

Complementary and Alternative Medicines Patients Are Talking About: Melatonin

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Melatonin (N-acetyl-5-methoxytryptamine) is a hormone produced by the pineal gland in the brain in response to darkness. Melatonin is made available when tryptophan is converted to serotonin and then enzymatically converted to melatonin in the pineal gland. Serum levels are low during the day, with peak levels occurring from 2–4 am.

Route of Administration

Melatonin is extracted from the pineal gland of beef cattle or synthesized chemically from 5-methoxytryptamine. Synthetic melatonin is taken orally as a tablet, sublingually, as an intramuscular injection, or as an IV infusion.

Dosing and Cost

Dosing of melatonin varies from 5 mg daily for relief of jet lag to 75 mg daily for chronic insomnia (Natural Medicines Comprehensive Database, 2005). Clinical trial doses range from 10–40 mg daily. The monthly cost for a 3 mg daily dose is about \$5, which is not covered by insurance.

Indications

Melatonin is marketed commercially for the relief of jet lag and insomnia. Other reported uses are for the treatment of tinnitus and cachexia, as oral contraception when combined with progestin, and for cancer treatment as combination therapy prior to or during interleukin-2 treatment. Melatonin also is believed to possess antioxidant properties (ThomsonTM Micromedex, 2005).

Regulation

As a dietary supplement, defined by the Dietary Supplemental Health and Education Act of 1994, melatonin does not fall under postmarket regulation by the U.S. Food and Drug Administration (FDA). The FDA is responsible, however, for taking action against any unsafe products once reported.

Safety and Efficacy

Supplements with melatonin appear to have a good safety profile. Ten clinical trials from 1992–2003 involving the use of melatonin for the treatment of cancer or supportive care were included in a systematic review reporting that, despite differences in tumor type and dosing, melatonin diminished the risk of mortality at one year (Mills, Wu, Seely, & Guyatt, 2005). Conflicting evidence exists regarding whether melatonin protects against chemotherapy-induced tox-

icities (Cerea et al., 2003; Ghielmini et al., 1999; Persson, Glimelius, Ronnelid, & Nygren, 2005). Table 1 offers a summary of the studies.

Interactions

Because the metabolism of melatonin occurs via the liver enzyme cytochrome P450 1A2, drugs that alter the activity of 1A2 may increase or decrease the effects of melatonin supplements (Natural Standard, 2005). Common drugs that increase the side effects of melatonin are anastrozole, cimetidine, ciprofloxacin, and interferon. Common drugs that decrease the therapeutic effects of melatonin are insulin, nafcillin, omeprazole, and ritonavir. Increased daytime drowsiness is reported with concurrent use of zolpidem, lorazepam, codeine, and alcohol. Because long-term effects of melatonin have not been examined in women who are trying to conceive, pregnant, or nursing, caution is warranted.

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