Melatonin Use in Children and Adolescents: Therapeutic Strategies and Clinical Protocols

Uso da Melatonina em Crianças e Adolescentes: Estratégias Terapêuticas e Protocolos Clínicos

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ABSTRACT

The widespread availability of melatonin without a prescription, combined with the lack of specific medications for certain disorders with increasing morbidity rates, is significant factors contributing to the increased use of melatonin over the past decade. Despite its growing popularity, uncertainties surrounding optimal dosage and duration of exposure remain critical concerns, as these factors could increase the risk of overexposure and adverse effects. This study aims to update the therapeutic indications for melatonin, as well as assess its prescription and therapeutic strategies. A systematic review was conducted in accordance with the PRISMA guidelines, using the PubMed/MEDLINE and LILACS databases. The following search strategy was applied: (melatonin AND (children OR child OR adolescent)) Results indicate melatonin's use for sleep disorders, autism spectrum disorder, neurodevelopmental disorders, and attention deficit/hyperactivity disorder, along with a smaller number of studies exploring its therapeutic potential in conditions such as atopic dermatitis, obesity, functional abdominal pain disorders, bipolar disorder, neurogenetic syndromes, and Bourneville disease. Pediatric-appropriate prolonged-release melatonin in correct dosages has demonstrated positive results in clinical trials and represents the most widely adopted formulation. Dose titration constitutes a critical determinant of therapeutic success. Significant variations in dosage, adaptation time, and exposure time were observed across clinical trials, complicating the comparison of results.

Keywords: Melatonin. Sleep Disorders. Children.Adolescents. Insomnia.

RESUMO

A ampla disponibilidade da melatonina sem prescrição médica, aliada à escassez de medicamentos específicos para determinados transtornos com taxas crescentes de morbidade, são fatores significativos que impulsionaram o aumento do uso dessa substância na última década. Apesar da crescente popularidade, ainda persistem incertezas quanto à dosagem ideal e à duração do uso, aspectos que podem elevar o risco de superexposição e efeitos adversos. Este estudo tem como objetivo atualizar as indicações terapêuticas da melatonina, além de avaliar sua prescrição e estratégias terapêuticas. Foi realizada uma busca atualizada utilizando os descritores (melatonin AND (children OR child OR adolescent)). Os resultados apontam para o uso da melatonina em distúrbios do sono, transtorno do espectro autista, transtornos do neurodesenvolvimento e Transtorno de Déficit de Atenção e Hiperatividade, além de um número menor de estudos que investigam seu potencial terapêutico em condições como dermatite atópica, obesidade, distúrbios funcionais dor abdominal, transtorno afetivo bipolar, síndromes neurogenéticas e doença de Bourneville. A formulação de liberação prolongada apropriada para uso pediátrico, quando utilizada na dosagem correta, demonstrou bons resultados em ensaios clínicos e parece ser a mais utilizada. A fase de ajuste da dose é fundamental para o sucesso do tratamento. Observou-se grande variação entre os ensaios clínicos quanto à dosagem, ao tempo de adaptação e à duração da exposição, o que dificulta a comparação dos resultados.

Palavras-chave: Melatonina, Distúrbios do Sono, Crianças, Adolescentes, Insônia.

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The authors declare no conflicts of interest.

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INTRODUCTION

Melatonin (N-acetyl-5-methoxytryptamine) is a hormone synthesized in the human body by the pineal gland, an endocrine structure located between the cerebral hemispheres. The biosynthesis of melatonin begins with the conversion of the essential amino acid tryptophan into serotonin, which is subsequently transformed into melatonin, a process regulated by sympathetic noradrenergic stimulation in the pineal gland. Melatonin serves as the principal hormone responsible for transmitting photic environmental information to the body, exhibiting a circadian secretion pattern dictated by the light-dark cycle. Its production predominantly occurs at night due to reduced exposure to light, reaching peak levels during sleep when light stimulation is minimal. The regulation of melatonin synthesis is governed by the endogenous biological clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus, which orchestrates the circadian rhythms in mammals. The SCN synchronizes internal biological rhythms with external environmental cues via neural and humoral pathways[2].

Melatonin exerts its physiological effects through specific receptors, classified as MT1, MT2, and MT3, which are widely distributed throughout the body. Due to its high oil-water partition coefficient, melatonin readily diffuses into cells, where it acts as an antioxidant, modulates nuclear receptor activity, and inhibits calcium-calmodulin complex interactions. As melatonin levels rise toward the end of the day, they initiate physiological processes that prepare the body for sleep, including reductions in core body temperature, suppression of sympathetic nervous system activity, and increased sleep propensity. Consequently, melatonin plays a fundamental role in regulating the sleep-wake cycle[2,3].

In recent years, there has been a significant rise in the prevalence of biopsychosocial disorders, such as autism spectrum disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD). This increase can be attributed to a combination of factors, including advancements in diagnostic methods and increased diagnostic recognition and reporting[4]. Current estimates suggest that around 17% of children aged 3 to 17 are diagnosed with some form of neurodevelopmental disorder, encompassing ADHD, ASD, and cerebral palsy. On a global scale, one in every 36 children is diagnosed with ASD[5]. Additionally, research indicates that approximately 5% to 8% of children worldwide are affected by ADHD, with 70% of these cases presenting comorbid psychosocial conditions. While the exact causes of these disorders remain uncertain, evidence points to both genetic and environmental factors playing a role in their development[6]. Due to the absence of a clear etiological framework, current therapeutic approaches remain non-specific, leading to increased interest in alternative, accessible treatment options.

Among these alternatives , melatonin — widely available over the counter—has become a popular therapeutic choice for managing sleep disturbances in children with ASD and ADHD. However, the unsupervised use of melatonin in pediatric populations raises concerns regarding its safety, particularly given the limited research on the potential risks associated with uncontrolled administration. Furthermore, the incidence of sleep disorders has significantly increased, particularly during and after the COVID-19 pandemic, contributing to the surge in melatonin use among children[3]. In light of these concerns, this study aims to provide a comprehensive review of the current scientific literature on melatonin's therapeutic applications, focusing on its effects on circadian rhythm regulation and evaluating the considerations involved in prescribing it for pediatric and adolescent populations.

MATERIAL AND METHODS

Search strategy

For the literature search on the therapeutic use, indications, and impacts on the circadian cycle of children and adolescents, studies were selected following the standardized PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). A search was conducted for original articles in the PubMed/Medline (US National Library of Medicine) and Lilacs (Latin American and Caribbean Health Sciences Literature). This search was divided into two strategies: i) a direct search for research published in the databases, and ii) an indirect search through the reference lists of the included articles, utilizing the snowballing strategy.

The studies were initially retrieved using search filters developed by combining standardized MeSH (Medical Subject Headings) descriptors (available at http://www.ncbi.nlm.nih.gov/mesh) with the Boolean operators “AND” and “OR”: ((child) OR (children) OR (adolescent)) AND (melatonin). The search filters included: i) study types - clinical trials, randomized trials, and case reports, and ii) publications from the last 10 years.

Selection of Studies

The following inclusion criteria were applied: i) original article; ii) studies investigating the association of melatonin use in children and adolescents; iii) clinical trial, randomized trial, or case reports; iv) publications from the last 10 years (2014-2024); v) studies involving participants aged 1 to 17.5 years.

Selection was guided by the PICOS framework (Population, Interventions, Comparison, Outcomes, and Study design),. The population consisted of human studies involving individuals aged 1 to 17.5 years; the intervention was melatonin administration, compared with other age groups, a placebo, or no treatment; the outcomes included

therapeutic effects and indications; and study design were restricted to clinical trials, randomized clinical trials, and case reports. No language restrictions were applied. Studies not conducted in humans or not involving participants within the specified age range were excluded age range were excluded.

Data Extraction

The information extracted from the selected articles was systematized in Table 1 and categorized as follows: i) study characteristics (author, year, title); ii) indication and dosage (reason for melatonin use and administration details); iii) participants (number and comorbidities); and iv) results and conclusions (efficacy, safety, and main findings).

RESULTS

After the initial screening, 139 studies were identified, of which 18 were duplicates in the electronic databases. Following a review of titles and abstracts, 36 studies were excluded as they consisted of editorials, book chapters, theses, notes, or review articles. An additional 35 studies were excluded because they focused on the correct age group but were not directly related to melatonin. Furthermore, 29 studies discussed melatonin use but did not focus on the age range of 1 to 17.5 years. Of the remaining 21 articles, 17 were selected for data extraction after a full-text review. One additional study was identified through the references of the 17 included studies, resulting in a total of 18 studies included (Figure 1).

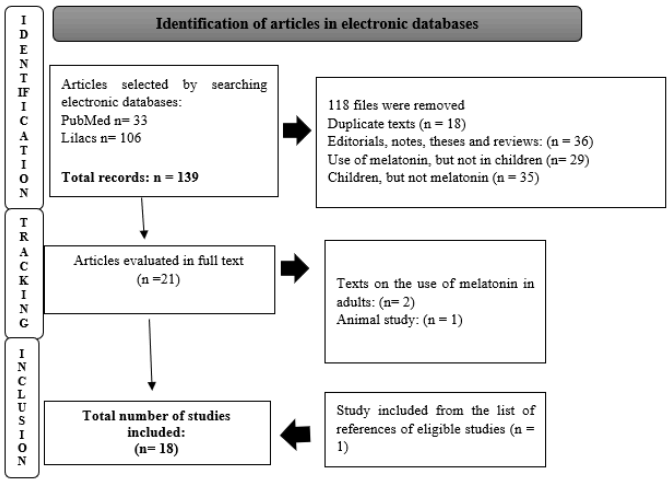


Figure 1. Flow diagram of survey results, based on preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement

Among the 18 studies, seven focused on the relationship between melatonin and sleep disorders[7,8,9,10,11,12,13]. Five studies explored the use of melatonin in children with ASD[7,9,14,10,15], while three examined melatonin in the treatment of attention deficit/hyperactivity disorder (ADHD)[7,14,15]. Two studies focused on its use in children with epilepsy[16,17], and another two investigated its effects on children with neurodevelopmental disorders[18,14]. Additional studies included two articles exploring the use of melatonin for headaches[19,20], one examining its use in children with atopic dermatitis and sleep disturbance[11], and one addressing obesity associated with the MC4R gene[17]. Further research covered its use in pediatric functional abdominal pain disorders[21], its application in children undergoing elective surgery[22], and melatonin use in children with bipolar affective disorder treated with olanzapine and lithium carbonate. Other studies examined neurogenetic disorders[9], seizures[13], Angelman syndrome and Bourneville disease[9], as well as a study on healthy individuals[23]. All studies reported positive effects of melatonin. The specific information extracted from the included studies is summarized in Table 1.

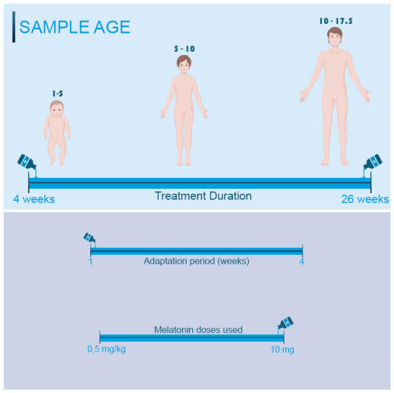
Table 1. Information about the characteristics of the study (author, year); indication and dosage (reason for using melatonin and details of administration); participants (number and comorbidity); and conclusion (efficacy) extracted from the articles included in this study

Source	Indication/ Dosage	Sample	Comorbidity	Effect
Mostafavi, *et al.*,2014	Two groups: i) "olanzapine (5-10 mg/day) and lithium carbonate (3-4 mg/day) and melatonin (3mg/day)" or ii) "placebo and lithium carbonate (3- 4mg/day) and melatonin (3mg/day)", for 12 weeks	48 patients aged between 11 and 17.	Bipolar Affective Disorder on Olanzapine and Lithium Carbonate	+
Jain, *et al.*,2015	Placebo or 9 mg sustained release melatonin for 4 weeks, followed by a 1-week washout and 4-week crossover condition.	Eleven young people aged between 6 and 11.	Epilepsy	+
Chang, *et al.*,2016	Melatonin 3mg and then placebo, versus first placebo and then melatonin.	Patients aged 1 to 18.	Atopic dermatitis and sleep disorders	+
Gringras, *et al.*,2017	PedPRM 10mg X Placebo, for 13 weeks for the children.	196 young people between 2 and 17.5 years old.	ASD, ADHD and sleep disorders	+
Ibekwe *et al.*,2017	Melatonin, orally - 3 mg (< 15 kg) or 6 mg (> 15 kg), about 1 hour before the EEG	173 children between 4 and 9 months.	Sleep disturbance, seizures and NDD	+
Impellizzer *et al.*,2017	Groups: i) oral midazolam (0.5 mg/kg, max. 20 mg) and ii) 40 oral melatonin (0.5 mg/kg, max. 20 mg).	80 children aged between 8 and 14.	Elective surgery.	+
Van Maanen *et al.*,2017	26 children received 3mg of rapid-release melatonin, 28 children placebo and 30 received light therapy, all for 3 to 4 weeks.	84 children (average age 10.0 years, 61% boys).	19 children ADHD, 4 with ASD, 4 with ASD and ADHD	+
Maras, *et al.*,2018	PedPRM (2/5 mg) or placebo for 13 weeks. For the following 39 weeks: 2.5 or 10 mg of PedPRM. Total 52 weeks.	125 young people 2 and 17.5 years old) with ASD or NDDs.	ASD and NDDs with/without ADHD comorbidity.	+
Schroder, *et al.*,2019	2 mg PedPRM or placebo once-daily 30-60 min After 3 weeks: 5 mg for 10 weeks until 91-week. Second dose optimization (2, 5 or 10 mg/day) for those who did not improve the sleep. Groups used 2, 5 or 10 mg of PedPRM followed by 2-week placebo period. Overall study period 2.2 years.	Children (aged 2 to 17.5 years) with: (1) ASD, or NGD, or Angelman syndrome and Bourneville disease together with chronic sleep disorders.	ASD, or NGD, or Angelman syndrome and Bourneville disease together with chronic sleep disorders.	+
Bravaccio, *et al.*,2020	3 mg/day melatonin versus nutritional supplements melatonin 1 mg/day, 20 mg tryptophan and 1.4 mg vitamin B6 for two months.	Thirty-four children aged between 7 and 17	Chronic headache (with or without sleep disturbances)	+
Gelfand, *et al.*,2020	"high-dose" or "low-dose" dose melatonin (<40 kg: 4 mg vs. 1 mg; ≥40 kg: 8 mg vs. 2 mg)	84 children and adolescents aged 4 -17 years.	Migraine Episodic migraine	+
Yuge, *et al.*,2020	1.2 or 4mg/melatonin/ oral/ once a day before bedtime, starting with 1 mg a day, for 26 weeks *versus* placebo.	99 young people aged between 6 and 15.	NDD	
Malow, *et al.*,2021	2-week placebo followed by a 13-week randomized PedPRM or placebo. 2, 5 or 10 mg of PedPRM every night for up to 104 weeks, followed by a 2-week placebo period to assess abstinence.	80 young people aged 2 - 17.5.	ASD and sleep disorders	+
RongGe; Wan;Yang, 2021	Oral melatonin (Puritan's Pride, Inc., Oakdale, NY, United States) 3 mg, once a night during treatment.	A 7-year-old male patient	Epilepsy, sleep disorder. obesity, genetic abnormality	+
Jalilolghadr, *et al.*,2022	Melatonin (Weber Nature Company)/ 3mg in the evening (7pm) versus placebo. Total 4 weeks.	60 young people aged between 7 and 12.	Changes in sleep patterns and insomnia	+
Bonuccelli, *et al.*,2023	Group 1: liposomal melatonin two different doses: 3 mg for children aged 1 to 3 years old, and 5 mg for children between 4 and 6 years old. Group 2 placebo in vials of 0.75 mL and 1.25 mL.	150 patients aged between 1 and 6 years.	Normal	+
Dipasquale *et al.*,2023	Melatonin 3mg or 5mg in combination with *Lactobacillus Rhamnosus* versus placebo with *L. Rhamnosus* for 4 weeks.	42 patients aged between 4 and 18.	Pediatric functional abdominal pain disorders	+
Gelfand, *et al.*,2023	Placebo versus melatonin 3 mg versus melatonin 6 mg nightly for 8 weeks.	70 young people with 10–17-year-old.	Migraine	=

Legend: NDD: Neurodevelopmental disorders; PedPRM: pediatric-appropriate prolonged-release melatonin; AD: Atopic Dermatitis; ASD: Autism Spectrum Disorder; ADHD: Attention-deficit/hyperactivity

Figure 2 presents relevant data on the use of melatonin in pediatric populations, detailing the age range of participants (1 to 17.5 years) and the treatment durations,

which varied from 4 to 26 weeks, including an adaptation period of 1 to 4 weeks. Additionally, the figure includes a summary table of the referenced studies, indicating the respective authors and the administered doses of melatonin, which ranged from 0.5 mg/kg to 10 mg. This figure provides a comprehensive overview of the dosage regimens and treatment periods across different age groups, contributing to a better understanding of the therapeutic protocols applied in clinical studies.



Authors	Doses (mg)
Impellizzeri *et al.* 2017	0.5 mg/kg
Bravaccio *et al.* 2020	3
Dipasquale *et al.* 2023	3
Jalilolghadr *et al.* 2022	3
Malow *et al.* 2021	3
Mostafavi *et al.* 2014	3
RongGee *et al.* 2021	3
Van Maanen *et al.* 2017	3
Yuge *et al.* 2020	4
Chang *et al.* 2016	5
Gelfand *et al.* 2023	6
Ibekwe *et al.* 2017	6
Gelfand *et al.* 2020	8
Jain *et al.* 2015	9
Gringras *et al.* 2017	10
Maras *et al.* 2018	10
Schroder *et al.* 2019	10

Figure 2: Age of participants, treatment duration, and adaptation period in studies on melatonin use in pediatric populations. The table presents the authors, referenced studies, and administered melatonin doses, ranging from 0.5 mg/kg to 10 mg, highlighting the different therapeutic strategies and clinical protocols adopted.

DISCUSSION

Synthetic melatonin is widely used; however, the exposure duration and dosage are not fully established as safe for use in pediatric patients. The scientific studies analyzed indicate numerous benefits of melatonin in various scenarios, contributing to an improved quality of life. Children and adolescents with neurodevelopmental and psychiatric disorders, such as ASD, ADHD, and neurodevelopmental disorders (NDDs), generally experience a disproportionately high prevalence of insomnia compared to children with typical development. However, excessive use of melatonin can lead to a lack of control over the regulation of the circadian cycle. In children, this regulation is particularly delicate and can be affected by factors such as exposure to artificial light, screen use, exercise close to bedtime, and melatonin administration. In such cases, the body may mimic nocturnal metabolic processes during the daytime, leading to melatonin circulating in the bloodstream. Consequently, given that the hormone has been used by parents without proper monitoring, this group of children is at higher risk of adverse effects from the excessive use of this supplement. Data on the efficacy of current treatments for sleep disturbances are limited, and some medications carry significant side effects. Long-term treatment with melatonin, combined with sleep hygiene, could provide clinical benefits for children with these disorders and potentially improve their well-being. This study aims to clarify and update questions on the subject, disseminating reliable scientific data.

There is a positive relationship between melatonin use and sleep disorders, melatonin and ASD, and melatonin and ADHD. Children treated with pediatric-appropriate prolonged-release melatonin (PedPRM) slept, on average of 57.5 minutes longer per night, compared to 9.14 minutes in the placebo group. Sleep latency decreased by an average of 39.6 minutes with PedPRM and 12.5 minutes with placebo, without causing earlier awakening. The increase in total sleep time and reduction in sleep latency were greater with PedPRM than with placebo (68.9% versus 39.3%)[7]. Regarding melatonin and sleep disorders, the melatonin group showed no adverse events and improvement in sleep onset, maintenance, and duration, as well as nocturnal awakenings and daily performance. However, it was ineffective in addressing bedtime resistance and sleep-disordered breathing. Furthermore, the use of melatonin to facilitate sleep electroencephalograms (EEGs) proved effective, without affecting sleep architecture or epileptiform discharges, and induced a state of calm and relaxation[8,13].

Owing to its chronobiological properties, melatonin has multiple therapeutic applications and has been widely used to treat sleep disorders, such as insomnia and jet lag, as well as chemotherapy-related nausea. Research is also exploring its potential use in migraine, fibromyalgia, chronic pain, and age-related cognitive decline. In addition, melatonin possesses antioxidant and anti-inflammatory properties, making it a subject of study in chronic, neurodegenerative, and metabolic diseases, including Alzheimer's disease and diabetes. Melatonin also influences energy metabolism, mood regulation, intestinal motility, and immune function. As a result, the pharmacological effects of this hormone may lead to adverse events in individuals with specific health conditions, necessitating careful assessment prior to clinical prescription[24].

In the context of headaches, a 91.7% reduction in headaches frequency was observed in the melatonin group. Both low and high doses of melatonin were associated with pain reduction in pediatric migraine; however, the study reported a high dropout rate. Higher doses and post-treatment napping were predictive of greater clinical benefit. The primary outcome measure was the change in mean pain score from baseline to 2 hours post-treatment, while secondary outcomes included 2-hour pain relief and pain-free rates. Compared with baseline recall at enrollment, headache days decreased during both the single-blind placebo phase and the double-blind phase, with no evidence of melatonin's superiority. Future preventive migraine trials in this age group may benefit from this findings, particularly regarding enrollment strategies during a single-blind placebo run-in[12,20].

Overexposure to melatonin (high doses or prolonged use) may occur when it is administered without medical supervision. Medication poisoning is relatively frequent in pediatric populations. Although melatonin is generally considered safe for children, side effects can be

more common. Mild symptoms include drowsiness, headaches, mood swings, agitation, nausea, irritability, gastrointestinal disturbances, and excessive nocturnal urination. More severe adverse effects, such as suppression of the hypothalamic-gonadal axis, potentially leading to precocious puberty, as well as immunological and hormonal disturbances, may also occur[19,25].

In a study of chronic sleep disorders in patients with ASD, NDDs, or Angelman syndrome and Bourneville disease, PedPRM primarily improved externalizing behaviors, including hyperactivity, inattention, and conduct problems, in children with neurogenetic disorders. Approximately 53.7% of patients in the PedPRM group showed improvements in externalizing behavior[9]. In a clinical trial involving 80 children and adolescents aged 2–17.5 years with ASD and sleep disorders, extended-release melatonin effectively maintained improved sleep quality over time, without significant adverse effects on physical growth or pubertal development. Additionally, melatonin improved sleep quality in children with atopic dermatitis (AD) and suggested a reduction in severity of the dermatological condition [10,11].

In children with ASD and NDDs with or without ADHD comorbidity, PedPRM proved effective and safe for long-term treatment (up to 52 weeks) of insomnia symptoms, leading to improvements in both children's sleep and caregivers' quality of life. Overall, 76% of children experienced long-term benefits with an increase of at least 60 minutes in sleep duration [18,14,15]. A study also investigated children with ASD, and children with ASD plus comorbid ADHD, and found that sleep latency was significantly reduced during melatonin treatment (β = -0.33, $p < 0.01$), when compared with placebo group. No significant effects of phototherapy were observed. Both melatonin and phototherapy reduced sleep latency and advanced sleep onset, as measured by diaries and actigraphy; however, melatonin demonstrated stronger effects on sleep onset[14].

Regarding children with epilepsy, melatonin was associated with reductions in sleep latency and wakefulness after sleep onset, although no clear effects on seizure frequency were observed. Furthermore, abnormalities in the melanocortin 4 receptor (MC4R) gene are liked to obesity, epilepsy, and sleep disorders. Melatonin showed positive results as an adjuvant therapy in children with epilepsy and MC4R-associated obesity[16,17]. In studies involving pediatric functional abdominal pain disorders, the combination of melatonin and Lactobacillus led to clinical improvements. Children premedicated with melatonin and midazolam prior to elective surgery showed no significant differences in preoperative anxiety levels compared to controls. In contrast, in children with bipolar affective disorder with olanzapine and lithium carbonate, melatonin reduced increases in total cholesterol and systolic blood pressure compared with placebo, although no significant effects were observed on diastolic blood pressure or triglycerides. Thus, melatonin was effective in mitigating some metabolic side effects of olanzapine, particularly preventing rises in cholesterol and systolic blood pressure[21,22,2].

In a study involving healthy individuals, significant differences in sleep latency were reported between groups (10.8 ± 5 minutes inthe melatonin group versus 18.1 ± 13.4 minutes in the placebo group, $p = 0.002$). No differences were observed in EEG abnormalities. Liposomal melatonin demonstrated greater bioavailability, producing faster effects at lower doses. The study concluded that melatonin administration could improve clinical neurophysiology practice by reducing unsuccessful EEG recordings[23,24].

Evidence from pediatric studies indicates that melatonin is effective in treating sleep disorders, including difficulties with sleep initiation, nocturnal awakenings, and delayed sleep onset, especially in children with ASD, attention-deficit hyperactivity disorder, intellectual disabilities, and other neurological conditions. In some regions, the prescription of melatonin for pediatric use has recently been subject to regulatory revisions, which warrant careful consideration and further discussion.

CONCLUSION

The widespread availability of melatonin without a prescription, combined with the lack of specific medications for certain disorders with increasing morbidity rates (e.g., autism, neurodevelopmental disorders), is driving the increased use of melatonin over the past decade. Dosage and treatment duration are critical determinants of overexposure risk and adverse events, warranting further investigation.

Clinical trials have revealed substantial variability in therapeutic applications, dosing regimens, adaptation periods, and treatment durations. Reported applications of melatonin primarily involve improving sleep duration and quality in children and adolescents with ASD, other neurodevelopmental disorders, epilepsy, headaches, and attention-deficit and learning disorders. Pediatric-appropriate prolonged-release melatonin (PedPRM), administered at appropriate dosages has demonstrated favorable clinical outcomes. The dosage adjustment phase is particularly crucial for achieving successful treatment.

In conclusion, under medical supervision and in accordance with established guidelines, melatonin use may confer substantial health benefits in children and adolescents. Nevertheless, despite its demonstrated therapeutic potential, further controlled clinical trials are essential to establish standardized dosing protocols, long-term safety, and efficacy in pediatric populations. Such studies would address current gaps in knowledge and provide evidence-based guidance for clinicians in the pediatric prescription of melatonin.

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