

Review article

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Complementary and alternative medicine for rheumatic diseases

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Abstract: The use of complementary and alternative medicine is not uncommonly encountered in our patients. This manuscript reviewed the latest evidence on other modalities in treating rheumatic diseases. Treatments that are found to be helpful for rheumatoid arthritis include herbs, fish oil, and acupuncture. Fish oil, vitamin D, N-acetylcysteine, and cognitive behavior treatments are helpful for systemic lupus erythematosus. Hydrotherapy and massage are potentially beneficial for fibromyalgia patients. Diet supplement is not found to be beneficial for osteoarthritis. CAM modalities will need further studies.

Keywords: alternative, complementary, herbs, acupuncture, rheumatic diseases

Introduction

Medicine can be classified into modern and traditional medicine. Modern medicine is based on the scientific researches with clearly defined underlying philosophy and clinical methods. Traditional medicine is based on beliefs and experiences in different cultures for promotion of physical and mental well-being. It is not universally accepted as being evidence-based.

Complementary and alternative medicine (CAM) may indicate alternative medical systems (e.g., holistic medicine, traditional Chinese medicine (TCM), body-based and manipulative therapies (e.g., chiropractic, massage, reflexology), mind-based interventions and spiritual medicine (e.g., prayer, hypnotherapy, yoga, Tai Chi, Qi Gong), biologically based therapy (e.g., diet

supplement and Herbs), energy therapies (e.g., magnets, Reiki, pulsed electric field), procedures (e.g., acupuncture, colon cleansing, mineral baths, chelation, hydrotherapy), and miscellaneous (e.g., copper bracelets, snake oil, leech therapy, dimethyl sulfoxide, venoms, exercise). A few of them are based on evidence. The manuscript reviewed evidence on CAM in various rheumatic diseases.

Rheumatoid arthritis

Botanical medicine has been used for thousands of years in various cultures. Black cohosh (*Actaea racemosa*) (升麻) have been shown to reduce IL-6, TNF- α , and IFN- γ production. It inhibits the production of proinflammatory cytokines and alters the expression of other biochemical mediators, including nitric oxide and COX-2. *Centella asiatica* (崩大碗) is widely used for treating high blood pressure (BP), enhancing memory, relieving anxiety, and prolonging longevity. It is shown to suppress nitric oxide production. *Urtica dioica* (蕁麻) is demonstrated to inhibit TNF- α , IL-1 β , and nitric oxide. It inhibits maturation of dendritic cells by reducing the expression of CD83+ and CD86+ cells; it is also shown to reduce induction of primary T-cell responses. *Angelica Sinensis* (當歸) is the aqueous extract that significantly inhibits the production of TNF- α and IL-1 β . Licorice (甘草) is demonstrated to inhibit lipopolysaccharide-stimulated nitric oxide, IL-1B, IL-6, and PGE2 production. *Tripterygium wilfordii* (雷公藤) consists of more than 70 constituents, including glycosides and alkaloids. It inhibits the nitric oxide production, suppresses the IL-2 and PGE2 production. Advanced and sophisticated research have demonstrated the possible efficacy of botanical medicine. *Tripterygium wilfordii* is being investigated in clinical trials. [1]

Li et al. studied 32 patients who were divided into the TCM group who received *Ganoderma lucidum* (lingzhi) (4 g) and San Miao San (2.4 g) daily and placebo group. The primary outcome was the number of patients achieving American College of Rheumatology (ACR) 20% response. Secondary outcomes were the changes in the ACR components, plasma levels, and ex-vivo-induced

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cytokines and chemokines and oxidative stress markers. 15% of the TCM group achieved ACR20 when compared with 9.1% of the placebo group ($P > 0.05$). The pain score and patient's global score improved significantly only in the TCM group. [2]

Proudman et al. studied 139 subjects with rheumatoid arthritis of <12 months duration and DMARD-naïve. They received none ($n = 53$) or Omega-3 fats, EPA, and DHA ($n = 86$). All patients received methotrexate, sulphasalazine, and hydroxychloroquine according to an algorithm taking disease activity and side-effects into account. The primary outcome measure was failure of the triple DMARD therapy. It was found that, in the fish oil group, failure of the triple DMARD therapy was lower (HR = 0.28 (95% CI 0.12 to 0.63; $p = 0.002$). The rate of ACR remission was significantly greater in the fish oil group than the control group (HRs = 2.17 (95% CI 1.07 to 4.42; $p = 0.03$). [3]

Tam et al. divided 29 patients with rheumatoid arthritis into three groups namely electro-acupuncture (EA) ($n = 12$), TCA ($n = 10$), Sham acupuncture (Sham) ($n = 7$). At week 10, the pain score remained unchanged in all three groups. The tender joint count significantly reduced for the EA and TCA groups. The physician's global score was significantly reduced for the EA group, and the patient's global score was significantly reduced for the TCA group. [4]

Systemic lupus erythematosus

In Systemic lupus erythematosus (SLE), several diet supplements were investigated for their efficacy, as shown in table 1.

Schoindre et al. studied 170 subjects with SLE whose 25-hydroxy vitamin D (25(OH)D) levels were measured and prospectively followed up for 6 months. It was found that lower 25(OH)D levels were associated with significantly high SLE activity by a SELENA-SLE Disease Activity Index (SLEDAI) score ≥ 6 ($p = 0.02$, with an odd ratio of 0.93 (95%CI (0.873 to 0.989)). [5]

Table 1

	Proposed mechanism	Results
Vitamin D supplement	Increase regulatory T cells and decrease Th17, Th1 and memory B cells.	Lower levels associated with more active disease
Omega3 Fish Oil	IL6, Leukotriene are derived from omega6 fatty oil	Significant decline in systemic lupus activity measure- Revised (SLAM-R)
N-acetylcysteine	Regulates T cell through mitochondrial transmembrane potential by glutathione (precursor of NAC)	Significantly reduce SLEDAI

Not found to be helpful: other vitamins, DHEA supplement

In Duffy's study, 52 SLE patients were divided into four groups: (1) 3 g Omega-3 polyunsaturated fatty acids (MaxEPA) and 3 mg copper, (2) 3 g MaxEPA and placebo copper, (3) 3 mg copper and placebo fish oil, and (4) both placebo capsules. A significant decline in the Systemic Lupus Activity Measure - Revised (SLAM-R) score from 6.12 to 4.69 ($p < 0.05$) was observed in the group taking fish oil compared with placebo. [6]

In Lai's study, 36 SLE patients were recruited. They received daily placebo or 1.2 g, 2.4 g, or 4.8 g of N-acetylcysteine. It was shown that 2.4 g and 4.8 g NAC reduced the SLEDAI score after 1 month ($P = 0.0007$), 2 months ($P = 0.0009$), 3 months ($P = 0.0030$), and 4 months ($P = 0.0046$). [7]

Mood disorders affect up to 65% of the SLE patients over their lifetime, and the rate of psychiatric disorders are higher. Mind-body intervention is commonly used and focuses on reducing pain, stress, anxiety, fatigue, and modify distorted or unhelpful thinking styles. These therapies include cognitive behavioral therapy, meditation, and group psycho-educational program.

Fibromyalgia

In Terry et al.'s review, five systemic reviews evaluating the effectiveness of homeopathy, chiropractic, acupuncture, hydrotherapy, and massage were studied. The authors suggested that acupuncture, chiropractic should not be recommended for inconsistent findings and lack of evidence. Homeopathy was shown to be favorable in four trials over control conditions. However, no conclusion could be made because of the paucity and disappointing quality of the available randomized controlled trials. [8]

There is moderate evidence that hydrotherapy has short-term beneficial effects in pain reduction and improvement of quality of life. Massage therapy (combination of Swedish massage and Shiatsu) has also been shown to be beneficial for fibromyalgia, but rigorous

research is needed to confirm and ascertain its safety and effectiveness.

Osteoarthritis

In Bannuru et al's network meta-analysis in examining the efficacy of treatments of primary Osteoarthritis (OA) knee, it showed that naproxen, ibuprofen, diclofenac, intra-articular hyaluronic acid, and intra-articular corticosteroids were statistically significantly superior to acetaminophen for pain reduction. Functionally, intra-articular hyaluronic acid was statistically significantly better than intra-articular placebo and intra-articular corticosteroids. Celecoxib, of note, is not superior to acetaminophen. [9]

Hochberg et al. studied 606 subjects with Kellgren and Lawrence grades 2–3 knee OA and moderate to severe pain. They were divided into two groups who received either 400 mg chondroitin sulphate plus 500 mg glucosamine three times a day, or 200 mg celecoxib every day for 6 months. The primary outcome was the mean decrease in Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain from baseline to 6 months. Secondary outcomes include WOMAC function and stiffness, visual analog scale for pain, presence of joint swelling/effusion, rescue medications consumption, and Outcome Measures in Rheumatology Clinical Trials and Osteoarthritis Research Society International (OMERACT-OARSI) criteria. No differences were found for stiffness, functional limitations, joint swelling, and effusion after 6 months of treatment. [10]

Among older women with OA (N = 82), Tai Chi Chuan increased endurance during knee flexion and extension and bone mineral density, while also decreasing fear of falling. [11] Tai Chi Chuan also caused significant improvements in pain related to knee OA, physical functioning, and gait following a six-week Tai Chi intervention (N = 40). The study suggested Tai Chi has beneficial effects for gait kinematics (such as stride length) among older adults. [12]

Recommendations from the American College of Rheumatology (ACR)

The ACR recognizes the interest in CAM modalities. It supports rigorous scientific evaluation of all modalities and the integration of those modalities that are proven to be safe and effective by scientific clinical trials. The ACR advises caution for those not studied scientifically. In the absence of such rigorous clinical trials, the ACR

recommends advising patients to be cautious of potential harm of unproven treatments.

Summary

Treatments that are found to be helpful for rheumatoid arthritis include herbs, fish oil, and acupuncture. Fish oil, vitamin D, N-acetylcysteine, and cognitive behavior treatments are helpful for systemic lupus erythematosus. Hydrotherapy and massage are potentially beneficial for fibromyalgia patients. Diet supplement is not found to be beneficial for OA. CAM modalities will need further studies.

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