REVIEW

Multiple Sclerosis

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La esclerosis múltiple

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Alan Gaby, MD, is internationally recognized as an expert in the field of nutritional therapy. He has recently completed a 30-year project, a textbook titled *Nutritional Medicine*. This article is adapted from chapter 137 of the textbook with permission from www.doctorgaby.com, Concord, New Hampshire; 2011.

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Multiple sclerosis (MS) is a chronic progressive demyelinating disease of the central nervous system. Common manifestations include paresthesias, diplopia, loss of vision, numbness or weakness of the limbs, bowel or bladder dysfunction, spasticity, ataxia, fatigue, and mental changes. Four main patterns of MS are recognized: relapsing remitting, primary progressive, secondary progressive, and progressive relapsing. The cause of MS is unknown, although it appears to be an autoimmune disease. Much of what is known about MS has been learned from an animal model of the disease, experimental allergic encephalomyelitis.

Conventional therapy may include immunomodulating drugs (such as certain types of beta interferon) to reduce the frequency of relapses, glucocorticoids to treat acute exacerbations, and amantadine to treat fatigue. Other medications are used for specific MS-related symptoms.

ENVIRONMENTAL FACTORS

A meta-analysis of 13 studies showed that exposure to organic solvents was associated with an increased risk of developing MS. The estimated relative risk in individuals exposed to solvents was 1.7 to 2.6.[1] In patients with a history of exposure to solvents or other toxic chemicals, a detoxification (depuration) program aimed at reducing the body burden of xenobiotic chemicals might help retard or reverse the disease process.[2]

DIETARY FACTORS

Low-fat Diet

Beginning in 1949, Swank treated 150 MS patients (mean age, 34 years) with a low-fat diet. After adjustments in the protocol during the first 3 years, the recommended diet was as follows: intake of saturated fat was restricted to 20 g/day. Whole milk, cheese, margarine, other sources of hydrogenated oils, and shortenings were prohibited. Patients were encouraged to eat fish three or more times a week. The diet was supplemented with 5 g/day of cod liver oil and 10 g/day to 40 g/day of vegetable oils high in polyunsaturated fatty acids. During the first 7 years, the frequency and severity of disease exacerbations appeared to be reduced. Patients who began treatment early in the course of the disease and before severe disability had developed had the best outcomes, with only 8% of patients deteriorating during an average follow-up period of 3.6 years. In contrast, about 65% of late cases deteriorated during the same period.[3] Relapses became progressively less severe and less prolonged as patients continued the diet, and many patients reported a decrease in fatigue after 2 to 3 years.[4,5]

After 34 years of follow-up,[6-8] data on 144 of the original patients were available. Among the 70 patients who had maintained saturated fat intake at 20 g/day or less (mean, 17 g/day), the mortality rate was 31% and the average degree of deterioration was minimal. In contrast, among the 74 patients who had consumed more than 20 g/day of saturated fat, serious disability was common and the mortality rate was 80%. Outcomes were similar in patients who consumed 20 g/day to 30 g/day of saturated fat and in those who consumed more than 30 g/day. Minimally disabled patients who adhered to the diet showed little or no deterioration, and 95% were still alive after 34 years. However, discontinuation of the diet, even after 5 to 10 years, was in almost all cases followed by reactivation of the disease. Among patients who were moderately or severely disabled, those who adhered to the diet had slower disease progression than those who did not adhere. Fifteen of the patients who adhered to the diet were followed for approximately 50 years. Thirteen were ambulatory, active, and normal in all respects, whereas the other two needed assistance to walk.[9]

A limitation of Swank's observations is that nonadherence to the diet may have been a result in some cases, rather than a cause, of clinical deterioration (ie, some patients may have discontinued the diet because they thought it was not working). Nevertheless, the impressive long-term results in a high percentage of patients are reason enough to recommend this type of diet for MS patients. Two more recent, shorter-term trials using diets similar to the Swank diet have also shown benefits.

Sixteen patients with early MS (mean disease duration, 1.6 years) were advised to limit intake of saturated fat from meat and dairy products, eat fish three to four times a week, increase intake of vegetables, eat one to two fresh fruits per day, use whole grain breads, reduce intake of refined sugar, and limit consumption of coffee and tea to 2 cups per day. They were also advised to avoid foods to which they were allergic or intolerant, stop smoking, and minimize alcohol consumption. In addition, they were prescribed 5 mL/day of fish oil and a multivitamin. During the 2-year study, the mean annual exacerbation rate was 0.06 episodes per person, as compared

with 1.39 episodes per person prior to the study (96% reduction; $P < .001$). Exacerbations occurred only in the two patients who continued to smoke. After 2 years, the degree of disability (as determined by the Extended Disability Status Scale) decreased by a mean of 25% compared with baseline ($P < .01$).[10]

Thirty-one patients with relapsing remitting MS were randomly assigned, in double-blind fashion, to one of two interventions for 1 year: a low-fat diet (15% of total energy as fat) with 6 g/day of fish oil, or an American Heart Association (AHA) Step 1 diet (30% of total energy as fat) with 6 g/day of "placebo" (olive oil). All but one of the patients had been on disease-modifying therapies for a mean of 1.1 years and continued those treatments during the study. After a mean follow-up period of 11 months, measures of physical functioning and mental health were significantly better in patients assigned to the low-fat diet than in those assigned to the AHA diet.[11]

Several different components of the Swank diet may have contributed to the observed benefits. While restricting saturated fat intake appeared to be necessary to achieve good results, the omega-6 fatty acids from vegetable oil and the omega-3 fatty acids and vitamin D from cod liver oil may have also played a role in the positive outcomes. The influence of each of these nutrients on MS is discussed below.

Allergy

Several investigators have reported that many attacks of MS can be traced to allergic reactions to foods.[12-15] Avoidance of the offending foods resulted in symptomatic improvement, and reintroduction of those foods was followed by exacerbations. The possibility that food allergy plays a role in the pathogenesis of MS is further supported by the finding of abnormal jejunal mucosa (partial villous atrophy, subtotal villous atrophy, or inflammatory cell infiltration) in some MS patients.[16] These intestinal changes are seen in gluten enteropathy (celiac disease), but they can also result from allergic reactions to cow's milk, egg, or other foods.

One investigator failed to observe any improvement in six MS patients who adhered to a gluten-free diet for 9 months to 2 years.[17] However, in my experience MS is more often exacerbated by dairy products than by gluten grains. I have seen a few patients with early MS who remained symptom-free as long as they excluded dairy products from their diet. Whenever they resumed eating dairy products, their neurological symptoms would recur. Epidemiological studies support a possible association between dairy product consumption and MS incidence.[18-20]

Allergic reactions to molds, tobacco, and house dust have also been identified as triggering factors in MS. I saw a 42-year-old woman who developed MS shortly after her house flooded and became infested with mold. Her symptoms resolved when she took a 10-day trip to a dry climate, but recurred when she returned to her house. She eventually moved to a different house, after which her symptoms improved considerably.

NUTRITIONAL SUPPLEMENTS

Fatty Acids

The low–saturated fat diet pioneered by Swank for the treatment of MS (see above) includes supplementation with both omega-6 and omega-3 fatty acids. The evidence summarized below suggests that these fatty acids may have contributed to the excellent long-term outcomes observed by Swank.

Omega-6 Fatty Acids

Omega-6 essential fatty acids (EFAs) play a role in the synthesis and/or metabolism of myelin. EFA-deficient animals had a reduced quantity and concentration of myelin in brain tissue.[21,22] EFA deficiency also increased the susceptibility of rats to the development of experimental allergic encephalomyelitis (an animal model of MS) in some,[23,24] but not all,[25] studies. In guinea pigs, supplementation with linoleic acid decreased the severity of experimental allergic encephalomyelitis when the disease was mild or moderate but not when it was severe.[26]

The mean concentration of linoleic acid in serum, serum lipids, lymphocytes, and cerebrospinal fluid was significantly lower in patients with MS than in controls in most,[27-32] but not all,[33] studies. The reduced concentrations of linoleic acid may be due in part to malabsorption, since 42% of 52 MS patients were found in one study to have increased fecal fat excretion.[34] However, another study found that absorption of EFAs was normal in patients with MS.[32]

While decreased concentrations of linoleic acid are not specific to MS (they are also seen in patients with other neurological illnesses and in acute non-neurological illnesses),[31] patients with MS may be especially susceptible to the effects of omega-6 fatty acid deficiency. That possibility is suggested by the observation that erythrocytes and lymphocytes from MS patients and from their close relatives showed abnormal electrophoretic mobility in vitro.[35-38] This abnormality was reversed in some cases by supplementation with evening primrose oil (which contains the omega-6 fatty acids, linoleic acid, and gamma-linolenic acid).[35,39,40]

Several clinical trials have examined the effect of linoleic acid supplementation in patients with MS. Linoleic acid was derived from sunflower oil or from unspecified sources and was given in dosages of 11.5 g/day to 23 g/day for 2.0 to 2.5 years. The control group received olive oil or oleic acid. Some studies observed fewer or less severe relapses in the active-treatment group than in the control group,[41,42] but other studies found no benefit.[43,44] A pooled analysis of three of these trials revealed that linoleic acid significantly ($P < .05$) decreased the rate of deterioration in patients who had minimal or no disability at baseline and decreased the severity and duration of relapses irrespective of baseline disability and illness duration.[45]

Omega-3 Fatty Acids

Omega-3 fatty acids play a role in normal brain function, and a deficiency of these fatty acids may increase the susceptibility of myelin to becoming damaged. The content of eicosapentaenoic acid (EPA) in erythrocyte phospholipids and the concentration of docosahexaenoic acid (DHA) in adipose tissue were significantly lower in patients with MS than in controls.[46] In uncontrolled trials, MS patients receiving fish oil or cod liver oil showed neurological improvement or had fewer exacerbations than expected.[47,48] In a double-blind trial, fish oil supplementation resulted in clinical benefit that was of borderline statistical significance.

Three hundred twelve patients with relapsing remitting MS were randomly assigned to receive, in double-blind fashion, 10 g/day of fish oil or placebo (olive oil) for 2 years. All patients were advised to increase dietary intake of omega-6 polyunsaturated fatty acids and to avoid a high intake of animal fat. After 2 years, 51% of the patients in the fish oil group and 41.4% of those in the placebo group were improved or unchanged, as determined by the Kurtzke Disability Status Scale score ($P = .07$).[49]

Vitamin B_{12}

Vitamin B_{12} plays a role in the synthesis and integrity of myelin. Patients with MS have been reported to have an increased prevalence of low serum and/or cerebrospinal fluid vitamin B_{12} levels, possibly as a result of a disorder of vitamin B_{12} binding or transport.[50,51] In one report, of 10 patients who had both MS and vitamin B_{12} deficiency, only two were anemic, although nine had macrocytosis. Two of the 10 patients had pernicious anemia, but the deficiency was unexplained in the other cases.[52] Of 52 patients with MS, 11.9% were found to have vitamin B_{12} malabsorption.[34] Another study found that MS patients had normal serum vitamin B_{12} levels but a significant decrease in unsaturated vitamin B_{12}-binding capacity.[53] Thus, MS is associated in some cases with abnormalities of vitamin B_{12} absorption or utilization, although the relationship of these abnormalities to the disease process is not clear.

Vitamin B_{12} has been used empirically to treat MS. In two uncontrolled trials, intramuscular administration of vitamin B_{12} was followed by an improvement in neurological function. The doses varied, but one effective regimen was 1000 μg once a week.[54,55] In another study, no objective neurological improvement was seen in 26 patients who received 100 μg of vitamin B_{12} intramuscularly every other day for 3 months, but 25% of the patients reported improvements in appetite and overall well-being. Two of the patients who believed they definitely benefited from vitamin B_{12} were given a placebo for 2 months and reported the same benefit.[56] The authors therefore concluded that the positive response to vitamin B_{12} was a placebo effect. However, the possibility of a carryover effect from the previous vitamin B_{12} treatment cannot be ruled out. In a study of six patients with chronic progressive MS, no neurological improvement was seen after oral administration of 60 mg/day of methylcobalamin for 6 months, although both the visual and brainstem auditory evoked potentials appeared to improve.[53]

While there is no definitive evidence that vitamin B_{12} is beneficial for MS patients, vitamin B_{12} injections are inexpensive and relatively safe. Therefore, a clinical trial (perhaps 1000 μg once a week for 4 to 8 weeks, followed by maintenance treatment if improvement occurs) would be reasonable, particularly for patients with chronic fatigue.

L-Carnitine and Acetyl-L-carnitine

Carnitine plays a role in energy production by facilitating the transport of fatty acids into mitochondria. L-carnitine has been used successfully to treat fatigue in various clinical situations. Acetyl-L-carnitine (ALC) functions as a neurotransmitter and also appears to be a precursor to carnitine. In clinical trials, administration of L-carnitine improved medication-induced fatigue in patients with MS, and treatment with ALC relieved MS-related fatigue.

Of 170 patients with MS, 80% suffered from fatigue. The mean serum carnitine concentration was significantly lower in MS patients receiving immunosuppressive drugs (but not in untreated patients) than in healthy controls. Drug-treated patients with low serum carnitine levels received 3 g/day to 6 g/day of L-carnitine. Sixty-three percent of the patients experienced an improvement in fatigue after 3 months. The most pronounced improvements were seen in patients treated with cyclophosphamide or interferon. L-carnitine caused dose-related gastrointestinal side effects in some cases.[57]

Thirty-six patients with MS-related fatigue were randomly assigned to receive, in double-blind fashion, ALC (1 g twice a day) or amantadine (a drug used to treat MS-related fatigue; 100 mg twice a day) for 3 months. After a 3-month washout period, each patient received the alternate treatment for an additional 3 months. An improvement in fatigue, as demonstrated by a lower score on the Fatigue Severity Scale (FSS), was seen in 70% of patients during treatment with ALC and in 43% of patients during treatment with amantadine ($P = .07$). The improvement was clinically meaningful (defined as a reduction of 0.5 or more in the FSS score) in 29% of patients during treatment with ALC and in 21% of patients during treatment with amantadine. Compared with amantadine, ALC significantly improved the mean FSS score ($P < .04$); this difference was due to a nonsignificant improvement during ALC treatment combined with a worsening of the mean score during amantadine treatment. One patient discontinued ALC and five discontinued amantadine because of side effects.[58] Thus, ALC was more effective and better tolerated than amantadine in the treatment of MS-related fatigue.

Vitamin D

Populations around the world that have a greater amount of sunlight exposure or higher dietary vitamin D intake have a lower incidence of MS.[59,60] In addition, a prospective cohort study of more than 187 000 women found that higher vitamin D intake was associated with a lower incidence of MS. Women in the highest quintile of vitamin D intake had a 33% lower incidence of MS, when compared with women in the lowest quintile (*P* for trend = .03).[61]

In mice, administration of 1,25-dihydroxyvitamin D_3 (the biologically active form of vitamin D) completely prevented the development of experimental autoimmune encephalomyelitis, an animal model for MS. Discontinuation of 1,25-dihydroxyvitamin D_3 resulted in a resumption of disease progression.[62]

In addition to the possible role of vitamin D in preventing MS, vitamin D deficiency may contribute to the high prevalence of osteoporosis that is seen in MS patients. Of 52 women with MS, 23% were found to have vitamin D deficiency (serum 25-hydroxyvitamin D < 25 nmol/L). Dietary intake of vitamin D was below the Recommended Dietary Allowance in 80% of the patients, and 40% reported no weekly sunlight exposure.[63] Vitamin D status should therefore be assessed in patients with MS, and deficiencies should be treated appropriately.

Although the research cited above suggests that vitamin D might help prevent MS, there is conflicting evidence regarding whether vitamin D supplementation affects disease activity or progression in patients with existing MS. Furthermore, preliminary data suggest that people with MS may fare better with moderate doses of vitamin D (such as 1000 IU/day) than with large doses (such as 13 000 IU/day).

Twelve patients with active MS received progressively increasing doses of vitamin D_3 (from 28 000 IU once a week to 280 000 IU once a week, with the highest dose being given for 6 weeks). The patients also received 1200 mg/day of calcium. Disease progression and disease activity (assessed clinically) did not change, but the number of gadolinium-enhancing lesions per patient (a possible objective measure of disease activity) decreased from 1.75 at baseline to 0.83 at the end of the study (*P* = .03). However, that improvement may have been a statistical artifact (regression to the mean), since the presence of active disease was one of the inclusion criteria for the study. No adverse effects were seen, and no patient had hypercalcemia or hypercalciuria.[64]

Forty-nine patients (mean age, 40.5 years) with MS (mean disease duration, 7.8 years) were randomly assigned to receive, in open-label fashion, vitamin D_3 or no vitamin D_3 (control group). The weekly dosage was as follows: weeks 1-2 (0 IU), weeks 3-4 (28 000 IU), weeks 5-10 (70 000 IU), weeks 11-16 (112 000 IU), weeks 17-22 (224 000 IU), weeks 23-28 (280 000 IU), weeks 29-40 (70 000 IU), weeks 41-49 (28 000 IU). Control patients were permitted to take up to 4000 IU/day of vitamin D, if desired. The mean number of relapses compared with the year prior to the trial decreased by 41.1% in the vitamin D group and by 16.7% in the control group (*P* = .17 for the difference between groups). The proportion of patients with relapses was nonsignificantly lower in the vitamin D group than in the control group (16% vs 37%; *P* = .09).[65]

Sixty-six patients (aged 18-55 years) with MS who were receiving interferon beta-1b were randomly assigned to receive, in double-blind fashion, 20 000 IU of vitamin D_3 once a week or placebo for 1 year. The mean T2 burden of disease on magnetic resonance imaging (MRI) scans increased less in the vitamin D group than in the placebo group, but the difference was not significant (*P* = .11). Patients in the vitamin D group had a significantly lower number of T1 enhancing lesions (*P* = .004), as well as a tendency to reduced disability accumulation (*P* = .07) and improved timed tandem walk (*P* = .076). The number of adverse events and the annual relapse rates were similar between groups.[66]

Twenty-three patients (aged 29-49 years) with relapsing-remitting MS were randomly assigned to receive, in double-blind fashion, high-dose or low-dose vitamin D_2 for 6 months. Patients in the high-dose group initially received 6000 IU twice a day plus an additional 1000 IU/day that was given to both groups. The number of high-dose capsules was adjusted during the study to maintain a serum 25(OH)D level of 130 nmol/L to 175 nmol/L. It was not stated how much vitamin D patients in the high-dose group ended up taking. The patients in the low-dose group received 1000 IU/day. There were no significant differences between groups in either of the two primary endpoints; ie, the number of new gadolinium-enhancing lesions and the change in the total volume of T2 lesions. The median Expanded Disability Status Scale score (a secondary endpoint) was significantly higher (worse) in the high-dose group than in the low-dose group (3 vs 2 on a 10-point scale; *P* = .04). The relapse rate (a secondary endpoint) was 36.4% (4 of 11) in the high-dose group and 0% (0 of 12) in the low-dose group (*P* = .04).[67]

Based on the available evidence, supplementation with moderate doses of vitamin D seems reasonable for MS patients, but the use of large doses may not be appropriate.

In mice, administration of niacinamide (500 mg/kg of body weight per day subcutaneously) prevented demyelination and improved behavioral deficits in mice with experimental autoimmune encephalomyelitis.[68] The amount of niacinamide used in this study is equivalent to 35 g per 70 kg of body weight per day, which would be hepatotoxic in humans. However, much lower (and apparently safe) doses of niacinamide have been shown in some studies to inhibit the progression of another autoimmune disease, type 1 diabetes. Clinical trials are therefore warranted to determine whether non-hepatotoxic doses of niacinamide would be beneficial for MS patients.

L-Threonine for Spasticity

Spasticity is a common problem in MS patients, and is an important cause of pain and disability. Glycine is an inhibitory neurotransmitter in the spinal cord, and its concentration is low in the brain of animals with spasticity. While glycine crosses the blood-brain barrier poorly, L-threonine crosses more readily and may be converted to glycine in brain tissue.[69] In clinical trials, administration of L-threonine in doses of 3.0 g/day to 7.5 g/day for periods of 2 to 8 weeks appeared to produce moderate improvement in patients with spasticity due to MS.[69-71] In one study, 3 g/day of L-threonine was as effective as 6 g/day. While no serious side effects were reported, longer-term studies are needed to determine whether L-threonine is safe and effective for patients with MS-related spasticity.

Folic Acid

Of 21 patients with MS, five had a subnormal serum folate concentration.[72] It is not known whether folate deficiency can exacerbate MS. However, because folate deficiency has adverse effects on overall health and on the neurological system, folate status should be evaluated in MS patients and deficiencies should be treated appropriately.

Other Nutrients

In animal studies, deficiencies of vitamin A,[73] vitamin B complex,[74] pantothenic acid,[75] or copper[76] resulted in demyelination or impaired myelin production in the central nervous system. While deficiencies of these nutrients are unlikely to be an important factor in most cases of MS, marginal deficiencies might conceivably have a modest adverse effect on the outcome of the disease.

OTHER TREATMENTS

Candidiasis

Several investigators have reported that some patients with MS had marked improvement after going on an "anti-Candida" program consisting of oral nystatin, with or without dietary restriction of refined sugar, yeast-containing foods, and carbohydrates.[77,78] The possibility that overgrowth of *Candida albicans* in the gastrointestinal tract or on other mucosal surfaces could trigger or exacerbate MS is plausible, considering that infection with this organism may result in the formation of autoantibodies that cross-react with various tissues and organs.[79] That possibility is further supported by the observation that the prevalence of chronic sinusitis was significantly greater in MS patients than in matched controls ($P < .0001$), and that first attacks of MS frequently followed an attack of sinusitis by 1 month.[80] Sinusitis is often treated with antibiotics, which may lead to Candida overgrowth.

I saw a 35-year-old male who was diagnosed with MS shortly after receiving a 30-day course of antibiotics for prostatitis. He experienced a rapid resolution of symptoms after treatment with oral nystatin (1 million units 4 times per day). He discontinued nystatin after 3 months, and his neurological symptoms recurred shortly thereafter. He then resumed nystatin for an additional year and remained asymptomatic during that time and for several more years, after which he was lost to follow-up. I have seen a few other MS patients in whom nystatin therapy was apparently responsible for marked clinical improvement.

The possibility that candidiasis is a contributing factor to MS should be considered in patients who have had recurrent vaginal yeast infections or a history of treatment with antibiotics, oral contraceptives, or systemic glucocorticoids.

Estriol

Women with MS experience a significant decrease in relapses during pregnancy, a time when estriol levels are high. Animal models of MS have shown that estriol can reduce disease severity. In an uncontrolled trial, administration of estriol was of possible benefit for women with MS.

Twelve non-pregnant women (mean age, 44 years) with MS received 8 mg/day of estriol for 6 months. After 3 and 6 months of treatment, the median number of gadolinium-enhancing lesions (a radiological measure of disease activity) decreased by approximately 80% compared with baseline. When estriol was discontinued, the number of lesions increased to pretreatment levels. When estriol treatment was resumed, the number of lesions again decreased significantly. Improvement was seen only in the six patients with relapsing remitting MS, not in the four with secondary progressive MS.[81]

Further research is needed to determine whether these radiological improvements translate to clinical benefits, and whether men with MS may also be candidates for estriol treatment.

Dehydroepiandrosterone (DHEA)

The mean plasma concentration of dehydroepiandrosterone (DHEA) was nonsignificantly lower by 18% in patients with active MS than in matched controls, although the levels were within the normal range.[82] DHEA secretion in response to ACTH stimulation was significantly lower in MS patients than in controls in one study[83] but not in another study.[82] It is not clear whether these alterations in DHEA secretion or metabolism are clinically significant. Nevertheless, administration of DHEA would be of potential benefit for selected patients with MS, since it has been found to be of value in the treatment of other autoimmune diseases.

Serum concentrations of DHEA and DHEA-sulfate have been found to be significantly lower in MS patients suffering from persistent fatigue than in MS patients without fatigue.[84] I have seen two patients with MS in whom supplementation with physiological doses of DHEA resulted in improvement of fatigue. It would seem reasonable to consider administering

physiological doses of DHEA (such as 5-15 mg/day for women, 10-20 mg/day for men) to MS patients whose serum DHEA-sulfate concentration is below or in the bottom 10% to 20% of the normal range for young adults of the same gender.

Padma 28

Padma 28 is a Tibetan herbal mixture consisting of 22 ingredients combined in a specific order. It has been reported to exert an immunomodulatory effect by affecting suppressor lymphocytes and may also induce the synthesis of interferon in humans.[85] In a randomized controlled trial, treatment with Padma 28 appeared to be beneficial for patients with chronic progressive MS.

One hundred patients with chronic progressive MS were randomly assigned to a control group or to receive Padma 28 (two tablets three times per day) for 1 year. Of the 50 patients assigned to receive active treatment, 44% experienced positive effects such as improved general condition, increased muscle strength, improvement or disappearance of disorders affecting the sphincter, and a decrease in paresis. The frequency of improvement was 52% in patients with recurrent attacks and 33% in patients with slowly progressive disease. In the control group, none of the 50 patients improved and 40% deteriorated.[85]

At the time of this writing, Padma 28 is not available in the United States because of regulatory action taken by the US Food and Drug Administration related to unapproved claims of efficacy. However, an almost identical product, Padma Basic, is readily available.

Adenosine-5'-monophosphate

In an uncontrolled trial published in 1953, administration of a series of intramuscular injections of adenosine-5'-monophosphate (AMP) was followed by clinical improvement in a high proportion of MS patients.

Sixteen patients with a history of MS for 5 to 20 years and severe disabilities received intramuscular injections of AMP in varying doses for 6 to 10 months. After AMP treatment, 86% of the patients reported an improvement in endurance and 72% reported a reduction in bladder disabilities. Impaired coordination, visual disturbances, spasticity, and paresthesias did not improve. A dose of 100 mg in aqueous solution three times a week was more effective than 20 mg in gelatin three times a week.[86]

Controlled trials are needed to confirm this early report. At the time of this writing, AMP for intramuscular administration is available only through some compounding pharmacies.

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