Melatonin as a sleep aid: Are you prescribing it correctly?

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Difficulty achieving regular restorative sleep is a common symptom of many psychiatric illnesses and can pose a pharmaceutical challenge, particularly for patients who have contraindications to benzodiazepines or sedative-hypnotics. Melatonin is commonly used to treat insomnia and circadian rhythm disorders in hospitalized patients because it is largely considered safe, nonhabit forming, unlikely to interact with other medications, and possibly protective against delirium.[1] We support its short-term use in patients with sleep disruption, even if they do not meet the diagnostic criteria for insomnia or a circadian rhythm sleep-wake disorder. However, this use should be guided by consideration of the known physiological actions of melatonin, and not by an assumption that it acts as a simple sedative-hypnotic.

How melatonin works

Melatonin is an endogenous neurohormone involved in circadian rhythm regulation (sleep/wake regulation), a fundamental process in the functioning of the CNS and in the development of psychiatric disorders.[2] Melatonin is commonly described as a sleep-promoting neurotransmitter, but it is more accurately described as a "darkness hormone."[3] With an onset at dusk and offset at sunrise, melatonin is the signal for biological night, not the signal for sleep. Melanopsin-containing retina neurons sensitive to blue light sense the diminishing light of the evening and communicate this cue to the brain's master clock in the suprachiasmatic nucleus (SCN) of the hypothalamus (via the retinohypothalamic pathway). The SCN then releases its inhibition on the pineal gland, allowing it to release melatonin into the bloodstream and CSF. The timing of this release is known as the dim-light melatonin onset (DLMO).

Selecting the optimal timing and dose

Studies in laboratory and home settings have consistently shown that the DLMO precedes the onset of sleep by approximately 2 to 4 hours.[4] Thus, we recommend scheduling melatonin administration for 2 to 4 hours before the intended bedtime.

Lower doses better replicate physiological levels of melatonin. A lower dose is also less likely to lead to a compromise of the entrainment process and the induction of a delayed sleep phase due to the lingering presence of melatonin, or the phase-delaying effects of a strong melatonin signal much later than the ideal DLMO. Giving higher doses at bedtime will induce sleep but may cause a circadian phase delay, effectively "jet lagging" the patient. We recommend prescribing low-dose melatonin (LDM; 0.5 to 1 mg) 2 to 4 hours before the intended bedtime rather than

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higher doses (≥5 mg) given at bedtime as is common practice and recommended by many melatonin manufacturers. LDM better simulates the natural release and function of melatonin and avoids potential adverse circadian phase delays. The successful use of melatonin in hospitalized patients suggests there is a unique opportunity to use this safe and effective medication with a relatively well-understood mechanism of action for nonhospitalized patients who are having difficulty sleeping. Considering the known physiological actions of melatonin can help guide the optimal timing and dosage of melatonin for this purpose.

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