

Role of melatonin in children with insomnia and ADHD: Mini-review

Ansab Akhtar *

Assistant Professor, Chandigarh College of Pharmacy, Chandigarh Group of Colleges, Landran, Mohali-140307 (Punjab)-India.

International Journal of Science and Technology Research Archive, 2021, 01(02), 010–012

Publication history: Received on 28 July 2021; revised on 04 September 2021; accepted on 06 September 2021

Article DOI: <https://doi.org/10.53771/ijstra.2021.1.2.0039>

Abstract

Melatonin is a hormone released from the pineal gland. In numerous clinical studies it has been investigated exogenously to treat children suffering from insomnia with attention deficit hyperkinetic disorder (ADHD), taking methylphenidate. The main purpose was to alleviate sleep disturbances. Subjects were selected for clinical studies in ADHD children taking methylphenidate and suffering from insomnia. Melatonin was administered in children for few weeks before bedtime with defined sleep hygiene. Constant monitoring of sleep qualities was done either subjectively or objectively. The studies have reported its efficacy and safety. Moreover, melatonin has been reported to alleviate the symptoms of ADHD associated insomnia. It has shown its effects in terms of reduced sleep latency and better sleep quality. Moreover, no serious adverse effects were reported. Cognitive functions were not much affected. The clinical studies hypothesize that melatonin has the potential to normalize the sleep disorders in ADHD children.

Keywords: Melatonin; ADHD; Insomnia; Children; Sleep latency

1. Introduction

Attention deficit hyperkinetic disorder (ADHD) has been widely recognized to be associated with insomnia in children. The disorder has affected intellectual and social life. The brain stimulant drug methylphenidate is generally used to attenuate the signs and symptoms of ADHD (1). However, insomnia episodes get worsened with the use of this drug. Sleep dysregulation is quite prevalent in ADHD patients taking methylphenidate. To counter that, melatonin, a hormone can be beneficial to regulate circadian rhythm. Sleep is an important phenomenon occurring majorly at night and hugely impacts human behavior, cognition, and attention. Melatonin is usually released from the pineal gland in the brain in response to the presence or absence of light/darkness, which in turn is accountable for the sleep-wake clock (2). The melatonin treatment combined with proper sleep hygiene can potentially shorten the sleep latency, thereby mitigating the problems pertaining to sleep disorders.

2. Methods used in clinical studies

There are several clinical trial studies conducted in the recent past to find out the safety and efficacy of melatonin adjusted with or without sleep hygiene regimen in children as well adults. An open-label study in a small sample size and randomized placebo-controlled double-blind trials were done in children in the age range of 5-15 years with an average body weight of 20-50 kg. Studies were conducted in hospitals, research institutes, or pharmacies under strict ethical guidelines. The parents and children consented to the study protocols. Almost 50-100 subjects were screened on the basis of exclusion and inclusion criteria like ADHD diagnosis, comorbidity, premedication, aggressive attitude, and willingness to participate, etc. Grouping of the selected subjects was done in a randomized way as treatment and placebo-controlled groups. The dose of melatonin was around 3-6 mg according to the body weight of individuals.

* Corresponding author: Ansab Akhtar
Division of Pharmacology, UIPS, Panjab University, Chandigarh, 160014, India.

Administration of melatonin to the patients was directed almost one hour before going to bed. Sleep hygiene was maintained by fixed bedtime, minimum light, dark, and sound of the room and the surroundings. Instruments like actigraphy, somnology, or questionnaires were applied to record the sleeping pattern, sleep onset, sleep latency, sleep disturbances, and wakefulness, etc. The studies lasted several weeks to months, and only a small number of patients were dropped out during the study period, which did not alter overall results. The results were compared with the baseline and placebo-controlled groups using different statistical methods like t-test or ANOVA with the help of the software (3-7).

3. Results and outcomes

Upon investigation by the researchers and experts at specified intervals during and at the end of the studies, the results revealed that melatonin treatment reduced the sleep-onset time, sleep latency, and enhanced total sleep duration in ADHD children. Hence, the potential drug melatonin resolved the problems of sleep-onset insomnia and sleep disturbances upto a great extent. Significant differences were depicted in melatonin-treated groups as compared to placebo groups. Additional outcomes were reported in terms of reduced wakefulness, movement, and variability during and between the nights. Further, there were more improvements realized when treatment duration increased and gave significantly improved benefits as compared to the baseline readings. The effects of the melatonin treatment were revealed in adolescents like parents and caregivers as well. The onset of sleep time in the range of 20-40 min was perceived as normal. However, exceeding 60 min was in the category of faulty sleep patterns. In clinical trials with melatonin revealed the attainable efficacy and acceptable safety. Interestingly, the effectiveness of the melatonin treatment was least in curing the core symptoms of ADHD. At the same time, the quality of life and cognitive performance were improved only very slightly. In the recorded revelations, no serious adverse effects were noted down. Headache and irritation type of mild condition was found only in few cases. Even the stimulant drug did not reveal any life-threatening side effects. There was no mortality occurred in any of the studies (3-7).

4. Discussion

In addition to basic findings, advanced studies were necessitated in order to corroborate and validate earlier reports. Almost all the studies conducted on children suffering from ADHD and sleep-onset insomnia revealed that melatonin had the potential to relieve sleep disorders. Series of reports justified the use of melatonin in a fixed dosage regimen. However, attention deficiency, hyperactive behavior, tiredness, speaking difficulty, concentration ability was not much changed. The reason could be the different molecular or neurochemical mechanisms of ADHD and insomnia. It has also given an inference of the essentiality of separate therapy for ADHD-related pathological hallmarks. The studies gave a fair indication that these approaches like melatonin in combination with sleep hygiene, subject variability, and dosage regimen fluctuations were significantly effective and safer to larger parameters. Still, cautions have to be built to produce a declined level of toxicity.

Table 1 Schematic illustration of the clinical studies

Items	Descriptions
Individuals	Children, Parents, Physicians, Pharmacists
Treatments	Methylphenidate, Melatonin, Placebo
Strategies	Sleep hygiene with balance dark/light, Sound, Fixed bedtime, and Properly made bed, Consent of participants
Parameters	Sleep latency, Sleep onset time, Total sleep time, and Cognitive functions
Instruments	Somnology, Actigraphy, Electronic sleep diary, Questionnaire, ABC-J, SPSS software
Statistical tests	t-test, ANOVA, Linear regression analysis, Pearson test, Wilcoxon signed-rank test
Outcomes/measurements	Safety, Efficacy, Sleep quality, Wakefulness, Movements
Adverse effects	Irritation, Lethargy, Migraine, Diarrhoea, Headache, and Dizziness

Most of the results of the latest study pertaining to melatonin efficacy were in line with previously reported studies with smaller samples or limited study design. The novel approaches also made the inroads to counter the extra insomnia behavior added by methylphenidate. Hence natural distortions of melatonin secretion or occurring as a result of ADHD have the potentiality to be compensated through exogenous melatonin treatment. Even though it has not been approved, still in few countries, people have started taking melatonin. Its safe nature and difference from conventional hypnotics make this agent quite promising (3-7). All of the studies have been illustrated in a brief overview in the Table 1.

4.1. Advantages

The novelties and advancements in the studies can be counted as the inclusion of adult subjects, maintenance of sleep hygiene, recording of sleep patterns both objectively and subjectively, and taking the consideration of comorbidity and medication history of patients. The intensive monitoring and analysis of a wide variety of parameters gave the inference of the least errors.

Limitations and future perspectives

Despite extensive clinical studies done on this topic, there are limitations associated with these studies such as smaller sample size, few adverse effects, and shorter durations. So, future studies can be warranted in the direction of a sizeable population, including the subjects of a wide variety of demographic, ethnic, and social backgrounds. Likewise, advanced techniques and a controlled environment to record the outcomes will provide more defined accuracy. This approach can potentially exclude bias. The exploitation of the field can further be done by determining the mechanistic aspects of melatonin.

5. Conclusion

In a nutshell, the series of studies outcomes on ADHD children suffering from sleep disturbances can be concluded that melatonin dose of 3-5 mg gave profound relief in terms of both efficacy and safety. Years of studies gave some concrete evidence for its effectiveness and tolerance. The clinical trial results can be translated to the approval of exogenous melatonin for human use.

Compliance with ethical standards

Acknowledgments

No funding is received for the manuscript.

Disclosure of conflict of interest

Author declares no conflict of interest.

References

- [1] Abikoff H, Hechtman L, Klein RG, Weiss G, Fleiss K, Etcovitch J, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2004;43(7):802-11.
- [2] Ferracioli-Oda E, Qawasmi A, Bloch MH. Meta-analysis: melatonin for the treatment of primary sleep disorders. *PloS one*. 2013;8(5):e63773.
- [3] der HEIJDEN KBV, Smits MG, Van Someren EJ, Ridderinkhof KR, Gunning WB. Effect of melatonin on sleep, behavior, and cognition in ADHD and chronic sleep-onset insomnia. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2007;46(2):233-41.
- [4] Gi CVTP, Broeren JP, Starreveld JS, Versteegh FGA. Melatonin for treatment of sleeping disorders in children with attention deficit/hyperactivity disorder: a preliminary open label study. *European journal of pediatrics*. 2003;162(7):554-5.
- [5] Mohammadi MR, Mostafavi SA, Keshavarz SA, Eshraghian MR, Hosseinzadeh P, Hosseinzadeh-Attar MJ, et al. Melatonin effects in methylphenidate treated children with attention deficit hyperactivity disorder: a randomized double blind clinical trial. *Iranian journal of psychiatry*. 2012;7(2):87.
- [6] Weiss MD, Wasdell MB, Bomben MM, Rea KJ, Freeman RD. Sleep hygiene and melatonin treatment for children and adolescents with ADHD and initial insomnia. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2006;45(5):512-9.
- [7] Yuge K, Nagamitsu S, Ishikawa Y, Hamada I, Takahashi H, Sugioka H, et al. Long-term melatonin treatment for the sleep problems and aberrant behaviors of children with neurodevelopmental disorders. *BMC psychiatry*. 2020;20(1):1-14.