# Melatonin Treatment for Insomnia in Pediatric Patients with Attention-Deficit/Hyperactivity Disorder

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## Request

Is there a role for the use of melatonin to treat insomnia in pediatric patients with attention-deficit/hyperactivity disorder?

## Response

### BACKGROUND

The prevalence of sleep disturbances in the pediatric population is pervasive. In clinical studies, sleep problems range from 10% to 45% and by parent reports from 25% to 40%, varying by age.[1,2] Common sleep disturbances include bedtime resistance, morning and night awakening, complaints of fatigue, and sleep-onset delays.[2]

Sleep disturbances have detrimental effects on children's academic performance, social functioning, overall health, and family life. Daytime somnolence results in performance impairments including reduced concentration and memory.[1-4] Children with sleep problems exhibit mood dysfunctions such as hyperactivity, irritability, and impulsiveness and have increased accidental injuries and negative health effects.[1,4] Families experience im-

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**OBJECTIVE:** To evaluate the efficacy and safety of melatonin for the treatment of insomnia in pediatric patients with attention-deficit/hyperactivity disorder (ADHD).

**DATA SOURCES:** Literature was accessed through MEDLINE (1948–August 2009), EMBASE (1950–August 2009), and Scopus (1960–August 2009) using the terms melatonin, attention-deficit/hyperactivity disorder (ADHD), pediatric, insomnia, sleep disorder, and sleep. In addition, reference citations from publications identified were reviewed for relevant information.

**STUDY SELECTION AND DATA EXTRACTION:** All English-language articles and human studies were identified and evaluated. Results from all identified randomized trials (n = 5), safety studies (n = 1), long-term follow-up studies (n = 1), post hoc retrospective analyses (n = 1), meta-analyses (n = 2), review articles (n = 9), and letters (n = 1) were summarized.

**DATA SYNTHESIS:** Pediatric insomnia is prevalent in children with ADHD and impacts academic performance, social functioning, overall health, and family life. First-line therapy includes ruling out differential diagnoses, optimizing ADHD stimulant treatment, and initiating good sleep hygiene and behavioral therapy. Adjuvant pharmacotherapy is then an option and melatonin is often prescribed. Melatonin regulates circadian rhythm sleep disorders such as sleep-onset insomnia (SOI) in children with ADHD. Four studies in children with ADHD and insomnia showed improvement in sleep onset and sleep latency. Studies included children 6–14 years old and melatonin doses ranged from 3 to 6 mg administered within a few hours of a scheduled bedtime. In all studies, adverse events were transient and mild. The available melatonin studies are limited by small size and short duration; variable SOI criteria, ADHD criteria, and treatment assessments; and lack of generalizability.

**CONCLUSIONS:** Available data suggest that melatonin is a well-tolerated and efficacious treatment option for pediatric patients with chronic SOI and ADHD. Regulated melatonin products and larger, well-designed trials to establish optimal dosing regimens and long-term safety are needed.

**KEY WORDS:** attention-deficit/hyperactivity disorder, children, insomnia, melatonin, pediatric, sleep disorder.

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paired daytime function and reduced overall well-being due to stress.[1,2,4] The consequences of sleep disorders are not just short-term; there is potential for long-term impact if sleep disturbances persist during critical pediatric developmental stages.[1,2]

The prevalence of pediatric insomnia is greater in children with neurodevelopmental or psychiatric comorbidities, as high as 50–77%.[4] ADHD is one of the most common neuropsychiatric disorders, with a worldwide prevalence of 8%, and it is estimated that 50–60% of children with ADHD experience sleep problems.[4,5] Two meta-analyses and one systematic literature review evaluated the association between sleep disturbances and ADHD in children.[5-7] The relationship between sleep disturbances in children with ADHD compared to children without ADHD is not well understood due to conflicting evidence in subjective and objective sleep measurements. Subjective studies demonstrated that parents of children with ADHD report higher rates of sleep problems than parents of controls (25–50% compared to 7%). Results from objective sleep measurements (polysomnography and actigraphy) varied substantially. Two consistent findings in both subjective and objective measures noted that total sleep time did not differ, but children with ADHD were more restless during sleep compared to controls. In studies that analyzed the effect of stimulant medication on sleep parameters in children with ADHD, subjective and objective findings were typically not in agreement, except for prolonged sleep latency and later onset to first rapid eye movement cycle.[6,7] Possible reasons for discrepancies between subjective and objective measures may be due to small sample sizes, other psychiatric comorbidities, heterogeneity of subjects, inadequate control populations, and differences in stimulant regimens.[5,7]

## MANAGEMENT OF INSOMNIA IN CHILDREN WITH ADHD

Despite the substantial prevalence and impact of pediatric sleep disturbances, there is a lack of robust efficacy and safety data supporting the use of hypnotic prescription and over-the-counter (OTC) drugs.[1] The Food and Drug Administration has approved few medications for sleep initiation or maintenance in pediatrics. Prescribers rely on case reports and small studies to recommend off-label use of drugs or parents turn to OTC medications.[3,4]

In children with ADHD, no specific guidelines for the management of pediatric insomnia have been developed. Optimal control of ADHD daytime symptoms should be achieved along with first-line sleep hygiene and behavioral therapy. Sleep disturbances in these patients may be the result of preexisting ADHD symptoms that could respond to dose adjustment or switching to a stimulant agent with fewer sleep difficulties, such as atomoxetine.[1,4,8,9] Differential diagnoses for sleep disorders should be ruled out with polysomnography assessment and temporal relationships with new stimulant, change in stimulant administration, or environmental changes should be considered.[5,9] If adjuvant pharmacologic treatment is necessary, patients should be monitored by specialists for improvements in sleep and changes in cognition, behavior, academic performance, and quality of life.[1,3] Medications should be used in a conservative approach with the lowest effective dose for short courses with appropriate monitoring and realistic treatment expectations.[1,4]

## MELATONIN USE IN SLEEP DISORDERS

First discovered in 1958, melatonin (*N*-acetyl-5-methoxytryptamine) is synthesized primarily in the pineal gland. Melatonin synthesis and secretion are synchronized with the 24-hour day/night cycle: light inhibits melatonin secretion and darkness promotes its secretion.[10-12] Endogenous 24-hour melatonin secretion is a reliable marker for the circadian phase profile.[13] As a small lipid soluble indoleamine, melatonin's highest concentrations are in the cerebrospinal fluid (CSF). Melatonin binds to melatonin 1a and melatonin 1b receptors, found in high density in the suprachiasmatic nucleus of the hypothalamus.[10-12] The suprachiasmatic nucleus is the circadian pacemaker that entrains light-dark input from the retina, regulating melatonin secretion.[14] Melatonin's chronobiotic properties regulate physiological sleep by phase shifting the circadian system (advancing or delaying sleep onset) and resetting sleep-wake cycles. Due to its hypnotic properties, an increase in melatonin correlates with the onset of sleep propensity.[10-12] Differences in circadian phase positions can be measured by dim-light melatonin onset (DLMO). DLMO is a rise in endogenous melatonin secretion in dim light settings, which promotes sleep onset. Delays in DLMO can result in sleep-onset insomnia (SOI).[13,14]

In children with ADHD, SOI is characterized by delays in sleep onset, time to awakening, and DLMO, suggesting a circadian rhythm sleep disorder that could benefit from the chronobiotic effects of melatonin. In a retrospective study of 120 psychotropic medication–naïve children aged 6–12 years with ADHD, actigraphic measures of sleep-wake rhythm and DLMO were assessed.[15] Children with ADHD and SOI (ADHD-SOI) compared to children with ADHD without SOI (ADHD-noSOI) had significantly later sleep onset (mean ± SD, 21:38 ± 0:54 h vs 20:49 ± 0:49 h; $p < 0.001$) and wake-up time (7:29 ± 0:39 h vs 6:56 ± 0:46 h; $p = 0.002$). DLMO was significantly later in the ADHD-SOI group compared to the ADHD-noSOI group (20:32 ± 0:55 h vs 19:47 ± 0:49 h; $p < 0.001$).

An ideal hypnotic agent would have high oral bioavailability, rapid absorption, metabolism to an inactive product, quick onset (~30 min), short elimination half-life (~2–3 h), and sufficient duration of action without daytime drowsiness, and lack rebound, tolerance, or withdrawal.[1,2] Melatonin is hepatically metabolized via the cytochrome P450 system and

conjugated to a urinary active metabolite 6-sulfatoxymelatonin. The oral bioavailability of melatonin is relatively low and administration is recommended on an empty stomach. The onset of action and the elimination half-life of melatonin are both approximately 30–60 minutes.[10,11] Melatonin dose ranges are not established due to lack of pharmacokinetic data and interindividual response variation.[10,12]

Melatonin has been demonstrated to be a well-tolerated drug, with only mild adverse effects similar to those of placebo, such as drowsiness, headache, and gastrointestinal disturbances.[10] Cases of new-onset seizure with melatonin have been reported in studies with children and SOI. Development of mild generalized epilepsy was reported after 4 months of melatonin treatment; the boy's preexisting risk factors and seizure history were not described, but he continued melatonin with valproate initiation without seizure recurrence.[13] In dose-finding and efficacy studies, 42% of 144 and 55% of 42 children, respectively, were diagnosed with epilepsy. The studies did not evaluate a possible causal relationship between epilepsy and seizure development; melatonin treatment was continued and, if necessary, adjustments to anticonvulsant medications were made.[16] If melatonin must be started in a patient with a history of seizures, increased drug monitoring and adjustments in antiepileptic therapy may be considered.[12] Delay in sexual maturity and alterations in hormone levels have been reported in animal studies; melatonin's effect on onset of puberty in children is uncertain.[10,12]

Melatonin has been available as an OTC dietary supplement in the US since 1993.[8,11] Melatonin is commercially synthesized and is not regulated or required to meet quality control standards.[10] Use of melatonin products evaluated in clinical trials or that have been third-party tested for quality, purity, and potency are preferred. Melatonin is available in sublingual, liquid, capsule, and tablet formulations. Fast-release formulations are studied most, as short-acting medications provide benefit in sleep-onset disorders.[1,11] Although ramelteon is a melatonin receptor agonist indicated for the treatment of insomnia, its efficacy and safety have not been established in pediatric patients.[17]

## Literature Review

A literature search was conducted using MEDLINE (1948–August 2009), EMBASE (1950–August 2009), and Scopus (1960–August 2009) using the search terms melatonin, attention-deficit/hyperactivity disorder (ADHD), pediatric, insomnia, sleep disorder, and sleep. Reference citations from identified publications were reviewed for relevant information.

### MELATONIN USE IN CHILDREN WITH ADHD AND INSOMNIA

The use of melatonin for insomnia in pediatric patients with ADHD and sleep disorders has been assessed in 4 studies (Table 1).[18-21] Overall, melatonin use in stimulant- and nonstimulant-treated children with ADHD demonstrated clinical benefit in improving sleep onset and sleep latency with mild adverse effects.

In a small, open-label study by Tjon Pian Gi et al.,[18] the safety of melatonin use in children with insomnia and methylphenidate-treated ADHD was evaluated. During a 1-year period, 120 children with newly diagnosed ADHD and started on methylphenidate treatment were identified. Of those identified, 24 with new-onset insomnia received 3 mg of melatonin. Short-term (1–4 wk) and long-term (after 3 mo) effects of melatonin on time to fall asleep were evaluated. At short-term evaluation, sleep onset significantly improved (median increase 135 min, n = 24), which was sustained at long-term evaluation (n = 13). Insomnia relapsed when melatonin treatment was forgotten (n = 2) and at study end (n = 2); upon melatonin reinitiation, insomnia resolved. One case of restless sleep was reported. Although the study demonstrated benefit in sleep onset, it has several limitations. The short published research letter does not provide adequate details on the study methodology including diagnosis of sleep insomnia, optimization of stimulant therapy, or initiation of good sleep hygiene and behavioral therapy prior to melatonin intervention. The study outcomes may be confounded by subjective sleep assessments that introduce reporter bias, potential placebo effect, open-label design, and missing data on long-term effects. Moreover, the generalizability of the study is limited due to the small sample of subjects from a single center and undocumented methylphenidate regimens.

In a large, 4-week, randomized, double-blind, placebo-controlled study, Van der Heijden et al.[19] assessed the use of melatonin on sleep, behavior, cognition, and quality of life in medication-free children with ADHD. One hundred and five children aged 6–12 years with SOI and nonstimulant-treated ADHD received weight-based melatonin doses at a scheduled administration time. The weight-based melatonin treatment was defined as 3 mg for less than 40 kg and 6 mg for greater than or equal to 40 kg. The study showed significant improvements in sleep parameters (sleep onset, total sleep time, sleep latency, DLMO) and specific core problems (anger, sleep, attention) reported by parents. Improvements were not seen in behavior problems, quality of life, or cognition parameters. Reported adverse events were mild and similar between doses at 4 weeks (headache, hyperactivity, dizziness, abdominal pain) and 2-year follow-up (bedwetting, abnormal feces, drowsiness). Study strengths included a large trial with well-defined diagnostic criteria for ADHD and SOI, randomization stratified on important patient characteristics (psychiatric comorbidities, age group, body weight), assessment of treatment adherence, inclusion of both objective and subjective outcome measures, and 2-year safety follow-up. Despite these strengths, the methodology had several flaws. The most critical observation is that melatonin improved sleep parameters, but did not positively impact dis-

ease outcomes such as problem behaviors, cognitive performance, and quality of life. Although positive disease measures are difficult to achieve, improvements in ADHD are of considerable importance in this patient population. SOI diagnosis, although well defined, was based on subjective Dutch criteria. Although sleep assessments around holidays and time changes were prohibited, children went to bed whenever they felt tired rather than at a scheduled time. A significant portion of pre- and posttreatment data was missing (31%), limiting data analysis. Although sleep parameters were measured objectively with actigraphy, polysomnography is considered the gold standard for sleep assessment.[4,12] Lastly, the generalizability of the study is limited by its exclusion of stimulant-treated children with ADHD and its completion in the Netherlands, where cultural differences can influence sleep patterns, parental reporting, and school attendance.

Hoebert et al.[20] conducted a 3-year follow-up assessment, of the Van der Heijden et al.[19] trial to assess the relapse rate of SOI after discontinuation of melatonin and the long-term efficacy and safety of melatonin treatment. Subjects were offered extended melatonin treatment under physician care and were encouraged to discontinue treatment for at least 1 week each year to reassess treatment need. Ninety-four parents of children with ADHD and SOI who participated in the melatonin study completed a questionnaire. At a mean 3.7 years follow-up, 61 (65%) parents reported that their children were

**Table 1.** Clinical Studies Evaluating Melatonin Use in Children with ADHD and Insomnia

| Reference, Design | Population | Intervention | Efficacy | Safety |
|---|---|---|---|---|
| Tjon Pian Gi (2003)[18] OL safety | N = 24[a] SOI (100%), ADHD (100%), concurrent methylphenidate (100%) | Melatonin 3 mg[b] Short- (1–4 wk, n = 24) and long-term (after 3 mo, n = 13) evaluation | Significant improvement in sleep onset at short-term evaluation (median increase 135 min); remained similar at long-term evaluation Relapse insomnia reported twice when melatonin was forgotten, twice when discontinued; sleep improved when reinitiated | Restless sleep (n = 1) |
| Van der Heijden (2007)[19] R, DB, PC, 2-y follow-up | N = 105; mean age 9 y (range 6–12) SOI (100%), ADHD (100%), stimulant-free (100%), mean body weight 32–33 kg | Randomized to fast-release melatonin weight-based dosing (<40 kg = 3 mg [n = 44], ≥40 kg = 6 mg [n = 9], placebo [n = 53]) at 19:00 h | Significant improvements in sleep onset (+27 ± 48 min; $p < 0.001$), total sleep time (+20 ± 62 min; $p = 0.01$), sleep latency (-21 ± 33 min; $p = 0.001$), DLMO 44 ± 68 min; $p < 0.0001$); significantly improved anger, sleep problems, and attention problems reported by parents ($p = 0.002$), but not reported by teachers ($p = 0.41$); no improvement with other behavior problems, quality of life, or cognition parameters ($p > 0.05$) | Adverse events similar to placebo, most common were headache, hyperactivity, dizziness, abdominal pain; 7 of 19 pts. with 2-y follow-up on melatonin reported mild adverse events (bedwetting, abnormal feces, drowsiness) |
| Hoebert (2009)[20] long-term follow-up[19] | N = 94 parents; mean pt. age at follow-up 12 y[c] SOI (100%), ADHD (100%), stimulant-free (100%) | Melatonin intervention as above[19]; parental survey with mean 3.7-y follow-up | 65% (n = 61) Using melatonin daily at follow-up; mean dose 4 mg, mean administration time 20:00 h, mean duration 18 mo (range 1–57); 92% (n = 60) had delayed sleep onset with temporary discontinuation; 90% (n = 85), 71% (n = 67), 61% (n = 57) of parents stated melatonin was effective for SOI, behavior, and mood, respectively | No serious adverse events; mild in 20% (n = 19) (>3% frequency: dizziness, bedwetting, sleep maintenance insomnia); no cases of epilepsy |
| Weiss (2006)[21] R, DB, PC crossover | N = 28; mean age 10 y (range 6–14) SOI (100%), ADHD (100%), concurrent methylphenidate (67%), concurrent dextroamphetamine (30%) | Pts. received 10 days sleep hygiene[d] (n = 28); nonresponders (n = 19) randomized to 5 mg short-acting melatonin or placebo 20 min before bedtime for 10 days followed by 5 days washout before crossover (30 days total) Melatonin responders (n = 17) received OL melatonin for 3 mo | Significant improvements in SOL with sleep hygiene and melatonin by somnolog and actigraph measures (–25 min; $p < 0.01$ and –16 min; $p < 0.01$, respectively); no improvements in SOL during OL period, but total sleep duration continued to improve (+23 min; $p < 0.01$) | Adverse events similar to placebo, except severe migraine (n = 1) |

ADHD = attention-deficit/hyperactivity disorder; DB = double-blind; DLMO = dim light melatonin onset; OL = open-label; PC = placebo-controlled; R = randomized; SOI = sleep-onset insomnia; SOL = sleep-onset latency .

[a]Ages not provided.

[b]Administration time not provided.

[c]Age range not provided.

[d]Sleep hygiene = consistent bedtime and awakening time with target sleep duration of at least 9.5 h and discontinuation of caffeine and naps.

still using melatonin daily, with a mean dose of 4 mg, mean administration time of 20:00 hours, and mean duration of 18 months (range 1–57). Seventy-one percent (n = 67) of children temporarily discontinued treatment and 92% (n = 60) of those subjects experienced a delay in sleep onset. Twenty percent (n = 19) reported adverse effects; none were reported as serious and no new cases of epilepsy developed on melatonin. Twenty-two (23%) respondents reported that children had discontinued melatonin due to SOI improvement (n = 8), physician initiative (n = 4), lack of efficacy (n = 3), adverse effects (n = 3), patient refusal (n = 1), change in therapy (n = 1), and unknown reasons (n = 2). Upon discontinuation, there were no reports of rebound insomnia, withdrawal symptoms, or dependence. Overall, 90% (n = 85) of parents believed melatonin to be an effective treatment for SOI in their children with ADHD and 71% (n = 67) and 61% (n = 57) of parents reported improvements in daytime behavior and mood, respectively.[20] The study demonstrated that improvements in SOI are not sustained after discontinuation of treatment, suggesting that long-term melatonin therapy may be necessary in this patient population. Although the sample size was large and survey response rate was high (93%), the retrospective follow-up assessment is limited. Survey efficacy data were restricted to subjective opinion and adverse event data were confounded by recall bias.

In a small, randomized, double-blind, placebo-controlled crossover study by Weiss et al.,[21] the efficacy and safety of sleep hygiene and melatonin for SOI in stimulant-treated children with ADHD were evaluated. Twenty-eight children, aged 6–14 years, underwent a 10-day structured sleep hygiene regimen with scheduled bedtime and wake-up routines. If subjects continued to have a mean or 30% variability in sleep latency that was greater than 60 minutes, the children were randomized into a 30-day crossover study with melatonin and placebo. Of the 28 subjects, 5 responded to sleep hygiene therapy alone. After withdrawals, 19 children were randomized to 10-day melatonin or placebo treatment followed by a 5-day washout period and then were crossed over to the opposite treatment and washout. Those who responded to melatonin therapy (n = 17) continued into an open-label 3-month follow-up. A 5-mg dose of short-acting melatonin was administered to children 20 minutes prior to an agreed-upon fixed bedtime. Sleep latency by actigraphy and somnolog measures significantly improved after 10-day treatments of sleep hygiene and melatonin; sleep latency did not significantly improve with continued treatment. All adverse events were mild or moderate, except one report of severe migraine. This study had several strengths. The crossover design allowed each subject to serve as his/her own control to reduce between-subject variability. This is the only published study to evaluate both sleep hygiene and melatonin. Pertaining to sleep hygiene, children and parents established realistic sleep expectations, agreed on a scheduled bedtime and awakening time with a targeted sleep duration of 9.5 hours, and eliminated caffeine and naps. Included children were optimized on stimulant therapy for 2 months prior to enrollment and were maintained on that optimized regimen. Exclusion criteria eliminated external factors that could influence sleep such as stressful lifestyles, unwillingness to adhere to sleep hygiene, and living in multiple households. Study flaws included insomnia diagnosis based on parental somnologs over a short, 10-night period and study population of primarily (91%) boys.

## Summary

To establish strong, evidence-based recommendations for the use of melatonin to treat insomnia in children with ADHD, more vigorous efficacy and safety data are needed. Although the few clinical studies available evaluated the effectiveness of melatonin to phase shift the circadian system, melatonin's effect on sleep quality has not been thoroughly investigated in this patient population. In the absence of recommended pharmacologic treatment for pediatric insomnia and limited data and known adverse effects of prescription agents, the following information is available regarding melatonin therapy.

In children with ADHD and sleep disorders, differential diagnoses should be ruled out, ADHD stimulant treatment should be optimized, and sleep hygiene and behavioral therapy should be implemented prior to melatonin adjuvant therapy consideration. Melatonin use in patients with ADHD has been most extensively researched in patients between the ages of 6 and 14 years suffering from chronic SOI. Initial doses have most often ranged from 3 to 6 mg and administered within a few hours prior to a scheduled bedtime. Without a regulated melatonin dietary supplement available, products used in clinical trials or that have undergone third-party testing are preferred. The goal of therapy should be to achieve sleep improvements with the lowest effective dose. Treatment duration should be as short as possible with interruptions in therapy to reassess continued need for melatonin. Patients should be monitored for improvements in sleep and changes in cognition, behavior, academic performance, quality of life, and adverse events. Most studies have shown improvements in sleep onset (~0.5–2 h), sleep duration (~0.33–1 h), and sleep latency (~20 min). In short-term studies, adverse events were infrequent and mild, such as transient headaches and dizziness. However, long-term effects of melatonin are unknown.

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Tratamiento del Insomnio con Melatonina en Pacientes Pediátricos con Síndrome de Hiperactividad/Déficit de Atención

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EXTRACTO

**OBJETIVO:** Evaluar la eficacia y seguridad de melatonina para el tratamiento del insomnio en pacientes pediátricos con síndrome de hiperactividad/déficit de atención (ADHD).

**FUENTES DE DATOS:** Se realizó una búsqueda en MEDLINE (1948–agosto 2009), Embase (1950–agosto 2009), y Scopus (1960–agosto 2009) utilizando los términos "melatonin", "attention-deficit/hyperactivity disorder (ADHD)," "pediatric," "insomnia," "sleep disorder," y "sleep," Además se revisaron las referencias bibliográficas de los artículos identificados en las búsquedas para localizar la información relevante contenida en ellas.

**SELECCIÓN DE LOS ESTUDIOS Y EXTRACCIÓN DE DATOS:** Se evaluaron todos los estudios realizados en humanos publicados en inglés. Se analizaron los resultados de todos los ensayos clínicos aleatorizados (n = 5), estudios de seguridad (n = 1), estudios de seguimiento a largo plazo (n = 1), estudios retrospectivos post-hoc (n = 1), meta-análisis (n = 2), artículos de revisión (n = 9), y cartas (n = 1).

**SÍNTESIS DE DATOS:** El insomnio pediátrico es prevalente en niños con ADHD y afecta al rendimiento académico, las relaciones sociales, el estado de salud y la vida familiar. La primera de línea de tratamiento incluye diagnóstico diferencial, optimización del tratamiento del ADHD con estimulantes e iniciación de una buena higiene del sueño y terapia comportamental. Posteriormente, existe la opción de la farmacoterapia adyuvante y a menudo se prescribe melatonina. La melatonina regula los trastornos del ritmo circadiano del sueño, tales como la dificultad para conciliar el sueño (SOI), en los niños con ADHD. Cuatro estudios en niños con ADHD e insomnio mostraron una mejora en el inicio y la latencia del sueño. Los estudios incluían niños de 6 a 14 años y las dosis de melatonina variaban de 3 a 6 mg administrados pocas horas antes de acostarse. En todos los estudios los efectos adversos fueron leves y transitorios. Los estudios disponibles sobre melatonina se ven limitados por el escaso número de sujetos y la corta duración, la variabilidad de los criterios para evaluar la SOI, el SAHD y la eficacia del tratamiento y la imposibilidad de generalización de los resultados obtenidos.

**CONCLUSIONES:** Los datos disponibles sugieren que melatonina es un tratamiento bien tolerado y eficaz para pacientes pediátricos con SOI y ADHD crónicos. Se necesita disponer de preparados regulados con melatonina y ensayos clínicos bien diseñados con mayor número de sujetos para establecer los regímenes óptimos de dosificación y la seguridad a largo plazo de estos tratamientos.


Traducido por Juan del Arco

Traitement par la Mélatonine de l'Insomnie chez des Enfants Présentant un Trouble de Déficit de l'Attention avec ou sans Hyperactivité

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RÉSUMÉ

**OBJECTIF:** Évaluer l'efficacité et l'innocuité de la mélatonine lorsqu'utilisée pour le traitement de l'insomnie chez des enfants présentant un trouble de déficit de l'attention avec ou sans hyperactivité.

**REVUE DE LA LITTÉRATURE:** Les articles pertinents ont été identifiés à l'aide d'une recherche dans les banques de données informatisées MEDLINE (1948–août 2009), EMBASE (1950–août 2009), et Scopus (1960–août 2009) en utilisant les mots mélatonine, trouble de l'attention avec ou sans hyperactivité (TDAH), pédiatrique, insomnie, trouble du sommeil, et sommeil.

**SÉLECTION DES ÉTUDES ET DE L'INFORMATION:** Tous les articles publiés en langue anglaise et les études chez l'humain ont été sélectionnés et évalués. Les résultats d'essais cliniques randomisés (n = 5), d'une étude sur l'innocuité, d'une étude à long terme, d'une analyse rétrospective, de méta-analyses (n = 2), d'articles de revue (n = 9), et de lettres ont été retenus pour cet article.

**RÉSUMÉ:** On observe souvent de l'insomnie chez les enfants présentant un TDAH et cette insomnie a des conséquences sur les performances académiques, le fonctionnement social, l'état de santé général, et la vie familiale. Le traitement de choix inclut un diagnostic différentiel, l'optimisation du traitement du TDAH par les stimulants et l'initiation d'une bonne hygiène du sommeil et une thérapie comportementale. En deuxième ligne, on trouve la pharmacothérapie adjuvante et la mélatonine est souvent prescrite à ce stade. La mélatonine agit sur la modulation du rythme circadien du sommeil lors de trouble d'endormissement chez les enfants présentant un TDAH. Quatre études chez les enfants présentant un TDAH avec insomnie ont montré une amélioration dans la latence d'endormissement. Les sujets d'études avaient de 6–14 ans et les doses de mélatonine variaient de 3 à 6 mg administrées quelques heures avant le sommeil. Dans toutes les études, les effets indésirables étaient légers et transitoires. Plusieurs faiblesses sont notées dans ces études; études de courte durée, faible nombre de sujets, définition des troubles d'endormissement non uniformes, critères de définition du TDAH différents d'une étude à l'autre, critères d'évaluation du traitement variables et comparaison des résultats difficile.

**CONCLUSIONS:** Les données actuellement disponibles suggèrent que la mélatonine peut représenter une option de traitement efficace et bien tolérée chez des enfants présentant un TDAH accompagné d'insomnie. Une réglementation de la mise en marché des produits de mélatonine et des études à plus grande échelle avec un bon devis afin d'établir les doses optimales et l'innocuité à long terme sont requises.

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