

# Nonpharmacologic Approaches to Rheumatologic Conditions

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According to the Arthritis Foundation, 50% of Americans with arthritis do not think anything can be done to help them (1). Many of these individuals cannot—or will not—tolerate pharmacologic therapies. This discussion will explore alternatives for controlling pain associated with rheumatologic conditions. Suitable interventions will be described, as will some available evidence to support these approaches.

## When Pharmacologic Agents Are Not Optimal

*Laverne, a 78-year-old woman, is a retired nurse who had severe bilateral knee osteoarthritis (OA), the most common rheumatologic condition. Unable to walk, she was in a wheelchair. Her history included atrial fibrillation (for which she was taking warfarin), congestive heart failure, chronic renal insufficiency, severe gastrointestinal (GI) bleed secondary to non-steroidal anti-inflammatory drug (NSAID)-induced gastritis, and an allergy to morphine (nausea, vomiting).*

Laverne represents a typical patient seen in the clinic. Surgery was not an option because of her cardiovascular disease. NSAID use was relatively contraindicated. In Laverne's case, a colleague recommended acupuncture.



I knew nothing about its effects—I did not set up expectations for her but simply said, “Let’s give it a try.” She came back glowing and said that it was the most wonderful experience. In the following years, she did very well with regular acupuncture treatments.

Overall, pharmacologic agents are not optimal when patients have allergies, adverse events (AEs), or interactions; an increased risk of concomitant disease; or when the agents are cost prohibitive.

Patient preference can also play a key role. Many patients in our clinic say, “I tend to avoid pharmaceuticals.” Luckily, in integrative medicine we stand in both realms—pharmacologic and nonpharmacologic—so conventional and nonconventional treatments are used as appropriate.

### *A Brief Note on Cyclooxygenase-2 Inhibitors*

Cyclooxygenase-2 (COX-2) inhibitors are used frequently in caring for patients with rheumatologic conditions. An American Heart Association review (2) discussed some of the issues with COX-2 inhibitors in terms of cardiovascular disease, specifically myocardial infarction, which approaches twice the normal risk rate. The studies from which these data were generated are not very rigorous, but they are provocative. Many rheumatologic conditions confer an inherent increased risk of cardiovascular disease and complications, so it is important to keep this in mind when considering these agents.

### **Overview of Therapeutic Options**

When treating joint pain in any rheumatologic condition, much depends on approach and perspective. Especially important is the type of practitioner being asked to consult. In general, primary care providers use analgesics; rheumatologists use NSAIDs, corticosteroids, nonbiologics, and biologics; surgeons use operative interventions; and manual medicine practitioners favor manipulation. The following review of manual medicine, botanicals, nutrition, mind-body medicine, tai chi, and acupuncture is not meant to be comprehensive but rather to encourage further study or research into these modalities.

### **Manual Medicine**

There are many different forms of manual medicine, including osteopathic manipulation, physical therapy, and chiropractic manipulation. A patient with arthritis, such as OA of the knee, will frequently overcompensate in order to maintain activity and function. This compensatory stress on other muscles causes increased or recurring pain.

The patient is straining muscles that are normally not used in walking, for example, so, it is important to develop techniques to break that cycle. The osteopathic practitioner identifies myofascial trigger points, areas of muscle tension, which are monitored and treated while the muscles are actively or passively shortened.

Physical therapy can include specific exercises, thermotherapy, electrical stimulation, and other modalities. Objective measures are made of strength, mobility, and balance. One study assigned 80 patients with OA of the knee to either a physical therapy program or a control of a subtherapeutic ultrasound twice weekly for 4 weeks (3). A significant benefit of physical therapy was seen at 4, 8, and 52 weeks. After 52 weeks, the percentage of patients receiving joint replacement was 20% in the placebo group and only 5% in the physical therapy group, so physical therapy can be a very useful intervention.

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Chiropractic manipulation restores joint mobility by manually applying controlled, sudden force to hypomobile joints. There is a paucity of peer-reviewed literature available for this modality, but anecdotal reports seem to be favorable.

### **Botanicals and Supplements**

#### *Glucosamine/Chondroitin*

Glucosamine is a monosaccharide involved in proteoglycan synthesis. It is derived from shellfish, so caution should be exercised in patients with shellfish allergies. The standard dose is 1500 mg per day. A 3-year, randomized, double-blind, placebo-controlled trial (4) showed improvements in symptoms and preservation of joint space relative to placebo in patients taking 1500 mg glucosamine daily.

Chondroitin, a glycosylate, comes from animal cartilage, mainly from bovine trachea in the United States. The clinical trial dose is 1200 mg daily. Two meta-analyses (5,6) found that chondroitin was superior to placebo in relieving pain and was well tolerated.

The most cited trial of these agents was the 6-month, randomized, double-blind, placebo-controlled Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT) (7), involving 1583 patients with OA of the knee. Eighty percent of the patients had mild pain at baseline, while 20% had moderate-to-severe pain. There were 4 arms in the study, in addition to placebo: glucosamine alone (500 mg tid), chondroitin alone (400 mg tid), glucosamine/chondroitin (500 mg tid/400 mg tid), and the NSAID celecoxib alone (200 mg qd). The results were surprising: the percentage of patients in each group who experienced pain relief was comparable: 64% in the glucosamine group, 65% in the chondroitin group, 67% in the glucosamine/chondroitin group, 70% in the celecoxib group, and 60% in the placebo group. Although 67% of participants who took the combined treatment had reduced pain, combined treatment was deemed ineffective. This trial was expensive and was clearly underpowered for such a large placebo response, but it confirmed that these supplements are safe for use over a minimum 6-month period.

### *Turmeric*

Turmeric is one of the most potent natural anti-inflammatories available and is a popular component in many over-the-counter nutraceuticals. Turmeric itself is not very bioavailable, but when combined with piperine from black pepper, the bioavailability increases by nearly 2000% (8). Many recent studies on autoimmunity have focused on turmeric, including one conducted at the University of Arizona (9). This study sought to determine whether turmeric functions as an anti-arthritic agent and, if so, to determine its possible mechanisms. Home-prepared turmeric was compared with commercial products in rats using an *in vivo* streptococcal cell wall-induced model of rheumatoid arthritis (RA). This study represents the first documentation of a curcumin-containing extract tested *in vivo* for anti-arthritic efficacy. Pretreatment with turmeric completely inhibited the onset of RA in this animal model, and treatment of “pre-existing” RA resulted in a significant attenuation of symptoms.

### *Licorice*

Licorice root has several active components—glycyrrhizic acid, glycyrrhizin, and carbenoxalone—and can potently inhibit cortisol metabolism. Basically, these components inhibit 11 beta-hydroxysteroid dehydrogenase, which is

the enzyme that converts active hydrocortisone to inactive cortisone. By inhibiting this degradation, more active endogenous product is built up. It is a useful agent when you are considering corticosteroids but want to avoid a corticosteroid burst. However, currently there is no evidence to support a safety benefit of increased endogenous steroid levels versus exogenously supplied corticosteroid.

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### *Nutrition*

Nutritional interventions can have a significant impact on patients’ lives and are often underestimated by practitioners. Patients often forget to take a midday dose of medication but they rarely forget lunch. Meals are administered like clockwork, and a diet incorporating substances shown to have beneficial effects can clearly affect disease course.

### *Fish Oil*

Fish oil is used for a wide variety of conditions, from its FDA-approved prescriptive use for hypertriglyceridemia, to over-the-counter (OTC) products used for joint aches and pains. More than 13 randomized controlled studies demonstrate clinical symptom improvement when using fish oil in RA (10). Both eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have shown benefits, although EPA is most often associated with anti-inflammatory effects.

Many effects of essential fatty acids are attributable to a decrease in inflammatory cytokine production and T-cell reactivity (11). A goal of using fish oil is to alter the availability of inflammatory precursors. Most fats located in the inflammatory cell membrane are omega-6 fats, which are readily assimilated into the arachidonic acid pathway. Omega-3 fats, obtained from fish or flax seed, are anti-inflammatory in that they are not good substrates for the arachidonic acid pathway.

Some studies (12,13) have shown that the addition of a small amount of EPA and DHA to a standard American diet can markedly change leukotriene production, which is one of the markers of the inflammatory reaction. After

as little as 6 weeks, the inflammatory potential of the neutrophils was diminished. Clinically, a number of randomized, placebo-controlled, double-blind studies of fish oil in RA have demonstrated efficacy. Benefits include reduction in overall pain and NSAID use (14), as well as decreased fatigue and duration of morning stiffness and improvements in grip strength and joint pain (15).

### *Elemental Diets*

Elemental diets provide the minimum amount of nutrients needed for survival: amino acids, monosaccharides, disaccharides, medium-chain triglycerides, vitamins, and trace elements (no intact proteins). In one study (16), 30 patients with active RA were treated with either 2 weeks of an elemental diet or 15 mg prednisolone daily over the same time period. Symptomatic improvement was seen in 78% of the diet group and 78% of the corticosteroid group, so elemental diets may be as clinically useful as a low-dose course of corticosteroids.

Caloric restriction has previously been shown to extend lifespan by as much as one-third, and additionally has a positive impact on autoimmune conditions.

### *Vegetarian Diets*

One fascinating controlled study in Belgium placed 53 patients sequentially on a 7- to 10-day juice fast, followed by a gluten-free vegan diet for 3½ months, and finally a lactovegetarian diet for 8½ months (17). The patients were compared to a group eating their “normal diet.” The modified diet group experienced changes in many objective and subjective categories that persisted throughout the whole year, including improvements in inflammatory markers and patient-reported pain symptoms. The caveat in this study was that there was no way to accurately monitor patient compliance. As an aside, juice fasts often help patients with arthritis at times when pain is flaring (18).

### *Caloric Restriction*

Caloric restriction has previously been shown to extend lifespan by as much as one-third, and additionally has a positive impact on autoimmune conditions (19). The NZB mouse model (20) uses animals that spontaneously

develop systemic lupus and lupus nephritis; the model has been repeatedly used in caloric restriction studies. Almost 100% of female NZB rats that are placed on a high-calorie diet (20 calories per day) were dead within a year. However, if this caloric intake is reduced by half, mortality decreases to 20%. Males fare a little better in this animal model, from 50% mortality with a high-calorie diet to 0% with caloric restriction. Thus, the impact of just caloric intake can be significant in these animals, and perhaps in humans, too.

### **Mind-Body Medicine**

Mind-body medicine is a very powerful and important intervention that can include journaling, biofeedback, and cognitive behavioral therapy, including stress reduction. Most studies show improvements in overall health, pain, quality of life, and inflammatory markers (21-23). Since there is high intrasubject variability and these diseases fluctuate naturally, there is some heterogeneity in the data.

### **Acupuncture**

Experimental evidence supporting the use of acupuncture in the care of patients with arthritis is not conclusive, but its use in OA is promising. Most trials are underpowered, nonrandomized, and unblinded. One study (24) randomized 570 OA patients to receive either real acupuncture, sham acupuncture, or an education-only control group. Significant improvement was seen in pain and function for the acupuncture group over the other 2 interventions, with no AEs. There are fewer studies of acupuncture in patients with RA, but symptomatic improvements are frequently seen, even in the absence of radiological and serological changes (25). One caveat regarding the use of acupuncture, however, is that a long treatment regime may not be financially viable for some patients.

### **Tai Chi**

A recent study published in the *New England Journal of Medicine* involved 66 fibromyalgia patients who were randomized to experience either tai chi sessions or a combination of stretching and education. All interventions were scheduled for 1 hour twice weekly for 12 weeks, with an additional 20 minutes per day of recommended at-home practice (26). Assessment was made at 12 and 24 weeks. The tai chi group had significant improvements in quality of life and overall health relative to the stretching/education group. Despite certain limitations in the evidence, tai chi can be

recommended to patients with rheumatoid arthritis as a complementary and alternative medical approach (23).

**Conclusions**

Many options exist for treating pain and inflammation. Most nonpharmacologic approaches can be used along with conventional therapy, in an effort to taper pharmacologic agents to the lowest possible dose that provides adequate relief. There may also be greater safety and greater patient autonomy with these interventions, so it is worthwhile to consider all possibilities. ■



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