

*Aktuelne teme/  
Current topics*

COMPLEMENTARY AND ALTERNATIVE  
MEDICINE FOR MULTIPLE SCLEROSIS  
TREATMENT: YES OR NO?

KOMPLEMENTARNA I ALTERNATIVNA  
MEDICINA U LEČENJU MULTIPLE  
SKLEROZE: DA ILI NE?

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(THC)

**Ključne reči**

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(THK)

*Abstract*

Multiple sclerosis (MS) is the most common chronic immune-mediated inflammatory disease of the central nervous system in young adults which is characterized by inflammatory demyelination and neurodegeneration with unpredictable effects lasting for the rest of their lives. The aim of the multiple sclerosis treatment is to prevent the demyelination and the reduction of axonal loss. Drugs approved for use in multiple sclerosis which reduce the frequency of exacerbations or slow disability progression are referred as disease-modifying drugs (DMDs). Complementary and alternative medicine (CAM) treatments of multiple sclerosis include: dietary supplementation, herbal medicine intake, vitamin D3 and vitamin B supplementation and some relaxation techniques. Patients' symptoms improve with some complementary and alternative therapies when used in addition to the conventional treatments or for specific symptom alleviation. These therapies must go hand in hand with the traditional disease treatment. Additionally, are proofs that  $\Delta$ -9-tetrahydrocannabinol (THC) improves multiple sclerosis spasticity better than baclofen.

Multiple sclerosis (MS) is an inflammatory disease in which the myelin sheaths around the axons of brain and spinal cord neurons are damaged by autoantibodies, resulting in demyelination and scarring. New symptoms may occur in discrete attacks (relapsing forms) or slowly accumulate over time (progressive forms). Between attacks, symptoms may go away completely. Permanent neurologic problems often occur, especially as the disease progresses. Neurological symptoms include sensory disturbances, optic neuritis, limb weakness, ataxia, bladder dysfunction, spasticity, cognitive deficits and fatigue. Our team has several interesting review articles on the treatment of MS [1, 2]. The aim of the treatment is to prevent demyelination and to reduce the axonal loss [1]. It would be of interest to combine an anti-inflammatory agent with a neuroprotective agent, to cover more of the pathologic spectrum of multiple sclerosis [2].

Treatment and management of MS should be targeted toward relieving symptoms of the disease, treating acute

exacerbations, shortening the duration of an acute relapse, reducing frequency of relapses, and preventing disease progression. Drugs approved for use in MS that reduce the frequency of exacerbations or slow disability progression are referred to as disease-modifying drugs (DMDs). These DMDs can be further classified as immunomodulating (or receptor modulating) or immunosuppressive. Some immunosuppressants are also FDA-approved as antineoplastic agents. Drugs that treat MS-related symptoms (eg, acute exacerbations, cognitive dysfunction, fatigue, spasticity, bowel and bladder problems, and pain) but do not modify the course of the disease are referred to as symptom-management medications [1].

According to the National Institutes of Health, almost 40 % of adult Americans spent \$33,9 billion on complementary and alternative medicine (CAM) in 2007 alone. Recently MS patients avail themselves of CAM. Some studies estimate their CAM usage as high as 80 percent. Some CAM

therapies are recommended by physicians, as enough evidence has accumulated to support their use. Hospitals often incorporate massage therapy, meditation, and visualization techniques to reduce pain or help with rehabilitation. The goal of the CAM in MS is to draw attention to the existing evidence for the effectiveness or ineffectiveness of these therapies and to highlight the need for more rigorous studies into the safety and efficacy of CAM. Furthermore, very little data is available on how CAM therapies interact with conventional therapies or what are the long-term effects of many treatments [3]. MS sufferers who use CAM, experience improved disease symptoms after the combination of these therapies with conventional treatments. Since these therapies are not harmful to patients then no problem with their use is anticipated. Caution against hot yoga though is expressed as MS patients can be sensitive to heat. The recent studies found that over 50-60% of people with MS may use complementary and alternative medicine possibly because conventional treatments lack effectiveness [1]. The percentages vary depending on how alternative medicine is defined [4]. The evidence for the effectiveness for such treatments in most cases is weak or absent [4, 5]. Treatments of unproven profit used by people with MS include: dietary supplementation, herbal medicine including ginkgo biloba [3], folic acid [3], vitamin D3 supplementation [5, 6, 7]; and regimens [4, 8, 9]; relaxation techniques such as gymnastics exercises, Chinese soft martial art technique Tai chi chuan, reiki, ayurveda and yoga [4]. Usage of medical cannabis is also documented as potentially beneficial [4, 10, 11]. Other techniques include parts of physiotherapy and rehabilitation as a hyperbaric oxygen therapy [12], reflexology and acupuncture [4], massage, magnetic therapy [3]; self-infection with hookworms [13]. Reflexology is CAM treatment, which involves applying manual pressure to points on the feet, and has positive effect on MS-related paresthesia. The paresthesia is similar to pins and needles; a person with MS may feel burning, prickling, or itching sensation on the skin. This is one CAM that may be considered as an alternative to conventional treatments in cases where the conventional treatment has adverse side effects for a patient [3]. Magnetic therapy treatment is effective for fatigue, a common symptom of MS. In magnetic therapy, patients are exposed to low frequency, pulsed electromagnetic fields on a regular basis. It is unclear how magnetism works to relieve fatigue, but it has few side-effects and is regarded as relatively benign. Ginkgo biloba supplementation is potentially effective for the relief of fatigue in MS. However, the authors have no good handle on how Ginkgo biloba affects that symptom [3].

Spasticity in MS is characterized by increased muscle tone and resistance to movement. It occurs most frequently in muscles that function to maintain upright posture. The muscle stiffness greatly increases expended energy to perform daily activities which in turn contributes to fatigue. Spasticity reduction gives the patient more freedom of movement with less energy expenditure, as well as avoiding complications such as pain, contractures, and decubitus [14].

Pharmacologic treatment of spasticity includes a skeletal muscle relaxant baclofen used as a first-line agent. Baclofen

can be titrated easily in divided doses. Adverse effects include fatigue and weakness. Baclofen overdose can lead to coma, respiratory depression, hyporeflexia, and flaccidity [15].

Recently, randomized, double-blind, placebo-controlled studies have confirmed the clinical efficacy of cannabinoids for the treatment of spasticity in patients with MS [11, 16, 17]. A review of six randomized controlled trials of a combination of  $\Delta$ -9-tetrahydrocannabinol (THC) and cannabidiol (CBD) extracts for the treatment of MS related muscle spasticity reported a trend of reduced spasticity in treated patients. Thus, cannabinoids seem to provide neuroprotective and anti-inflammatory benefits in MS. A small study done on whether or not cannabis could be used to control tremors of MS patients was conducted. The researchers concluded that the mood enhancing or cognitive effects that cannabis had on the brain could have given the patients the effect that their tremors were getting better [18].

Since the beginning of the 20th century, most countries have enacted laws against the cultivation, possession or transfer of cannabis. The plant has been a subject to legal restrictions with the possession, use, and sale of cannabis preparations containing psychoactive cannabinoids currently illegal in most countries of the world though simultaneously cannabis is the most-used illicit drug in the world [3]. A number of investigators have suggested that this is an important factor in marijuana's effects, perhaps because cannabinoids accumulate in the body, particularly in the lipid membranes of neurons [11]. Based on these data, nabiximols (USAN, trade name Sativex - GW Pharma Ltd), a 1:1 mix of  $\Delta$ -9-tetrahydrocannabinol and cannabidiol extracted from cloned Cannabis sativa chemovars, received approval for treating MS-related spasticity in various countries around the globe [17]. In Germany, a cannabis extract was approved in 2011 for the treatment of moderate to severe refractory spasticity in multiple sclerosis. It is commonly used off label for the treatment of anorexia, nausea, and neuropathic pain [19]. Sativex is the first cannabinoid preparation to be approved as a symptomatic treatment option. Sativex has been licensed for symptom improvement in adult patients with moderate to severe spasticity due to MS who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy [14].

Recently, American Academy of Neurology (AAN) published a guideline on complementary alternative therapies, such as medical marijuana, to treat MS. Another systematic review published by the AAN discussed the efficacy and safety of medical marijuana in selected brain and nervous system disorders, such as epilepsy, Parkinson's disease, MS and Tourette syndrome [20].

## CONCLUSION

It is vital for patients and physicians to distinguish between disease-modifying therapies and symptom-alleviating therapies. Disease-modifying therapies positively affect the course of the disease, whereas symptom-alleviating therapies offer relief for specific symptoms of a disease. Although CAM treatments may affect the course of MS patients

should not stop using the FDA-approved drugs that have been proven in clinical trials to reduce inflammation and relapse and slow the progress of the disease.

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### Sažetak

Multipla skleroza (MS) je najčešća hronična imunološka i inflamatorna bolest centralnog nervnog sistema koja pogađa mlade ljude i koju karakteriše inflamatorna demijelinizacija i neurodegeneracija sa nepredvidivim efektima koji traju do kraja života. Cilj lečenja MS je da spreči demijelinizaciju i smanji gubitak aksona. Lekovi koji se koriste za lečenje MS smanjuju učestalost pogoršanja (egzacerbacije) i usporavaju progresiju bolesti, klasifikuju se kao lekovi koji modifikuju bolest (LMB). Lečenje MS komplementarnom i alternativnom terapijom (KAT) uključuje: dijetetske dodatke ishrani, unos biljnih lekova, vitamina D3 i B vitamina, kao i neke tehnike relaksacije. Simptomi bolesti se smanjuju sa nekim komplementarnim i alternativnim načinima lečenja kada se primenjuju zajedno sa konvencionalnom terapijom ili sa specifičnom simptomatskom terapijom. Ove vrste lečenja moraju da idu pod ruku sa tradicionalnim terapijama. Osim toga, postoje dokazi da  $\Delta$ -9-tetrahidrokanabinol (THK) smanjuje spasticitet uzrokovan MS-om bolje od baklofena.

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