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Uses of Complementary and Alternative Medicine in Multiple Sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a chronic, disabling, recurrent demyelination of the central nervous system (CNS). It could affect different regions in the brain and spinal cord, and according to the domain which is affected, it could cause different symptoms such as motor, sensory, or visual impairment; fatigue; bowel, bladder, and sexual dysfunction; cognitive impairment; and depression. MS patients also face reduced quality of life. Drugs that are used in MS are not fully efficient and patients suffer from many symptoms and adverse effects. Today there is an increasing trend of using complementary and alternative medicine (CAM). People are more likely to use this type of treatment. Using appropriate lifestyle and CAM therapy can subside some of the symptoms and could improve the quality of life in these patients. Many people with MS explore CAM therapies for their symptoms. This review is aimed to introduce CAM therapies that could be used in MS patients.

Key words: Complementary and alternative medicine, Multiple sclerosis, Natural cure, Phytotherapy

INTRODUCTION

Multiple sclerosis (MS; also known as disseminated sclerosis or encephalomyelitis disseminated) was described by Charcot and Vulpain in 1866 for the first time.[1] MS is a chronic, disabling, incurable recurrent demyelination of the central nervous system (CNS) by which about 2.5 million people in the world have been affected.[2-4]

MS is an inflammatory disease of the CNS. The inflammation causes damage and forms plaques or lesions that are located primarily in the CNS white matter. At the site of the inflammatory lesions, the myelin sheath is destroyed in the process of demyelination. When myelin is lost, transmission of signals through nerves is slowed down or blocked. In some cases, the myelin sheaths around axons can be rebuilt on reducing inflammation. This process is called remyelination and is performed by oligodendrocytes. If there are not enough oligodendrocytes at the lesion site, remyelination will not occur or will be done partially. Therefore, nerves will carry out their functions in an abnormal pathway, and the axons continue to remain for long periods without damage. The lost myelin sheath can be replaced by scar tissue where it is called MS; multiple means many and sclerosis means scar formation.[1]

When the axons are damaged, they do not completely lose their function. As the disease progresses, oligodendrocytes and,

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ultimately, axons are destroyed, leading to a worsening of the symptoms. There is strong evidence that the destruction is caused by the immune system, which indicates that MS is an autoimmune disease.[1]

Prevalence of MS

The prevalence of MS in the Northern Hemisphere is more than in the Southern Hemisphere.[3] Probably more than 2 million people in the world have been affected with MS, and mainly they experience the first symptoms between the ages of 20 and 40 years. Women are two times more likely to develop the disease.[5] Iran is located in a low-risk area for MS[6] and prevalence of MS in different regions of Iran varies from 5.3 to 74.28 per 100,000.[7]

Pathology

MS affects neurons, the cells of the brain and spinal cord that carry information, create thoughts and perception, and allow the brain to control the body. Around these neurons is a fatty acid layer that is known as the myelin sheath. Myelin sheath helps the neurons to transfer signals. MS causes gradual destruction of myelin and transection of axon in the brain and spinal cord. According to the area of demyelination in the brain and spinal cord, MS manifests its symptoms.[3,8]

Pathologically, MS is detected by appearance of demyelinated areas and perivascular T cell inflammation in the white matter of CNS. However, some axons may be not affected by this pathological process.[3,8]

Severity of demyelination is determined by the preservation or destruction of oligodendrocytes. It is indicated that in the early stage of disease, more oligodendrocytes are preserved in plaque lesion. Thus, some degree of remyelination is still possible. In other patients in whom oligodendrocytes are destroyed completely, the possibility of remyelination is very low.[3,8]

Causes

Today, the prevailing theory is that MS is caused by the immune system attacking the nervous system and, thus, is commonly known as an autoimmune disease.[3,9] There is also a more trivial theory which says that MS is not an autoimmune disease but is a metabolic neurodegenerative disorder. However, the main cause of MS is still unknown.[3,10]

Although the exact mechanism of the disease is unknown, there is considerable evidence toward the autoimmune nature of the disease. It has been observed that the levels of immunoglobulin G (IgG) in the cerebrospinal fluid of MS patients are increased, as it is thought that IgG is produced in the CNS. With immunofluorescent and immunoperoxidase techniques, IgG has been detected in the white matter of normal-appearing brain as well as in MS plaque tissue. According to the features previously observed, autoimmune IgG extracted from the brains of MS patients has anti-myelin basic protein (anti-MBP) activity.[4]

In MS, immune dysfunction can be detected locally in the CNS and cerebrospinal fluid, as well as systemically in peripheral circulation. Autoimmune nature of MS has long been suspected. It is known that patients with MS have inflammation and demyelination in their CNS and oligoclonal bands in their cerebrospinal fluid.[3]

MS symptoms

Mainly, every function that is completely or partially controlled by the CNS could be lost. According to the CNS domains which may be affected and how badly is the are damaged, the type and severity of symptoms widely vary.[1]

Relapse-remitting MS (RRMS) type mainly starts with sensory disturbance, unilateral optic neuritis, diplopia (internuclear ophthalmoplegia), Lhermitte's signs (limbs and trunk paresthesia associated with the curvature of the neck), limb weakness, clumsiness, gait ataxia, and neurological bladder and bowel dysfunction. Many patients suffer from fatigue that worsens in the afternoon and is associated with increased physiological body temperature. Some patients have recurrent stereotypical phenomena (sudden pain or paresthesia, trigeminal neuralgia, episodic clumsiness or dysarthria, and tonic limb posturing), which is very common in MS.[1] Cognitive impairment in MS patients leads them to spend more time for their tasks.[11]

Types of MS

Three types of MS have been identified:

- RRMS
- Primary progressive multiple sclerosis (PPMS)
- Secondary progressive multiple sclerosis (SPMS).

MS patients may experience new symptoms in each relapse or slowly over the time. Clinically, most patients with MS suffer from relapsing–remitting type of the disease, which depends on the final phase of the disease. Following this, the most common type of the disease is its neurodegenerative phase called SPMS. Currently there is no cure for MS. Various treatments can slow the appearance of new symptoms, although they have their own side effects.[3]

Treatment of MS

Currently, there is no cure for MS. However, treatments for slowing the disease process or for the MS symptoms are available. Medications to modify the disease process constitute disease-modifying therapy. Four classes of drugs have been approved for the remission phase of MS: (1) interferon-β, (2) glatiramer acetate, (3) mitoxantrone (a chemotherapy agent), and (4) fingolimod.[1,12,13] Interferon beta-1b (Betaseron®) and interferon beta-1a (Avonex®) successfully reduce the number and severity of the disease relapses. Glatiramer acetate is an alternative drug for interferon-β in RRMS.[3]

For relapse phase of MS, corticosteroids are the choice treatment for exacerbations.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

According to the National Institute of Health (NIH), alternative therapies are classified into five categories:[14,15]

- Biologically based therapies
- Alternative medical system
- Mind–body intervention
- Manipulative and body-based methods
- Energy therapies.

Complementary and alternative medicine (CAM) therapies have been suggested for MS symptoms [Figure 1] however studies on their efficacy and safety are very limited. A study in California and Massachusetts shows that 60% of MS patients use CAM for treatment, and each individual uses two or three different forms of CAM. Another study in British Columbia has shown that 67% of MS patients use CAM.[15]

Biologically based therapies

Biologically based therapy includes herbs, diet, and bee venom therapies.[14,15]

Herbs

Herbs can be classified as herbal medicine, food, and spices. Herbs that are commonly used in MS are listed in Table 1.[15-37]

Other herbs

Potentially useful

- Herbs that are rich in γ-linoleic acid, such as flax seed and rapeseed, also could be useful in MS treatment due to their intervention in fatty acid metabolism and lymphocyte functions[38-40]
- Herbs, fruits, and berries that are rich in flavonoids, such as blueberry, could be helpful.[3]

Potentially harmful

- Some plants such as *Echinacea*, *Astragalus* (黃耆 Huáng Qí), and *Spirulina* should be avoided in progressive systemic immune diseases such as MS because of their immune-stimulating properties[19,41-43]
- Since fatigue is one of the most common symptoms in MS, MS patients prefer to use herbal energy enhancers. However, it should be considered that some plants such as tea, coffee, and guarana which contain caffeine and cola, *Citrus aurantium*, and *Ephedra* (麻黃Má Huáng) could be harmful for MS patients and might worsen the symptoms because of their CNS stimulating properties.[19,44,45]

Diet and nutritional supplements

Vitamins and minerals: The advantages of vitamins and minerals as supplements are not clearly understood.[15]

Antioxidant vitamins: Antioxidant vitamins, including vitamins A, C, and E, seem to be useful in MS because of their ability to fight against free radicals, thus proving to be useful in preventing myelin injury and damage.[15]

Non-vitamin antioxidant supplements such as α-lipoic acid, Coenzyme Q10 (Co Q10), grape seed extract, oligomeric proanthocyanidine (OPC), and pycnogenol are more expensive than vitamins, and their efficacy in MS patients and safety are not known.[15]

Vitamin D and calcium: MS prevalence is very high in areas with low vitamin D intake.[46] Vitamin D deficiency is associated with increased progression of MS.[47] Vitamin D level in the body is influenced by two factors: Vitamin D intake through food sources such as milk, eggs, fish, and vegetables and the amount of sun exposure because cholesterol, which is made in the skin, is converted into cholecalciferol or D_3, the active form of vitamin D, by UV B irradiation. Vitamin D resulting from each route will

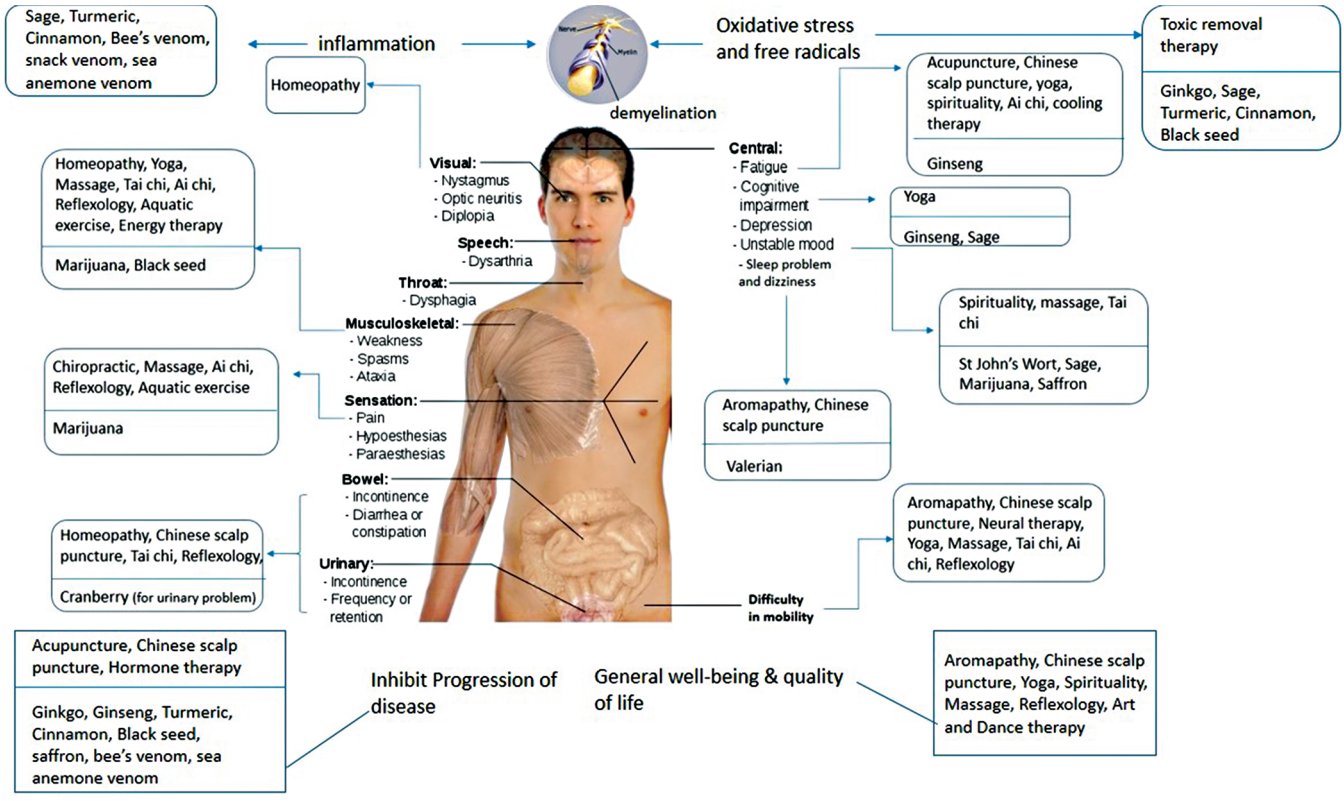

Figure 1. schematic explain of MS symptoms and related Complimentary and alternative therapy

Table 1. Proved effects of medicinal herbs in EAE model and MS symptoms

Type	Common name	Scientific name	Ingredient	Effect in MS
Herbal medicine	St John's wort	*Hypericum perforatum*	Hypericin	Anti-depression activity[15]
	Valerian (纈草 Xié Cǎo)	*Valeriana officinalis*	Not defined	Sedation through GABA-ergic system, increase fatigue[15]
	Ginkgo (銀杏 Yín Xìng)	*Ginkgo biloba*	Ginkgolides	Decrease the exacerbation in MS patients[15]
	Evening primrose oil (月見草 Yuè Jiàn Cǎo Yóu)	*Oenothera biennis*	γ-linoleic acid	Intervention in fatty acid metabolism and lymphocyte functions; could be useful in MS treatment[19,26,29,35]
	Ginseng (人參 Rén Shēn)	*Panax ginseng*	Ginsenosoides	Effective in increasing body resistance to stress, trauma, and fatigue by modulating immune function; improves memory, learning performance, and motor activity; protects against the neurodegenerative process[24]
	Sage	*Salvia officinalis*	Not defined	Improves cognitive function, modulates mood, enhances the memory of young people[24]
	Marijuana (大麻 Dà Má)	*Cannabis spp.*	Cannabinoides	Improves some MS-related symptoms including spasticity, pain, tremor, and depression; improves tremor[15]
Spices	Turmeric (薑黃Jiāng Huáng)	*Curcuma longa*	Curcumin	Suppresses exacerbation in neurodegenerative disease[24]
	Cinnamon (肉桂 Ròu Guì)	*Cinnamomum zeylanicum*	Cinnamaldehyde, sodium benzoate	Treats relapse-remitting EAE.[18,20,25,27,28,31,32,36]
	Saffron (番紅花 Fān Hóng Huā)	*Crocus sativus*	Not defined	Reduces clinical symptoms in the EAE mice model, delayed onset of disease, anti-depression[16,17,21]
	Black seed	*Nigella sativa*	Thymoquinone	Inhibits oxidative stress, leading leading to improved EAE, effective in MS-associated muscle spasticity[20,30,33]
Herbal food	Cranberry	*Vaccinium spp.*	Not defined	Treats urine infections and inhibits some bacteria in MS patients[23,34]

EAE: Experimental Autoimmune Encephalomyelitis, MS: Multiple sclerosis

be transported to the liver to be hydroxylated.[46] In cytoplasm, calcitriol links to intracellular receptors and then passes through the nuclear membrane. The hormone–receptor complex binds to DNA and regulates the expression of several genes including interleukin (IL) 1, IL2, and tumor necrosis factor-alpha (TNF-α), which reduces inflammatory reactions. Therefore, D3 is known to be an immune regulator and an anti-inflammatory agent. Some studies show that administration of vitamin D3 in experimental allergic encephalomyelitis (EAE) mice and rat model may modulate the severity of disease. It could also reduce the complications associated with the disease, including muscle weakness and bone fragility.[15,46,48]

Vitamin B_{12}: Vitamin B_{12} deficiency may cause damage to the spinal cord and optic nerve. MS patients with B_{12} deficiency may benefit from its supplements.

Antioxidants and polyunsaturated fatty acids: Inflammatory conditions and lack of antioxidant defense mechanisms increase the reactive oxygen spies (ROS), which can damage lipids, proteins, and nucleic acids. This damage leads to mitochondrial dysfunctions and induces cell death. Low levels of antioxidants, such as tocopherol, carotene, retinol, and ascorbic acid, and inhibition of antioxidant enzymes in a patient with MS causes oxidative stress leading to cell damage or death. Supplementation of antioxidants may be useful in MS.[49]

Risk of developing MS increases with high levels of saturated fatty acids in the diet. Many studies report omega-3 fatty acids as immune system regulators which act by reducing the levels of inflammatory cytokines such as TNF-α, IL-1, IL-2, and vascular cell adhesion molecule (VCAM1). The beneficial effects of omega-3 fatty acids in inflammatory diseases such as rheumatoid arthritis and MS have been observed. A study reported that administration of omega-3 fatty acids for 3 months could reduce the level of inflammatory cytokine. In addition, omega-3 fatty acids may reduce the level of matrix metalloproteinase (MMP). MMP is zinc-dependent endopeptidase that plays an important role in the migration of inflammatory cells in the CNS fluid, which breaks down blood–brain barriers. Studies show that MS patients have higher level of MMP compared with normal individuals. Chemical compounds of yarrow extract have beneficial effects in preventing or treating neurodegenerative disease.[50]

Linoleic acid: Studies on the relationship between MS prevalence and dietary fatty acids have shown the effectiveness of linoleic acid in MS. It is suggested that linoleic acid has a role in regulation of cell-mediated immunity. Prostaglandin derivatives of linoleic acid show immunosuppressive effect.[51] Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are effective in alleviating the symptoms of MS patients. EPA and DHA are α-linoleic acid derivatives, and they are found in fish oil.[52]

Flavonoids: Flavonoids are colored antioxidants that are found in plants. These substances are responsible for the color of fruits and vegetables. Epidemiological studies show that fruits and vegetables rich in flavonoids can be used for their anti-viral, anti-allergic, anti-inflammatory, and anti-tumor properties.[51]

Luteolin, a regulator of the immune system, can be effective in neurodegenerative diseases like MS by inhibiting the inflammatory responses. It is found in leaves of artichoke (朝鮮薊 Cháo Xiān Jì), rosemary (迷迭香Mí Dié Xiāng), thyme (百里香 Bǎi Lǐ Xiāng), and chamomile (洋甘菊 Yáng Gān Jú).[51]

Quercetin is another flavonoid which exists in onion, apple, and *Gingko biloba*.[51]

Special diet: Low-fat diet (intake of saturated fat less than 20 g/day, avoiding whole milk, cheese, margarine, and other sources of hydrogenated oil, encouraging eating fish three or more times per week and vegetables with high polyunsaturated fat content, using cod-liver oil supplement 5 g/day) could reduce the severity of disease and the frequency of an exacerbation episodes of MS. Mortality rate and serious disability in MS patients who ate saturated fat more than 20 g/day were more than in those on low-fat diet.[19,53]

Venom therapy

Venom therapy involves the use of bee's venom, snake venom, and sea anemone venom.

Bee's venom: Although *Apis mellifera* or bee's sting can cause pain, its venom containing peptide, enzyme, and amines[54] can inhibit migration of leukocytes and decrease the amount of TNF-α leading to anti-inflammatory effects.[54,55] Melittin, one of its components, known as anti-inflammatory, and adolapin, another component, may play a role in analgesia by inhibition of cyclooxygenase. Bee's venom also can reduce the symptoms of EAE in rat.[55] In bee's venom therapy, patients may be at risk of allergic reactions. Nine patients with MS were treated with bee's venom; no serious allergic reactions were seen. However, four patients showed some neurological symptoms that need to be studied further.[56]

Although new information about the efficacy of the venom therapy in the treatment of MS has been obtained, further clinical trials studies are needed.

Snake venom: Snake venom contains various compounds such as polypeptides, protein, and phospholipase. Venom of the Malayan pit vipers (*Calloselasma rhodostoma*), called Ancord, has an anticoagulant polypeptide. It also can delay inflammatory demyelination in animal models.

In inflammatory conditions, fibrin is deposited. Since the brain is permeable to protein in MS, deposition of fibrins leads to damage to axons and inflammatory demyelination. Therefore, fibrin exhaustion by the venom of snakes can inhibit inflammatory reaction.

Overall, there is no clinical trial proving the efficacy of snake venom therapy and studies are usually limited to experimental models.[54]

Sea anemone venom: Stichodactyla helianthus is a sea anemone which can produce peptide and protein as venom. In EAE models, voltage-gated potassium channels (Kv channels) are expressed. Venom of *S. helianthus* can block these channels. In addition, by blocking of Kv channels (especially Kv1.3), production of cytokine and proliferation of T-cell are reduced. Therefore, venom of sea anemone may play a role as an immunosuppressive agent and may be useful in MS.[56]

Alternative medical system

The six most used CAM therapies in MS include reflexology, massage, yoga, relaxation, meditation, aromatherapy, and acupuncture.[57]

Homeopathy

Homeopathy is a treatment system whose basic principle is "let like be treated by like." This means that an individual who has an illness or a condition could be treated with a medicine that produces similar symptoms when a healthy individual uses it. Homeopathic medicines are given in a highly dilute form, so they are nontoxic. The system uses a very wide range of natural substances.[58]

Some kinds of homeopathic treatment are used frequently in MS symptoms. For example, for bladder symptoms and urinary retention, *Causticum* could be used. Bowel dysfunction, mainly constipation, may be treated by *Opium*, *Alumina*, *Nux vomica,* and sulphurarte. Daily use of phosphorus has been reported to be helpful for optic neuritis; combination with *Hypericum* makes it more effective. *Gelsemium* for double vision, *Cuprum metalicum, Cuprum arsenicum*, *Nux vomica* (馬錢子Mǎ Qián Zǐ), and *Ignatia* for cramp and spasm, and *Secale* for sensory symptoms have been reported to be effective in MS patients.[58]

Aromatherapy

Aromatherapy is the use of essential oil to improve health and well-being. In pain management, it has been commonly used. Aromatherapy in MS patients could be effective for some symptomatic relief, such as helping in sleep, relaxation, mobility of joints and muscle, and improvement in the feeling of well-being.[59]

Acupuncture

Acupuncture (針灸Zhēn Jiǔ) is a frequently used method in neurological conditions such as spasticity, stroke, and fibromyalgia. Studies show that acupuncture could be helpful for treating MS associated with fatigue. Acupuncture could release some neurohormones and opioids that affect the disease process and these substances could also slow down or even reverse the progression of MS.[60]

Chinese scalp puncture: Chinese scalp puncture is a combination of Chinese needling method and Western medical knowledge of the cerebral cortex, and has been shown to be a very effective technique for treating MS and other CNS disorders. In this technique, different areas in the brain, such as motor area, sensory area, foot motor and sensory area, balance area, hearing and dizziness area, and tremor area, are stimulated in MS patients. After treatment, patients can stand and walk without any problem. Patients have more energy, and their urinary problem and dizziness are solved. This technique not only relives symptoms but also increases the quality of life and slows or reverses the progression of physical disability. It also reduces the number of relapses and helps patients to remain in remission.[61]

Neural therapy: Neural therapy is a modified form of acupuncture that was investigated by Gibson for amelioration of symptoms of MS. This treatment is cheap and effective for MS and is very useful for patients with the ambulatory problems. It is suggested that this treatment restores the conduction capacity in intact demyelinated axons. However, this treatment is almost new.[51]

Mind–body interventions

Mind–body interventions include meditation such as yoga and prayer.[14,15]

Yoga

Yoga mainly improves the general well-being, including improvement of mobility, muscle strength, and balance.[57] It is an

ancient Indian mind–body technique that focuses on meditation, mind fullness, breathing, and activity or posture. Yoga exercises can improve the muscle tone and reduce fatigue and spasticity. In a study on MS patients who attended weekly Iyengas classes – the most common type of yoga – for 9 months, significant improvement in fatigue was observed compared with the control group.[62]

Yoga intervention significantly improves fatigue, mobility, activity, and mental function.[63,64] Some forms of yoga, such as Bikram yoga which is done in hot temperature, are contraindicated in neurological disorder.[64]

Spirituality

Some studies explore spiritual well-being in some neurological disorders such as MS. Patients aim to achieve spiritual selves through meditation and praying.[65,66] In a research conducted in Switzerland on 150 patients with MS during 8 weeks, it was observed that meditation can reduce the symptoms of MS, such as fatigue, anxiety, and depression, and can improve the quality of life.

Manipulative and body-based methods

Manipulative and body-based methods include massage, reflexology, and chiropractic medicine.[14,15]

Chiropractic

Many of the musculoskeletal symptoms associated with MS could be managed with physical therapies. Chiropractic is one of these therapies. It has shown efficacy in the treatment of chronic spinal pain, so it could be used for treatment of pain in MS patients. Although chiropractic could be one of the choices for pain management, more studies are needed to show its efficacy in MS patients.[67,68]

Massage

A clinical trial shows that massage could be helpful in MS patients. Patients who had massage showed lower anxiety and lesser depressed mood.[51] The main benefits of using massage for MS patients include reduced pain, reduced spasms, improved circulation, increased joint and limb mobility, and improved general well-being.[57]

Tai Chi is an ancient Chinese traditional exercise that is a mixture of mind–body therapy and exercise in the form of slow rhythmic movements. It was originally meant for self-defense, but is used today to improve health, especially position, energy, and balance. In a study on MS patients, depression, spasticity, walking, and bladder dysfunction were found to improve.[69]

Ai chi is a combination of Tai chi and Qigong shiatsu techniques and is practiced by standing in deep water and deep breathing, with slow movements of the arms and legs. It is successfully used in pain management, MS, chronic obstructive pulmonary disease (COPD), diabetes, and arthritis. In a study on 73 patients with MS during 20 weeks, Ai chi was found to significantly reduce pain, spasticity, and fatigue.

Reflexology

Reflexology, also known as zone therapy, is done by applying pressure with the thumb on specific points of the feet related to the internal body organs and glands. Reflexology could improve paresthesia, urinary symptoms, muscle strength, and spasticity.[51] It has been reported to be useful in reducing pain, stopping spasms, reducing bladder and bowel problems, and improving walking and the quality of life.[57] In a study on 71 patients with MS, the symptoms of lack of sensation, muscle weakness, and cramps improved after they received 11 weeks of reflexology.[70]

Aquatic exercise

Aquatic exercise includes pool therapy, hydrotherapy, and balneotherapy which are used routinely for management of pain in patients with neuralgic pain. Warm water also increases the blood flow, which causes muscle relaxation.

Energy therapies

Energy therapy includes magnetic field therapy and therapeutic touch.[14,15]

Magnetic field induces electrical field and subsequently stimulates tissue and neuron. One study shows that repetitive stimulation has an antispastic effect on MS.[53] The mechanism is still unclear.

Other CAM therapies

Hyperbaric oxygen therapy is breathing oxygen at a higher level than the atmospheric pressure in a chamber for 20-90 min each session for 4 weeks. The UK Federation of MS therapy suggested it as a useful, cost-effective method with few side effects. However, some studies showed no significant improvement.[19,71,72]

Art and dance therapy could be effective in the emotional state of MS patients and could improve their well-being.

MS symptoms often worsen in heat and warm environment. Cooling therapy is a method used to reduce body temperature. Cold bath or shower reduces fatigue.[19]

Toxin removal therapy

Toxic metals can cause neurodegenerative disease. Chelation therapy is a method in which toxic metals are removed from the body with chelators such as ethylenediamine tetraacetic acid (EDTA), vitamins, and minerals by excreting them in urine. A study on patients with MS showed that the level of toxic metal in urine reduces after chelation therapies.[19,73] Furthermore, chelation therapy can reduce lipid peroxidation and oxidative DNA damage.[69]

Mercury, silver, copper, lead, and zinc are used as amalgam for filing of teeth. Mercury vapor can be produced in the mouth while chewing foods or drinking warm liquids. Removing dental fillings can be beneficial.[19,74,75]

Hormone therapy

Higher prevalence of MS in women and late onset in men show that the level of testosterone has a predictive effect on MS. Studies on animal models show that treatment with a high dose of testosterone in male and female mice is effective. Supplement therapy with testosterone in men could be considered as a choice, but high dose of testosterone in women has several adverse effects. Pregnancy and high dose of estradiol have a protective effect. Estradiol reduced severity of disease in EAE animal modeles. In

a clinical trial, oral treatment with estradiol was found to reduce inflammatory lesions in the brain.[1,76,77]

CONCLUSION

CAM has different definitions and is considered conventional or unconventional in different countries. It is not routinely taught in medical universities. Patients and health care professionals have a problem finding information regarding different kinds of CAM and usefulness of each. In addition, MS patients experience many problems after receiving conventional therapies. Discussing the available CAMs with their holistic nature may establish stronger patient–physician relationship leading to improved health and satisfaction. In addition, CAM helps patients as a friendly palliative care with low adverse effects by improving the quality of life. Anyway, long-term large-scale studies are needed to show the effectiveness of each CAM therapy.

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