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Melatonin: A Promising Natural Agent in the Prevention of ALS

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A number of years ago, experimental studies suggested melatonin could block key steps in the development of Alzheimer's disease, primarily by acting as a brain antioxidant and inhibiting the build-up of beta-amyloid plaque in the brain (a hallmark feature of Alzheimer's disease). In recent years, several clinical studies have gone on to suggest melatonin supplementation (3-9 mg per day) can block the progression of mild cognitive impairment (MCI) to full-blown dementia and Alzheimer's disease in a significant number of human subjects compared to placebo.[1-4]

A recent animal study goes a step further, suggesting melatonin also blocks key steps in the development of Lou Gehrig's disease (also known as amyotrophic lateral sclerosis or ALS), a disease that causes progressive muscle weakness and eventual death due to the failure of respiratory muscles.

After screening more than a thousand FDA-approved drugs several years ago, a research team determined melatonin is a powerful antioxidant which blocks the release of enzymes that activate programmed cell death (apoptosis) of nerve cells involved in the development of ALS. They later followed up using a transgenic mouse model of ALS, demonstrating that melatonin injections delayed symptom onset and reduced mortality from ALS in mice. In this model, mice were bred to carry the gene that encourages the development of Lou Gehrig's disease.[5]

Melatonin and ALS Inhibition

The researchers involved in the recent animal study stated: "We demonstrate that melatonin significantly delayed disease onset, neurological deterioration and mortality in ALS mice." More specifically, melatonin was shown to inhibit nerve degeneration and nerve cell death of the motor nerves involved in ALS.

These nerves are the motor nerves in the ventral horn of the spinal cord, which supply life-force energy to the muscles of the body, including respiratory muscles. When these nerve cells die, muscles become paralyzed and unable to function.

Melatonin was shown to block nerve cell death in the ventral horn motor nerves by inhibiting several key pathways within these nerve cells that otherwise cause nerve cell death in ALS. These pathways include inhibiting the Rip2/caspase-1 pathway, blocking the release of mitochondrial cytochrome c, and reducing the over expression and activation of caspase-3. The researchers went on to state: "Moreover, for the first time, we determined that disease progression was associated with the loss of both melatonin and the melatonin receptor 1A (MT1) in the spinal cord of ALS mice."

One of the researchers, Dr. Robert Friedlander, explained that the research team saw similar results

in a Huntington's disease animal model in an earlier project, whereby melatonin injections inhibited the same nerve cell death pathways when injected into animals bred to be genetically predisposed to Huntington's disease.[5]

Aging and Melatonin

Melatonin is a hormone synthesized in the pineal gland in the brain. Upon darkness, it is released, which helps to induce sleep and increase depth and quality of sleep. Melatonin is also a powerful brain antioxidant and immune modulator, and also demonstrates some impressive anti-cancer properties, especially with respect to breast and prostate cancer.

As we age, melatonin secretion drops off markedly, which explains many cases of insomnia and sleep disturbances that arise by age 40. Some research now suggests the age-related decline in melatonin also makes us more susceptible to dementia, Alzheimer's disease, immune-system weakness, and breast and prostate cancer.[6]

Emerging research also suggests the decline in melatonin may trigger the development of ALS and possibly Huntington's disease in those who are genetically predisposed to these neurodegenerative conditions. Although speculative at this point, impressive animal model studies have elucidated the pathways and mechanisms through which melatonin may be protective in preventing the onset of these neurological conditions or slowing their progression.[5]

Melatonin research continues to show its impressive biological effects in preserving health and preventing a number of diseases and health challenges. For the sake of general wellness, sleep quality, immune system support and prevention of various degenerative diseases, many health experts recommend taking a melatonin supplement after 40 years of age. This practice compensates for the decline in melatonin synthesis and secretion by the pineal gland as we age, helping to ensure more optimal brain and body levels of this important protective compound.

Melatonin is best taken one hour before bedtime each night. I personally take a supplement of this nature that also includes other synergistic nutrients that help support brain health, well-being and memory. Here is an example of such a supplement (one capsule) and the recommended dosage, which is based on age:

- Melatonin – 500 mcg (0.5 mg)
- 5-hydroxytryptophan (5 HTP) – 10 mg
- Gamma amino butyric acid (GABA) – 25 mg
- Bacopa monnieri – 15 mg (std to 20 percent bacosides)

The correct sleep-aid dosage is the one that helps induce a good night's sleep with no excessive morning grogginess. Suggested daily dosage based on age is as follows:

- Ages 40-49 – 1-2 capsules one hour before bedtime
- Ages 50- 59 – 2-3 capsules one hour before bedtime
- Ages 60-69 – 3-4 capsules one hour before bedtime
- Ages 70-plus – 4 capsules one hour before bedtime

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