Complementary and Integrative Methods in Fibromyalgia

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Educational Gaps

1. Clinicians should recognize that chronic widespread musculoskeletal pain without laboratory or physical examination evidence of joint or muscle inflammation is a common problem in the pediatric population.
2. Pediatricians should be aware of safe and likely effective lifestyle and complementary and integrative therapies that can be used for children with chronic widespread pain and fibromyalgia.

Objectives After completing this article, readers should be able to:

1. Understand the definition and epidemiology of fibromyalgia in pediatric populations.
2. Articulate a framework to assess the desirability of a complementary therapy based on safety and efficacy and assess the utility of the most common complementary therapies used for fibromyalgia.
3. Discuss the rationale for seeking complementary and alternative therapies in patients with fibromyalgia.

CASE

Maria is an 11-year old girl brought to the pediatrician by her mother who is concerned about her daughter feeling fatigued and experiencing pain throughout her body for the previous 8 months. The pain involves multiple joints, waxes and wanes, and is not associated with joint swelling. The pain has no accentuation in the morning. Maria also says she has pain in her thighs and upper arms in the muscle groups. She has had no fevers, weight loss, rashes, or oral ulcers. Because of her symptoms, she has missed 14 days of school in the current school year. She says she has less energy, sleeps more than in the past, and has had to stop playing softball.

On examination, her vital signs are normal. She is well nourished and in no distress. She has a subdued affect. Aside from tenderness to palpation and pain on passive but full range of motion of the knees, ankles, wrists, and elbows, the examination findings are normal. Results of screening for clinical depression

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ABBREVIATIONS

ACR	American College of Rheumatology
CAM	complementary and alternative medicine
5-HTP	5-hydroxytryptophan
SAM-e	S-adenosylmethionine

were negative. The results of laboratory testing for evidence of inflammation, organ dysfunction, and autoimmune disease were also negative.

DEFINITION

Fibromyalgia is a common syndrome of unknown origin characterized by widespread pain and muscle tenderness often accompanied by chronic fatigue, sleep disturbance, and depressed mood. (1) The diagnostic label *fibromyalgia* is not universally used in pediatric contexts; some use the term *amplified musculoskeletal pain* to describe a larger category of pain syndromes. In this classification, fibromyalgia is then categorized as belonging to the subset of *diffuse idiopathic musculoskeletal pain* in contrast to *localized idiopathic musculoskeletal pain*, which would include complex regional pain syndrome. (2)

EPIDEMIOLOGY

Fibromyalgia affects 2% of the adult US population (approximately 6 million people). (3)(4) Chronic widespread musculoskeletal pain affects 6% to 7% of school-aged children, (5) with most studies finding greater prevalence in females. (6)

PATHOGENESIS

No single origin has been confirmed as the cause of fibromyalgia. The most frequently cited theory to explain the manifestations of fibromyalgia is that of a neuroendocrine-mediated syndrome that involves a central pain processing system, (7) resulting in hyperalgesia (exaggerated perception of painful stimuli) and allodynia (the perception of minor stimuli as painful). (7) Some investigators (8)(9)(10) concentrate on possible deficiencies in the hypothalamic-pituitary-adrenal axis. Others speculate that hormonal fluctuations and sympathetic nervous system dysfunction lead to fibromyalgia, (8) whereas some literature describes hormone and neuropeptide-mediated pain signaling and perception. (11)

CLINICAL ASPECTS

Clinical diagnosis in adults is most often based on the 1990 American College of Rheumatology (ACR) criteria (1), which includes the following:

- Continuous presence of widespread musculoskeletal pain (on the left and right sides of the body and above and below the waist) of undefined cause for 3 months or more.
- Tenderness on pressure in 11 of 18 tender point sites on digital palpation, which are 9 bilateral pairs under the

lower sternomastoid muscle, the second costochondral junction, medial fat pad of the knee, insertion of the suboccipital muscle, upper midtrapezius muscle, supraspinatus muscle, and outer upper quadrant of the buttock. (1)

Yunus and Masi (12) have defined juvenile primary fibromyalgia syndrome as generalized musculoskeletal aching at 3 or more sites for 3 months or more, 5 tender points (in contrast to the 11 tender points in adults), normal rheumatologic serologic test results, and at least 3 non-specific symptoms (of a list of 10). Many clinicians, however, use the 1990 ACR adult criteria despite these not being validated in children. (6)

The 2010 ACR criteria (13) focus more on global symptoms rather than individual tender points and can be used in adolescents. In the 2010 ACR criteria, the manual tender point examination is eliminated, and a widespread pain index and symptom severity score are incorporated. The widespread pain index is a count of areas of pain throughout the body (19 possible), whereas the symptom severity score assesses the severity of fatigue, waking unrefreshed, cognitive symptoms, and other somatic symptoms. (13)

We offer a practical pediatric definition for fibromyalgia that consists of a normal rheumatologic workup with predominant symptoms of widespread pain and symptoms consistent with the 2010 ACR diagnostic criteria for fibromyalgia (13) because this eliminates the need for a manual tender point examination, which can be performed with varying consistency.

Because of its association with high levels of physical impairment, school absences, anxiety, and depression in adolescents, fibromyalgia can have a debilitating effect on quality of life. (5) Kashikar-Zuck et al (5) recently reported that more than 80% of individuals diagnosed as having juvenile fibromyalgia continued to experience symptoms in adulthood, with 51% meeting ACR diagnostic criteria as adults.

The American Pain Society recommends that the diagnosis of juvenile primary fibromyalgia syndrome be made only after a developmental assessment of the child and parents, including behavioral observation, pain history, psychosocial distress, and functional status, (14) to rule out other potential causes of widespread chronic pain.

MANAGEMENT

No randomized trials have assessed specific complementary and alternative medicine (CAM) therapies for the treatment of pediatric fibromyalgia. Despite the lack of strong evidence-based therapies, the practicing clinician can gain insights from data from adult trials and consider therapeutic options with a favorable risk-benefit ratio.

As is true of many conditions that are poorly understood and often resistant to conventional treatments, fibromyalgia often compels patients to seek CAM therapies and practitioners. (15)(16)(17) The definition of CAM itself is nebulous; the National Center for Complementary and Alternative Medicine at the National Institutes of Health notes, “While the terms are often used to mean the array of health care approaches with a history of use or origins outside of mainstream medicine, they are actually hard to define and may mean different things to different people.” Furthermore, integrative medicine is operationally defined as combining conventional treatments with CAM interventions for which there is “emerging evidence that some of the perceived benefits are real or meaningful.” (18)

A survey of 110 patients with juvenile fibromyalgia at a pediatric rheumatology clinic found the most frequently used CAM therapies (>10 patients reporting) were vitamins or herbal remedies and massage. Most patients perceived these treatments to be helpful. (19)

Cohen et al (20) developed criteria to assess the appropriateness of a particular CAM intervention. Therapies that are safe and effective are recommended, whereas those that are unsafe or ineffective are discouraged. Effective risky therapies should be monitored (ie, assessed regularly for safety and clinical course), and ineffective risky therapies should be avoided. Areas where either (but not both) safety and efficacy are questioned should be approached with caution. A rational expectation of benefit, based on weak clinical trial evidence or biological plausibility, may be desirable in cases where more evidence-based treatment options are unavailable or undesirable or when patient preference drives the consideration of a particular intervention. In most cases, it is recommended that the treatment of pediatric fibromyalgia begin with nonpharmacologic means, including education, exercise, and psychological therapies, with secondary options of muscle relaxants, analgesics, or tricyclic antidepressants. (21)(22)

The following therapeutic choices will include those that can be classified as CAM, (18) as well as other types of interventions that are not necessarily CAM but are in prevalent use (such as lifestyle interventions) by CAM and integrative medicine practitioners. Not every intervention that has been studied in fibromyalgia is included. We have attempted to focus on safe and low-impact interventions that can be readily used by pediatric patients.

Furthermore, it is essential to assess and address factors that affect pain perception, such as emotional stress, parental psychological health, and family interactions. A number of these and other environmental influences can affect the course of pain syndromes in children. (23)

INITIAL RECOMMENDATIONS

Lifestyle change, including exercise and stress reduction interventions, are recommended as initial therapies because a variety of benefits can be obtained, from symptomatic relief to reduced risk of many chronic conditions. (24) Furthermore, lifestyle changes can be empowering to patients, allowing them to experience influence over a condition that is all too often debilitating.

Exercise

Moderate low-impact aerobic exercise has been found to improve physical function, mood, symptom severity, and self-efficacy in patients with fibromyalgia, (25) as well as increase energy in patients with unexplained fatigue. (26) Other trials have confirmed the benefits of low-impact aerobic exercise and muscle strengthening for fibromyalgia. (27)(28) Pain, the most characteristic symptom of fibromyalgia, was reduced in persons exercising at low to moderate intensity 2 or 3 times per week with positive effects on depressed mood, quality of life, and physical fitness. (29) Aerobic exercise, performed twice weekly for 8 months, can alleviate symptoms and demonstrate anti-inflammatory effects. (30)

A systematic review has confirmed that among myriad treatments proposed for fibromyalgia, exercise, specifically mild- to moderate-intensity aerobic and weight-bearing exercise, has consistently been effective in alleviating pain, fatigue, and depression and improving health-related quality of life in persons with fibromyalgia. (31)

Mind-Body Therapies

Among the more promising interventions for fibromyalgia are mind-body therapies that address psychological and somatic symptoms. (32) The National Institutes of Health defines mind-body therapies as “interventions that use a variety of techniques designed to facilitate the mind’s capacity to affect bodily function and symptoms.” (33) In adults, significant benefits of Tai Chi, a Chinese mind-body practice that involves meditation, deep breathing, and slow, gentle movements, (34) have been demonstrated in individuals with fibromyalgia. A number of trials have assessed various forms of mindfulness meditation, with promising results in outcomes that range from pain to physical function to tender points. (35)(36)(37)(38) Sibinga et al (39) have developed an 8-week mindfulness-based stress reduction program tailored to urban youth, involving didactic instruction, experiential meditation instruction, and group discussions.

Diet and Obesity

It is unclear whether obesity is directly associated with the development or exacerbation of fibromyalgia symptoms.

Weight loss is associated with improvement in fibromyalgia symptoms and quality of life, but this association may be confounded by the effects of exercise. Given the increased prevalence of childhood obesity, it is prudent to address obesity in the clinical setting to reduce lifetime risk of chronic disease. One survey found that 42% of patients report symptom exacerbation associated with the intake of particular foods. (40) Some believe that systematic elimination diets may improve pain perception, stiffness, mood, and fatigue, although clinical trial data supporting this approach are weak. (41)

SECONDARY RECOMMENDATIONS

The following approaches should generally be recommended after starting with initial lifestyle change. These approaches involve some type of therapeutic intervention, whether pharmacologic (ie, nutritional supplementation) or practitioner dependent (massage and acupuncture), and thus have long-term financial considerations associated with them.

Nutritional Supplementation

One survey found that 68% of patients with fibromyalgia tried nutritional supplements to control fibromyalgia symptoms, (42) although no specific dietary supplement is consistently effective in controlling fibromyalgia symptoms. (41) The ω 3 fatty acids have mild anti-inflammatory properties, decreasing synthesis of thromboxane A₂ from arachidonic acid. Intake of ω 3 fatty acids is inversely associated with major depression, (43)(44) a strong comorbidity with chronic fatigue syndrome and fibromyalgia. (45) Furthermore, serum levels of the ω 3 fatty acid eicosapentaenoic acid are significantly lower in patients with chronic fatigue syndrome than in healthy controls. (46) Supplementation with ω 3 fatty acid has some evidence of efficacy in treating a number of non-specific symptoms associated with fibromyalgia, including fatigue, arthralgias, (47) depression, (48) and anxiety. (49)

Selected research has focused on neurotransmitter modulation as a therapeutic intervention. Preliminary research suggests a possible benefit of 5-hydroxytryptophan (5-HTP), a precursor that can increase serotonin synthesis. (50) In adults, 100 mg given 3 times daily has produced benefit. Furthermore, S-adenosylmethionine (SAM-e) is a naturally occurring substance produced from homocysteine and 5-methylene tetrahydrofolate, related to vitamin B₁₂ and folate synthesis, and associated with serotonin turnover. Two small randomized trials have found benefit of SAM-e supplementation in tender points, pain perception, and fatigue when dosed at 800 mg/d in adults. (51) Acetyl-L-carnitine, structurally related to acetylcholine, is a precursor

to acetyl coenzyme A. One randomized clinical trial found a reduction in tender points, pain perception, and depression at a dose of 500 mg 2 or 3 times daily in adults. (52) Both 5-HTP and SAM-e should not be used in conjunction with other serotonergic antidepressants. Small clinical trials have found no adverse effects of 5-HTP (53)(54)(55) and SAM-e (56) for other conditions in children. Dosing should be proportionally lower than adult doses.

We suggest ω 3 fatty acids as an initial recommendation, with 5-HTP and SAM-e as secondary choices. The ω 3 fatty acids have more potential benefits in other areas related to chronic widespread pain and fibromyalgia, whereas 5-HTP and SAM-E essentially work as serotonergic antidepressants. Although there are no major documented adverse effects associated with 5-HTP and SAM-E, they are theoretically more risky than ω 3 fatty acids, which are generally recognized as safe (as major constituents of foods, fatty fish in particular). Furthermore, dosing of SAM-e and 5-HTP is not well established in pediatric populations.

Massage Therapy

Massage therapy has produced short-term beneficial effects in treating fibromyalgia symptoms in randomized trials. (57) Despite the lack of a complete understanding of the mechanisms, massage clearly improves chronic pain conditions in adults and children. (58)(59) Massage therapy has been evaluated and found efficacious as an adjunct treatment for pain secondary to cancer, (60)(61)(62) low back pain, (63) procedural pain, (64) and rheumatoid arthritis. (65) In a randomized, open-label clinical trial, a series of classic Swedish massage therapy sessions were found to be as effective as conventional analgesia for chronic rheumatic pain. (65)

Acupuncture

Acupuncture (66) and sham acupuncture (67) symptomatically improve pain associated with fibromyalgia. Acupuncture (performed by licensed practitioners) demonstrates minimal risk, (67) reduces anxiety, (68) and may be effective for fatigue (69) in cancer. (70) Many of the higher-quality clinical trials of acupuncture in chronic pain conditions have found significant nonspecific (placebo) effects in addition to relatively modest specific effects of acupuncture needling. (71) Nevertheless, a meta-analysis of 17,922 patients found consistently significant differences between verum (true) and sham acupuncture in a variety of pain conditions. (71) Younger children may be needle averse, and thus a judicious approach to using verum acupuncture in collaboration with highly trained acupuncturists is advisable. As with many CAM interventions, financial cost is a consideration.

Contextual factors and the therapeutic relationship are important factors in the overall effectiveness of a therapy, especially with subjective outcomes, such as in chronic pain syndromes, (72)(73) and perhaps stronger with alternative therapies associated with elaborate rituals and distinct contexts. (74) There is an ethical imperative to provide therapeutic options that are safe and effective for symptomatic relief, with appropriate informed consent, without endorsing approaches that are unsafe or ineffective. (20) There is emerging literature on the psychobiology of the placebo effect, with clinically significant effects demonstrated in a variety of contexts. (74)(75) Intentional use of placebo in clinical practice is routine (76) and has complex ethical implications. (74)

Pharmacotherapy

Three drugs have received Food and Drug Administration approval for treating fibromyalgia in adults, but efficacy is limited (77)(78)(79)(80)(81) and toxicity is a concern. (78)(79)(82) Of note, these drugs (duloxetine, pregabalin, and milnacipran) have been rejected by European regulatory authorities. (80) None of these drugs are approved by the Food and Drug Administration for fibromyalgia in pediatric populations. One 5-year survey of patients from 114 rheumatology practices found a total of 74 different medications used to treat adult fibromyalgia, suggesting that no specific drug or class of drugs is especially useful in fibromyalgia. (83) If nonpharmacologic means are ineffective, inappropriate, or undesirable in a particular case, muscle relaxants, analgesics, or tricyclic antidepressants can be tried. (21)

PROGNOSIS

It is possible to reduce symptom burden and improve the quality of life in children with fibromyalgia. It is advisable to follow-up every 4 to 8 weeks in the initial stages of treatment, with less frequent visits subsequently. There is no strong research evidence indicating the long-term prognosis of any of the interventions discussed in this article. Nevertheless, interventions that are safe and well tolerated can reasonably be tried sequentially or in rational combinations.

CASE REVISITED

For Maria, a graduated exercise program focused on outdoor social activities, involving 5- to 15-minute intervals of low-impact aerobic exercise 3 times weekly, was initially recommended. Most of the time, these activities involved playing in the neighborhood park. These activities were particularly empowering for Maria because she often felt socially isolated because of her chronic pain. She was able

to strengthen friendships with neighborhood children. She usually felt invigorated the day she played at the park and occasionally the following day. However, painful episodes would recur, and Maria would feel dejected that she could not “live a normal life” like her neighborhood friends.

Subsequently, referral for individualized mindfulness training empowered Maria to “live in the moment” and reduce her fear of not being like her friends. Mindfulness training also gave her tools to reduce stress in her daily life. Maria’s mother noticed less behavioral outbursts in the subsequent months. Supplementation with ω 3 fatty acids was recommended at 1 tsp (containing approximately 1 g of eicosapentaenoic acid and docosahexaenoic acid) per day.

Because of her improvement with the CAM therapies, conventional pharmaceuticals, such as amitriptyline, were not needed. During particularly stressful times, flare-ups would occur, but overall Maria found her pain and quality of life generally improved and her symptoms more manageable. In the following years, Maria integrated aerobic exercise and mindfulness knowledge into her life and despite the flare-ups has led an active, productive life.

Summary

- On the basis of expert opinion, juvenile primary fibromyalgia syndrome involves chronic widespread musculoskeletal pain throughout the body, accompanied by fatigue, waking unrefreshed, cognitive symptoms, and other somatic symptoms. (12)(13) A negative rheumatologic workup is necessary before making this diagnosis. (2)(12)
- On the basis of observational studies, children with fibromyalgia often present with debilitating and severe symptoms. (5) Patients should not be dismissed or disregarded because the pathophysiologic cause of their symptoms is unknown. Effective symptomatic treatments can significantly improve quality of life.
- No randomized trials have revealed the efficacy of any individual complementary and alternative medicine intervention in juvenile primary fibromyalgia syndrome, although consideration can be given to the use of adult data modified for children for those therapies considered to be safe.
- On the basis of some research evidence and expert opinion, less invasive interventions are preferred, (6)(21) and those with a favorable benefit-risk ratio, such as graded exercise, (31) mind-body therapies (35)(36)(37)(38), ω 3 fatty acid supplementation, (45) and massage therapy, (57) can initially be recommended.

NOTE: The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Complementary and Alternative Medicine or the National Institutes of Health.

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Parent Resources from the AAP at HealthyChildren.org

- English: <http://www.healthychildren.org/English/health-issues/conditions/treatments/Pages/Complementary-and-Alternative-Medicine.aspx>
- Spanish: <http://www.healthychildren.org/English/health-issues/conditions/treatments/Pages/Complementary-and-Alternative-Medicine.aspx>

PIR Quiz

1. Which of the following is the most frequently cited theory to explain the cause of fibromyalgia?
 - A. Deficiencies in the hypothalamic-pituitary-adrenal axis.
 - B. Hormonal fluctuations.
 - C. Hormone- and neuropeptide-mediated pain signaling and perception.
 - D. Neuroendocrine-mediated syndrome that involves a central pain processing syndrome.
 - E. Sympathetic nervous system dysfunction.
2. In diagnosing fibromyalgia in a 15-year-old girl, which of the following is MOST likely to be identified?
 - A. Knee swelling.
 - B. Positive rheumatologic serologic test results.
 - C. Tenderness on pressure in 11 of 18 tender point sites.
 - D. Unilateral upper extremity stiffness.
 - E. Widespread musculoskeletal pain.
3. Among the following, the intervention that you would recommend to your patient with fibromyalgia as MOST likely to be beneficial is:
 - A. Dietary supplementation.
 - B. Exercise.
 - C. Massage therapy.
 - D. Mindfulness meditation.
 - E. Weight loss.
4. Your patient with fibromyalgia asks about dietary changes that might be beneficial. You recommend that she try eating which of the following foods 2 to 3 times per week?
 - A. Citrus fruits.
 - B. Pecans.
 - C. Salmon.
 - D. Turkey.
 - E. Yellow squash.
5. Your patient with fibromyalgia has been exercising regularly and has modified her diet. She has tried medical massage and acupuncture. Her muscle pain and fatigue have not responded to any of these interventions. Among the following, you are MOST likely to recommend:
 - A. Atypical antidepressant.
 - B. Monoamine oxidase inhibitor.
 - C. Selective serotonin reuptake inhibitor.
 - D. Serotonin-norepinephrine reuptake inhibitor.
 - E. Tricyclic antidepressant.

REQUIREMENTS: Learners can take *Pediatrics in Review* quizzes and claim credit online only at: <http://pedsinreview.org>.

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