Pediatric insomnia: clinical, diagnosis, and treatment

Silvia Miano, Rosa Peraita-Adrados

Summary. Pediatric insomnia is an extrinsic sleep disorder subdivided into two categories: behavioral insomnia and insomnia related to medical, neurological, and psychiatric diseases. This review will cover several types of insomnia, comorbidities and specific pediatric therapies according to clinical characteristics and age. Behavioral insomnia should be differentiated from pediatric insomnia due to medical conditions, mostly occurring during the first year of life. Multiple night awakenings and diurnal hypersomnolence are strong indicators of insomnia due to medical conditions. Insomnia during adolescence and pediatric insomnia associated with psychiatric comorbidity, cognitive disabilities and epilepsy, will be discussed in terms of diagnosis, clinical features and implications for treatment.

Key words. Children. Insomnia. Treatment.

Sleep & Epilepsy Center; Neurocenter of Southern Switzerland; Civic Hospital (EOC) of Lugano; Lugano, Switzerland (S. Miano). Sleep and Epilepsy Unit; Clinical Neurophysiology Department; Gregorio Marañón University Hospital; Faculty of Medicine; Complutense University of Madrid; Madrid, Spain (R. Peraita-Adrados).

Corresponding author:
Silvia Miano MD, PHD.
Sleep & Epilepsy Center.
Neurocenter of Southern Switzerland.
Civic Hospital (EOC) of Lugano.
Via Tesserete 46. CH-6900 Lugano (Switzerland)

Fax:
+41 91 811 6915.

E-mail:
silvia.miano@gmail.com

Accepted:
30.08.13.

How to cite this paper:
Miano S, Peraita-Adrados R. Pediatric insomnia: clinical, diagnosis, and treatment. Rev Neurol 2014; 58: 35-42.

Versión española disponible en www.neurologia.com

Introduction

Pediatric insomnia can be intrinsic or idiopathic in nature, or due to external causes. The International Classification of Sleep Disorders (ICSD), second edition (2005) [1] defines pediatric insomnia as an extrinsic sleep disorder subdivided into two categories: behavioral insomnia and insomnia related to medical, neurological, and psychiatric diseases. Idiopathic insomnia is an intrinsic sleep disorders that can start early and is characterized by a lifelong inability to obtain adequate sleep, presumably due to an abnormality in neurological control of the sleep-wake system [1,2]. Pediatric insomnia is also distinguished by age, in relationship to several etiological factors (Table I) [2,3]. This review will cover several types of insomnia, comorbidities and specific pediatric therapies according to clinical characteristics and age.

Diagnosis

The behavioral insomnia of childhood (BIC) is based on the criteria described in the ICSD, second edition (2005) [1]. The child shows a pattern consistent with either the sleep-onset-association type or limit-setting type of insomnia. Typical of the sleep-onset-association type are that: falling asleep becomes an extended process that requires special conditions; sleep onset associations are highly problematic or demanding, in the absence of the associated conditions; sleep onset is significantly delayed or sleep is otherwise disrupted; and night-time awakenings require caregiver intervention for the child to return to sleep. In limit-setting type, the individual has difficulty initiating or maintaining sleep; the individual stalls or refuses to go to bed at an appropriate time or refuses to return to bed following a night-time awakening; the caregiver demonstrates insufficient or inappropriate limit-setting to establish appropriate sleeping behavior in the child; the sleep disturbance is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, or medication use. In the mild form of BIC the major sleep episode is reduced by less than one hour, with up to three episodes per night of stalling, calling out, or leaving the bedroom. In the moderate form, the major sleep episode is reduced by one to two hours, with three to four episodes per night of stalling, calling out, or leaving the bedroom. In severe cases, the major sleep episode is reduced by at least two hours, with five or more episodes per night of stalling, calling out, or leaving the bedroom [1].

Etiology

BIC in childhood represents a complex combination of biological, circadian, neurodevelopmental, environmental, and behavioral variables. Difficulty falling asleep is generally associated with either a parent who provides poor or inconsistent limits at bedtime, or a child who requires a parent to help him or her fall asleep, inducing a negative sleep on-

Table I. Different types of insomnia related to age and etiology.

	First year of life	Preschooler	Adolescence
Behavioral insomnia	Sleep onset association type, bedtime struggles, night awakenings (that can be aggravated by the association with excessive use of liquid such as water or milk)	Behavioral insomnia (Limit setting problems)	Inadequate sleep hygiene
Insomnia related to medical, neurological, psychiatric, environmental or social factors	Infant colic, food allergy, gastro-esophageal reflux (mostly milk allergy), otitis	Nightmares and fear at bedtime	Substance abuse

set association (SOA). Difficulties maintaining sleep are most often a consequence of a negative SOA that is required to help a child return to sleep following normal night-time arousals (the child loses or never acquires the ability to self-soothe at bedtime or during night awakenings and asks for the same condition of bedtime also thorough the night to fall asleep). This is a developmental skill that occurs between 3 and 6 months in typically developing, healthy infants, but some do not acquire the ability to self-soothe and have high risk to develop BIC. Bedtime refusal is when a child refuses to get ready for bed, go to bed, or stay in bed. Some parents may set few, if any, limits at bedtime (for instance, allowing children to fall asleep in front of the television), or they may set inconsistent limits [1,2].

There is increasing evidence that sleep disruption and/or insufficient sleep has deleterious effects on children's cognitive development (learning, attention, memory consolidation, executive function), mood regulation chronic irritability, poor modulation of affect), and disruptive behavior, as well as health (metabolic and immune function, accidental injuries) and overall quality of life, with deleterious effect on parents mood and family functioning [4,5]. Behavioral disturbances staring form preschool age correlated with the specific kind of BIC: awakenings are correlated with externalizing symptoms while bedtime problems are associated with internalizing symptoms [3].

Differential diagnosis

Behavioral insomnia should be differentiated from pediatric insomnia due to medical conditions, mostly occurring during the first year of life. Multiple night awakenings, and diurnal hypersomnolence are strong indicators of insomnia due to medical conditions (which represents 20% of cases). Gastro-esophageal reflux and food allergies are usually associated with insomnia and sleep disordered breathing [6,7]. Medical insomnia can be aggravated in combination with behavioral insomnia due to the early alteration of sleep quality inducing wrong associations at bedtime. In these cases the therapy is combined (medical therapy plus behavioral therapy). Normal infant colic starts at evening and occurs in infants less than 3 months old. It has been hypothesized that in the evening, peak serotonin concentration causes intestinal cramps associated with colic because serotonin increases smooth intestinal muscle contractions. Melatonin has the opposite effect of relaxing smooth intestinal muscles. Both serotonin and melatonin exhibit a circadian rhythm with peak concentrations in the evening [8]. However, serotonin intestinal contractions are unaffected by melatonin during the first 3 months because only serotonin circadian rhythms are present at birth. Melatonin circadian rhythms appear at 3 months of age. Colic cramps disappear at 3 months of age. The persistence of infant colic seems to be caused by an immaturity of circadian rhythms, but unfortunately there is no data confirming that the administration of melatonin improves sleep of infants with persisting colic (usually occurring randomly over the 24 hours) [8].

Treatment of pediatric insomnia

Behavioral therapy

The American Academy of Sleep Medicine has published recommendations for behavioral treatment of bedtime problems and night awakenings in infants and young children [4]. Behavioral therapy is largely subdivided into the follow interventions:

– Unmodified extinction, which involves parents putting the child to bed at a designated bedtime and then ignoring the child until morning. The objective is to reduce undesired behaviors by eliminating parental attention.

– Graduated extinction which involves parents ignoring bedtime crying and tantrums for established periods before briefly checking on the child. A progressive (graduated) checking schedule or fixed checking schedule may be used. The goal is to teach the child to develop 'self-soothing' skills, eliminating any associations.
– Positive or faded bedtime routines with response costs. Positive routines involve parents developing a stable bedtime routine characterized by enjoyable and quiet activities, while faded bedtime routines involve temporarily delaying the bedtime to more closely coincide with the child's natural sleep onset time, then anticipating the bedtime as the child gains success in falling asleep quickly. Response costs involve taking the child out of bed for prescribed brief periods if the child does not fall asleep. These strategies rely on stimulus control as the primary agent of behavior change and target physiological arousal at bedtime, such as in adult psychophysiological insomnia.
– Other interventions include scheduled awakenings which involve parents awakening their child prior to a typical spontaneous awakening, and providing responses such as feeding, rocking, soothing.
– Parental education/prevention, which involves parental education to prevent the development of sleep problems. All these techniques have provided efficacy and evidence to be a standard therapy for BIC.

In sum, behavioral treatments provide beneficial effects on secondary outcomes, including daytime functioning of the child and parental well-being [4].

Drug therapy

Two benzodiazepines, flurazepam and delorazepam, one antihistamine (niaprazine) and one phenothiazine (rimeprazine) have been shown to be effective in short-term treatment of insomnia in young children, although none of these agents are approved for pediatric insomnia. Niaprazine associated with behavioral therapy in short-term treatment can be the best choice of treatment in order to improve the compliance of children and parents or caregivers with the behavioral therapy. Short-acting benzodiazepines may have a role in brief treatments of pediatric insomnia associated with an anxiety or mood disorder, psychosis, aggression, medication- induced activation, or anticipatory anxiety [9]. Melatonin and other kinds of medication such as neuroleptics or antidepressives like trazodone can be used in specific comorbidities (circadian rhythm disorders, insomnia during adolescence, anxiety, mood disorders, attention deficit and hyperactive disorder, autism and other cognitive disabilities (for more details see below) [10-12]. However, large-scale clinical trials of pediatric insomnia treatment are warranted to provide information to the clinician on the safety and efficacy of prescription agents for the management of pediatric insomnia [13].

An anonymous questionnaire examining the prescribing practices of members of the British Association for Community Child Health and the British Academy of Childhood Disability, revealed that autism (68%) and attention deficit hyperactivity disorder (44%) were the most frequent clinical diagnoses in the children prescribed melatonin, and that over 95% of respondents found melatonin 'usually' or 'always' effective, whereas adverse events were reported by 18% of respondents including: new onset seizure activity, increased seizure frequency, hyperactivity, agitation/behavioural changes, worsening sleep pattern, nightmares, and constipation [14].

In addition, many medications that are commonly used as hypnotics in children are being used for their sedative adverse effects rather than for primary effects on sleep/wake mechanisms or hyperarousal. Despite the widespread use of prescription therapies such as clonidine, antidepressants, mood stabilizers, and antihistamines, little data exist on their efficacy for the treatment of insomnia in children and adolescents [13].

Special forms of pediatric insomnia

Insomnia during adolescence

A particular form of insomnia brought by adolescence is the delayed sleep phase syndrome (DSPS), due to changes in the activities and social life of adolescences. Late-night socializing or other activities make it impossible to get to sleep, leading to insufficient sleep and sleep debt which may cause daytime sleepiness and reduction of overall functioning [15]. Diagnostic criteria of delayed sleep phase syndrome according to ICSD are as follows: The patient complains of an inability to fall asleep at the desired clock time, an inability to awaken spontaneously at the desired time of awakening, or excessive sleepiness [1]. There is a phased delay of the major sleep episode in relation to the desired time

for sleep. The symptoms are present for at least one month. An important distinctive feature is that patients will have a habitual sleep period that is sound and of normal quality and duration, then will awaken spontaneously and maintain stable entrainment? to a 24-hour sleep-wake pattern at a delayed phase. A strict schedule is not required.

The diagnosis is based on sleep-wake logs that are maintained daily for a period of at least two weeks, showing a delay in the timing of the habitual sleep period and one of the following measurements should demonstrate a delay in the timing of the habitual sleep period: twenty-four-hour polysomnography (or by means of 2 consecutive recordings and 1 multiple sleep latency test) or continuous temperature monitoring showing that the time of the absolute temperature nadir is delayed into the second half of the habitual (delayed) sleep episode. Any other sleep disorder causing inability to initiate sleep or excessive sleepiness should be excluded. A transitory delay of sleep onset can be associated with the start of major mental disturbances, in particular in the excited phase of bipolar affective disorder and during schizophrenic decompensation. The prevalence of DSPS is about 7% in adolescents, even if it rarely occurs during childhood, and typically there is a 10:1 male:female ratio [1,16].

Hypersensitivity to evening light could be a precipitating or maintaining factor [17]. A reduced sleep time in adolescents affected by DSPS following sleep deprivation has been found, suggesting that DSPD patients may have a diminished ability to compensate for lost sleep [18]. Occupational, school, and social dysfunctions may be relevant complications, since absenteeism and chronic tardiness are not tolerated in school and adolescents with DSPS come to be judged as lazy, unmotivated, or mentally ill by their families, peers, and school environment. Chronic sedative or alcohol use or abuse accompanies some cases as a complicating feature [1,16,19].

It has been demonstrated that long-term treatment with oral melatonin, 3 to 5 mg/day for an average period of 6 months, can be beneficial for adolescents with DSPS in terms of sleep-wake schedule and school performance [20].

Insomnia and psychiatric comorbidity

Many psychiatric disorders (affective disorders, psychosis, anxiety disorders, including posttraumatic stress disorder, substance abuse disorders, eating disorders, and attention deficit/hyperactivity disorders) are associated with sleep disturbances, and the relationship is often bidirectional. The spectrum of associated sleep disorders includes insomnia, hypersomnia, nocturnal panic, sleep paralysis, hypnagogic hallucinations, restless legs/periodic limb movements of sleep, obstructive sleep apnea, and parasomnias [21].

Anxiety disorders are one of the most prevalent categories of childhood psychiatric disorders including separation anxiety disorder, generalized anxiety disorder, social phobia, specific phobias, obsessive compulsive disorder, posttraumatic stress disorder, panic disorder (with or without agoraphobia), and anxiety disorder. Anxiety is characterized as a state of hypervigilance or hyperarousal and is closely related to sleep dysregulation. The majority of children and adolescents with anxiety disorders have transient sleep problems, and up to 50% have chronic sleep disturbance. The most common sleep problems in children with anxiety disorders include sleep initiation and maintenance problems, frequent nocturnal awakenings, bedtime refusal, cosleeping, nightmares, and nocturnal fears [22]. Anxiety symptoms are strongly associated with specific sleep habits: sleeping with the lights on, requiring a toy/object for sleep onset, sensitivity to noises, fear of the dark or of being alone, requiring bedtime rituals, nightmares, and crying during sleep. Recurrent nightmares are frequently noted in children with anxiety disorders and can be a hallmark of traumatic experience or abuse. In the acute phase, physiological hyperarousal, sleep difficulties, and flashbacks are predominant, whereas in the chronic phase detachment, sadness, numbing, dissociation, and even increased sleep are predominant [22].

Major depressive disorder (MDD) occurs in approximately 2% of children and up to 8% of adolescents. About 2/3 of children suffering from early onset/pre-pubertal MDD reported disorders with initiating and maintaining sleep, and half of them early final awakening [22].

Pharmacological interventions such as trazodone may be warranted in cases of MDD or anxiety disorder associated with insomnia that do not respond to non-pharmacologic interventions alone (cognitive-behavioral therapy) [10].

Sleep issues are relevant to the management of children with attention deficit hyperactivity disorder (ADHD). Several sleep phenotypes are associate with ADHD: a 'primary' form due to an hypoarousal state similar to narcolepsy; a phenotype associated with delayed SOI; another form associated with sleep disordered breathing; a form associated with restless legs syndrome and/or periodic

limbs movements disorder; and finally, a form associated with epilepsy/or electroencephalographic (EEG) intercritical discharges during sleep [23].

Actigraphic monitoring of sleep in combination with dim-light melatonin-onset measurements have revealed delayed sleep onset, delayed dim-light melatonin onset, time of awakening suggestive of delayed circadian pacemaker in children with ADHD, and insomnia compared with children with ADHD without insomnia [24]. Moreover, it has been recently suggested that the core endophenotypic characteristic of pediatric bipolar sleep is a phase-delayed circadian sleep-wake cycle, rather than decreased need for sleep per se, with many similarities to the insomnia of ADHD-SOI children. ADHD-SOI may be a phenotype with a higher risk for bipolar disorder [25]. Melatonin treatment was found to be safe, effective, and well tolerated in several studies of children with ADHD and delayed sleep onset. Research evidence supports the use of melatonin in children with ADHD suffering from chronic sleep-onset insomnia, in order to prevent the aggravation of psychiatric comorbidities [22,23,26,27].

Insomnia and cognitive disabilities

The majority of the studies about sleep problems in children with mental disabilities reported unspecific sleep problems such as disorders of initiating and maintaining sleep, sleep-wake deregulation or sleepiness. The lack of knowledge about specific sleep disorders like sleep breathing disorders or periodic limb movements disorders in mentally retarded children may be due to two factors: 1) parents do not perceive their child as having a sleep problem, or 2) they tend to underestimate sleep problems [28]. Epilepsy and other neurological impairments increase the risk and the severity of insomnia and of sleep-wake behavior. Severe locomotor disablity, blindness and active epilepsy are predictors of increased daytime sleep and increased number of wake-sleep transitions. The prevalence of insomnia is markedly higher, occurring in about 30-50% of school-aged children with intellectual disability. The treatment of choice for disorders of initiating and maintaining sleep in children with cognitive disability is again melatonin along with cognitive-behavioral techniques [29]. Persons with intellectual disability (ID) and sleep problems exhibit more daytime challenging behaviors than persons with ID without sleep problems. Several reports suggest that melatonin is not only effective in the treatment of insomnia, but also decreases daytime challenging behavior, and a randomized controlled trial in a population of children, adolescents and young adults with intellectual disability and chronic insomnia demonstrated that treatment with melatonin (administered at a dosage of 5 mg (< 6 years: 2.5 mg) during 4 weeks decreases daytime challenging behavior, probably by improving sleep maintenance or by improving circadian melatonin rhythmicity [30].

A recent randomized placebo trial of immediate release melatonin administered 45 minutes before the child's bedtime for a period of 12 weeks (dosage from 0.5 mg capsule, to 2 mg, 6 mg, and 12 mg depending on the response to treatment) demonstrated an increase of total sleep time and a slight improvement of family functioning outcomes [31].

It has been reported that in some patients with intellectual disability and sleep problems, the initial good response to melatonin disappeared within a few weeks after starting treatment, returning only after considerable dose reduction, hypothesizing that this loss of response is associated with slow melatonin metabolism. As melatonin is metabolised in the liver almost exclusively by cytochrome P450 enzyme CYP1A2, the loss of response is probably due to decreased activity/inducibility of CYP1A2. Further, they suggested a melatonin clearance test in patients with loss of response to melatonin [32,33].

Insomnia is the predominant sleep concern in children with autistic spectrum disorder (ASD), and its nature is most likely multifactorial, with neurochemical (abnormalities in serotonergic transmission or melatonin levels), psychiatric (anxiety), and behavioral (poor sleep habits) and etiological factors involved. Children with ASD experience sleep problems similar to those of typically developing children, although the prevalence is markedly higher, occurring in 44-83% of school-aged children with ASD. Caregivers usually report that insomnia is the most frequent sleep disorder, described as disorders of initiating and maintaining sleep, restless sleep, bedtime resistance, co-sleeping, alterations of sleep hygiene, and early awakenings in the morning. Both pharmacologic and behavioral interventions have been suggested for the treatment of sleep problems in autistic children [34]. The most common types of behavioral interventions are complete extinction (removing reinforcement to reduce a behavior) and various forms of graduated extinction. There is some evidence that low melatonin concentration caused by a primary deficit in acetylserotonin methyltransferase activity is a risk factor for ASD. Sleep problems usually start at the same age as developmental regression, suggesting a higher vulnerability at this stage of life. Melatonin has

Table II. Clinical features and treatment of pediatric insomnia related to other conditions (medical, psychiatric, neurological factors).

	Age at onset	Type of insomnia	Behavioral treatment	Drug therapy
Medical conditions (gastroesophageal reflux, food allergy, otitis)	First year of life	Disorders of initiating and maintaining sleep with multiple night awakening and diurnal hypersomnolence	Extinction or graduated extinction, bedtime routines	Yes (specific treatment of medical conditions and/or niaprazine)
Infant colic	First year of life	Disorders of initiating and maintaining sleep	Extinction or graduated extinction, bedtime routines	None or melatonin (fast release, after 6 months of age)
Anxiety and depressive disorders	School age and adolescence	Sleep onset delay, bedtime struggles, nightmares, early morning awakenings	Bedtime routines, relaxing therapy, cognitive therapy	Melatonin (fast plus delay controlled in case of early morning awakening), trazodone or short term benzodiazepine with hypnotic effect, or zolpidem in adolescents
ADHD and sleep onset insomnia	School age, prepubertal age, adolescence	Sleep delayed phase syndrome	Cognitive therapy, light and chronotherapy	Melatonin (fast plus controlled release)
Intellectual disabilities (and autism)	Any age	Disorders of initiating and maintaining sleep	Extinction or graduated extinction, bedtime routines	Melatonin (fast plus controlled release)
Epilepsy	Any age	Disorders of initiating and maintaining sleep and diurnal hypersomnia	Extinction or graduated extinction, bedtime routines	Melatonin (fast plus controlled release)

ADHD: attention deficit hyperactivity disorder.

shown promising results in the treatment of insomnia in children with ASD, and a dual treatment of melatonin with behavioral techniques is considered the best choice [34]. Recently, one hundred and sixty children with autism spectrum disorders suffering from insomnia, were assigned randomly to either a combination of controlled-release melatonin and cognitive-behavioral therapy, controlled-release melatonin, four sessions of cognitive-behavioral therapy, or placebo drug treatment condition for 12 weeks. Melatonin treatment was mainly effective in reducing insomnia symptoms, while cognitive-behavioral therapy had a light positive impact mainly on sleep latency, suggesting that some behavioral aspects might play a role in determining initial insomnia. The combination treatment group showed a trend to outperform other active treatment groups, with fewer dropouts and a greater proportion of treatment responders achieving clinically significant changes. This study demonstrates that adding behavioral intervention with melatonin treatment seems to result in a better treatment response, at least in the short term [12].

Insomnia and epilepsy

Several factors influence the relationship between epilepsy and sleep, such as disorders of initiating and maintaining sleep due to a behavioral insomnia secondary to changes in sleep habits like co-sleeping or parental presence at sleep onset, the presence of specific sleep disorders such as rapid eye movement (REM), parasomniac disorders like sleepwalking, sleep terrors, and confusional arousals. Another important factor influencing sleep disturbances is the 'interference' of interictal activity and seizures with sleep quality and the effects on both sleep and coexisting sleep disorders of antiepileptic drugs [35]. Several studies of sleep problems in children with epilepsy have been conducted, and parents report a higher rate of sleep problems, disturbed daytime behavior, poor-quality or non-restorative sleep, and anxieties about sleeping, with a significant association with poor seizure control. Nocturnal seizures, polytherapy, developmental delay, refractory epilepsy, and epileptic syndromes are usually associated with poor sleep habits and sleep disorders [35].

There is evidence that subjects with intractable epilepsy have low levels of baseline melatonin (but increase dramatically after the seizure period), and that melatonin therapy may help control seizures in children and adolescents with epilepsy, improving sleep efficiency and reducing sleep disruption. It has been shown that, in a model of chronic epilepsy, ramelteon, a selective melatonin receptor agonist, has

anticonvulsant properties [36]. In addition, melatonin therapy may help control seizures in children and adolescents with epilepsy, improving sleep efficiency and reducing sleep disruption. The mechanism whereby treatment of a sleep disorder improves a seizure disorder is unknown, but is probably linked to stabilization of sleep as a result of preventing the unsteadiness of EEG oscillations [35].

Table II summarizes clinical features and treatment of the specific forms of pediatric insomnia.

Conclusions

Pediatric insomnia is a common, long-lasting, and challenging sleep disorder with increased risk to develop learning disability and behavioral problems. Although recently the randomized-controlled trials and the population studies with a large numbers of children have been increased, further research is needed regarding the most appropriate treatment regimes for both the general pediatric population and subpopulations in terms of commonly prescribed medications to treat both the primary disorder and comorbid insomnia [13]. Special attention has to be paid to the comorbid conditions, such as respiratory problems, epilepsy, mood disorders, ADHD, and intellectual disability, in order to improve both chronic insomnia and comorbid condition, considering that sometime insomnia is associated with multiple comorbidities. This review is an attempt to help clinicians by increasing a awareness and knowledge of pediatric insomnia.

References

1. American Academy of Sleep Medicine. The International Classification of Sleep Disorders, Second Edition (ICSD-2). Diagnostic and coding manual. Darien, IL: AASM; 2005.
2. Villa MP, Pagani J, Miano S. Insomnia from neonatal age to adolescence. Minerva Pediatr 2007; 59: 492-3.
3. Bruni O. Principi di medicina del sonno in età evolutiva. Milano: Mediserve; 2000.
4. Mindell JA, Kuhn B, Lewin DS, Meltzer LJ, Sadeh A; American Academy of Sleep Medicine. Behavioral treatment of bedtime problems and night wakings in infants and young children. Sleep 2006; 29: 1263-76.
5. Mindell JA, Telofski LS, Wiegand B, Kurtz ES. A nightly bedtime routine: impact on sleep in young children and maternal mood. Sleep 2009; 32: 599-606.
6. Kahn A, François G, Sottiaux M, Rebuffat E, Nduwimana M, Mozin MJ, et al. Sleep characteristics in milk-intolerant infants. Sleep 1998; 11: 291-7.
7. Katz ES, Mitchell RB, D'Ambrosio CM. Obstructive sleep apnea in infants. Am J Respir Crit Care Med 2012; 185: 805-16.
8. Weissbluth L, Weissbluth M. Infant colic: the effect of serotonin and melatonin circadian rhythms on the intestinal smooth muscle. Med Hypotheses 1992; 39: 164-7.
9. Younus M, Labellarte MJ. Insomnia in children: when are hypnotics indicated? Paediatr Drugs 2002; 4: 391-403.
10. Owens JA, Rosen CL, Mindell JA, Kirchner HL. Use of pharmacotherapy for insomnia in child psychiatry practice: a national survey. Sleep Med 2010; 11: 692-700.
11. Marcus RN, Owen R, Manos G, Mankoski R, Kamen L, McQuade RD, et al. Safety and tolerability of aripiprazole for irritability in pediatric patients with autistic disorder: a 52-week, open-label, multicenter study. J Clin Psychiatry 2011; 72: 1270-6.
12. Cortesi F, Giannotti F, Sebastiani T, Panunzi S, Valente D. Controlled-release melatonin, singly and combined with cognitive behavioral therapy, for persistent insomnia in children with autism spectrum disorders: a randomized placebo-controlled trial. J Sleep Res 2012; 21: 700-9.
13. Mindell JA, Emslie G, Blumer J, Genel M, Glaze D, Ivanenko A, et al. Pharmacologic management of insomnia in children and adolescents: consensus statement. Pediatrics 2006; 117: 1223-2.
14. Waldron DL, Bramble D, Gringras P. Melatonin: prescribing practices and adverse events. Arch Dis Child 2005; 90: 1206-7.
15. Stores G. Sleep disorders in general and in adolescence. J Fam Health Care 2009; 19: 51-3.
16. Sack RL, Auckley D, Auger RR, Carskadon MA, Wright KP Jr, Vitiello MV, et al; American Academy of Sleep Medicine. Circadian rhythm sleep disorders: part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm. Sleep 2007; 30: 1484-501.
17. Aoki H, Ozeki Y, Yamada N. Hypersensitivity of melatonin suppression in response to light in patients with delayed sleep phase syndrome. Chronobiol Int 2001; 18: 263-71.
18. Uchiyama M, Okawa M, Shibui K, Liu X, Hayakawa T, Kamei Y, et al. Poor compensatory function for sleep loss as a pathogenic factor in patients with delayed sleep phase syndrome. Sleep 2000; 23: 553-8.
19. Carskadon MA, Acebo C, Jenni OG. Regulation of adolescent sleep: implications for behavior. Ann N Y Acad Sci 2004; 1021: 276-91.
20. Szeinberg A, Borodkin K, Dagan Y. Melatonin treatment in adolescents with delayed sleep phase syndrome. Clin Pediatr 2006; 45: 809-18.
21. Abad VC, Guilleminault C. Sleep and psychiatry. Dialogues Clin Neurosci 2005; 7: 291-303.
22. Ivanenko A, Johnson K. Sleep disturbances in children with psychiatric disorders. Semin Pediatr Neurol 2008; 15: 70-8.
23. Miano S, Parisi P, Villa MP. The sleep phenotypes of attention deficit hyperactivity disorder: the role of arousal during sleep and implications for treatment. Med Hypotheses 2012; 79: 147-53.
24. Van der Heijden KB, Smits MG, Gunning WB. Sleep hygiene and actigraphically evaluated sleep characteristics in children with ADHD and chronic sleep onset insomnia. J Sleep Res 2006; 15: 55-62.
25. Staton D, Hill CM, Chen W. ADHD, sleep onset, and pediatric bipolar disorder. J Sleep Res 2008; 17: 240.
26. Van der Heijden KB, Smits MG, Van Someren EJ, Ridderinkhof KR, Gunning WB. Effects of melatonin on sleep, behavior, and cognition in ADHD and chronic sleep-onset insomnia. J Am Acad Child Adolesc Psychiatry 2007; 46: 233-41.
27. Hoebert M, Van der Heijden KB, Van Geijlswijk IM, Smits MG. Long-term follow-up of melatonin treatment in children with ADHD and chronic sleep onset insomnia. J Pineal Res 2009; 47: 1-7.
28. Stores G. Sleep studies in children with a mental handicap. J Child Psychol Psychiatry 1992; 33: 1303-17.
29. Zucconi M, Bruni O. Sleep disorders in children with neurologic diseases. Semin Pediatr Neurol 2001; 8: 258-75.
30. Braam W, Didden R, Maas AP, Korzilius H, Smits MG, Curfs LM. Melatonin decreases daytime challenging behaviour in persons with intellectual disability and chronic insomnia. J Intellect Disabil Res 2010; 1: 52-9.
31. Gringras P, Gamble C, Jones AP, Wiggs L, Williamson PR, Sutcliffe A, et al; MENDS Study Group. Melatonin for sleep

problems in children with neurodevelopmental disorders: randomised double masked placebo controlled trial. BMJ 2012; 345: e6664.
32. Braam W, Van Geijlswijk I, Keijzer H, Smits MG, Didden R, Curfs LM. Loss of response to melatonin treatment is associated with slow melatonin metabolism. J Intellect Disabil Res 2010; 54: 547-55.
33. Braam W, Keijzer H, Struijker-Boudier H, Didden R, Smits M, Curfs L. CYP1A2 polymorphisms in slow melatonin metabolisers: a possible relationship with autism spectrum disorder? J Intellect Disabil Research 2013; 57: 993-1000.
34. Miano S, Ferri R. Epidemiology and management of insomnia in children with autistic spectrum disorders. Paediatr Drugs 2010; 12: 75-4.
35. Parisi P, Bruni O, Villa MP, Miano S, Luchetti A, Curatolo P. The relationship between sleep and epilepsy: the effect on cognitive functioning in children. Dev Med Child Neurol 2010; 52: 805-10.
36. Fenoglio-Simeone K, Mazarati A, Sefidvash-Hockley S, Shin D, Wilke J, Milligan H, et al. Anticonvulsant effects of the selective melatonin receptor agonist ramelteon. Epilepsy Behav 2009; 16: 52-7.

Insomnio pediátrico: clínica, diagnóstico y tratamiento

Resumen. El insomnio pediátrico es un trastorno de sueño extrínseco que puede subdividirse en dos categorías: insomnio conductual e insomnio relacionado con trastornos médicos, neurológicos y psiquiátricos. En esta revisión presentamos varios tipos de insomnios, comorbilidad y terapias específicas de acuerdo con la edad y con las características clínicas. El insomnio conductual se debe diferenciar del insomnio pediátrico por causas médicas, ya que este último aparece, normalmente, en el primer año de vida. Los despertares nocturnos frecuentes y la somnolencia diurna excesiva indican un insomnio debido a causas médicas. El insomnio del adolescente y el insomnio pediátrico asociado a trastornos psiquiátricos, alteraciones cognitivas y epilepsia se discutirán en términos de diagnóstico, hallazgos clínicos e implicaciones terapéuticas.

Palabras clave. Insomnio. Niños y adolescentes. Tratamiento.