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Benefits of Melatonin in Health Through the Regulation of Biological Rhythms: An Update on its Therapeutic Use

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Abstract

Melatonin is one of the major hormones related to circadian cycle regulation in the human body. More and more studies are showing benefits of its therapeutic use, both in supplemental form and with food sources. Benefits include improvements in metabolism, antioxidant profile and sleep quality. However, there is still a need to establish the best dietary sources for this nutrient and safe supplementation doses for specific population groups.

Keywords: Melatonin; Supplementation; Food sources

Introduction

One of the main sleep-related hormones is melatonin, which regulates biological rhythms and has important antioxidant, immune and antitumor function [1,2]. In the human body melatonin can be synthesized by the pineal gland, retina, bone marrow, skin and cells of the gastrointestinal tract. Thus, being synthesized in different places, its effects do not have a specific target organ either [3]. Melatonin synthesis occurs from the neurotransmitter serotonin in the following sequence: tryptophan → serotonin → N-acetyl serotonin → melatonin [1,2]. In this sense the cells of the suprachiasmatic nucleus (SCN) receive from the retina information related to the period of the day and send to the pineal gland the command to produce melatonin. So pineal synthesizes melatonin and distributes it as a signal for its production to the body. Once released, melatonin coordinates circadian and neuroendocrine processes by activating two melatonin receptors called MT1 and MT2, coupled to G protein [4,5].

Secretion of this hormone begins at dusk approximately 2 hours before bedtime. Maximum plasma levels are reached between 3:00 AM and 4:00 AM, coinciding with the lowest body temperature and varying according to everyone's chronotype, seasonal changes and dark light cycle [2,3]. Once produced, melatonin is distributed to all body tissues, but is not stored. Approximately 90% of circulating levels are metabolized in the liver and its major metabolite (6-sulfatoxymelatonin) excreted in the urine [2]. Melatonin levels decrease with age and are inversely related to poor sleep quality, so deficiency of this hormone may be responsible for decreased sleep quality [3]. In addition, melatonin levels may be lower when cardiovascular disease is present [5]. Because of its metabolic effects, such as improved insulin resistance, antioxidant power and circadian rhythm control, more and more studies are examining the melatonin benefits for health [5,6].

Thus, melatonin supplementation has been considered. Koziod et al., by a randomized trial in 33 healthy subjects showed that supplementation of melatonin 5 mg for 2 months, improved lipid profile, antioxidant and blood pressure [7]. Two other studies observed, in addition to improvements in metabolic profile, improvements in insomnia levels and sleep quality with supplementation 10mg/day of melatonin [8,9]. In 33 patients with traumatic brain injury, supplementation of 2mg/day of melatonin for 4 weeks also showed objective and subjective improvements in sleep quality [10]. Despite the numerous benefits already described with supplementation, some small reports of adverse effects such as dizziness, nausea, drowsiness and headache in relation to placebos are observed. It

is also noteworthy that further investigation of supplementation for population groups such as pregnant women, children, infants is still needed to obtain greater safety [11].

Regarding diet, it is possible to observe a positive correlation between the consumption of melatonin food sources and improvement of its circulation level. A study of healthy Japanese women evaluating the consumption of 350g of vegetables for 65 days showed a significant increase of 6-sulfatoxymelatonin in the urine of these volunteers, indicating an improvement in circulating melatonin concentrations [12]. In turn, Nagata et al., using a frequency questionnaire of food intake, showed a positive association between the consumption of vegetables and urinary excretion of 6-sulfatoxymelatonin [13]. With respect to tropical fruits, it is possible to observe a considerable increase of 6-sulfatoxymelatonin in the urine with the consumption of pineapple, banana, and orange [14]. Animal studies assessing the intake of fermented goat milk and bean sprouts also show improvements in melatonin biomarker levels as well as antioxidant capacity [15,16].

When it comes to melatonin in food, it stands out that it has already been detected and quantified in roots, buds, leaves, flowers, fruits and seeds. Higher concentrations can be found in plant reproductive organs, particularly seeds, which may be related to species survival through antioxidant defense [5]. Melatonin concentrations may also change within varieties of the same species, which may be related to the detection technique, extraction, as well as the environmental conditions that the specie variety was subjected to such as soil type, climate and solar incidence. The processing level of a food (cooking, fermentation, baking) can also influence melatonin concentrations, which shows the need to build consistent food composition tables for it [5,6].

Conclusion

In this sense, it is observed that both in supplemental form and in diet, melatonin can have beneficial effects both in improving circadian rhythm, as well as in anti-inflammatory and metabolic processes. Despite this, the literature shows that there are still several gaps, especially when it comes to the benefit of dietary sources. Thus, further studies are needed to establish concrete and safe recommendations.

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