

Complementary and Alternative Medicine: Is There a Role in Multiple Sclerosis?

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Despite effective conventional therapies for multiple sclerosis (MS), many people with MS explore complementary and alternative medicine (CAM) therapies for their symptoms. Common CAM therapies that people use include dietary modification, nutritional and herbal supplementation, and mind-body therapies. There is a revival of interest among MS researchers about the therapeutic potential of low-fat diet and essential fatty acid supplementation in MS. The efficacy of specific vitamin supplementation remains unclear. Recently, cannabis and yoga have been studied in more controlled studies and have provided evidence that they may have some benefit. The research on CAM therapies in MS is still exploratory, but considering peoples' interest and common use of these therapies, further research in this area is clearly warranted.

Introduction

Multiple sclerosis (MS) remains a chronic neurologic illness that has a significant impact on the lives of patients and their families. MS can cause motor, sensory, or visual impairment; fatigue; bowel, bladder, and sexual dysfunction; cognitive impairment; and depression. Current conventional treatments, including drugs that modify the course of MS, have limitations that include high cost of drugs, partial efficacy, and side effects.

There are several recent surveys that indicate that people with MS often explore complementary and alternative medicine (CAM) treatments [1,2•,3•,4,5]. The reasons people use CAM therapies include dissatisfaction with conventional medicine because it is only partially effective and causes side effects, and the appeal of following a "holistic approach" that includes CAM therapies and desire to have more self-control over disease management [2•,3•,6]. Recent review articles about CAM use in MS indicate that many people with MS use CAM thera-

pies and that most people use CAM as complement rather than an alternative to conventional therapy for MS [7,8].

Surveys indicate that people using CAM therapies are generally well educated and tend to use CAM in conjunction with the conventional therapies for MS [1,2•,3•,5]. Some of the common reasons for which people use CAM therapies include improvement of general well-being, treatment of fatigue, pain, spasticity, mood disorders, and cognitive difficulties. Importantly, people who use CAM therapies usually do not discuss these therapies with neurologists but are more likely to discuss these with non-neurologist care providers [4]. Interestingly, people with MS using CAM therapies perceive significant differences in the benefit from individual therapies. For instance, in a survey of 1913 people in Oregon with MS, perception of benefit for the most commonly used individual CAM therapies ranged from 22% to 52% [4].

Despite the high rate of CAM therapy use among people with MS and their reporting deriving benefit from some of these therapies, there is a paucity of well-designed clinical trials assessing the efficacy of CAM therapies in the treatment of MS. In this article, we review recent literature on the efficacy of some CAM therapies in the treatment of MS.

Diet and Multiple Sclerosis

The role of diet in MS can be approached from at least two different perspectives. One approach involves exploring diet as a possible culprit in the causation of MS and another looks at dietary recommendations after patients develop MS.

Dietary risk factors and the development of multiple sclerosis

The literature indicating diet as a possible environmental factor in the etiology of MS remains controversial. There has been special interest in looking at the fat content of diet and the role of specific essential fatty acid supplementation, antioxidants, and various nutritional supplements in MS. A case-control study of 197 MS patients and 202 matched control subjects explored the relationship between the different nutritional factors and risk of MS [9]. This study suggested a possible protective role of plant-derived components such as vegetable pro-

tein and dietary fiber, especially from cereal, vitamin C, thiamine, riboflavin, calcium, and potassium toward the risk of MS. The study also showed a significant positive association of high-caloric diet and animal fat intake and the risk of developing MS.

Researchers in the recent literature agree that intake of polyunsaturated fatty acids is possibly beneficial [7,8]. Thus, the idea that dietary modifications can influence the outcome in MS after the onset of disease is now considered plausible. Recent literature on nutrition and MS emphasizes the detrimental effects of malnutrition in MS and recommends a healthy eating regimen following the diagnosis [10,11].

Low-fat diet and essential fatty acid supplementation

Omega-3 essential fatty acids possess potent immunomodulatory activities [12]. Fish oil supplements are enriched in the omega-3 essential fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which may have immunomodulatory effects that could benefit inflammatory diseases and ischemic heart disease [12,13•].

A strong proponent of low-fat diet with essential fatty acid supplementation as a treatment for MS has been Dr. Roy Swank. He developed the so-called "Swank diet," which was widely used by people with MS prior to the advent of disease-modifying therapies and is still popular among many MS patients [14]. This diet contains 10 to 15 g/d of saturated fats and includes cod liver oil supplementation. Dr. Swank recently published long-term (approximately 50 years) survival and follow-up information of 144 MS patients who participated in a study assessing the effects of the Swank low-fat saturated diet in MS. In this study that started in 1951, 144 subjects were divided into two groups: "good dieters" and "bad dieters". Good dieters included 70 subjects that adhered strictly to a low-fat diet, consuming less than 20 g/d of fat, and bad dieters included 74 people who consumed more than 20 g/d of fat. After 34 years, there had been 23 deaths in the good dieters group versus 58 deaths in the bad dieters group. Patients were then not followed for the next 15 years, and in the year 2000 investigators contacted the subjects again. There were 15 survivors, all of whom had followed the low-fat diet. These people were found to be otherwise healthy MS patients and most (13 of 15) were still ambulatory. Dr. Swank inferred that consumption of saturated animal fat is somehow related as a cause of MS, and that patients who followed the Swank low-fat diet may have longer survival and decreased disability [15]. Although this is a unique long-term follow-up of an intervention for MS, the lack of a comparative control group makes it difficult to generalize the findings [16]. However, further investigation of low-fat diet and omega-3 fatty acid investigation may well be warranted.

A 1-year partially blinded, randomized trial involving 31 relapsing-remitting MS patients looked at low-fat dietary intervention with omega-3 fatty acid supplementa-

tion [17•]. This study included two arms that were randomized into one of the two dietary interventions: the "fish oil" and the "olive oil" groups. The fish oil group was prescribed a low-fat diet (total fat, including the fatty acids from fish oil supplementation intake, not to exceed 15% of total daily calories) that was similar to the Swank diet and also took 6 fish oil capsules (equivalent to 1 g of fish oil; containing 65% omega-3 fatty acids; EPA 1.98 g/d, and DHA 1.32 g/d). The olive oil group followed the American Heart Association Step I diet (total fat \leq 30% of total daily calories and saturated fats $<$ 10% of total daily calories) with an olive oil supplement (6 capsules of 1 g of olive oil per day). Subjects were blinded to the type of oil supplement they were taking. The primary outcome of the study was the Physical Component Scale (PCS) of the Short Form Health Survey Questionnaire (SF-36). Modified Fatigue Impact Scale (MFIS) and Mental Health Inventory (MHI) were used as secondary outcomes of the study. The subjects were followed for an average of 11 ± 2.9 months.

The fish oil group had a significant clinical benefit as seen on the PCS ($P = 0.05$) and the MHI ($P = 0.05$) scores as compared with the olive oil group after 6 months of the study. When data were analyzed after 12 months, the fish oil group maintained higher PCS scores (although not statistically significant) as compared with the olive oil group, but the MHI scores were similar in the two intervention groups. Interestingly, at the 6-month time-point, the olive oil group showed reduced fatigue as compared with the fish oil group ($P = 0.035$), and the trend was maintained for 12 months. Both groups showed a decrease in the relapse rate as compared with their relapse rates during the 1 year preceding the study. This small pilot study suggested that a diet low in saturated fats and fish oil supplementation might benefit the physical health and mental well-being of people with MS.

Another 2-year, open-label uncontrolled study was recently conducted in 16 newly diagnosed MS patients and used dietary advice in addition with fish oil and vitamin supplementation intervention. The study objectives included assessing the effect of this intervention on MS annual exacerbation rate and disability as measured by Expanded Disability Status Score (EDSS) [18]. The dietary advice included reduction of saturated fat from meat and dairy products, increased fish intake (up to three to four times per week), increased intake of vegetables and fruits daily, as well as reduction of sugar-containing products. The supplementation included 5 mL of fish oil (containing 0.4 g of EPA and 0.5 g of DHA, 1.0 mg of vitamin A, 10 μ g of vitamin D, and 5.5 mg of vitamin E). The subjects also received a vitamin B complex and 200 mg of vitamin C supplementation in addition to fish oil supplementation. People who had past or current treatment with interferons or treatment with immunosuppressive agents within the past 1 year were excluded from the study.

Thirty-five patients were screened for the study and 16 were eligible. All 16 subjects (four men and 12 women) completed the study. Mean age of the subjects was 32 years and mean duration of the disease was 1.6 years. The study showed significant reduction in the mean annual exacerbation rate ($P < 0.001$ compared with prestudy rate) and EDSS ($P < 0.01$ compared with prestudy score). The mean prestudy annual exacerbation rate was 1.39 and decreased to 0.06 after the first and second year of the study. The mean prestudy EDSS was 2.16, which decreased to 1.63 after 2 years. The study also showed significant alteration in the lipid profile of the patients, with increases in the plasma total phospholipid omega-3 fatty acids levels and decreases in the omega-6 fatty acids levels. The reduction in relapse rate and improvement in EDSS are very impressive, even for an open-label study. The results of this trial are appealing, but the trial lacked an appropriate comparison group and was not randomized or blinded. The positive results could well represent "regression towards the mean" and physiologic placebo effects. However, like the other trials, it does suggest a possible benefit to omega-3 fatty acid supplementation and a low-fat diet.

These recent publications on the potential therapeutic effects of a low-fat diet and omega-3 fatty acid supplementation certainly have methodologic problems and are not definitive. However, given the low cost and safety of a low-fat diet and fish oil supplementation, these studies provide additional impetus for performing larger and better designed trials.

Nutritional Supplements

Antioxidants

There is mounting scientific data supporting the role of immune-mediated mechanisms in the pathogenesis of MS. T cells, B cells, and macrophages, along with soluble mediators of inflammation, appear to cause demyelination and axonal and neuronal injury in MS. One common pathway of tissue injury in MS is oxidative stress mediated by reactive oxygen species [19]. The notion that oxidative stress-mediated lipid peroxidation of brain tissue contributes to the pathogenesis in MS is emphasized in recent studies [19–21]. Serum lipid peroxidation generation can be estimated by thiobarbituric acid (TBA) reactivity and has been used to assess the oxidative stress levels. Because of the interest in free radical injury in MS, it is not surprising that various antioxidants such as lipoic acid, vitamin C, vitamin E, and flavonoids, among others, are being explored as having a potential role in prevention or treatment of MS. A recent article reviewed the use of antioxidants and polyunsaturated fatty acids in MS [22]. Another publication addressed the relationship of vitamin E and oxidative stress in neurologic diseases including MS [23]. Although there are no clinical trials

of these vitamin supplementations, in a recent article one author has recommended specific vitamin supplementations in MS [24].

Lipoic acid

Lipoic acid (LA), also called alpha lipoic acid and thioctic acid, is a natural antioxidant that serves as an important cofactor for mitochondrial dehydrogenases [25]. LA has been shown to be effective in treating diabetic neuropathy due to its potential antioxidant properties in randomized, placebo-controlled trials [26,27]. In recent years, LA has been shown to be effective in treating the animal model of MS (ie, experimental autoimmune encephalomyelitis [EAE]) [28•,29•]. In addition, LA has been shown to inhibit human T-cell migration and thus makes an attractive candidate for a possible immune modulator in MS [30].

There is a single pilot study of oral LA in 37 MS subjects [31•]. The study was placebo controlled and randomized and had four comparison groups: placebo and three different doses of LA (600 mg twice a day; 1200 mg once a day, and 1200 mg twice a day). The trial explored the pharmacokinetics and tolerability of oral LA in MS and studied its effects on serum matrix metalloproteinase-9 (MMP-9) and soluble intercellular adhesion molecule-1 (sICAM-1). Participants took the study capsules for 14 days. Pharmacokinetic studies showed considerable variability in the peak LA levels after ingestion among subjects, but people who took 1200 mg of LA had significantly higher peak serum LA levels than those taking 600 mg. The study found that oral LA up to doses of 1200 mg twice a day was safe and generally well tolerated by people with MS.

Importantly, the study showed that higher doses of LA led to reduced levels of serum MMP-9 levels ($T = -0.263$; $P = 0.04$) and serum sICAM-1 levels ($P = 0.03$). Because MMP-9 and sICAM-1 are important factors affecting the T-cell migration into the central nervous system, LA may prove useful in treating MS by inhibiting MMP-9 activity and interfering with T-cell migration into the central nervous system [31•]. Further long-term studies of LA in MS are planned as extension of these results.

Vitamin C and vitamin E

There are two recent epidemiologic studies addressing the association of vitamin C and vitamin E and the risk of developing MS. The case-control study by Ghadirian et al. [9] included 399 subjects (197 cases and 202 control subjects) and suggested that there could be a protective role of vitamin C for the risk of MS (odds ratio of 0.58; $P = 0.008$). This study did not find any significant association of vitamin E and risk of MS [9].

On the contrary, a prospective case-control study involving two large cohorts of nurses (the Nurses' Health study, which followed 81,683 women for 12 years, and the Nurses' Health study II, which followed 95,056 women for 6 years) did not find that higher intakes of dietary

vitamin C reduced the risk of MS in women [32•]. This study also did not find vitamin E to have any significant impact on the risk of MS.

A case-control study of 24 MS patients and 24 age-matched control subjects looked at the levels of antioxidants (vitamin C, beta-carotene, alpha-tocopherol) and lipid peroxidation (estimated by TBA reactivity) activity in the serum [33]. The study showed an inverse relationship between the antioxidants' levels and lipid peroxidation activity.

Another study looked at the cerebrospinal fluid (CSF) and serum levels of alpha-tocopherol in 36 patients with MS and 32 control subjects. This study did not find any significant differences in the mean CSF vitamin E levels and the CSF/serum vitamin E ratio between the two groups; this suggested that CSF vitamin E concentrations are not a marker of activity of MS activity [34].

There are no clinical trials of vitamin C or E intake and effect on MS. The role of antioxidants such as vitamin C and E in MS treatment remains to be explored.

Other Supplements

Vitamin B₁₂

The relationship of vitamin B₁₂ and its role in MS pathogenesis or treatment remains controversial [35–39]. One of the recent studies that yielded positive results with vitamin B₁₂ supplementation was a small study by Kira et al. [40] in which a massive dose (60 mg/d for 6 months) of vitamin B₁₂ supplementation was given to six subjects with chronic progressive MS. This study showed no clinical improvement in motor disability in these subjects but showed improved visual and brainstem evoked-potential responses as compared with the pretreatment period [40].

On the contrary, Wade et al. [41] conducted a placebo-controlled, double-blind randomized study of 138 MS subjects of weekly vitamin B₁₂ injections in combination with noradrenergic agents (lofepramine and L phenylalanine, called the "Cari Loder regime") or placebo. The subjects included 35 relapsing-remitting, 44 primary progressive, and 59 secondary progressive MS subtypes. All study participants received weekly vitamin B₁₂ for 24 weeks and were divided into two groups of 69 subjects each. The combination group received daily lofepramine and L phenylalanine and the control group took placebo tablets. Primary outcome of the study was a change in the Guy's Neurological Disability Scale (GNDS). The study showed that all subjects receiving vitamin B₁₂ injections showed improvement in their GNDS scores at week 24, although the change was not statistically significant. The authors also found that the combination group had slightly more improvement in the GNDS scores as compared with the control group [41]. Because the findings were not statistically significant, the authors concluded that there was not enough evidence to routinely support the use of the Cari Loder regime in the treatment of MS.

Mastronardi et al. [42] conducted a study in EAE as well as nonautoimmune primary demyelinating transgenic mice using combination therapy with interferon- β plus vitamin B₁₂ and found significant clinical improvement in these mice. These authors suggested a possible synergistic effect of the combination therapy and possible role of this combination in MS treatment [42].

Despite the lack of objective data supporting its use in MS, many individuals with MS still use vitamin B₁₂ supplementation. In our survey of Oregonians with MS, about 30% of respondents had tried vitamin B₁₂ supplementation but only 9% found it to be "highly beneficial." Well-designed trials of vitamin B₁₂ supplementation in MS have yet to be performed.

Vitamin D

Epidemiologic data suggest that MS patients are more prone to osteoporosis and hence are at increased risk for bone fractures [43–45]. Studies besides these indicate that vitamin D deficiency in people with MS potentially contributes to or worsens osteoporosis [46]. Because of these reasons, prophylaxis with vitamin D and calcium in MS patients is widely recommended. More recently there has been emerging evidence for vitamin D as an environmental factor affecting autoimmune disease prevalence [47•].

Models of MS based on EAE have been effectively treated with vitamin D [48–50], and thus vitamin D may have the potential for immunomodulatory effect in MS [51]. A prospective case-control study supported a protective effect of vitamin D intake on risk of developing MS [52•]. There is a recent open-label pilot study that assessed the safety and tolerability of oral calcitriol with 1 year of intervention in relapsing-remitting MS patients that found this intervention to be safe and tolerable [53]. Further studies may be warranted to understand the relationship of vitamin D and MS.

Yoga

Experts agree that exercise should be an active part of MS management [54–56], and clinical studies have demonstrated the benefits of exercise in MS [57–60]. These benefits include improvement in functional capacity, quality of life, and fatigue. Yoga is a CAM approach that may be considered equivalent to conventional exercise.

Yoga is an ancient Indian practice that combines specific breathing techniques, meditation, and certain forms of exercise/postures. Surveys indicate that yoga is practiced by 13% to 23% of people with MS and that more than half of these find it to be highly beneficial [2•,3•,4,5]. In our survey of Oregonians, we compared the "very beneficial" ratings of yoga to ratings of conventional exercise modalities, such as water aerobics, swimming, stretching, and walking, by the respondents. A significantly higher percentage of respondents rated yoga (49%) as "very beneficial" compared with walking (40%; $P = 0.001$).

For other conventional exercise modalities, we found that “very beneficial” rating of yoga was similar to water aerobics (49%; $P = 0.96$), swimming (45%; $P = 0.17$), and stretching (44%; $P = 0.06$) [4].

There is a single 6-month, randomized controlled trial of yoga in MS. In this study, 69 MS patients were randomized into one of three arms: yoga, exercise on a stationary bicycle, and a “wait-list” group. Both the yoga and stationary bicycle groups regularly attended group classes and were encouraged to continue their particular group’s exercise modality at home. This study showed that subjects in the yoga arm of the study improved significantly on measures of fatigue as compared with the waiting list group. Similar improvements in fatigue were seen in the conventional exercise group. The study did not find any improvement in cognitive functions in either yoga or the exercise group [61•]. This study provides support for the notion that yoga can improve fatigue among people with MS. Because of the low impact of exercises involved in yoga and potential beneficial effect on fatigue, yoga may be a worthy exercise technique for MS.

Cannabis

Cannabis remains a controversial intervention for MS-related symptoms [62]. It has been used for symptoms in MS such as pain, spasticity, mood, tremors, fatigue, or bladder dysfunction. There has been a tremendous interest in use of this therapy from patients, the general public, and media. Many patients report subjective improvement in various MS-related symptoms despite negative objective improvement [63]. A recent survey of 220 MS patients in Halifax, Nova Scotia assessed the patterns and prevalence of cannabis use among patients with MS. The survey found that up to 36% of respondents had used cannabis for any purpose ever in their lives and 14% were using cannabis for symptom treatment at the time of the survey [64]. Recent review articles explore the therapeutic potential of cannabinoids for the treatment of MS [65].

Several clinical trials have recently been conducted to address the efficacy of cannabis in MS-related symptoms. A randomized, double-blind, placebo-controlled crossover study trial by Vaney et al. [66•] examined the efficacy, safety, and tolerability of an orally administered cannabis extract in the treatment of poorly controlled spasticity in patients with MS. Fifty-seven patients that were part of an inpatient rehabilitation program were enrolled in this trial. The study used cannabis-extract capsules standardized to 2.5 mg of tetrahydrocannabinol (THC) and 0.9 mg of cannabidiol (CBD) each, and used up to 30 mg of THC as the maximum dose. The study concluded that *Cannabis sativa* plant extract might lower spasm frequency and increase mobility with tolerable side effects in MS patients with persistent spasticity not responding to conventional medications [66•].

The Cannabinoids in MS (CAMS) [67] study tested the efficacy and long-term safety of cannabinoids in MS. This was a placebo-controlled, 15-week study that included 630 patients with stable MS and spasticity. The preliminary results from the 12 months of follow-up in these subjects showed a small but significant treatment effect on the primary outcome (muscle spasticity) as assessed by Ashworth scale ($P = 0.04$). There was improvement in some aspects of disability as well as subjective improvement in patients’ symptoms of muscle spasms, pain, and sleep [68•].

Wade et al. [69•] conducted a parallel group, double-blind, randomized, placebo-controlled study to assess the benefit of cannabis-based medicinal extract (CBME) on MS-related symptoms. The study included 160 MS patients who had significant problems in at least one of the following: spasticity, spasms, bladder problems, tremor, or pain. Oromucosal sprays of matched placebo or whole-plant CBME containing equal amounts of delta-9-THC and CBD at a dose of 2.5 to 120 mg of each daily were given in divided doses. There was no significant change in the primary outcome measure of Visual Analogue Scale (VAS) score for each patient’s most troublesome symptom as compared with placebo. However, there was a significant reduction in the spasticity VAS scores (a secondary outcome) in the CBME group as compared with the placebo group ($P = 0.001$) [69•].

Fox et al. [70] studied the effect of cannabis on tremor in 14 patients with MS in a randomized, double-blind, placebo-controlled crossover trial. These researchers used oral cannador (cannabis extract) in MS patients with upper limb tremors. The investigators used a 50% change on a tremor index as the primary outcome and did not find improvement in any of the objective measures of upper limb tremor as compared with placebo. Patients did report more subjective relief from their tremors while on cannabis extract compared with placebo [70].

Brady et al. [71] conducted a 16-week open trial in 21 patients to evaluate the safety, tolerability, dose range, and efficacy of two whole-plant extracts of cannabis in patients with advanced MS and refractory lower urinary tract symptoms. After completion of 6 weeks, patients were followed in a long-term extension arm. Besides proving to be safe, significant improvement in most of the outcomes, including urinary frequency, urgency incontinence pad weights, cystometry, and VAS for secondary troublesome symptoms, was seen. There was also a significant decrease in urinary urgency, the number and volume of incontinence episodes, frequency, and nocturia with cannabis ($P < 0.05$). The trial also showed significant improvements in patient self-assessment of pain, spasticity, and quality of sleep ($P < 0.05$) with the intervention [71].

Based upon these studies, it appears cannabis may have some role in treatment of spasticity and bladder symptoms. Further studies are warranted, particularly for symptoms such as spasticity, in which there are controlled

trials suggesting benefit. Legal issues in some countries, like the United States, will make it difficult to recommend cannabis even if there are convincing clinical trials.

Ginkgo

Ginkgo biloba is an herb that has been used in China for centuries that is now commonly used by people worldwide, including people in the United States with MS [2•,4]. Ginkgo contains constituents that include flavonoids, terpenoids, and organic acids and has both antiplatelet and antioxidant activities [72–74]. Ginkgo also has effects on the neurotransmitters involved in cognition [75–77]. In 1998, a meta-analysis of published studies suggested that ginkgo biloba was effective in slowing progression of Alzheimer's disease [78].

Ginkgo attracted the interest of MS researchers because of its potential as a disease modulatory agent as well as a treatment for cognitive dysfunction in MS. However, ginkgolide B, which is a specific compound found in ginkgo biloba extracts that had beneficial effects on EAE, did not have effects on exacerbations in a double-blind, placebo-controlled trial of MS [79,80].

Ginkgo biloba has been studied as a treatment for cognitive dysfunction in MS in two clinical trials. One small pilot study suggested that ginkgo biloba might be beneficial for treatment of cognitive dysfunction [81]. Another double-blind, placebo-controlled study assessed the effects of a standardized ginkgo biloba extract given at 120 mg twice a day for 12 weeks on cognitive performance in 43 subjects with MS. At the end of the study, the group taking ginkgo biloba extract significantly ($P = 0.015$) improved on the Stroop test, attention, and executive functions [82•]. The subjects in the ginkgo biloba group also reported significantly fewer cognitive difficulties on the Retrospective Memory Scale of the Perceived Deficits Questionnaire when compared with the placebo group ($P = 0.016$.) This trial was limited by a short duration and small sample size but warrants a larger and longer trial before we can recommend ginkgo biloba extract for MS-related cognitive deficits.

Bee Venom

Bee sting therapy has been used by a small number of MS patients despite no reasonable justification of its benefit in MS. There has been a single, randomized, crossover study in 26 MS patients with 24 weeks of medically supervised bee sting therapy [83]. Patients received bee venom three times per week. The study examined the cumulative number of new gadolinium-enhancing lesions on T1-weighted MRI of the brain as the primary outcome. Secondary outcomes included lesion load on T2-weighted MRI, relapse rate, disability, fatigue, and health-related quality of life. This study showed that although bee sting therapy was well tolerated, there was no significant improvement on any of

the primary or secondary outcomes [83]. In our opinion, bee sting therapy has no significant advantage over other treatment options in MS and we would discourage its use.

Conclusions

The role of CAM therapies in MS is evolving. Many researchers now agree that diet and omega-3 fatty acid supplementation may have some beneficial effect in MS. Based on recent literature, promising areas of CAM research in MS may include the immunomodulatory effects of low-fat diet and omega-3 fatty acid supplementation, use of cannabis for certain symptoms like spasticity, and ginkgo biloba for cognitive dysfunction. Recent studies also indicate that yoga may be as beneficial as conventional exercise for reducing fatigue. Several of the CAM therapies may be used in conjunction with the current conventional therapies for MS. Because most of these therapies have minimal side effects and can be used in conjunction with the currently approved therapies for MS, neurologists should become more familiar with these options and have open discussions with their patients about CAM therapies they may be trying. Clearly, more research is warranted in this field.

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