic score, pain and depression scores after up to 24 weeks of follow-up, but no significant between-group differences.

A three-month programme of once-weekly joint interventions with BAT, the effect of Qigong was not more positive than usual treatment in a pilot RCT involving 36 FM patients carried out by Mannerkorpi *et al.* The treatment group improved in terms of movement harmony (81).

In an uncontrolled pilot study of external Qigong, Chen *et al.* (82) studied 10 women with FM over a 3-week period and after three months follow-up, and observed improvements in pain, functioning, depression and self-efficacy.

More recently, Haak *et al.* (83) randomly assigned 57 FM women to a 7-week Qigong intervention group or a waiting list control group, and obtained significant improvements in pain, psychological health and distress at the end

of the treatment and after four months follow-up. This is so far the only RCT in which Qigong has been used as the sole treatment for FM.

Very recently, Lynch *et al.* (84) conducted an RCT of eight weeks Chaoyi Fanhuan Qigong involving 100 FM patients; the controls were in a delayed practice group. Pain, impact, sleep, physical function and mental function scores were recorded at baseline, and significantly improved after eight weeks, four months and six months.

Taggart *et al.* (85) treated 39 women with FM by means of 2-weekly Tai Chi sessions over six weeks in an uncontrolled pilot study. The dropout rate was high (18 patients), but there were significant improvements in symptoms and the quality of life as measured using FIQ and SF-36.

Wang *et al.* (86) have recently conducted a single-blind, randomised trial to compare Tai Chi with wellness education plus stretching twice a week for 12 weeks in 66 FM patients. The treatment group achieved clinically and significantly important improvements in the FIQ total score and quality of life, and the differences between the groups were maintained after 24 weeks.

Very recently, Jones *et al.* (87) compared an FM-modified 8-form Yang-style Tai Chi programme with education in a parallel-group RCT involving 101 FM patients. After 12 weeks, those who underwent Tai Chi treatment showed clinically and statistically significant improvements in FIQ scores (primary endpoint) and in other endpoints such as pain severity and interference, self-efficacy, and functional mobility.

Romero-Zurita *et al.* (88) analysed the effects of a 28-week programme of thrice-weekly Tai Chi training sessions on 32 women with FM. The results of this open study indicated a significant overall improvement in the various endpoints.

An RCT of Reiki by Assefi *et al.* (89) involving 100 FM adults failed to demonstrate the benefit of the energy therapy; four groups received twice-weekly treatment for eight weeks given by a Reiki master or actors randomised to use direct touch or no touch; neither

Reiki nor touch had any effect on pain or any of the secondary endpoints.

Stiller studied the efficacy of Rogers' model therapeutic touch (TheT) in relieving FM pain and anxiety in 42 patients in a randomised crossover trial (TheT followed by placebo or placebo followed by TheT) (90). During the TheT phase, the participants experienced greater reduction in pain and anxiety than during the placebo (mattress pad) phase.

Da Silva *et al.* (91) compared eight weekly sessions of Relaxing Yoga or relaxing Yoga plus Touch Therapy (Tui Na) in an RCT involving 40 women with FM. Both groups showed improvements in FIQ and VAS scores, but the post-treatment data and the follow-up scores after 4-6 weeks showed better results in the first group, thus suggesting a negative effect of passive therapy on FM symptoms.

In an uncontrolled study, Curtis *et al.* (92) found that twice-weekly yoga sessions for eight weeks led to a significant decrease in pain and catastrophising, and a significant increase in acceptance and mindfulness, in 22 female FM patients; furthermore, total salivary cortisol levels were significantly higher after the treatment.

Carson *et al.* (93) have very recently published the preliminary findings of an RCT of an 8-week Yoga of awareness programme involving 39 FM patients, eighteen of whom were allocated to a waiting list group that received the same treatment. The post-treatment results were good in both groups, with a 31.9% improvement in the FIQ Revised total score. The patients in the immediate treatment group maintained most of their gains at the end of a 3-month follow-up period.

Carbonell-Baeza *et al.* (94) carried out a controlled study of 59 female FM patients in order to compare the effects of a 3-month programme of once-weekly Biodanza sessions with those of usual care. The outcome measures included pain thresholds, body composition, physical fitness and psychological outcomes, and significant interaction effects were found for the pain threshold of various TPs, the percentage of body fat, and the FIQ total score.

Altan *et al.* (95) carried out the first clinical study to investigate Pilates in FM treatment. Fifty women with FM were randomly assigned to a 12-week programme of thrice-weekly one-hour Pilates exercise sessions given by a certified trainer or a domiciliary programme of relaxation/stretching exercises. In the first group, both pain and the FIQ scores had improved at the end of the 12-week programme, but only FIQ scores after 24 weeks (the end of the follow-up); the results were significantly superior to those obtained in the second group (no improvement), but only after 12 weeks.

Finally, in their previously cited review (26), Hassett *et al.* state that Tai Chi and Qigong offer some promise of efficacy, but need more rigorous assessment, whereas a recent systematic review by Langhorst *et al.* (33) led the authors to recommend Qigong, Tai Chi and Yoga strongly, at the same time as dance therapy and Reiki are not recommended. In a very recent meta-analysis Mist *et al.* (96) conclude that alternative exercise programs are somewhat efficacious for FM pain, but the majority of studies had lower methodological quality.

Dietotherapy

Dietary solutions may be considered biology-based practices (*i.e.* the third level of the NCCAM classification) founded on the hypothesis that the ingestion or non-ingestion of specific foods change the level of pain or other patient symptoms. Some authors have investigated their usefulness in the treatment of FM.

Michalsen *et al.* (97) conducted a two-month observational study of 16 patients with RA and 35 with FM in order to evaluate whether a Mediterranean diet or an 8-day fasting period was associated with changes in fecal flora, and whether such changes were associated with clinical outcomes. Neither treatment affected the microbiologically assessed intestinal flora, leading to the conclusion that clinical outcomes were not related to any alterations in the flora. In another two-month observational study, Donaldson *et al.* (98) evaluated 30 FM patients following a mainly raw

vegetarian diet (raw fruits, salads, carrot juice, tubers, grain products, nuts, seeds, and a dehydrated barley grass juice product, avoiding alcohol, caffeine, foods containing refined sugar, corn syrup, refined and/or hydrogenated oil, refined flour, dairy products, eggs and any meat) that led to significant results in terms of FIQ, SF-36 subscale and Quality of Life Survey scale scores, which were maintained for up to seven months.

Azad *et al.* (99) assessed the effect of a vegetarian diet on 78 subjects participating in a 6-week RCT versus the administration of AMT. In the diet group, the only significant positive changes were in VAS scores; there were no changes in the other FM symptoms.

Kaartinen *et al.* (100) carried out an open, non-randomised controlled study compared the effects of a strict, low-salt, uncooked, lactobacteria-rich vegan diet on the symptoms of 18 FM patients during and after a 3-month intervention period with those observed in a control group of 15 patients following an omnivorous diet. There were significant improvements in VAS scores, joint stiffness, quality of sleep, Health Assessment Questionnaire (HAQ), and General Health Questionnaire (GHQ).

Holton *et al.* (101) recently examined the effects of monosodium glutamate (MSG) as compared to placebo on the symptoms of 30 FM/irritable bowel syndrome (IBS) patients who initially experienced plus than 30% remission of symptoms on an excitotoxin elimination diet. They were randomised to a 2-week double-blind placebo-controlled crossover challenge with MSG or placebo for 3 consecutive days each week. Total symptom score, IBS Quality of Life Questionnaire and the FIQ revised significantly got worse; a non-significant negative trend on VAS emerged.

Dietary supplements

Dietary supplements (also known as food or nutritional supplements) are preparations intended to provide nutrients such as vitamins, minerals, fibre, fatty acids or amino acids in the case of their absolute or relative deficiency. In the United States, they are defined

in the Dietary Supplement Health and Education Act of 1994 as any product that contains a vitamin, mineral, herb or other botanical, amino acid, concentrate, metabolite, constituent or extract, or a combination of any of the same, or is a substance historically used by man to supplement the diet.

S-adenosyl methionine

This amino acid derived from methionine and adenosine triphosphate is probably the most widely studied of the supplements used to treat FM.

At the end of the 1980s, Tavoni *et al.* (102) conducted a short-term, double-blind, placebo-controlled, cross-over study of 34 FM patients divided into two equal groups. There was a significant improvement in depression and a reduction in the number of tender points in the S-adenosyl methionine (SAME) group.

Jacobsen *et al.* (103) orally administered SAME 800 mg/day to 44 patients with primary FM in a six-week, double-blind and placebo-controlled study, and observed good benefits in terms of clinical disease activity, pain experienced during the previous week, fatigue, and morning stiffness in the active treatment group, although the improvement in mood was uncertain. There was no difference in TPC and isokinetic muscle strength between the two groups.

Di Benedetto *et al.* (104) carried out an RCT in which 30 FM patients were treated with oral and parenteral SAME for six weeks, and compared the results with those obtained in a control group treated with transcutaneous electrical nerve stimulation (TENS). Unlike TENS, SAME significantly decreased the total TPC, and had a significant beneficial effect on depression and the subjective symptoms of pain and fatigue. Grassetto *et al.* (105) used the same procedure for the same period in an uncontrolled open study: there was a significant decrease in the tenderness of painful sites in 47 patients, and an improvement in general well-being, depression and anxiety scores.

Volkman *et al.* (106) performed a 10-day double-blind, placebo-controlled, cross-over study of intravenous SAME 600 mg/day involving 34 FM patients.

There was no significant between-group difference in the primary outcome of the improvement in TPC, although there was a trend in favour of SAME.

Other authors have investigated the usefulness of SAME in patients with secondary FM and found significant improvement in symptoms and mood (107, 108).

Magnesium

At the beginning of the 1990s, it was hypothesised that FM is due to deficiencies in the substances needed for ATP synthesis, and some authors tried to demonstrate the pivotal role of magnesium and malate in mitochondria. Magnesium (MAG) deficiency causes the swelling and disruption of mitochondrial cristae, and decreases the number of mitochondria per cell. Observing that this abnormality had been reported in muscle biopsies of the TPs of FM patients, they suggested a possible correlation between mitochondrial damage and myalgia and, in an open clinical setting, treated 15 FM patients with an oral preparation containing elemental MAG and malic acid at total daily doses of respectively 300-600 mg and 1200-2400 mg for eight weeks. There was an improvement in the TP index and pain, and myalgia recurred within 48 hours in six patients who were switched to placebo tablets for two weeks (109).

A few years later, Russell *et al.* (110) conducted a 4-week randomised, double-blind, placebo-controlled, cross-over pilot study of 24 FM patients using a fixed dose of the same compound, followed by a 6-month, open-label, dose escalation trial. Only the dose escalation and longer treatment duration led to significant reductions in the severity of pain and tenderness measures.

Very recently, Bagis *et al.* (111) investigated the effect of MAG citrate on FM symptoms in a controlled study involving 60 premenopausal patients with FM and 20 healthy women. The patients were divided into three groups: MAG citrate, AMT, and MAG citrate plus AMT. TPC, TP index, and FIQ, and Beck depression scores decreased significantly with MAG citrate treatment.

The combined amitriptyline plus magnesium citrate treatment proved effective on all parameters except numbness.

Other supplements

– Soy

Wahner-Roedler *et al.* (112) tested the efficacy of soy in an RCT in which 50 FM patients randomly assigned to receive soy or placebo casein shakes once a day for six weeks. There was no significant benefit in either group, particularly in terms of FIQ scores.

– 5-hydroxytryptophan

Caruso *et al.* (113) conducted a double-blind, placebo-controlled study of the efficacy and tolerability of 5-hydroxytryptophan (5-HTP) in 50 FM patients. There were significant improvements in all of the studied clinical parameters, and only mild and transient side effects were reported. Sarzi-Puttini *et al.* (114) obtained the same results in a 90-day open study of 50 FM patients, in whom there were significant improvements in TPC, anxiety, pain intensity, quality of sleep, and fatigue.

– Melatonin

Citera *et al.* (115) investigated the effect of melatonin (ML) 3 mg given at bedtime to 21 patients with FM in an open 4-week pilot study. There were good improvements in TPC and pain severity, sleep VAS scores, and patient and physician global assessments.

In a very recent study, Hussain *et al.* (116) tested the value of ML as an adjuvant treatment in an 8-week double-blind, controlled study of 101 FM patients randomised to receive fluoxetine, ML, or fluoxetine plus one of two different doses of ML. The combination of fluoxetine and ML led to a significant improvement in FIQ scores, and the authors concluded that the use of ML (alone or combined with fluoxetine) was effective.

– Anthocyanidins

These food supplements belong to the flavonoid group of plant-derived chemicals frequently used for chronic disease. Edwards *et al.* (117) tested its efficacy in an RCT in which only 12 FM patients were randomly assigned

to one of three doses of anthocyanidins or placebo group. The total duration of this cross-over study was 52 weeks, and every treatment administered for 12 weeks. Only sleep disturbances significantly improved, whereas no improvements were observed in pain or fatigue.

– *Deutrosulfazyme*

This colloidal-ionic formula contains all-natural, plant-based organic substances, including traces of ionic minerals, enzymes, amino acids and deuterium sulphate as traces.

Nieddu *et al.* (118) conducted a single-blind, cross-over RCT involving 40 female FM patients who had failed to respond to conventional therapy. They were assigned to receive deutrosulfazyme for six months (31 patients) or placebo (9 patients) for three months followed by deutrosulfazyme for three months. TPC and FIQ scores improved with the active treatment.

– *L-acetyl-carnitine*

Rossini *et al.* (119) conducted a multicentre double-blind RCT in which 102 FM patients were randomised to receive high-dose L-acetyl-carnitine (LAC) or placebo for 10 weeks; the follow-up period was four weeks. The “total myalgic scores” and TPC were similar until the sixth week of treatment. They significantly improved by the tenth week in the treatment group, and differences between the groups was statistically significant.

– *Chlorella pyrenoidosa*

Merchant *et al.* (120) investigated the usefulness of this unicellular green alga in a 2-month pilot study of 18 FM patients. The average TP index had significantly decreased at the end of the treatment period, but only seven patients declared that it had improved their symptoms in the post-treatment interviews and self-assessment questionnaires.

The same first author later conducted a double-blind, placebo-controlled RCT trial in which 55 FM patients received 10 g pure chlorella tablets for two or three months (121). The authors reported an improvement in pain and the overall quality of life.

Homoeopathy

In this form of AM, practitioners treat patients using highly diluted preparations that are believed to cause healthy people to manifest symptoms that are similar to those of patients. Homoeopathic remedies may not contain any pharmacologically active molecules and must not have any pharmacological effects. Its fundamental concepts are so far away from modern scientific views that no scientifically plausible physical mechanism can be suggested.

Fisher *et al.* have investigated the value of homoeopathy (HO) in treating FM. In their first study (122), 24 FM patients were given a placebo or a remedy containing highly diluted *Arnica montana*, *Bryonia alba* and *Rhus Toxicodendron* for three months. In comparison with placebo, the HO treatment led to a significant improvement in pain and sleep VAS. In a subsequent RCT, 30 FM patients were assigned to receive a tablet containing placebo or a 6C dilution of *Rhus Toxicodendron* for two months. The treatment significantly improved in pain, sleep disturbances and tenderness (123).

The effect of a 6X dilution of *Rhus Toxicodendron* on pain was studied by Gemmell *et al.* (124) in a small study of only three FM patients using a time-series design. The subjects rated and recorded their pain levels daily using a numerical scale, and visual data analysis indicated that the treatment was ineffective.

Bell *et al.* (125) compared individually selected homoeopathic remedies (not clearly defined) with placebo in a 4-month RCT involving 62 FM patients, and reported significant improvements in TP pain, TPC, depression, and quality of life and global health.

Relton *et al.* (126) randomly allocated 47 FM patients to usual care or usual care plus adjunctive care by a homoeopath in a 22-week RCT. McGill pain score and FIQ fatigue and tiredness upon waking scores improved in the group receiving homoeopathic care, which also had a small effect on pain scores and a large effect on function.

Although recognising that some RCTs have found that homoeopathy is better than the control interventions in allevi-

ating the symptoms of FM, a recent review by Perry *et al.* (127) raised doubts and uncertainties concerning their methods and positive results. Even if the mainly positive results suggest potential for future research (as also highlighted by Baranowski) (28), Porter *et al.* (27) do not offer any conclusions concerning this type of treatment.

Miscellanea

Aromatherapy

Aromatherapy is a form of AM that uses volatile plant materials known as essential oils and other aromatic compounds for the purpose of altering a person’s mind, mood, cognitive function or health.

Rutledge *et al.* (128) conducted a randomised pilot study to determine the effects of essential oils combined with a 12-week exercise programme on exercise volume, pain, physical performance, and physical function in 43 women, 20 of whom were randomised to 024 oil (*Aloe vera*, eucalyptus, lemon, orange, camphor, rosemary and peppermint) and 23 to sham oil (peppermint oil alone). There was no significant difference between the groups after 12 weeks. Although the use of aromatherapy is well known and widespread, no other studies have been found.

Music therapy and vibration

Music therapy consists of an interpersonal process in which a trained music therapist uses music to help clients to improve or maintain their health. Whole body vibration is an increasingly popular training method that is now widely used in physical therapy, rehabilitation and professional sports.

Chesky *et al.* (129) conducted an RCT of one session of music listening and the bodily application of musically fluctuating vibrations involving 13 FM patients and 13 controls who received a vibration known to be outside the therapeutic range. No between-group differences were found, but there were some positive results in terms of the TP index in both groups, and in terms of the TP pain in the treatment group.

More recently, Alentorn-Geli *et al.* (130) investigated the effectiveness of a 6-week traditional exercise pro-

gramme with supplementary whole-body vibration in 36 women with FM who were randomly assigned to exercise and vibration, exercise alone or a control group. The exercise therapy was administered twice a week, and the patients were assessed by means of VAS and FIQ at baseline and after six weeks. Pain and fatigue scores significantly decreased from baseline only in the first group.

Religiosity and spirituality

There is evidence that religiosity and spirituality may be related to health as a growing body of observational data supports the hypothesis that they may be associated with physiological processes (131).

Dedert *et al.* (132) investigated the associations of religiosity and spirituality with psychological measures of stress in a sample of 91 FM women who provided self-reports of religiosity and spirituality and underwent measurements of their diurnal salivary cortisol profiles as an indicator of neuroendocrine regulation. The patients reporting a medium or high degree of religiosity had rhythmic cortisol profiles characterised by high morning and low evening levels, whereas the cortisol rhythms of those reporting a low degree of religiosity seemed to be flattened. However, no significant effects of religiosity or spirituality on perceived stress were observed, although the authors concluded that religiosity might have a protective effect on the physiological effects of stress.

Baetz *et al.* (133) found that spirituality and/or religion may be a factor that can influence the experience of chronic pain or fatigue when they used the Canadian Community Health Survey data relating to 37,000 subjects to analyse four conditions: FM, back pain, migraine headaches and chronic fatigue syndrome. The religious subjects were less likely to have chronic pain and fatigue than those who were spiritual but were not affiliated with regular worship attendance. The subjects with chronic pain and fatigue were more likely to use prayer and seek spiritual support as a method of coping than the general population, and those who were both

religious and spiritual were more likely to have a better sense of psychological well-being and to use positive coping strategies.

Hypnotherapy

Hypnotherapy uses hypnosis to induce a deep state of relaxation during which the subconscious or unconscious mind is highly receptive to new perspectives and ideas.

In a controlled study, Haanen *et al.* (134) randomly allocated 40 patients with refractory FM to treatment with hypnotherapy or physical therapy for 12 weeks, and followed them up after 24 weeks. In comparison with the controls, the patients in the hypnotherapy group experienced a significantly better outcome in terms of pain experience, fatigue upon awakening, sleep patterns and global assessment after 12 and 24 weeks, but not in terms of the total myalgic score measured by means of a dolorimeter.

Castel *et al.* (135) randomly assigned 45 FM patients to hypnosis with relaxation suggestions, hypnosis with analgesia suggestions, or relaxation alone. Before and after the session, pain intensity was measured using VAS, and the sensory and affective dimensions were measured using the MGPIQ. Hypnosis followed by analgesia suggestions had a greater effect on the intensity of pain and the sensory dimension of pain than hypnosis followed by relaxation suggestions; the effect of hypnosis followed by relaxation suggestions was not greater than that of relaxation alone.

In another study, Castel *et al.* (136) recently compared the efficacy of two psychological treatments for FM with each other and with standard care. Ninety-three FM patients were randomly assigned to multicomponent CBT, multicomponent CBT with hypnosis or pharmacological treatment (the control group). The outcome measures of pain intensity, catastrophizing, psychological distress, functionality, and sleep disturbances were assessed after the 14 weekly treatments, and after six months follow-up. The patients who received multicomponent CBT alone or with hypnosis showed greater improvements than those receiving standard care, and

hypnosis enhanced the effectiveness of multicomponent CBT.

Cannabis

Fiz *et al.* (137) have very recently described the patterns of cannabis use and associated benefits reported by 28 FM patients (cannabis smokers, oral users and combined users), and compared their quality of life with that of 28 non-cannabis using FM patients. After two hours of cannabis use, there was a statistically significant reduction in pain and stiffness VAS scores, an improvement in relaxation, greater somnolence and an increased feeling of well-being. The SF-36 mental health summary score was significantly higher among the cannabis users.

Capsaicin

This is a herbal medicine extracted from chili peppers. McCarty *et al.* (138) compared the efficacy of the local application of capsaicin with that of a placebo in an RCT involving 45 FM who were randomly assigned to four different treatment groups. Four weeks of double-blind capsaicin treatment did not lead to any significant improvement in pain (apart from tenderness) or in the quality of sleep.

Vitamin D

Observational and circumstantial evidence suggests that vitamin D may play a role in the etiology of chronic pain conditions, and may be one of the major causes of unexplained muscle and bone pain. The symptoms of vitamin D deficiency are similar to those of FM, but there is still little evidence to support the use of vitamin D to treat chronic pain in adults.

Arvold *et al.* (139) examined the association between the symptoms of vitamin D deficiency and the symptomatic response to cholecalciferol treatment in an 8-week double-blind RCT in patients with various diseases. One hundred of the 610 patients had mild to moderate vitamin D deficiency and 38 were severely deficient; these patients were treated in an unblinded manner. The treated group showed a significant improvement in FIQ scores, whereas the placebo-treated participants did not.

Table III. Acupuncture, electroacupuncture, hydrotherapy, thermotherapy.

First author	Year	CAM	Combined therapy	Control group ^o	Type of study [§]	Number of patients	Duration	Effectiveness*	Effectiveness vs. comparator*	Follow-up
Sprott	1998	AP			open	29	6 w	yes		no
Clarke	2004	AP	life style counselling		open	20	12w	yes		no
Harris	2005	AP		TP	RCT	114	different	yes	no	no
Assefi	2005	AP		TP	RCT	100	12w	no	no	6m
Targino	2008	AP	amitriptyline + exercise	TP	RCT	58	10w	yes	yes	2y
Cassisi	1994	AP		TP	RCT	42	10w	yes	no	6m
Iannucelli	2012	AP	pharma-therapy		open	30	10w	yes	no	
Deluze	1992	EAP		PL	RCT	70	3w	yes	yes	no
Martin	2006	EAP		PL	RCT	50	3w	yes	yes	7m
Ceccherelli	2012	EAP	amitriptyline + exercise + educational or group therapy + supplements		open	52	7w	yes		6m
Buskila	2001	BT		PL	RCT	48	10d	yes	no	3m
Dönmez	2005	BT	pressure shower or massage	TP	RCT	30	2w	yes	yes	6m
Zijlstra	2005	ThT	exercise + education	TP	RCT	134	2w	yes	yes	3m
Evcik	2002	BT		TP	RCT	42	3w	yes	yes	6m
De Andrade	2008	ThT	exercise	TP	RCT	46	12w	yes	no	no
Altan	2004	BT		TP	RCT	50	12w	yes	no	12w
Guenther	1994	HE		TP	RCT	25	5w	yes	no	no
Eksioglu	2007	HE	amitriptyline	TP	RCT	50	8w	yes	yes	2m
Fioravanti	2007	TT		TP	RCT	80	12d	yes	yes	16w
Brockow	2007	TT	rehabilitation	TP	RCT	139	3w	yes	yes	6m

AP: acupuncture; EAP: electroacupuncture; BT: balneotherapy; ThT: thalassotherapy; HE: hydroelectric therapy; TT: thermotherapy.

^oTP other therapies or "usual care" or "treatment as usual"; PL placebo or no treatment group or sham therapy; *effectiveness and effectiveness vs. comparator are evaluated at least on pain parameters; [§]randomised control trial (RCT), case control trial (CCT).

The severely deficient patients did not show any improvement in symptoms. Matthana (140) conducted a prospective cohort study aimed at defining the relationship between vitamin D deficiency and FM in 100 female patients, 61 of whom were vitamin D deficient and received vitamin D supplementation. TPC and the revised FIQ scores before and after treatment showed that only 42 women showed a significant improvement, which was more significant when their blood levels exceeded 50 ng/mL.

Discussion

FM is a common disorder characterised by a wide range of symptoms whose pathogenesis is still relatively unclear. Although no definite therapy is known, some effective treatments are available and recommended for disease management (3-5, 141, 142). The non-pharmacological approach is particularly interesting because, as pointed out by a number of authors, pharmacological therapy is often unsatisfactory. Conse-

quently, bearing in mind that optimal treatment requires a multidisciplinary approach, various non-pharmacological treatments have been recommended as adjuncts to pharmacological treatment.

Non-pharmacological (particularly CAM) treatments have been welcomed by the general public over the last decades (and are slowly gaining greater acceptance among scientists and researchers) because they are perceived as being more natural and having fewer adverse effects. Slowly recognising the merit of some CAM therapy agents, the FDA has also recently proposed guidance for industry on CAM products (143).

However, the suggested treatments are many and very different from each other, and this makes it very difficult to evaluate them. Some have been widely studied and the available data suggest a certain efficacy, whereas others have only been described anecdotally or their initially promising results have not been supported by subsequent studies (Tables III-VII). Furthermore,

expert opinions vary and there is still no form of official consensus.

In an attempt to understand how different authors have approached the subject, we analysed some reviews (26, 142, 144) and systematic reviews (27-29, 33, 145, 146) and found that their conclusions concerning the efficacy of CAM in treating FM are often conflicting.

We believe that the first problem is the role and competence of the authors themselves insofar as they may be rheumatologists, physiatrists, psychologists, epidemiologists or other specialists, but it is not clear whether they are experts in managing FM or whether they really know CAM treatments.

Another potential bias comes from what they intend to demonstrate with their studies or systematic reviews, and whether their data analyses are always independent and impartial.

Systematic reviews have used different methods to analyse and rate the quality of the studies, particularly in the case of RCTs, but we believe that assessing the results of pharmacologi-

Table IV. Biofeedback, manual therapy, body-mind technique.

First author	Year	CAM	Combined therapy	Control group ^o	Type of study [§]	Number of patients	Duration	Effectiveness* (only for depressive symptoms)	Effectiveness vs. comparator*	Follow-up
Ferraccioli	1987	BFB		PL	CCT	12	7w	yes	yes	6m
Buckelew	1998	BFB	relaxation + exercise	TP + PL	RCT	119	6w-2y	yes	yes	2y
Van Santen	2002	BFB		TP + PL	RCT	143	24w	no	no	no
Babu	2007	BFB		PL	RCT	30	6d	yes	yes	no
Hassett	2007	BFB			open	12	10w	yes		3m
Brattberg	1999	MG		PL	RCT	48	10w	yes	yes	6m
Ekici	2009	MG		TP	RCT	50	5w	yes	no	no
Sunshine	1996	MG		PL	RCT	30	5w	yes	yes	no
Field	2002	MG		TP	RCT	24	5w	yes	yes	no
Alnigenis	2001	MG		PL	RCT	37	4w	no	no	28w
Blunt	1967	CP	stretching + soft tissue therapy	TP	RCT	21	4w	yes	no	no
Panton	2009	CP	resistance training	TP	RCT	21	16w	yes	no	no
Gamber	2002	OP		TP	RCT	24	6m	yes	yes	no
Kaplan	1993	MT			open	77	10w	yes		no
Sephton	2007	MT		PL	RCT	91	8w	yes	yes	2m
Astin	2003	MT	Qigong	TP	RCT	128	8w	yes	no	24w
Keel	1998	Integrated group therapy	CBT + physical exercise + relaxation + information	TP	RCT	32	15w	yes	yes	3m
Rucco	1995	AT		TP	RCT	53	16w	yes	no	6m
Fors	2002	GI		TP+PL	RCT	55	4w	yes	yes	no
Menzies	2006	GI	usual care	PL	RCT	48	6w	yes	yes	10w
Mannerkorpi	2004	BAT	Qigong	PL	RCT	36	3m	no	no	no
Kendall	2000	BAT		TP	RCT	20	20w	no	no	18m
Hsu	2010	BAT		PL	RCT	45	3w	yes	yes	6m
Bennett	1996	Group therapy	various	PL	CCT	133	6m	yes	yes	2y

BFB: biofeedback; MG: massage; CP: chiropractic; OP: osteopathy; AT: autogenic training; GI: guided imagery; MT: meditation; CBT: cognitive-behavioural therapy; BAT: body awareness technique.

^oTP other therapies or "usual care" or "treatment as usual"; PL placebo or no treatment group or sham therapy; *effectiveness and effectiveness vs. comparator are evaluated at least on pain parameters; [§]randomised control trial (RCT), case control trial (CCT).

cal and non-pharmacological treatments is methodologically different. Furthermore, the reviewed studies are not homogeneous, frequently have different outcome measures, and the criteria used to determine their inclusion or exclusion are often arbitrary: for example, the EULAR recommendations (3) were based on expert opinion, changes in pain were only assessed by means of VAS and function by the FIQ, and no conclusions were reached concerning CAM treatments. In an attempt to overcome this, the OMERACT 9 workshop (147) sought to establish a consensus on core domain for assessment in FM studies, identifying specific key domains, and proposed a multidimensional core set of symptoms for evaluating FM in clinical trials.

Another problem is the diagnosis of FM

because it is not always clear whether it always refers to a defined illness, or whether FM study groups are real or as homogenous as they should be. Did all of the studies recruit patients strictly in accordance with the universally recognised classification or diagnostic criteria (148)? For example, Porter *et al.* (27) systematically reviewed CAM treatments for FM and chronic fatigue syndrome, but drew their conclusions without specifying the differences between the two diseases.

Other methodological obstacles highlighted by most reviews are the lack of established placebo procedures (or sham treatment or control groups), difficulties in blinding, short or non-existent follow-ups, unclear randomisation procedures, treatments that differ greatly between individuals, and inter- and

intra-operator differences. Finally, it has to be remembered that negative results are less likely to be published and, given the heterogeneous nature of FM, that the lack of clinical effectiveness of a single therapeutic approach is not only understandable but can be expected.

Some systematic reviews have come to different conclusions: Porter *et al.* (27) found both AP and MT promising, but had nothing precise to say about BT, whereas Baranowsky *et al.* (28) concluded that BT and HT were supported by the best evidence, mindfulness MT led to positive results, and that the evidence concerning AP was equivocal. Terhorst *et al.* (29) concluded that BT, mind-body and AP trials all showed evidence of effectiveness, whereas, very recently, Langhorst *et al.* (33) strongly recommended meditative movement therapies

Table V. Magnet therapy, energy and movement therapy.

First author	Year	CAM	Combined therapy	Control group ^o	Type of study [§]	Number of patients	Duration	Effectiveness*	Effectiveness vs. comparator*	Follow-up
Colbert	1999	MF		PL	RCT	25	16w	yes	yes	no
Alfano	2001	MF		PL	RCT	56	6m	yes	no	no
Shupak	2006	MF		PL	RCT	18	30m	yes	yes	no
Thomas	2007	MF		PL	RCT	17	1w	yes	yes	no
Sutbeyaz	2009	MF		PL	RCT	56	3w	yes	yes	12w
Chen	2006	QG			open	10	3w	yes		3m
Haak	2008	QG		PL	RCT	57	7w	yes	yes	4m
Linch	2012	QG		PL	RCT	100	8w	yes	yes	6m
Taggart	2003	TC			open	39	6w	yes		no
Wang	2010	TC		TP	RCT	66	12w	yes	yes	24w
Jones	2012	TC		PL	RCT	101	12w	yes	yes	no
Romero-Zurita	2012	TC			open	32	28w	yes		no
Assefi	2008	RK		PL	RCT	100	8w	no	no	no
Stiller	2006	TheT		TP	RCT	42	–	yes	yes	no
Da Silva	2007	YO		TP	RCT	40	8w	yes	yes	4-6w
Curtis	2011	YO			open	22	8w	yes		no
Carson	2012	YO		PL	RCT	39	8w	yes	yes	3m
Carbonell-Baeza	2010	BD		PL	CCT	59	3m	yes	yes	no
Altan	2009	PLT		TP	RCT	50	12w	yes	yes	24w

MF: magnetic field; QG: Qigong; TC: Tai Chi; RK: Reiki; TheT: therapeutic touch; YO: yoga; BD: Biodanza; PLT: Pilates.

^oTP other therapies or “usual care” or “treatment as usual”; PL placebo or no treatment group or sham therapy; *effectiveness and effectiveness vs. comparator are evaluated at least on pain parameters; [§]randomised control trial (RCT), case control trial (CCT)

Table VI. Dietotherapy, dietary supplements.

First author	Year	CAM	Combined therapy	Control group ^o	Type of study [§]	Number of patients	Duration	Effectiveness*	Effectiveness vs. comparator*	Follow-up
Michalsen	2005	DT			open	35	2m	no		no
Donaldson	2001	DT			open	30	2m	yes		7m
Azad	2000	DT		TP	RCT	78	6w	yes	no	no
Kaartinen	2000	DT		PL	CCT	33	3m	yes	yes	no
Tavoni	1987	SA		PL	RCT	34	15d	yes	yes	no
Jacobsen	1991	SA		PL	CCT	44	6w	yes	yes	no
Di Benedetto	1993	SA		TP	RCT	15	6w	yes	yes	no
Grassetto	1994	SA			open	47	6w	yes		no
Volkman	1997	SA		PL	CCT	34	10d	no	no	no
Ianniello	1994	SA		TP	CCT	20	4w	yes	yes	no
Tavoni	1998	SA		PL	RCT	30	15d	yes	yes	no
Abraham	1992	MAG	super malic		open	15	8w	yes		no
Russell	1995	MAG	super malic	PL	RCT/open	24	6m	no/yes	no	no
Bagis	2012	MAG		TP	CCT	60	8w	yes	no	no
Wahner-Rodler	2008	SO		PL	RCT	50	6w	no	no	no
Caruso	1990	5HTP		PL	CCT	50	3w	yes	yes	no
Sarzi	1992	5HTP			open	50	3w	yes		no
Citera	2000	ML			open	21	4w	yes		no
Hussain	2011	ML	fluoxetine	TP	RCT	101	8w	yes	no	no
Edwards	2000	AC		PL	RCT	12	12w	no	no	no
Nieddu	2007	DS		PL	RCT	40	6m	yes	yes	no
Rossini	2007	LAC		PL	RCT	102	10w	yes	yes	4w
Merchant	2000	CP			open	18	2m	yes		no
Merchant	2001	CP		PL	RCT	55	2-3m	yes	yes	no

DT: dietotherapy; SA: S-adenosylmethionine; MAG: magnesium; SO: soy; 5HTP: 5-hydroxytryptophan; ML: melatonin; AC: Anthocyanidins; DS: Deutrosulfazyme; LAC: L-acetyl-carnitine; CP: chlorella pyrenoidosa.

^oTP other therapies or “usual care” or “treatment as usual”; PL placebo or no treatment group or sham therapy; *effectiveness and effectiveness vs. comparator are evaluated at least on pain parameters; [§]randomised control trial (RCT), case control trial (CCT).

(Qigong, Tai Chi and Yoga), but only stated that AP can be considered.

The potential therapeutic properties of HO, dietary supplementation, BFB, BAT and other interventions are some-

times acknowledged and other times denied. In their review of oral and topical CAM treatments De Silva *et al.* (145) stated that, in most cases, there is no RCT-based evidence indicating that

they are efficacious, whereas a recent overview of systematic reviews by Terry *et al.* (149) concluded that there is some evidence that AP, homoeopathy, HT and MG (but not CP) may be beneficial.

Table VII. Homoeopathy, miscellanea.

First author	Year	CAM	Combined therapy	Control group ^o	Type of study ^s	Number of patients	Duration	Effectiveness*	Effectiveness vs. comparator*	Follow-up
Fisher	1986	HO		PL	CCT	24	3m	yes	yes	no
Fisher	1989	HO		PL	RCT	30	2m	yes	yes	no
Gemmel	1991	HO			open	3	2m	no		no
Bell	2004	HO		PL	RCT	62	4m	yes	yes	no
Relton	2009	HO		PL	RCT	47	22w	yes	yes	no
Rutledge	2007	ART	exercise	PL	RCT	43	12w	no	no	no
Chesky	1997	MC	vibration	PL	RCT	26	1 time	yes	no	no
Alentorn-Geli	2008	VB	exercise	TP	RCT	36	6w	yes	yes	no
Haanen	1991	HY		TP	RCT	40	12w	yes	yes	24w
Castel	2007	HY	suggestions	TP	RCT	45	1 time	yes	no	
Castel	2012	HY	CBT	TP	RCT	93	14w	yes	yes	6m
			Pharma-therapy							
Fiz	2011	CN		PL	CCT	56	2h	yes	yes	no
McCarty	1994	CAP		PL	RCT	45	4w	no	no	no
Arvold	2009	VD		PL	RCT	100	8w	yes	yes	1y
Matthana	2011	VD			open	61	1 time	yes		no

HO: homoeopathy; ART: aromatherapy; MC: music therapy; VB: vibration; HY: hypnotherapy; CBT: cognitive-behavioural therapy; CN: cannabis; CAP: capsaicin; VD: vitamin D.

^oTP other therapies or "usual care" or "treatment as usual"; PL placebo or no treatment group or sham therapy; *effectiveness and effectiveness vs. comparator are evaluated at least on pain parameters; ^srandomised control trial (RCT), case control trial (CCT).

The case of AP is exemplary insofar as the findings of many systematic reviews are radically different (as noted above). Mayhew *et al.* (30) concluded that it cannot be recommended for FM patients, and Martin-Sanchez *et al.* (32) found that there was no evidence demonstrating its superiority over placebo, but a consensus document from the US National Institutes of Health (NIH) stated that it may be useful as an adjunct or acceptable as an alternative treatment in a comprehensive management programme for FM patients (12). Lastly, Langhorst *et al.* initially claimed that it cannot be recommended (31) but subsequently stated that it can be considered for the management of patients with FM (33).

It is therefore clear that authors come to different conclusions depending on the results of their research and their previous thinking about a specific treatment. The aim of this review is not to demonstrate the unquestionable efficacy of a specific CAM treatment, but to suggest a different clinical approach to "real life" everyday practice by offering a general overview and proposing a different way of analysing the available literature.

Sarac *et al.* (144) pointed out that it is important to maintain an open mind towards CAM treatments when integrating clinical practice as it is known that

many traditional and more orthodox interventions are ineffective. In our own everyday experience, many patients indicate the beneficial effects of some CAM treatments, and we cannot believe that this is only due to a placebo effect.

This view is supported, for example, by a very recent meta-analysis of RCTs of AP for chronic pain by Vickers *et al.* (150), who concluded that AP was superior to both sham and no AP control treatments for each pain condition, thus suggesting that it is more than a placebo.

Another question is the multidimensional nature of FM, which has led many authors to suggest that FM patients should be managed by a multidisciplinary team using with a coordinated and comprehensive therapeutic approach (144, 151-156). Furthermore, the EULAR recommendations (3) indicates the use of a combination of pharmacological and non-pharmacological treatments tailored on the basis of individual pain intensity, function, and associated features such as depression, fatigue and sleep disturbance, and agreed in discussion with the patient. Finally, it needs to be borne in mind that the cost of treating FM has considerably increased over the last ten years: annual direct costs now range from \$ 4,500 to \$ 7,500 per patient (157). The

lack of validated therapeutic protocols and the generally poor response to all treatments may explain the frequent use of physiotherapy or CAM treatments, whose cost is almost always borne by the individual patient rather than the public health system. For this reason, it is important to assess the cost-benefit ratios of conventional and CAM therapies.

Conclusion

The world of unconventional medicine is highly variegated, and this is particularly true of CAM. Although still often neglected by scientific medicine, many patients are enthusiastic about the range of interventions available, and even the FDA is slowly recognising the merits of some CAM therapeutic agents. It is therefore likely that CAM treatments will continue to represent a resource in the future because, although there is a need for further safety and long-term efficacy studies, it is no longer possible to dismiss them as useless or ineffective. The therapeutic challenge raised by the inefficacy of many traditional interventions for FM has made resorting to the use of CAM and other non-pharmacological treatments, which should therefore be integrated into clinical practice with an open mind.

The aim of this wide-ranging review of the available literature was to iden-

tify and analyse the type of CAM treatments used by FM patients and their efficacy. Our evaluations took account of the quality and duration of the studies and follow-up periods, the presence of a control group, and the appropriateness of the randomisation and placebo procedures, bearing in mind that patients consider pain the most important of the many symptoms of FM (158, 159). Finally, we would like to make some clinical recommendations for everyday practice based on published findings and our own clinical experience. In line with the main guidelines and recommendations for the management of FM, CAM and other non-pharmacological treatments should be used in a multidisciplinary manner. Patient information and education are fundamental: it is important to explain the nature of the disease and avoid the suggestion that the symptoms are “in your head” because patients must understand mind-body relationships in order to better agree a therapeutic programme. As Hassett *et al.* (26) have pointed out, any multidimensional programme must include exercise, special attention to psychological aspects, regaining function, sleep hygiene and stress management. The absence of clear information concerning timing and follow-up prevents us from drawing any conclusions about the most appropriate duration of non-pharmacological CAM treatment but, if welcomed by a patient, we suggest periodic repetitions while monitoring the patient's symptoms and status. The quality of CAM providers is essential and adequate knowledge of CAM techniques is desirable for any physician dedicated to managing FM; it is essential to avoid any uncritical acceptance of CAM in the absence of any benefit for the patient.

List of abbreviations used

AIMS 1: Abnormal Involuntary Movement Scale
AM: Alternative medicine
AMT: Amitriptyline
AP: Acupuncture
AT: Autogenic training
BAT: Body awareness technique
BFB: Biofeedback
BT: Balneotherapy

CAM: Complementary and Alternative Medicine
CBT: Cognitive-behavioural Therapy
CCT: Case Control Trial
CP: Chiropractic
EAP: Electroacupuncture
EULAR: European League Against Rheumatism
FDA: Food & Drug Administration
FIQ: Fibromyalgia Impact Questionnaire
FM: Fibromyalgia
GI: Guided imagery
HAQ: Health Assessment Questionnaire
HO: Homoeopathy
HT: Hydrotherapy
LAC: L-acetyl-carnitine
MAG: Magnesium
MG: Massage
ML: Melatonin
MPI: Multidimensional Pain Inventory
MT: Meditation
PMR: Progressive Muscle Relaxation
RCT: Randomised control trial
SAME: S-adenosylmethionine
SF-36: 36-items Short Form Healthy Survey
TP: Tender Point
TPC: Tender Point Count
VAS: Visual Analogue Scale

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