

Melatonin Supplementation in Beta-Blocker - Induced Insomnia: A Literature Review

Kirtick Poovendran, Vishnupriya Krishnaveni, Pavana Chandran,
Mohammad Ibrahim Hashmi

International Faculty of Medicine, Tbilisi State Medical University, Tbilisi, Georgia

Corresponding Author: Kirtick Poovendran

DOI: <https://doi.org/10.52403/ijrr.20251217>

ABSTRACT

Beta-blockers, widely prescribed for cardiovascular diseases, have been linked to sleep disturbances, notably insomnia and vivid dreaming. This effect is primarily attributed to the suppression of endogenous melatonin secretion via β 1-adrenergic receptor blockade in the pineal gland [2]. Melatonin, a neurohormone produced by the pineal gland, regulates the circadian rhythm and promotes sleep onset. This review summarizes the available evidence on the relationship between beta-blocker therapy and melatonin suppression, and evaluates the therapeutic potential of melatonin supplementation in mitigating insomnia among these patients.

Keywords: beta-blockers, insomnia, melatonin, pineal gland, sleep disturbance, circadian rhythm, cardiovascular disease.

INTRODUCTION

Insomnia is a frequent complaint among patients receiving beta-blocker therapy, especially in the elderly. Beta-blockers reduce melatonin secretion, disrupting circadian rhythm and leading to difficulty in sleep initiation and maintenance. Exogenous melatonin has emerged as a potential therapy to counteract this deficiency. This literature review consolidates available data on the physiological mechanisms, clinical trials, safety, and therapeutic implications of

melatonin supplementation in beta-blocker-induced insomnia.

Mechanism of Beta-Blocker-Induced Insomnia

Lipophilic beta-blockers such as propranolol, metoprolol, and pindolol cross the blood-brain barrier and inhibit adrenergic stimulation of the pineal gland, leading to decreased melatonin synthesis [1]. In contrast, hydrophilic agents like atenolol have minimal central nervous system penetration and less effect on sleep patterns [1]. Clinical observations reveal increased nocturnal awakenings, vivid dreaming, and reduced REM sleep in patients on lipophilic beta-blockers [1]. Urinary 6-sulfatoxymelatonin, a marker of melatonin secretion, is significantly reduced in chronic beta-blocker users [1]. This reduction in the melatonin is the root cause for the sleep disturbance.

Role and Mechanism of Melatonin

Melatonin (5-methoxy-N-acetyltryptamine) is synthesized from serotonin in the pineal gland under control of the suprachiasmatic nucleus (SCN) of the hypothalamus. Its secretion peaks during darkness, inducing sleep by binding to MT1 and MT2 G-protein-coupled receptors in the SCN, retina, and hippocampus. These receptors regulate circadian phase and sleep initiation. Pharmacologic agents like CIRCADIN (prolonged-release melatonin), agomelatine, ramelteon, and tasimelteon act on these

receptors, demonstrating beneficial effects on sleep and mood regulation [4-5]. CIRCADIN's slow-release mimics physiological melatonin secretion, promoting sustained sleep.

Clinical Studies and Evidence

A controlled clinical trial conducted on ten volunteers receiving different beta-blockers over ten consecutive nights revealed that lipophilic agents (propranolol, pindolol, metoprolol) disrupted sleep architecture, increasing dream recall and nighttime awakenings, whereas atenolol did not affect sleep and reduced REM duration. A Taiwanese cohort study in elderly hypertensive patients demonstrated that beta-blocker initiation was associated with insomnia, with propranolol showing higher incidence than atenolol or bisoprolol [3].

Randomized controlled trials, such as Scheer et al. (2012), confirmed that melatonin supplementation (2.5 mg nightly for three weeks) improved sleep efficiency, total sleep time, and reduced sleep onset latency in hypertensive patients on beta-blockers [1]. These improvements persisted after discontinuation of melatonin, suggesting a potential regulatory effect on circadian rhythm [2].

Safety Profile and Pharmacology

Melatonin use is considered generally safe, with only minor issues such as light-headedness, mild headaches, or feeling sleepy during the day [4]. Still, it should be used carefully in older adults who often take several medications, as drug interactions can occur [4]. Research reviews show that taking melatonin for a short period can help people feel their sleep has improved, without causing serious side effects [5]. Continuous use might slightly decrease blood pressure, so patients already on blood pressure medicines should be monitored closely [4].

Clinical Implications and Future Directions

A lack of melatonin may play a role not only in sleep problems but also in broader bodily

dysfunctions such as elevated oxidative stress, nerve cell damage, and possibly cancer development [6]. Studies have found that people with certain cancers, including breast and colon cancer, often have lower melatonin levels, although a direct cause-and-effect relationship has not been proven [7]. Because of its heart-protective and antioxidant effects, melatonin may offer added benefits for those with cardiovascular conditions [6]. Future investigations should aim to determine the most effective dosage, ideal timing of use, and long-term effects on heart health. Well-structured randomised clinical trials are also needed to assess whether melatonin should be routinely prescribed for individuals with beta-blocker-induced sleep disturbances.

CONCLUSION

Evidence indicates that beta-blocker-induced suppression of melatonin contributes significantly to insomnia and altered sleep architecture. Melatonin supplementation appears to improve sleep parameters safely in the short term. Until large-scale trials establish definitive guidelines, melatonin should be considered as an adjunctive therapy in patients with beta-blocker-induced sleep disturbances, implemented with individualized dosing and careful monitoring.

Declaration by Authors

Ethical Approval: Not applicable

Acknowledgement: AI was used for language purposes only.

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Scheer, F. A., Morris, C. J., Garcia, J. I., Smales, C., Kelly, E. E., Marks, J., Malhotra, A., & Shea, S. A. (2012). Repeated melatonin supplementation improves sleep in hypertensive patients treated with beta-blockers: a randomized controlled trial. *Sleep*, 35(10), 1395–1402. <https://doi.org/10.5665/sleep.2122>

2. Stoschitzky, K., Sakotnik, A., Lercher, P., Zweiker, R., Maier, R., Liebmann, P., & Lindner, W. (1999). Influence of beta-blockers on melatonin release. *European journal of clinical pharmacology*, 55(2), 111–115.
<https://doi.org/10.1007/s002280050604>
3. Tikhomirova, O. V., Zybina, N. N., & Kozhevnikova, V. V. (2021). Vliyanie dlitel'nogo priema beta-adrenoblokatorov na sekretnost' melatonina, kachestvo sna i sosudistoe porazhenie golovnoy mozga [The effect of long-term beta-blockers on melatonin secretion, sleep quality, and vascular brain damage]. *Zhurnal nevrologii i psikiatrii imeni S.S. Korsakova*, 121(8), 7–12.
<https://doi.org/10.17116/jnevro20211210817>
4. Tuft, C., Matar, E., Menczel Schrire, Z., Grunstein, R. R., Yee, B. J., & Hoyos, C. M. (2023). Current Insights into the Risks of Using Melatonin as a Treatment for Sleep Disorders in Older Adults. *Clinical interventions in aging*, 18, 49–59.
<https://doi.org/10.2147/CIA.S361519>
5. Anghel, L., Baroiu, L., Popazu, C. R., Pătraș, D., Fotea, S., Nechifor, A., Ciubara, A., Nechita, L., Mușat, C. L., Stefanopol, I. A., Tatu, A. L., & Ciubara, A. B. (2022). Benefits and adverse events of melatonin use in the elderly (Review). *Experimental and therapeutic medicine*, 23(3), 219.
<https://doi.org/10.3892/etm.2022.11142>
6. Daliri, A. S., Goudarzi, N., Harati, A., & Kabir, K. (2025). Melatonin as a Novel Drug to Improve Cardiac Function and Quality of Life in Heart Failure Patients: A Systematic Review and Meta-Analysis. *Clinical cardiology*, 48(3), e70107.
<https://doi.org/10.1002/clc.70107>
7. Fares A. (2011). Night-time exogenous melatonin administration may be a beneficial treatment for sleeping disorders in beta blocker patients. *Journal of cardiovascular disease research*, 2(3), 153–155.
<https://doi.org/10.4103/0975-3583.85261>

How to cite this article: Kirtick Poovendran, Vishnupriya Krishnaveni, Pavana Chandran, Mohammad Ibrahim Hashmi. Melatonin supplementation in beta-blocker -induced insomnia: a literature review. *International Journal of Research and Review*. 2025; 12(12): 156-158. DOI: [10.52403/ijrr.20251217](https://doi.org/10.52403/ijrr.20251217)
