

Does Melatonin Have a Meaningful Role as a Sleep Aid for Jet Lag Recovery?

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BACKGROUND

Melatonin has long been used as an over-the-counter aid to assist with hastening sleep onset and treating symptoms of jet lag, with jet lag being the most common application. The effects of jet lag are greater based on an increase in the number of time zones travelled and when experiencing eastbound travel. Jet lag may have varying effects on an individual, and is associated with cognitive and physiological deficits. Insomnia and constant sleepiness may also occur during the day. Other negative effects may include reduced attention, altered mood states, diminished memory processing, and altered executive functioning. Melatonin has numerous commercially available preparations, and in most countries is not considered a regulated substance. Despite its widespread use as a sleep aid, and its promotion as such by celebrity entertainers and media-based physicians alike, it remains unclear whether or not there is sufficient evidence to support the recommendation of this substance as a sleep aid.

LITERATURE REVIEW

Most of the contemporary literature regarding melatonin suggests that overcoming the negative effects of jet lag requires adjusting the person's sleep phase into the new time zone of their destination, a concept referred to as sleep-phase shift. The general literature on this topic suggests that it is not the melatonin dosage quantity, but rather the time of day of administration, that benefits the patient.

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Burgess et al.¹ focused on the effects of air travel, sleep deprivation, and jet lag disorder. A meta-analysis of 10 trials was conducted in this study, all focusing on air travel in patients traveling eastward. Effects of melatonin for advancing sleep onset were found in all studies, yet the strength of such treatment was unknown, and the effect sizes could not be established. To analyze the results of the study, a phase response curve was generated for all patients. Results indicated that if 3 mg of exogenous melatonin is taken just prior to usual bedtime as a sleep aid, minimal phase advances occur (<0.5 hours in 3 days). Administration of exogenous melatonin near the end of sleep, closer to wake time, could inadvertently delay the circadian clock. The current study is difficult to compare to others for numerous reasons: varying doses of melatonin, the use of continuous release or an immediate release dose, the number of successive days of treatment, and if subjects were entrained to a 24-hour day, sleep/dark schedule, or free-running day. The ideal time to administer melatonin was found to be when the endogenous melatonin begins to taper off in the morning before waking. This ideal timing produces an optimal overlap, potentially stimulating a later dawn and creating phase delays. In addition, results found that the addition of morning intermittent bright light pulses (>3,000 lux) increased phase advance (1.5–1.7 hours). Both morning bright light and exogenous morning and afternoon melatonin administration increased the phase advance even further (2.5–2.6 hours). Final recommendations for further study suggest a lower dosage of melatonin to be used. There was no difference found in the phase advances between 3 mg and 0.5 mg doses.

In humans, melatonin is secreted by the pineal gland at night, creating biological rhythms that may induce sleep. However, a study by Kostoglou-Athanassiou found that exogenous administration of melatonin before sleep time between 10 and 12 PM in the travel destinations may help reduce jet lag symptoms when crossing more than five time zones.² It was determined that 0.5 to 5 mg of melatonin were equally effective in sleep-phase shifting. Those treated with 5 mg of melatonin, however, were found to fall asleep faster and experience more

effective sleep patterns. In addition, multiple dosages may be beneficial for the many effects of traveling across time zones.

The negative effects of jet lag require sleep-phase shifting to realign the person to normal time. However, melatonin may also be able to phase delay biological rhythms depending on when administered. Weingarten conducted circadian rhythm assessments in individuals whose phase shifts were analyzed when administered melatonin.³ A three pulse phase response curve to 3 mg of melatonin given to humans found that maximum phase advances of 3 mg of melatonin occur when it is taken about 5 hours before the dim light melatonin onset (DLMO), and phase delays occur when taken about 11 hours after the DLMO. The study established that the usage of exogenous melatonin can both phase advance and phase delay human circadian rhythms. Multiple dosages of melatonin were found to be more effective than a single dosage.

Gradually advancing sleep phases occurs by forcing sleep for at least 8 hours in participants and treating with melatonin. Burke et al. conducted 3 days of experimentation in which each day the wake time occurred 1 hour earlier than the previous day.⁴ Each afternoon, after being woken, participants were randomly assigned to receive either 0.5 mg or 3.0 mg of melatonin or a placebo. Larger changes in sleep-phase shifts were found to occur with melatonin compared to placebo. The largest sleep-phase advancement was found with the 3-mg dose. This difference was not found to be significant (participants were only slightly more tired at night); therefore, it was suggested to use the lower dosage to avoid drowsiness the following day.

In an interesting study combining the use of natural light and melatonin to alter the circadian clock, Revell et al.⁵ conducted a study using 36 healthy participants who were randomly assigned to four different conditions in which either dim light (1.9 lux) was administered with a placebo, dim light with melatonin (5 mg), bright light (3,000 lux) with placebo, or bright light with melatonin (5 mg). All melatonin was adminis-

tered in late afternoon, and light therapy exposure occurred in the morning. The study concluded that a greater sleep-phase shift was possible when the two treatments were administered together rather than alone. In addition, a dosage of 0.5 mg of melatonin was just as effective as 3 mg of melatonin when administered at nighttime.

BEST PRACTICE

Melatonin can be a useful tool to counter the effects of jet lag on human sleep-phase shifting when administered at the proper time. Greater effects seen in sleep-phase shift occur when the patient is treated in conjunction with light therapy. Although the current literature is not sufficient to evaluate all the various commercially available preparations of melatonin, it does seem that this over-the-counter supplement generally has a meaningful effect on human sleep, and in particular the treatment of jet lag. Larger trials of high-level evidence would be preferred to support a firm recommendation to take melatonin as routine therapy for those suffering from jet lag, but the current evidence is strong enough for clinicians to offer this as an option to patients.

LEVELS OF EVIDENCE

Two studies in this article were randomized trials (level 1), one was a systematic review and meta-analysis (level 1), and two were individual prospective studies (level 2b).

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