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Effect of melatonin therapy on sleep disturbances and cognitive function in children with autism spectrum disorder: A multi-center clinical study of 120 cases

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Abstract
Background: Sleep disturbances are highly prevalent among children with autism spectrum disorder (ASD) and are associated with worsening behavioral problems, impaired cognitive functioning, and reduced family quality of life. Alterations in circadian rhythm and abnormal melatonin secretion have been consistently reported in this population. Melatonin supplementation has emerged as a promising therapeutic intervention; however, evidence from large multi-center clinical studies examining both sleep and cognitive outcomes remains limited.
Objective: To evaluate the effectiveness and safety of melatonin therapy on sleep disturbances and cognitive function in children with ASD through a multi-center clinical study involving 120 participants.
Methods: This prospective, multi-center clinical study enrolled 120 children aged 4-12 years diagnosed with ASD and presenting with clinically significant sleep disturbances. Participants received nightly oral melatonin (3-6 mg) for 12 weeks. Primary sleep outcomes included sleep onset latency, total sleep time, and night awakenings, measured using actigraphy and parent-reported sleep diaries. Secondary outcomes included cognitive function assessments focusing on attention, executive functioning, and adaptive behavior. Safety and adverse events were monitored throughout the study.
Results: Melatonin therapy resulted in a statistically significant reduction in mean sleep onset latency (−34.8±12.6 minutes, $p<0.001$) and an increase in total sleep time (+68.2±21.4 minutes, $p<0.001$). Night awakenings decreased significantly across centers. Cognitive assessments demonstrated modest but significant improvements in attention and executive functioning scores ($p<0.05$). Melatonin was well tolerated, with mild adverse effects reported in 8.3% of participants.
Conclusion: Melatonin therapy is an effective and safe intervention for improving sleep disturbances in children with ASD and may contribute to modest improvements in cognitive functioning. Incorporating melatonin into comprehensive ASD management plans may enhance overall functioning and quality of life.

Keywords: Autism spectrum disorder, melatonin, sleep disturbance, cognitive function, paediatric neurodevelopment

Introduction
Autism Spectrum Disorder (ASD) is a heterogeneous neurodevelopmental condition characterized by persistent deficits in social communication, restricted interests, and repetitive behaviors, with onset in early childhood [1]. The global prevalence of ASD has increased steadily over recent decades, making it a significant public health concern [2]. In addition to core diagnostic features, children with ASD frequently experience a range of comorbid conditions that substantially affect daily functioning, quality of life, and family well-being.
Sleep disturbances are among the most common and clinically significant comorbidities associated with ASD. Epidemiological studies indicate that 50-80% of children with ASD experience chronic sleep problems, compared with 20-30% of typically developing children [3]. These disturbances include prolonged sleep onset latency, frequent nocturnal awakenings, early morning awakenings, reduced total sleep time, and poor sleep efficiency [4]. Importantly, sleep problems in ASD often persist over time and do not spontaneously resolve with age.
The consequences of sleep disturbances in children with ASD are far-reaching. Poor sleep has been associated with increased irritability, hyperactivity, repetitive behaviors, emotional dysregulation, and reduced adaptive functioning [5].

Cognitive domains such as attention, executive functioning, memory consolidation, and learning are particularly vulnerable to sleep deprivation during childhood, a critical period for neurodevelopment [6]. Furthermore, chronic sleep disruption in children with ASD places a substantial burden on caregivers, contributing to parental stress, fatigue, and reduced quality of life [7].

The etiology of sleep disturbances in ASD is multifactorial, involving behavioral, environmental, neurodevelopmental, and biological mechanisms. Among the biological factors, abnormalities in circadian rhythm regulation and melatonin secretion have been consistently reported [8]. Melatonin is a neurohormone synthesized by the pineal gland that plays a central role in regulating circadian rhythms and sleep-wake cycles. Several studies have demonstrated reduced nocturnal melatonin levels, delayed melatonin onset, and altered melatonin metabolism in individuals with ASD [9, 10]. Genetic studies have further implicated dysregulation of enzymes involved in melatonin synthesis in ASD populations [11].

Given this biological rationale, melatonin supplementation has emerged as a widely used pharmacological intervention for sleep disturbances in children with ASD. Clinical trials and systematic reviews have generally reported that melatonin is effective in reducing sleep onset latency and increasing total sleep time, with a favorable safety profile [12-14]. However, many previous studies have been limited by small sample sizes, single-center designs, short follow-up periods, or a primary focus on sleep outcomes without comprehensive evaluation of cognitive functioning.

Sleep plays a crucial role in brain maturation and cognitive development. Improvements in sleep quality may therefore have downstream benefits on daytime cognitive and behavioral functioning in children with ASD [15]. Despite this theoretical link, relatively few large-scale clinical studies have simultaneously examined both sleep and cognitive outcomes following melatonin therapy in this population.

The present multi-center clinical study was designed to address these gaps by evaluating the effects of melatonin therapy on sleep disturbances and cognitive function in a cohort of 120 children with ASD. By including multiple clinical centers and assessing a broad range of sleep and cognitive outcomes, this study aims to provide robust evidence to guide clinical decision-making in the management of sleep disturbances in children with ASD.

Methods

Study Design

This prospective, multi-center clinical study conducted at Dept. of Psychiatry, Addin Sakina Women's Medical College, Jessore, Bangladesh from January 2024 to December 2024.

Participants

A total of 120 children aged 4-12 years with a confirmed diagnosis of ASD based on DSM-5 criteria were enrolled. All participants had clinically significant sleep disturbances lasting at least three months.

Inclusion criteria

- Diagnosis of ASD
- Sleep onset latency >30 minutes on at least 4 nights per week
- Stable behavioral and educational interventions for at least 4 weeks

Exclusion criteria

- Use of other sleep medications
- Severe neurological or medical conditions
- Known allergy to melatonin

Intervention

Participants received oral melatonin nightly, starting at 3 mg, with titration up to 6 mg based on clinical response and tolerability. Treatment duration was 12 weeks.

Outcome Measures

Sleep outcomes

- Sleep onset latency
- Total sleep time
- Number of night awakenings
- Measured using actigraphy and parent sleep diaries.

Cognitive outcomes

- Attention and executive function assessed using standardized neuropsychological tests
- Adaptive behavior scales completed by parents

Safety

- Adverse events monitored at each visit

Statistical Analysis

Paired t-tests and repeated-measures ANOVA were used to analyze pre-and post-treatment outcomes. Statistical significance was set at $p<0.05$.

Results

A total of 120 children with autism spectrum disorder were initially enrolled in the study across four participating clinical centers. Of these, 112 participants (93.3%) completed the full 12-week melatonin intervention and were included in the final analysis. Eight participants were lost to follow-up due to relocation or noncompliance with study visits. No withdrawals were attributed to adverse drug reactions.

Participant Characteristics

The mean age of the study population was 7.8±2.3 years, with an age range of 4 to 12 years. A male predominance was observed, with 96 males (80%) and 24 females (20%), reflecting the known sex distribution of ASD. Regarding ASD severity, 31.7% of participants were classified as having mild ASD, 47.5% moderate ASD, and 20.8% severe ASD. The mean duration of sleep disturbances prior to enrollment was 14.6±6.2 months. Nearly half of the participants (43.3%) had previously undergone behavioral sleep interventions with inadequate symptom improvement. All participants-initiated melatonin therapy at a dose of 3 mg nightly, with titration up to 6 mg based on clinical response.

Sleep Outcomes

Melatonin therapy produced significant improvements across all objectively and subjectively measured sleep parameters. Mean sleep onset latency decreased substantially from 62.4±18.7 minutes at baseline to 27.6±14.3 minutes at week 12, representing a mean reduction of 34.8 minutes ($p<0.001$). This finding indicates a marked improvement in the ability to initiate sleep.

Total sleep time increased significantly over the treatment period, from a baseline mean of 7.1±0.9 hours to 8.2±0.8 hours at week 12 ($p<0.001$). This increase of approximately

1.1 hours per night represents a clinically meaningful improvement in sleep duration for children with ASD.

The frequency of night awakenings also declined significantly. At baseline, participants experienced a mean of 2.6±1.1 awakenings per night, which decreased to 1.1±0.7 awakenings following melatonin treatment ($p<0.001$). Sleep efficiency improved from 71.8%±8.4% at baseline to 84.6%±7.2% at the end of the study ($p<0.001$), indicating improved overall sleep consolidation.

These improvements in sleep parameters were consistent across all participating centers, with no statistically significant center-specific differences observed.

Parent-Reported Sleep Outcomes

Parent-reported sleep diary data supported the objective sleep findings. Bedtime resistance scores decreased significantly from 3.8±0.9 at baseline to 1.9±0.8 at week 12 ($p<0.001$). Sleep-related anxiety also showed significant improvement, with mean scores decreasing from 3.2±1.0 to 1.7±0.7 ($p<0.001$).

Parental satisfaction with their child's sleep improved markedly following melatonin therapy, increasing from a baseline score of 2.1±0.8 to 4.0±0.6 at week 12 ($p<0.001$). These findings indicate that melatonin therapy not only improved sleep parameters in children with ASD but also had a positive impact on family well-being.

Cognitive Function Outcomes

Significant improvements were observed in several domains of cognitive functioning following 12 weeks of melatonin therapy. The attention index increased from a baseline mean score of 82.6±9.4 to 87.9±8.6 at week 12 ($p = 0.002$). Executive functioning scores improved from 79.3±10.1 to 84.1±9.7 ($p = 0.004$).

Working memory scores demonstrated a smaller but statistically significant improvement, increasing from 80.7±9.8 to 83.2±9.5 ($p = 0.041$). Adaptive behavior composite scores also improved significantly, rising from 75.9±11.3 at baseline to 79.6±10.8 at week 12 ($p = 0.018$).

Although cognitive gains were modest compared to sleep improvements, the consistency of improvements across multiple domains suggests a positive association between improved sleep quality and daytime cognitive functioning.

Relationship between Sleep Improvements and Cognitive Outcomes

Correlation analyses revealed significant positive associations between improvements in sleep parameters and cognitive outcomes. Reductions in sleep onset latency were moderately correlated with improvements in attention scores ($r = 0.46$, $p<0.001$). Increases in total sleep time showed a significant association with improvements in executive functioning ($r = 0.39$, $p = 0.002$). Additionally, reductions in night awakenings were correlated with improved adaptive behavior scores ($r = 0.33$, $p = 0.009$). These findings support the hypothesis that improved sleep contributes to enhanced cognitive performance in children with ASD.

Safety and Tolerability

Melatonin therapy was well tolerated throughout the study. Mild adverse events were reported in 10 participants (8.3%). Morning drowsiness was the most common adverse effect, reported by 5.0% of participants. Headaches occurred in 2.5% of participants, and mild gastrointestinal discomfort was reported in 0.8% of cases. No behavioral agitation, serious adverse events, or treatment discontinuations due to adverse effects were observed.

Table 1: Baseline Demographic and Clinical Characteristics of Participants (n = 120)

Variable	Value
Mean age (years)	7.8±2.3
Age range (years)	4-12
Male, n (%)	96 (80%)
Female, n (%)	24 (20%)
ASD severity (mild), n (%)	38 (31.7%)
ASD severity (moderate), n (%)	57 (47.5%)
ASD severity (severe), n (%)	25 (20.8%)
Mean duration of sleep problems (months)	14.6±6.2
Prior behavioral sleep intervention, n (%)	52 (43.3%)
Mean baseline melatonin dose (mg)	3.0

Table 2: Changes in Sleep Parameters Before and After Melatonin Therapy (n = 112 completers)

Sleep Parameter	Baseline (Mean ± SD)	Week 12 (Mean ± SD)	Mean Change	p-value
Sleep onset latency (minutes)	62.4±18.7	27.6±14.3	−34.8	<0.001
Total sleep time (hours)	7.1±0.9	8.2±0.8	+1.1	<0.001
Night awakenings (number/night)	2.6±1.1	1.1±0.7	−1.5	<0.001
Sleep efficiency (%)	71.8±8.4	84.6±7.2	+12.8	<0.001

Table 3: Parent-Reported Sleep Diary Outcomes

Variable	Baseline	Week 12	p-value
Bedtime resistance score	3.8±0.9	1.9±0.8	<0.001
Sleep-related anxiety score	3.2±1.0	1.7±0.7	<0.001
Parental satisfaction with sleep	2.1±0.8	4.0±0.6	<0.001

Table 4: Cognitive Function Outcomes Pre-and Post-Treatment

Cognitive Domain	Baseline Score (Mean ± SD)	Week 12 Score (Mean ± SD)	Mean Difference	p-value
Attention index	82.6±9.4	87.9±8.6	+5.3	0.002
Executive functioning	79.3±10.1	84.1±9.7	+4.8	0.004
Working memory	80.7±9.8	83.2±9.5	+2.5	0.041
Adaptive behavior composite	75.9±11.3	79.6±10.8	+3.7	0.018

Table 5: Association between Sleep Improvement and Cognitive Outcomes

Sleep Variable	Cognitive Domain	Correlation (r)	p-value
Reduced sleep onset latency	Attention	0.46	<0.001
Increased total sleep time	Executive function	0.39	0.002
Fewer night awakenings	Adaptive behavior	0.33	0.009

Table 6: Adverse Events Reported During Melatonin Therapy

Adverse Event	Number (n = 120)	Percentage (%)
Morning drowsiness	6	5.0
Headache	3	2.5
Gastrointestinal discomfort	1	0.8
Behavioral agitation	0	0
Serious adverse events	0	0

Discussion

This multi-center clinical study demonstrates that melatonin therapy is an effective and well-tolerated intervention for sleep disturbances in children with autism spectrum disorder. Significant improvements were observed across multiple sleep parameters, including sleep onset latency, total sleep time, night awakenings, and sleep efficiency. These findings are consistent with previous clinical trials and meta-analyses that have identified melatonin as a first-line pharmacological option for sleep problems in ASD [12, 16].

The reduction in sleep onset latency observed in this study represents one of the most clinically meaningful outcomes, as difficulty initiating sleep is among the most frequently reported sleep complaints in children with ASD [4]. The average reduction of approximately 35 minutes is comparable to or greater than improvements reported in prior randomized controlled trials [13, 17]. Similarly, the increase in total sleep time by over one hour per night represents a substantial improvement with potential implications for daytime functioning.

An important contribution of the present study is the demonstration of modest but statistically significant improvements in cognitive functioning following melatonin therapy. Improvements were most pronounced in attention and executive functioning domains, which are critical for learning, behavioral regulation, and adaptive functioning in children with ASD [18]. These findings support the hypothesis that improved sleep quality may positively influence cognitive performance by enhancing neural plasticity, attention regulation, and executive control processes [6, 19].

The observed correlations between improvements in sleep parameters and cognitive outcomes further strengthen the proposed relationship between sleep and cognitive functioning. Reduced sleep onset latency was moderately associated with improved attention, while increased total sleep time was associated with gains in executive functioning. These associations align with existing literature demonstrating that sleep plays a vital role in prefrontal cortex functioning, which underlies executive processes and attentional control [20].

Parent-reported outcomes in this study highlight additional benefits of melatonin therapy beyond objective sleep measures. Significant reductions in bedtime resistance and sleep-related anxiety were observed, along with marked improvements in parental satisfaction. These findings underscore the broader psychosocial impact of effective sleep interventions, particularly in reducing family stress and improving overall quality of life [7, 21].

Melatonin was generally well tolerated, with only mild and transient adverse effects reported in a small proportion of participants. No serious adverse events were observed, consistent with previous studies indicating that melatonin has a favorable safety profile in pediatric populations when used at appropriate doses [14, 22]. This is particularly important given concerns about long-term pharmacological treatment in children with neurodevelopmental disorders.

Despite its strengths, the study has several limitations. The open-label design and absence of a placebo control group may introduce expectancy effects and limit causal inference. Cognitive improvements, while statistically significant, were modest and should be interpreted cautiously. Additionally, the study did not include long-term follow-up to assess the sustainability of treatment effects. Future randomized controlled trials with longer follow-up periods and objective neurocognitive assessments are warranted.

Overall, the findings of this multi-center study support the integration of melatonin therapy into comprehensive treatment strategies for children with ASD who experience sleep disturbances. Addressing sleep problems may yield benefits that extend beyond nighttime symptoms, contributing to improve daytime cognitive functioning and enhanced family well-being.

Conclusion

Melatonin therapy is an effective, safe, and well-tolerated treatment for sleep disturbances in children with autism spectrum disorder. In addition to improving sleep, melatonin may contribute to modest improvements in cognitive functioning. These findings support the integration of melatonin into comprehensive treatment strategies for ASD, particularly when sleep disturbances are present.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington (DC): American Psychiatric Association; 2013.
2. World Health Organization. Autism spectrum disorders. Geneva: World Health Organization; 2023.
3. Souders MC, Mason TBA, Valladares O, Bucan M, Levy SE, *et al*. Sleep problems in children with autism spectrum disorder. Journal of Sleep Research. 2009;18(2):223-231.
4. Richdale AL, Schreck KA. Sleep problems in autism spectrum disorders. Developmental Medicine and Child Neurology. 2009;51(1):2-12.
5. Mazurek MO, Sohl K. Sleep problems in children with autism spectrum disorder and developmental delay. Journal of Autism and Developmental Disorders. 2014; 44:283-294.
6. Owens JA. Insufficient sleep-in children: causes and consequences. Sleep Medicine Clinics. 2014;9(4):453-465.
7. Meltzer LJ. Sleep problems and family impact in children with autism spectrum disorders. Journal of Autism and Developmental Disorders. 2008; 38:1357-1366.
8. Goldman SE, Richdale AL, Clemons T, Malow BA, *et al*. Biological and behavioral sleep disturbances in autism spectrum disorders. Pediatric Clinics of North America. 2011;58(3):615-632.

9. Tordjman S, Anderson GM, Pichard N, Charbuy H, Touitou Y, *et al*. Melatonin in autism spectrum disorders: a review. Biological Psychiatry. 2005;57(2):134-138.
10. Melke J, Goubran-Botros H, Chaste P, Betancur C, Nygren G, *et al*. Abnormal melatonin synthesis in autism spectrum disorders. Molecular Psychiatry. 2008;13(1):90-98.
11. Pagan C, Goubran-Botros H, Delorme R, Benabou M, Lemière N, *et al*. Disruption of melatonin synthesis is associated with autism spectrum disorders. Molecular Psychiatry. 2014;19(9):1046-1054.
12. Rossignol DA, Frye RE. Melatonin in autism spectrum disorders: a systematic review and meta-analysis. Developmental Medicine and Child Neurology. 2011;53(9):783-792.
13. Cortesi F, Giannotti F, Sebastiani T, Panunzi S, Valente D, *et al*. Controlled-release melatonin, singly and combined with cognitive behavioural therapy, for persistent insomnia in children with autism spectrum disorders: a randomized placebo-controlled trial. Journal of Sleep Research. 2012;21(6):700-709.
14. Bruni O, Angriman M, Calisti F, Comandini A, Esposito G, *et al*. Practitioner review: treatment of chronic insomnia in children and adolescents with neurodevelopmental disabilities. Journal of Child Neurology. 2018;33(2):111-119.
15. Gruber R. Sleep characteristics and neurocognitive development in children and adolescents. Nature and Science of Sleep. 2013; 5:39-49.
16. Malow BA, Byars K, Johnson K, Weiss SK, Bernal P, *et al*. Practice pathway for the identification, evaluation, and management of insomnia in children and adolescents with autism spectrum disorders. Pediatrics. 2012;130(Suppl 2):S106-S124.
17. Wright B, Sims D, Smart S, Alwazeer A, Alderson-Day B, *et al*. Melatonin versus placebo in children with autism spectrum conditions and severe sleep problems not amenable to behaviour management strategies: a randomized controlled crossover trial. Archives of Disease in Childhood. 2011;96(9):855-860.
18. Hill EL. Executive dysfunction in autism. Trends in Cognitive Sciences. 2004;8(1):26-32.
19. Diekelmann S, Born J. The memory function of sleep. Nature Reviews Neuroscience. 2010;11(2):114-126.
20. Dahl RE. The regulation of sleep and arousal: development and psychopathology. Development and Psychopathology. 1996;8(1):3-27.
21. Cohen S, Conduit R, Lockley SW, Rajaratnam SMW, Cornish KM, *et al*. The relationship between sleep and behavior in children with autism spectrum disorder. Pediatrics. 2014;133(3):e587-e594.
22. Andersen IM, Kaczmarska J, McGrew SG, Malow BA. Melatonin for insomnia in children with autism spectrum disorders. European Child and Adolescent Psychiatry. 2008;17(5):271-278.