SCORE SOUTH CAROLINA OFFERING PRESCRIBING EXCELLENCE

FAQ– Summer 2014

IN THIS ISSUE: What is the Recommended Management of Insomnia in Children with ADHD?

Before deciding how to treat sleep disorders in children with ADHD, identify the underlying cause, which is likely to be multifactorial and vary from patient to patient. Sleep problems (e.g., poor sleep habits of child/family, obstructive sleep apnea, restless leg syndrome) can:

- mimic ADHD symptomatology,
- exacerbate underlying ADHD symptoms,
- be associated with or exacerbated by ADHD,
- and/or result from psychotropic medications used to treat ADHD.

Educating families about normal sleep development and engaging them in good sleep hygiene is essential in any treatment plan or discussion about use of behavioral interventions, diet changes, adjustments in stimulant dosing schedule, or an additional medication to treat pediatric insomnia.

Evidence supporting an increased prevalence of sleep problems in children with ADHD is unclear. Objective sleep studies have generally failed to find consistent differences in sleep architecture and patterns between children with ADHD and controls. In contrast, surveys of parents and children with ADHD consistently report higher rates of difficulty falling asleep, night time awakenings, poor sleep quality, and daytime sleepiness compared to children without ADHD. Sleep disturbances may be attributable to comorbid conditions or medication use (e.g., stimulants for ADHD or antidepressants). One parent survey reported a 3-fold increase in severe sleep difficulties (e.g., sleep onset delay or night awakenings) while their children were on stimulant therapy for ADHD. Objective sleep studies of stimulant medications show varied results, with some reporting delayed sleep onset, shorter sleep duration, and delayed onset rapid eye movement sleep. In addition, stimulants may also have a rebound effect when wearing off at the end of the day, resulting in increased arousal and hyperactivity.

Good sleep hygiene can improve sleep quality and effectively treat initial insomnia in children with ADHD. See SCORxE's Healthy Sleep Habits for Children at *http://www.sccp.sc.edu/sites/default/files/27842-SCORXE_HSH_PADS.pdf* to provide more information to children and their families. While ensuring good sleep hygiene, if stimulant use is a suspected cause, adjustments in the dosing schedule can help. Examples include:

- if the medication is wearing off at bedtime causing rebound arousal and hyperactivity, giving a late day dose of short-acting stimulant may be beneficial; in contrast,
- if the stimulant is lingering and causing a direct stimulatory effect, then earlier dosing, avoiding afternoon/evening doses, using a shorter acting or different formulation (e.g., with more prominent morning than afternoon release), or changing to a non-stimulant medication may be helpful.

The use of sleep-promoting medication is usually a final resort after all other attempts (e.g., behavioral interventions, adjusting primary ADHD medications as needed) to improve sleep have been unsuccessful. Although there is a scarcity of FDA-approved pediatric sleep medications, alpha-2-agonists (clonidine), antidepressants (trazodone and mirtazapine), antihistamines and hypnotics have been used in clinical practice. However, their continued effectiveness over time and effect on sleep quality have not been well studied, and long-term safety data for combination treatment are limited. Melatonin, a naturally occurring sleep hormone, is an alternative treatment that has been well tolerated and shown to have a relative phase delay in release in children with ADHD. In two well controlled studies in children with ADHD, melatonin was reported significantly better than placebo in reducing sleep onset latency and enhancing total time asleep in stimulant-treated and medication-free children up to 14 years of age with ADHD and chronic sleep-onset insomnia when given in doses of 3 to 6 mg 30 to 90 minutes before desired sleep onset. It should be noted that long-term data for melatonin is still needed to determine its effect on development during adolescence. Two hypnotics, zolpidem and eszopiclone, have been evaluated in the management of insomnia in children with ADHD in one large controlled trial each; neither medication was better than placebo at reducing sleep onset insomnia.

In summary: (1) good sleep hygiene is an ongoing issue that should always be addressed; (2) identify the underlying cause, including comorbid conditions and medications that may contribute to sleep difficulties; and (3) as a last resort, use a sleep promoting medication short-term because there is no long-term data for effectiveness or safety with any agents (including melatonin) used to address insomnia in children with ADHD.

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Select Sleep Aids for Insomnia in Pediatrics[1]

Generic Name (Brand Name)[2]	Dosage Forms[3]	FDA Approval	Initial Dose[4] (Maximum Daily Dose)[4]	Onset of Action	Administration	Evidence Base; limited data for ALL
Alpha-2-agonist[5]						
Clonidine (Catapres®) Rx	0.1, 0.2, 0.3 mg TAB	No	0.05 mg (0.8 mg/day)	30 – 60 minutes	HS	Retrospective chart review
Antidepressant						
Mirtazapine (Remeron®) Rx	15, 30, 45 mg SolTab 7.5, 15, 30, 45 mg TABs	No	7.5 mg (45 mg)	15 – 30 minutes	HS	Open-label trials
Trazodone (Desyrel®) Rx	50, 100, 150, 300 mg TAB	No	25 – 50 mg	1 – 3 hours	HS	Open-label trials
Antihistamine[6]						
Diphenhydramine (Benadryl®) OTC	CAPS, ChewTab. ELX, OSOLN, TAB	≥ 12 years	Age 2 to < 12: 1mg/kg/dose (50 mg) Age ≥ 12: 50 mg	Maximum Effect 1 – 3 hours after administration	30 minutes before HS	RCT
Doxylamine OTC	TAB	≥ 12 years	Age ≥ 12: 25 mg	30 minutes	30 minutes before HS	Anecdotal
Dietary Supplement						
Melatonin OTC	CAPS, TAB, Liquid, ODT	No	3 – 6 mg	30 – 120 minutes	30 – 90 minutes before HS	RCTs

CAPS = capsule; ChewTab = chewable tablet; ELX = elixir; ODT = orally disintegrating tablet; OSOLN = oral solution; OTC = over-the-counter; RCT = randomized controlled trial; Rx = prescription only; SolTab = soluble tablet; TAB = tablet

[1] Not all agents listed here have been well studied in the management of insomnia in children with ADHD; only melatonin has been studied and shown effective to treat insomnia in children with ADHD.
[2] Use caution when recommending OTC brand names because active ingredients may vary even if the brand name is identical.
[3] Some may be scored, varies with manufacturer.
[4] Dosing data for use in insomnia is limited. Always consider age and weight of child, especially when < 12 years old, starting with the lowest dose.
[5] ADHD approved extended release product, Kapvay® (clonidine), is not listed here due to lack of information.
[6] Some patients get hyperactive instead of sleepy.

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