Melatonin and Multiple Sclerosis: An Outline on Current Evidences

Seyed-Hossein Abtahi1,2, Zahra Nasri2,3, Niloofaralsadat Nourian1, Seyed-Mojtaba Abtahi2, Fatemeh Abrishamchi2, Masoud Etemadifar1 and Mahboobeh Fereidan-Esfahani1,2

1Isfahan Research Committee of Multiple Sclerosis (IRCOMS), Isfahan University of Medical Sciences, Isfahan, Iran
2Persia Research Center, Sady hospital, Isfahan, Iran
3Medical Students' Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
4Medical School, Islamic Azad University, Najafabad Branch, Najafabad, Iran
5Department of Neurology, Medical School, Isfahan University of Medical Sciences, Isfahan, Iran
6Department of Otolaryngology/Head and Neck Surgery, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

To date, in the literature, there have been a number of studies regarding the effects of Melatonin on MS course and pathogenesis; herein, we wish to bring a concise outline on such evidences to the readership.

Keywords: Melatonin; Multiple sclerosis; Sleep; Vitamin D

Multiple sclerosis (MS) is a complex demyelinating disorder resulting from multiplicity genetic and environmental risk factors. The substantial rise in MS prevalence and changing in the epidemiological pattern of MS have been shown in several population-based studies [1].

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Melatonin is mainly produced by pineal gland in dark phase and metabolized to principal metabolite 6-hydroxy-melatonin in the liver. Although, melatonin secretion has a constant rhythmic amplitude in each individual, significant differences has been shown among the general population [2].

Varied factors such as, high oxygen utilization; high concentration of polysaturated fatty acids; low concentrations of cytosolic antioxidants; and, existence of transition metals such as iron involved in the generation of hydroxyl radicals make the brain susceptible to radical damage [3]. On one hand, some theories for the role of oxidative stress, autoimmunity and inflammatory process have been proposed in the pathogenesis of MS lesions. On the other hand, the anti-inflammatory, immunomodulatory and antioxidative effects of melatonin have been previously well established [4]; theoretically, these protective effects could play an important role in MS pathogenesis, course and complications such as fatigue [5].

Some previous studies showed that the level of melatonin or its metabolites decreases in MS patients compared with normal controls and inversely might be correlated with MS disease activity [6,7]. Such findings could have been explained by the anti-inflammatory property of melatonin.

Complications such as sleep restriction and depression are common in MS. Melatonin secretion is directly affected by environmental stimuli such as light and in turn, regulates the sleep circle in humans. A recent study showed significant decrease in melatonin levels among patients with sleep restriction [6]. Relatively, increased risk of MS has also been shown in young patients with shift work [8]. Moreover, one of the routine treatments of MS patients i.e. Interferon-beta may result in increased level of serum melatonin, though, this medication was not shown to improve the sleep efficacy. Such results might have been due to other factors along with melatonin which could play a role in sleep disturbances; e.g. urinary complications; spasticity and muscle cramps; fatigue; depression; disease activity; and, location of CNS lesions.

In some reports, depression -- another common complication of MS -- has been associated with low nighttime level of serum melatonin [9]; a finding which can be speculatively explained by melatonin dysregulation in MS. However, some other studies [10,11] do not support such a linkage; this could be due to other confounding factors e.g. antidepressant agents, beta blockers or hormonal drugs, as well as age, light exposure and season.

Impressive geographical gradient with significantly higher incidence of MS in increasing altitude led scientists to evaluate the role of vitamin D in MS patients and also its relation with melatonin secretion [12,13]. Recently, Golan et al. [14] found that melatonin level is inversely related to 25-OH-D level. They adhered to the notion that “25-OH-D can bring a ‘message of light’ to the pineal gland and consequently decrease melatonin synthesis”. Such possible interconnectivities between vitamin D and melatonin are an engaging issue to be opened up in future works. Further clinical and experimental studies should consider the concurrent role of melatonin and vitamin D on MS-related symptoms and disease course.

References


*Corresponding author: Mahboobeh Fereidan-Esfahani, Isfahan MS Society, No.2, Behesht Building, Bozorgmehr Ave., Isfahan, Iran, Tel: +98.9380283952; E-mail: mf.esfahani@yahoo.com

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