

Medical News & Perspectives

Climbing Melatonin Use for Insomnia Raises Safety Concerns

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In recent years, Judith Owens, MD, MPH, has seen increasing numbers of her pediatric patients taking over-the-counter (OTC) melatonin supplements as a sleep aid. In some cases, parents decided on their own to give it to their children who had trouble sleeping; others tried it because a pediatrician recommended it.

"They end up on my doorstep in a sleep clinic because [melatonin] is not the magic bullet," Owens, director of the Center for Pediatric Sleep Disorders at Boston Children's Hospital and a professor of neurology at Harvard Medical School, said in an interview.



[Medical News website](#)

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Owens' patients are part of a larger trend. National Health Interview Survey [data](#) from interviews with 17 321 adults caring for children and teens aged 4 to 17 years found a 7-fold increase in melatonin use, to 0.7% of the youths in 2012, up from 0.1% in 2007.

Increasing use isn't confined to children and adolescents. More recent [data](#) from a total of 55 021 participants in 10 cycles of the National Health and Nutrition Examination Survey (NHANES) showed that melatonin use increased by 5-fold, to 2.1% of 5563 participants in the 2017-2018 cycle compared with 0.4% of 4865 participants in the 1999-2000 cycle.

The data also showed that more adults are using doses greater than 5 mg, which boost serum melatonin levels far beyond typical nighttime [peak concentrations](#) before declining after 4 to 8 hours. Prior to the 2005-2006 NHANES survey, no participants reported taking more than 5 mg per day but by 2018, about 1 in 8 melatonin users did so.

Sales data indicate the trend may be accelerating, with melatonin sales more than doubling to \$821 million in 2020 from \$339 million in 2017, according to data from [Statista](#). Market research company Technavio [predicts](#) continued growth in melatonin sales through 2026 due to an aging population that's at greater risk of sleep problems and increasingly hectic lifestyles that can result in anxiety and disordered sleep.



"It's a crazy situation that has gotten out of hand," said Owens, who also is president of the International Pediatric Sleep Association.

She and other sleep experts are concerned about the potential harm melatonin use without physician oversight may cause, particularly at higher doses and over the long-term. And US poison centers have reported a [startling increase](#) in the past decade of calls about children who have ingested melatonin.

"It's a bit alarming; just because the product is available over the counter doesn't mean it is totally harmless and doesn't have important physiological effects," senior author of the NHANES analysis, Naima Covassin, PhD, an assistant professor at the Mayo Clinic College of Medicine and Science in Rochester, Minnesota, said in an interview.

Resetting the Clock

Melatonin is a hormone secreted by the pineal gland that helps synchronize the body's

daily circadian rhythms with the light-dark cycle, Covassin said. Levels of melatonin slowly increase a few hours before bedtime, setting the stage for the body to switch gears for rest and other nighttime physiological activities.

"Melatonin can be very effective in resetting the clock and changing sleep timing by advancing or delaying it," Covassin said. "But it's often misused to help with insomnia."

Studies show melatonin is effective for improving sleep in [shift workers](#) or easing [jet lag](#). An American Academy of Sleep Medicine's (AASM) Best Practice Guide also [suggests](#) melatonin for rapid eye movement (REM) sleep disorder—a condition that disproportionately affects older adults and causes some people to act out dreams, sometimes violently.

Children with some neurodevelopmental conditions also may benefit. Owens explained that some evidence shows delayed melatonin release in children with attention-deficit/hyperactivity disorder (ADHD), and

some with autism release melatonin at the wrong time of day. A [practice guideline](#) from the American Academy of Neurology suggests melatonin for children with autism if behavioral approaches haven't helped and the sleep effects of medications and co-occurring conditions have been addressed. A recent [review](#) also noted evidence from randomized controlled trials that indicate melatonin reduces sleep onset delays in children with ADHD.

Most studies of the drug's use for insomnia have been small and of short duration and show very modest benefits, such as a 5- to 8-minute decrease in the time it takes to fall asleep, Covassin said. A 2017 [clinical practice guideline](#) from the AASM suggests against using melatonin for adults with insomnia who have difficulty falling or staying asleep.

"There aren't any medications recommended for long-term use for insomnia in children or adults," Jennifer Martin, PhD, president of AASM and professor of medicine at the David Geffen School of Medicine at the University of California, Los Angeles, said in an interview. "We always try nonmedication approaches first, and for most people, that works."

Self-medication

Insomnia rates have risen dramatically over the past 2 decades with roughly [one-third](#) of US adults experiencing insomnia. Similarly, a recent CDC [report](#) found that one-third of US children and adolescents aren't getting sufficient sleep. And older adults are more likely to have sleep difficulties, so the aging US population may contribute to the increase, Phyllis Zee, MD, PhD, director of the Center for Circadian and Sleep Medicine and professor of neurology at Northwestern University's Feinberg School of Medicine, noted in an interview. Additionally, 24/7 work schedules and constant social media use may also expose individuals to blue light at night, which can inhibit endogenous melatonin production, Covassin said.

These rising rates of sleep difficulties, coupled with a growing recognition that poor sleep has health consequences, have led more people to seek treatment, with some turning to melatonin, Owens said.

"[Melatonin] is an easy fix," Owens said.

The pandemic may have exacerbated some of these underlying trends.

"During the COVID-19 pandemic, we have seen increasing struggles with

sleep across the board," Martin said. Many people, she noted, are turning to supplements and home remedies instead of clinical best practices.

Safety concerns about prescription sleep medications may also cause patients or physicians to look for alternatives they perceive as safer, Zee said. In 2013, the US Food and Drug Administration (FDA) [warned](#) that using zolpidem could impair next-day driving and mental alertness. A year later, the agency issued a similar [warning](#) for eszopiclone. The FDA added [boxed warnings](#) in 2019 to the eszopiclone, zaleplon, and zolpidem labels, cautioning that people who take the medications may engage in "complex behaviors" like driving or walking while still asleep. The FDA identified 66 cases of complex behaviors in users over a 26-year period that resulted in serious injuries, including 20 deaths.

Growing concerns about adverse effects may have contributed to fewer prescriptions for insomnia medications including zolpidem between 2011 and 2018, according to a 2020 [research letter](#) in *JAMA*. Melatonin may be perceived as safe because it is "natural" or a supplement, Zee said. It might also be easier to obtain for those who don't have access to sleep specialists, she added.

"It is kind of self-medication," Zee said.

In most other countries, melatonin is only available by prescription. But in the US, it's regulated as a supplement with little oversight over product ingredients or manufacturing processes. Some studies have raised concerns about these OTC products' quality control and content. For example, a [study](#) of OTC melatonin supplements sold in Ontario, Canada, found that the melatonin content was as much as 478% higher than the label indicated in some products and could fluctuate substantially between lots. Eight out of 31 products tested also contained serotonin, a product of melatonin breakdown, at potentially clinically significant doses.

"It's cheap, available, and I think the marketers have done an excellent job of making it seem safe and not a big deal," Owens said.

Potential Risks

Melatonin supplements are "generally safe and well-tolerated, but they are not completely free of risks," Covassin said. The adverse effects may include headache, fa-

tigue, dizziness, or daytime sleepiness. Small studies have also documented potentially more severe consequences, including impaired [glucose tolerance](#) and [increased blood pressure and heart rate](#) in patients concurrently taking melatonin and antihypertensive medication.

"We know very little about long-term safety," Covassin said. For example, a recent [analysis](#) concluded that long-term studies are needed to assess melatonin's effects on puberty based on research of how it influences other hormones and sexual behavior in animals.

High doses may increase the risk of adverse effects, Zee explained. She noted that the pineal gland releases melatonin in picograms and that doses used to treat circadian shift disorders are typically small—about half a milligram, which is far lower than what is offered in many OTC products.

The dose of melatonin and when it's taken also affect how the user will feel. Owens explained that a 3- to 5-mg dose taken a half hour before bed will induce drowsiness. A much lower dose of about 0.5 mg taken earlier in the evening will shift bedtime earlier. A high dose of melatonin taken in the middle of the night could lead to morning drowsiness, Zee noted.

"If given at the wrong time of day, it can shift your clock in the wrong direction," Zee said. "Given at the right time of day, it can help you maintain a healthier clock. It goes both ways."

The same as with prescription drugs, inappropriate use or carelessness can have dire consequences. Between 2012 and 2021, US poison control centers fielded 260 435 calls about children who had ingested melatonin—a [530% increase](#) during the period. Most of the children were asymptomatic and recovered at home. But 4097 were hospitalized, 287 needed intensive care, 5 required mechanical ventilation, and 2 died.

Owens said she hopes the CDC report gives pause to clinicians and parents who use melatonin. Many products are fruit-flavored or sold as gummies or chewables and lack childproof packaging. She noted that parents calling melatonin "candy" or "vitamins" to get their child to take it might also send the wrong message.

"It's a drug," Owens said. "Like any other drug, you don't leave it on the kitchen counter for your toddler to get into."

Behavioral Is Better

The AASM [recommends](#) cognitive behavioral therapy for insomnia (CBT-I) as the first-line therapy for adults and children with insomnia. Martin said that mental health specialists typically provide this brief personalized behavioral therapy, which emphasizes working on habits and skills that can improve sleep.

Owens said she typically spends an hour with new patients trying to understand the underlying causes of their sleep difficulties. For example, a child with difficulty falling asleep might have an underlying circadian rhythm disruption, restless leg syndrome, or their bedtime may be too early. She said sleep problems could be an adverse effect of a medication the child takes or they may be related to how parents manage bedtime.

Medications or supplements including melatonin may be appropriate for children in some circumstances, Owens noted. For

example, she said that she frequently prescribes medication for patients with autism, anxiety, or depression. When she does recommend melatonin, she tells parents to purchase brands that offer pharmaceutical-grade melatonin.

The AASM has a public-facing [website](#) with information and tools for people with insomnia or other sleep difficulties and a directory of accredited sleep disorder centers. The Society of Behavioral Sleep Medicine also has a directory of CBT-I providers on its [website](#).

And Owens is working with her colleagues at the International Pediatric Sleep Association to develop guidelines for primary care physicians on using melatonin. Sometimes, she noted, it's appropriate to use drugs or supplements like melatonin in conjunction with behavioral interventions.

But she added a caveat: "Like any sleep-aid, [melatonin] is a Band-Aid, and it doesn't

fix the underlying issues, which are typically behavioral." ■

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