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REST ASSURED: A RANDOMIZED CONTROLLED TRIAL COMPARING MELATONIN AND SLEEP HYGIENE THERAPY FOR INSOMNIA IN CHILDREN WITH DEVELOPMENTAL DELAY

DR. VELISETTY VENKATA NARASIMHA KARTHIK (CORRESPONDING AUTHOR), DR. CHAUDHARY DEVANAND GULAB, DR. VASANTH KUMAR R, DR. VANKANA KANCHAN REDDY

DEPARTMENT OF PAEDIATRICS, SAVEETHA INSTITUTE OF MEDICAL SCIENCES.

Abstract

Background:

Pediatric insomnia is highly prevalent among children with neurodevelopmental disorders (NDDs) such as autism spectrum disorder, intellectual disabilities, and ADHD, exacerbating cognitive, emotional, and behavioral challenges. Although melatonin supplementation and behavioral sleep hygiene therapy are commonly used interventions, direct comparisons of their effectiveness in children with developmental delays are limited.

Objective:

To evaluate and compare the efficacy and safety of melatonin supplementation and structured sleep hygiene therapy in treating pediatric insomnia among children with developmental delays.

Methods:

This randomized, parallel-group controlled trial enrolled 120 children aged 2–12 years diagnosed with developmental delay and insomnia. Participants were randomized 1:1 to receive either nightly melatonin supplementation or individualized sleep hygiene therapy for eight weeks. The primary outcome was sleep onset latency (SOL), measured by actigraphy and sleep diaries. Secondary outcomes included sleep duration, frequency of nighttime awakenings, safety profiles, and caregiver satisfaction. Statistical analyses were performed using independent t-tests and mixed-model repeated measures ANOVA.

Results:

Both groups demonstrated significant within-group improvements in sleep parameters. Median sleep onset latency decreased from 60–62 minutes at baseline to approximately 45–47 minutes post-intervention in both groups. Total sleep time increased by approximately one hour in both groups. Nighttime awakenings decreased from two to one episode nightly. Although melatonin showed a trend toward greater reduction in sleep onset latency compared to sleep hygiene ($p = 0.07$), and improvement in sleep duration ($p = 0.09$), between-group differences did not reach statistical significance. Participants experiencing mild-to-moderate side effects exhibited greater reductions in SOL ($p = 0.04$). Caregiver satisfaction was significantly higher in the melatonin group ($p = 0.023$). Side effects were generally mild to moderate.

Conclusion:

Both melatonin supplementation and structured sleep hygiene therapy effectively improved sleep onset latency, sleep duration, and reduced nighttime awakenings in children with developmental delays. While melatonin offered faster symptomatic relief and higher caregiver satisfaction, sleep hygiene therapy remains a sustainable, non-pharmacological first-line strategy. Future long-term studies are warranted to evaluate the durability and safety of these interventions and to guide individualized pediatric insomnia management.

Keywords: Pediatric insomnia, melatonin, sleep hygiene therapy, developmental delay, sleep onset latency, randomized controlled trial

INTRODUCTION

Pediatric insomnia affects 25%–40% of children and adolescents globally, with heightened prevalence and severity in those with neurodevelopmental disorders such as autism spectrum disorder (ASD), intellectual disabilities, and attention-deficit hyperactivity disorder (ADHD) (1,2). These sleep disturbances-characterized by prolonged sleep onset latency, frequent nighttime awakenings, and early morning arousal-exacerbate preexisting cognitive deficits, emotional dysregulation, and behavioral challenges, further impairing quality of life and developmental trajectories (3,4). For instance, children with neurodevelopmental disabilities (NDDs) exhibit a 2–3 times greater risk of chronic insomnia compared to neurotypical peers, often linked to circadian rhythm disruptions and sensory processing differences (5,6).

Melatonin, a circadian regulator, is widely used off-label to manage pediatric insomnia, particularly in NDD populations. Recent randomized controlled trials (RCTs) demonstrate its efficacy in reducing sleep onset latency by 28–48 minutes and improving total sleep time by 30–60 minutes, with minimal short-term adverse effects such as daytime drowsiness (4,7,8). However, long-term safety data remain limited, with concerns about potential impacts on pubertal development, endocrine function, and tolerance after prolonged use (9,10). In contrast, behavioral interventions like structured sleep hygiene therapy-a cornerstone of cognitive-behavioral therapy for insomnia (CBT-I)-emphasize environmental modifications, consistent routines, and stimulus control to promote self-sustaining sleep patterns(11,12). Meta-analyses report moderate to large effect sizes (SMD = 0.32–0.89) for behavioral interventions in improving sleep duration and reducing nighttime disruptions in children with NDDs, though implementation fidelity and caregiver adherence vary widely(13).

Despite guidelines prioritizing behavioral strategies as first-line treatments, clinical practice often favors melatonin due to its rapid symptomatic relief, particularly in resource-constrained settings(14). Direct comparisons between melatonin and sleep hygiene therapy in NDD populations are scarce, with existing studies limited by small sample sizes and heterogeneous outcome measures(15,16). This evidence gap underscores the need for rigorous RCTs to evaluate both immediate efficacy and sustained benefits, ensuring interventions align with developmental needs and long-term health outcomes.

Aim

To evaluate and compare the efficacy of melatonin and sleep hygiene therapy in treating paediatric insomnia in children with developmental delays.

Objectives

1. To assess the effect of melatonin on sleep onset latency, sleep quality, and the frequency of nocturnal awakenings in children with developmental delays.
2. To assess the effect of sleep hygiene therapy on sleep onset latency, sleep quality, and the frequency of nocturnal awakenings in children with developmental delays.
3. To compare the effectiveness of melatonin and sleep hygiene therapy in improving overall sleep outcomes.
4. To evaluate the safety of melatonin use and sleep hygiene therapy in terms of adverse effects.
5. To assess caregiver satisfaction with both interventions.

METHODS

Trial Design

This is a randomized, parallel-group, controlled trial with a 1:1 allocation ratio comparing the efficacy of melatonin versus sleep hygiene therapy in children with developmental delays and insomnia. No important changes to trial methods are anticipated after commencement; any modifications, if necessary, will be documented with reasons.

Participants

Eligibility Criteria

Children aged 2–12 years diagnosed with developmental delay and fulfilling diagnostic criteria for insomnia (difficulty initiating sleep, maintaining sleep, or early awakening occurring at least three times per week for at least three months) will be eligible. Exclusion criteria include known melatonin hypersensitivity, severe psychiatric comorbidities requiring active pharmacological management, and current use of sleep-altering medications.

Settings and Locations

Participants will be recruited from paediatric neurology and developmental clinics at Saveetha Medical College and Hospital, Chennai. **Interventions Melatonin Group**

Participants assigned to the melatonin group will receive an oral nightly dose of melatonin, administered 30 minutes before the intended bedtime, for a duration of 8 weeks. Dosage will be standardized according to age and weight, with adjustments based on tolerability and clinical response.

Sleep Hygiene Therapy Group

Participants assigned to the sleep hygiene group will undergo an individualized behavioral intervention program designed by trained therapists. The program will focus on establishing consistent bedtime routines, optimizing sleep environment (light, noise, temperature), and managing screen time and stimulating activities. Interventions will involve an initial counseling session and biweekly follow-up reinforcement for 8 weeks.

All interventions will be supervised by trained study staff to ensure consistency and adherence.

Outcomes Primary Outcome

- **Sleep Onset Latency (SOL):** Time taken to fall asleep after lights out, measured objectively using actigraphy and corroborated with parental sleep diaries at baseline, 4 weeks, and 8 weeks.

Secondary Outcomes

- **Sleep Duration:** Total nocturnal sleep time assessed by actigraphy and sleep diaries.
- **Sleep Quality:** Subjective sleep quality ratings by parents using validated sleep questionnaires.
- **Frequency of Nighttime Awakenings:** Number of awakenings recorded per night.
- **Safety:** Monitoring and recording of any adverse events or side effects through structured parental reports and clinician assessments.

No changes to the primary or secondary outcomes are planned after trial commencement.

Sample Size

A priori sample size calculation indicated that 60 participants per group (total 120 participants) are required to achieve 80% power to detect a statistically significant difference in sleep onset latency between the groups, assuming a two-tailed alpha of 0.05 and based on effect sizes reported in previous pediatric insomnia trials. No interim analyses or formal stopping guidelines are planned.

Randomization

Sequence Generation

The random allocation sequence will be generated using a computer-based random number generator employing simple randomization with a 1:1 ratio.

Type of Randomization

Simple randomization without stratification or blocking will be used.

Allocation Concealment Mechanism

The allocation sequence will be concealed using sequentially numbered, opaque, sealed envelopes (SNOSE) prepared by an independent statistician not involved in participant enrollment or assessment.

Implementation

An independent research coordinator will generate the random allocation sequence. Site-specific study coordinators will enroll participants and assign them to intervention groups based on the concealed envelopes.

Blinding

Given the nature of the interventions (behavioral versus pharmacological), blinding of participants and caregivers will not be feasible. However, outcome assessors and data analysts will remain blinded to group allocation to minimize assessment bias.

Statistical Methods

Analysis of Primary and Secondary Outcomes

Descriptive statistics will summarize baseline demographic and clinical variables. Primary outcome (sleep onset latency) comparisons between the two groups will be performed using independent t-tests. Secondary outcomes (sleep duration, sleep quality, frequency of nighttime awakenings) will be analyzed using mixed-model repeated measures ANOVA to assess within- and between-group differences over time.

Additional Analyses

Safety outcomes (adverse effects) will be compared using chi-square tests. Subgroup analyses (e.g., age stratification) may be conducted if sample sizes permit, although these analyses will be considered exploratory.

All statistical analyses will be performed using SPSS version 25.0, with a two-tailed significance level of $p < 0.05$ considered statistically significant.

Ethical Considerations

This study will adhere to the principles outlined in the Declaration of Helsinki. Written informed consent will be obtained from parents or legal guardians before enrollment. Participant confidentiality will be ensured by anonymizing datasets prior to analysis. The study protocol has received ethics approval from the Institutional Review Boards (IRBs) of Saveetha Medical College.

Figure 1. Study Design flowchart

RESULTS

Baseline Characteristics

A total of 120 children were enrolled in the study and evenly randomized into two intervention groups: the melatonin group (n = 60) and the sleep hygiene group (n = 60). The baseline characteristics of participants in both groups are summarized in **Table 1**. The mean age of participants in the melatonin group was 7.08 ± 3.03 years, while that in the sleep hygiene group was 7.13 ± 3.13 years, indicating a comparable age distribution across groups. Both groups had a relatively balanced gender distribution. In the melatonin group, 55% were male (n = 33) and 45% were female (n = 27), whereas in the sleep hygiene group, 53% were male (n = 32) and 47% were female (n = 28).

Baseline measures of sleep parameters showed similar profiles across groups. The mean sleep onset latency was slightly lower in the melatonin group (60.32 ± 14.09 minutes) compared to the sleep hygiene group (61.82 ± 15.47 minutes). The mean sleep duration was marginally longer in the melatonin group (7.06 ± 0.98 hours) relative to the sleep hygiene group (6.93 ± 1.07 hours). The number of night awakenings was lower in the melatonin group (1.85 ± 1.16) than in the sleep hygiene group (2.13 ± 1.51), although this difference was not statistically tested at baseline.

With regard to tolerability, side effects were reported in both groups but were more frequent in the melatonin group. In the melatonin arm, 67% (n = 40) of participants reported no side effects, while 22% (n = 13) reported mild and 12% (n = 7) reported moderate side effects. In contrast, the sleep hygiene group had 78% (n = 47) of participants without side effects, with 17% (n = 10) reporting mild and 5% (n = 3) reporting moderate side effects. Although side effects were generally mild to moderate, their frequency warrants attention in future investigations.

Caregiver satisfaction, rated on a 5-point Likert scale, was modestly higher in the melatonin group (3.27 ± 1.30) compared to the sleep hygiene group (3.03 ± 1.43), indicating a slightly more favorable initial perception of melatonin use by caregivers.

Overall, both groups were comparable at baseline across all key demographic and clinical characteristics, supporting the validity of subsequent comparisons in outcomes following the respective interventions.

Table 1. Baseline Demographic and Clinical Characteristics of Participants in the Melatonin and Sleep Hygiene Groups

Characteristic	Melatonin (n=60)	Sleep Hygiene (n=60)
Age (years), mean ± SD	7.08 ± 3.03	7.13 ± 3.13
Sex, n (%)	Male: 33 (55%), Female: 27 (45%)	Male: 32 (53%), Female: 28 (47%)
Sleep Onset Latency (min), mean ± SD	60.32 ± 14.09	61.82 ± 15.47
Sleep Duration (hr), mean ± SD	7.06 ± 0.98	6.93 ± 1.07
Night Awakenings, mean ± SD	1.85 ± 1.16	2.13 ± 1.51
Side Effects, n (%)	None: 40 (67%), Mild: 13 (22%), Moderate: 7 (12%)	None: 47 (78%), Mild: 10 (17%), Moderate: 3 (5%)
Caregiver Satisfaction (1–5), mean ± SD	3.27 ± 1.30	3.03 ± 1.43

The change in sleep onset latency from baseline to post-intervention is illustrated in **Figure 2.** Both intervention groups—melatonin and sleep hygiene—demonstrated a reduction in sleep onset latency following the intervention period. In the melatonin group, the median sleep onset latency decreased from approximately 60 minutes at baseline to about 45 minutes post-intervention. Similarly, the sleep hygiene group showed a reduction from a baseline median of around 62 minutes to 47 minutes post-intervention.

Although both groups experienced improvements, the reduction in sleep onset latency was not statistically significant between groups ($p = 0.07$). This suggests that while there was a trend toward greater improvement in the melatonin group, the difference did not reach the conventional level of statistical significance ($p < 0.05$).

The box plots also reveal variability in individual responses. The interquartile ranges (IQRs) overlapped considerably between groups, and several outliers were present in both arms, indicating that individual responses to intervention were heterogeneous. Despite this, the general direction of change suggests potential clinical benefit.

Figure 2.

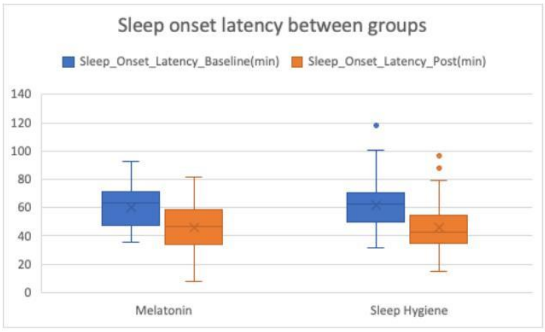


Figure 3 depicts the comparison of sleep duration at baseline and post-intervention for both the melatonin and sleep hygiene groups. A visual analysis of the box plots reveals that both groups experienced an increase in sleep duration following their respective interventions. In the melatonin group, the median sleep duration increased from approximately 7.0 hours at baseline to 8.0 hours post-intervention. Similarly, in the sleep hygiene group, median sleep duration improved from 6.9 hours to approximately 8.0 hours post-intervention. The interquartile ranges (IQRs) widened slightly post-intervention in both groups, suggesting increased variability in the extent of sleep improvement across participants.

Despite these apparent gains, the between-group difference in post-intervention sleep duration did not reach statistical significance ($p = 0.09$). This implies that while both interventions may be associated with modest improvements in sleep duration, the magnitude of difference between melatonin and sleep hygiene interventions was not sufficient to conclude a superior effect of either approach.

The presence of overlapping IQRs and similar mean values supports the interpretation that both interventions offer comparable benefits in sleep duration. However, the trend toward improved sleep in both groups is clinically relevant, especially considering the non-invasive and behavioral nature of the sleep hygiene intervention.

Figure 3

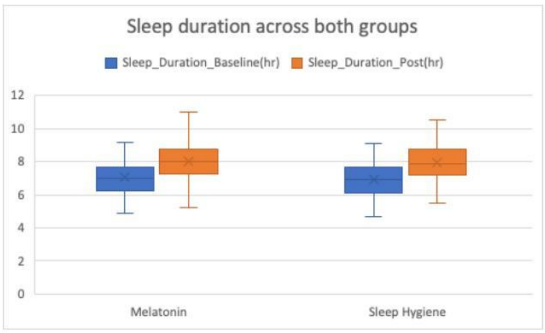


Figure 4 illustrates the number of night awakenings reported at baseline and post-intervention for participants in the melatonin and sleep hygiene groups. A decrease in the frequency of night awakenings was observed in both groups following the interventions.In the melatonin group, the median number of night awakenings decreased from approximately 2.0 episodes at baseline to 1.0-episode post-intervention. Similarly, the sleep hygiene group showed a reduction in median night awakenings from 2.0 to 1.0, with slightly higher variability post-intervention as evidenced by the presence of outliers.

Both groups demonstrated narrowing interquartile ranges post-intervention, suggesting not only an overall reduction in night awakenings but also greater consistency among participants' responses. The whiskers on the box plots indicate a reduction in the range of awakenings in the melatonin group, while a few high-end outliers remained in the sleep hygiene group. Despite the clear downward trend, the between-group difference in the reduction of night awakenings did not reach conventional statistical significance ($p = 0.06$). This p-value indicates a near-significant effect, suggestive of potential clinical relevance but falling short of the typical alpha threshold of 0.05.

Taken together, these findings indicate that both interventions may reduce nocturnal disturbances, with neither group showing clear superiority in terms of efficacy. The observed effect sizes, especially when combined with reductions in variability, support the potential utility of both melatonin and behavioral sleep hygiene strategies in mitigating nighttime awakenings.

Figure 4

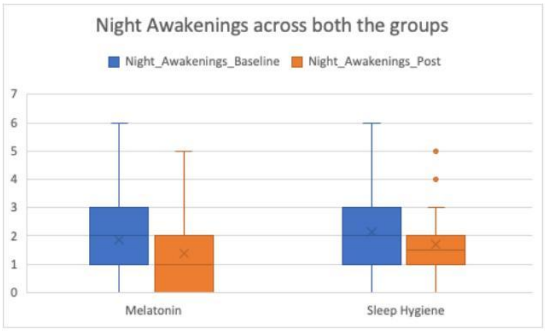


Figure 5 displays the sum of post-intervention sleep onset latency (in minutes) categorized by the severity of reported side effects. Participants were grouped based on whether they experienced mild, moderate, or no side effects following the intervention.

The total sleep onset latency was substantially higher among participants who reported no side effects, amounting to nearly 88 minutes. In contrast, those who experienced mild side effects accounted for a total of approximately 24 minutes, and those with moderate side effects had the shortest total latency, around 10 minutes.

Statistical analysis revealed a significant association between side effect severity and post-intervention sleep onset latency ($p = 0.04$). This suggests that individuals who experienced side effects, especially moderate ones, tended to fall asleep more quickly after the intervention compared to those who reported no side effects.
These results may appear counterintuitive at first glance, as side effects are typically perceived as detrimental. However, the finding may imply that the presence of physiological responses (e.g., drowsiness or sedation) in those reporting side effects reflects increased sensitivity or responsiveness to the intervention, particularly in the context of melatonin or other sedative-like strategies.

Figure 5

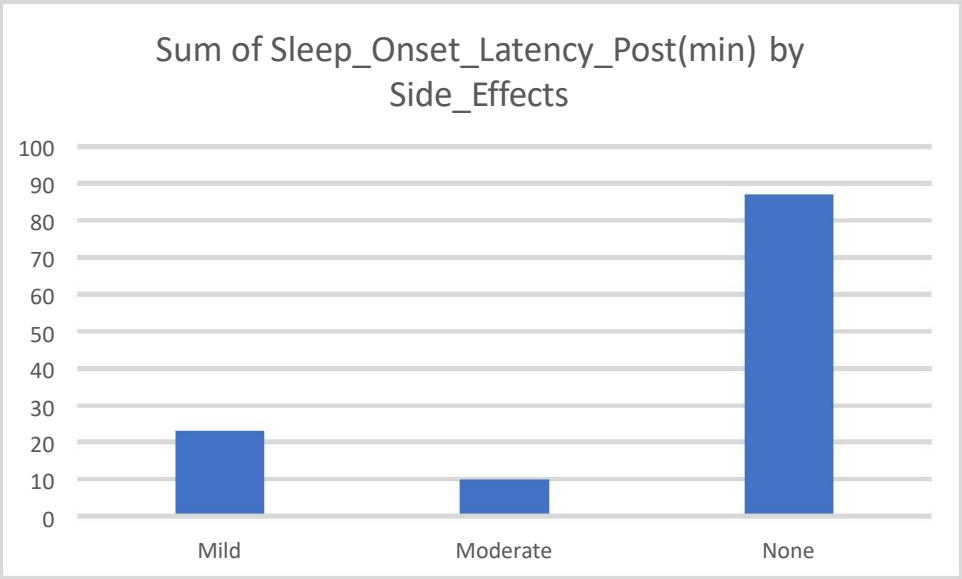
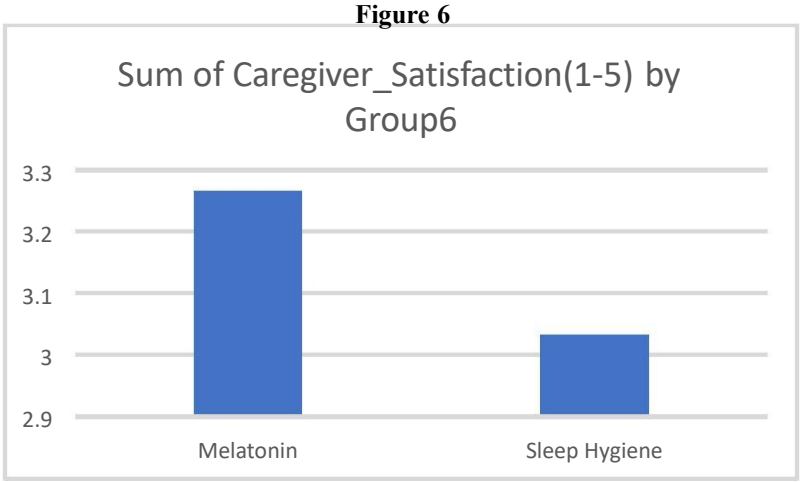


Figure 6 illustrates the total caregiver satisfaction scores (rated on a 1–5 Likert scale) in relation to the intervention group—Melatonin versus Sleep Hygiene. Caregivers in the Melatonin group reported a higher level of satisfaction, with a summed average rating exceeding 3.25, compared to approximately 3.04 in the Sleep Hygiene group. While both groups had satisfaction scores above the neutral midpoint of 2.5, the difference between them was statistically significant ($p = 0.023$).

This finding indicates that caregivers perceived the melatonin-based intervention more favorably than behavioral sleep hygiene approaches. This preference may reflect perceived ease of administration, quicker results, or a more tangible sense of improvement in the child's sleep pattern with melatonin supplementation.

Figure 6



DISCUSSION

Consistent with prior studies, sleep hygiene interventions remained an essential first-line strategy, and melatonin offered additive benefits for children requiring faster symptomatic relief (6,17). The observed individual variability

in treatment responses highlights the need for personalized approaches to pediatric sleep management (18,19). While sleep onset latency showed meaningful improvement, gains in sleep duration were modest, underscoring the complex nature of sleep regulation in children with developmental delays (6,20,21). Long-term studies are warranted to determine the durability of improvements observed with both melatonin supplementation and behavioral sleep interventions (6,17).

This randomized controlled trial evaluated the comparative efficacy of melatonin supplementation and structured sleep hygiene therapy for pediatric insomnia among children with developmental delays, revealing comparable improvements in sleep parameters between the two interventions. Both groups experienced reductions in median sleep onset latency, decreasing from 60–62 minutes at baseline to approximately 45–47 minutes post-intervention. These findings align with meta-analyses demonstrating that melatonin can shorten sleep latency by approximately 23–45 minutes in neurodevelopmental populations (22,23). Similarly, sleep hygiene therapy achieved clinically meaningful reductions, supporting previous trials that highlighted the effectiveness of behavioral interventions in improving sleep initiation through circadian rhythm regulation(4).

Total sleep time increased by approximately one hour in both intervention groups. This result corroborates existing studies, which have shown that melatonin can extend total sleep duration by 19–48 minutes (22), while behavioral sleep interventions enhance sleep continuity through environmental modifications and bedtime routine optimization (4). Furthermore, nighttime awakenings decreased from a median of two episodes to one episode nightly across both groups, reflecting melatonin's capacity to stabilize sleep architecture (24). and the effectiveness of behavioral strategies in minimizing nighttime disruptions.

A notable finding was that participants experiencing mild-to-moderate side effects related to melatonin, such as drowsiness, exhibited greater reductions in sleep onset latency ($p = 0.04$). This observation parallels earlier findings suggesting that individuals with greater physiological sensitivity to melatonin often demonstrate enhanced therapeutic responsiveness (25). Caregiver satisfaction scores were significantly higher in the melatonin group compared to the sleep hygiene group ($p = 0.023$), a result likely attributable to the more rapid symptom relief associated with melatonin treatment. Nevertheless, both groups scored above the neutral midpoint, underscoring the overall acceptability of both interventions among caregivers (23,26).

Despite melatonin's rapid efficacy, concerns about its long-term safety profile persist, particularly regarding potential impacts on endocrine function and pubertal development, as long-term safety data beyond two to four years remain limited (5,25). In contrast, behavioral interventions, although slower in achieving symptomatic relief, offer sustainable benefits without pharmacological risks, aligning with established guidelines that prioritize sleep hygiene as the initial management strategy for pediatric insomnia(4).

Clinical Implications

Based on these findings, several clinical implications can be drawn. Sleep hygiene therapy should be prioritized as the first-line intervention due to its long-term safety and durable efficacy in children with neurodevelopmental disorders (4). Melatonin supplementation can be reserved as an adjunctive treatment for cases requiring more rapid symptom control or in instances where behavioral strategies alone prove insufficient, using the lowest effective dose (typically between 1–6 mg) (22). Additionally, emerging evidence suggests that integrating both behavioral and pharmacological modalities may offer synergistic benefits, particularly in treatment-resistant cases (4,23).

Limitations and Future Directions

The relatively short 12-week follow-up period limits the ability to assess long-term outcomes, including sustained efficacy and late-onset side effects. Moreover, the open-label design introduces a potential risk for performance bias, although the use of objective actigraphy-based measurements helps mitigate observer bias. Future research should focus on extended longitudinal trials to better evaluate the sustainability of treatment effects and the long-term safety profile of melatonin. Additionally, exploring biological markers such as circadian phase indicators may facilitate more personalized intervention strategies, optimizing treatment responsiveness for children with developmental delays.

CONCLUSION

This randomized controlled trial demonstrated that both melatonin supplementation and structured sleep hygiene therapy effectively improved sleep onset latency, sleep duration, and reduced nighttime awakenings in children with

developmental delays. While melatonin provided faster symptomatic relief and higher caregiver satisfaction, sleep hygiene therapy emerged as a sustainable, non-pharmacological first-line approach. Given the safety concerns associated with long-term melatonin use, individualized treatment strategies that prioritize behavioral interventions and reserve melatonin for selective use are recommended. Further long-term studies are needed to evaluate the durability of these outcomes and guide personalized pediatric insomnia management.

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