The Use of Pharmacotherapy in the Treatment of Pediatric Insomnia in Primary Care: Rational Approaches. A Consensus Meeting Summary


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Objectives: To formulate a rational approach to the pharmacologic treatment of pediatric insomnia, and to develop clinical guidelines regarding indications, target populations, and parameters for the use of these medications, especially by community-based pediatricians.

Participants: A multidisciplinary task force developed under the auspices of the American Academy of Sleep Medicine, which included experts in pediatric sleep medicine, psychiatry, pharmacology, neurology, and general pediatrics.

Evidence: Review of existing data regarding current use of over-the-counter and prescription medications for pediatric insomnia in the primary care practice setting, and of empirical data on the pharmacology, safety, efficacy, and tolerability of medications commonly used for the treatment of pediatric insomnia.

Consensus Process: Group consensus definition of pediatric insomnia and clinical guidelines; working group recommendations regarding special populations and future directions.

Conclusions: Use of medications for pediatric insomnia should be diagnostically driven, and should be implemented in conjunction with empirically-based behavioral treatment strategies and adequate sleep hygiene. Specific target populations include children with neurodevelopmental disorders, pervasive developmental disorders, chronic medical conditions, and psychiatric disorders. Additional research, including clinical trials, is critically needed to provide an evidence-based approach to the use of these medications in clinical practice.

Key Words: Pediatric, Insomnia, Pharmacotherapy.


Recent studies suggest that medications for sleep problems are part of the increasing use of psychopharmacotherapy in children.1-3 Several survey studies of European physicians in clinical practice which included questions about the use of prescription and nonprescription medications specifically for sleep problems in children, have found that one of the primary indications for psychotropic use in children is sleep disturbances.4-9 Although little data on the use of soporific medications in the pediatric population in the United States exist, several lines of evidence suggest that this may be a common practice in the United States as well. For example, recent data from a national survey of 670 community-based pediatricians10 found that about 75% of practitioners had recommended nonprescription medications and more than 50% had prescribed a sleep medication for children with sleep problems in the previous 6 months. Although there were a number of special clinical circumstances in which medications were reported to be more commonly used, including children with special needs such as mental retardation, autism, and attention-deficit hyperactivity disorder, almost 40% of the respondents in the survey reported recommending medication for otherwise normal children with significant difficulty falling or staying asleep and “bedtime struggles/sleep-onset delay.” Antihistamines were the most commonly recommended nonprescription medication (68%) and α-receptor agonists were the most frequently prescribed sleep medications (31%); approximately 15% had prescribed an antidepressant for adolescent insomnia. In another recent study11 examining sleep medication prescriptions in a 39-month period for over 38,000 Medicaid recipients in Michigan, 20% of the children had received at least 1 dose of a sleep medication; many of these children were from special needs populations. Furthermore, there was a wide variation in prescribing practices by county and by individual practitioner.

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Unlike the solid body of evidence that exists for empirically supported nonpharmacologic or behavioral treatments for pediatric insomnia, there are relatively few empirical data to support the use of many of the more commonly used over-the-counter and prescription medications in the pediatric population, such as prescription and nonprescription antihistamines, chloral hydrate, \( \alpha \)-receptor agonists such as clonidine, melatonin, and antidepressants. As a result, sound clinical practice at all levels is compromised by the fact that there remains a significant lack of knowledge concerning the efficacy, tolerability, and safety profiles of soporific drugs in children. Indeed, a recent survey study of sleep knowledge among pediatricians suggests that at least some of these medications are prescribed by practitioners in the community not only frequently, but often inappropriately (eg, antihistamines for sleep terrors and melatonin for adolescents with poor sleep hygiene). Furthermore, the dramatic increase seen recently in clonidine overdose in pediatric patients between 1990 and 1997 may be at least a partial reflection of inappropriately prescribed sedative and hypnotic drugs.

Despite the lack of empirical supporting data, the development of a rational approach to the use of pediatric sleep medications, especially for the practicing pediatrician, is an important, timely, and appropriate task due to the widespread use of these medications in clinical practice, and the apparent need for safe and effective medications for some high-risk populations in particular. Recognizing this need, in March of 2003, the American Academy of Sleep Medicine established a multidisciplinary task force on Pharmacotherapy in Pediatric Sleep Medicine with the following charge: to develop a set of clinical experience-based general guidelines for primary care physicians regarding the use of medication as an adjunct in the treatment of pediatric insomnia and to develop a set of indications, target populations, and parameters for the use of these medications, based on the information that is currently available.

In addition, it was felt that the establishment of the task force would provide an opportunity to educate pediatricians about the diagnosis and management of sleep disorders in children. Finally, in order to help generate the data that are needed to eventually develop standards of practice for the use of these pharmacologic agents, an additional charge to the task force was to develop recommendations for and to advocate further research in this area.

The task force consisted of a panel of 13 experts in the fields of pediatric sleep medicine, psychiatry, neurology, developmental/behavioral pediatrics, pharmacology, and community-based pediatrics, as well as representatives from the American Academy of Pediatrics and the Food and Drug Administration. The task force met over a 2-day period to review the empirical data regarding the use of medications for pediatric insomnia, as well as the literature on current clinical practices. Three working groups (General Clinical Guidelines, Special Populations, and Research Recommendations) then convened to develop the summary recommendations presented below.

**SUMMARY OF RECOMMENDATIONS**

In order for the pediatric practitioner to develop a rational and diagnostically driven approach regarding the use of pharmacotherapy in the treatment of pediatric sleep problems, the task force agreed that it was important to first outline the clinical context in which these problems are likely to appear, including the definition of insomnia and the scope of the problem in clinical practice, and to emphasize both the importance of screening for sleep problems and of conducting a thorough diagnostic evaluation prior to treatment.

### Consensus Definition of Pediatric Insomnia

*Insomnia* is a symptom and not a diagnosis. The causes of insomnia are varied and range from the medical (ie, drug-related, pain-induced, associated with primary sleep disorders such as obstructive sleep apnea) to the behavioral (ie, associated with poor sleep hygiene or sleep-onset association disorder) and are often a combination of these factors. In adults, insomnia is generally defined as difficulty initiating and/or maintaining sleep and/or early morning awakening and/or nonrestorative sleep. However, the definition of insomnia or problematic sleep in children is much more challenging for a number of reasons. Clinically significant sleep problems, like many behavioral problems in childhood, may best be viewed as more loosely occurring along a severity and chronicity continuum that ranges from a transient and self-limited disturbance to a disorder that meets specific diagnostic criteria. Unlike strict research definitions of sleep problems, the validity of parental concerns and opinions regarding their child’s sleep patterns and behaviors and the resulting stress on the family must be considered in defining sleep disturbances in the clinical context. The relative prevalence and the various types of sleep problems that occur throughout childhood must also be understood in the context of normal physical, cognitive, and emotional phenomena that are occurring at different developmental stages. Parental recognition and reporting of sleep problems in children also varies across cultures and across age groups, with parents of infants and toddlers more likely to be aware of sleep concerns than those of school-aged children and adolescents. Thus, the range of sleep behaviors that may be considered “normal” or “pathologic” is wide, and the definitions are often highly subjective.

In order to more clearly define the clinical situations in which the use of pharmacotherapy for pediatric sleep problems might be appropriate, the task force members agreed that the development of a consensus definition of pediatric insomnia was a necessary and important first step. It should be noted that, in most instances, the standard adult definition of insomnia may be applied to adolescents and that pediatric insomnia refers largely to children under the age of 12 years. The key components of the consensus definition developed by the panel were as follows:

**Pediatric insomnia** may be defined as difficulty initiating or maintaining sleep that is viewed as a problem by the child or caregiver.

The significance of the sleep problem may be characterized by its severity, chronicity, and frequency and associated impairment in daytime function in the child or family.

The sleep problem may be due to a primary sleep disorder or occur in association with other sleep, medical, or psychiatric disorders.

### Scope and Impact of Pediatric Insomnia

The task force members emphasized the importance of underscoring the prevalence and impact of sleep problems in pediatric clinical practice in order to provide a rationale for developing pharmacologic treatment strategies. Although prevalence rates are at
best approximations because the definition of difficulty initiating or maintaining sleep in children varies across studies, approximately 25% of all children are reported to experience some type of sleep problem at some point during childhood. Specific studies have reported an overall prevalence of a variety of parent-reported sleep problems ranging from 25% to 50% in preschool-aged samples, to 37% in a community sample of 4- to 10-year-olds, upward of 40% in adolescents. Furthermore, sleep concerns are one of the most frequent parental complaints in pediatric practices, reported as the fifth leading concern of parents, following illness, feeding, behavior problems, and physical abnormalities.

Although in many children these sleep disturbances are transient, there is considerable evidence that sleep problems may persist or recur in a substantial percentage. In addition to their high prevalence and chronicity, recent evidence also suggests that sleep disorders may have significant short- and long-term consequences on children's academic and social functioning and on their health. A wealth of empirical evidence from several lines of research clearly indicates that children and adolescents experience significant daytime sleepiness as a result of inadequate or disturbed sleep and that significant performance impairments and mood dysfunction are associated with that daytime sleepiness. Higher-level cognitive functions, such as cognitive flexibility and the ability to reason and think abstractly, appear to be particularly sensitive to the effects of disturbed or insufficient sleep. Finally, health outcomes of inadequate sleep include an increase in accidental injuries (ranging from minor injuries to drowsy driving-related motor vehicle fatalities) and potential deleterious effects on the cardiovascular, immune, and various metabolic systems, including glucose metabolism and endocrine function. Sleep problems are also a significant source of distress for families and may be one of the primary reasons for caregiver stress in families with children who have chronic medical illnesses or severe neurodevelopmental delays.

Screening for Sleep Problems

A number of studies have suggested that screening for sleep problems in pediatric practice is inadequate and may result in significant underdiagnosis of sleep disorders. For example, in the recent survey of more than 600 community-based pediatricians cited above, more than 20% of the respondents did not routinely screen for sleep problems in school-aged children in the context of the well-child visit, and fewer than 40% questioned adolescents directly about their own sleep habits. Recognizing this gap, the task force recommended that all children be regularly screened for sleep problems in pediatric clinical practice. One simple sleep-screening algorithm is the BEARS. The key areas of inquiry that are included in the BEARS screening for sleep problems in children and adolescents are (1) bedtime resistance and delayed sleep onset; (2) excessive daytime sleepiness; (3) awakenings during the night; (4) regularity, pattern, and duration of sleep; and (5) snoring and other symptoms of sleep-disordered breathing. A number of other brief parent and self-report sleep survey tools have also been developed that can facilitate the screening process and yield important information about the nature and severity of any coexisting sleep complaints.

Evaluation of Sleep Complaints

The clinical evaluation of a child presenting with a sleep problem involves a careful medical history to assess for potential medical causes of sleep disturbances, such as allergies, concomitant medications, and acute or chronic pain conditions. A developmental history is important because of the aforementioned frequent association of sleep problems with developmental delays. Assessment of the child’s current level of functioning (school, home, etc) is key in evaluating possible mood, behavioral, and neurocognitive sequelae of sleep problems. Current sleep patterns, including usual sleep duration and sleep-wake schedule, are often best assessed with a sleep diary, in which parents record daily sleep behaviors for an extended period. A review of sleep habits, such as bedtime routines, daily caffeine intake, and the sleeping environment (temperature, noise level, etc) may reveal environmental factors that contribute to the sleep problems. Use of additional diagnostic tools such as polysomnographic evaluation are seldom warranted for routine evaluation of pediatric insomnia but may be appropriate if organic sleep disorders such as obstructive sleep apnea or periodic limb movements are suspected.

Finally, referral to a sleep specialist for diagnosis, treatment, or both diagnosis and treatment should be considered under the following circumstances: children or adolescents with persistent or severe bedtime issues that are not responsive to simple behavioral measures or that are extremely disruptive; children or adolescents with parasomnias who also present with symptoms of another underlying sleep disorder (e.g., sleep-disordered breathing) or for whom pharmacologic treatment is being considered; children with associated medical, psychiatric, or developmental conditions that create additional management challenges; and children and adolescents with circadian rhythm disorders.

MEDICATION GUIDELINES

Any discussion of the use of pharmacologic interventions in the treatment of pediatric insomnia must be prefaced by a statement regarding the importance of good sleep hygiene as a necessary component of every treatment package. Sleep hygiene refers to the basic environmental (e.g., temperature, noise level, ambient light), scheduling (e.g., regular sleep-wake schedule), sleep practice (e.g., bedtime routine), and physiologic (e.g., exercise, timing of meals, caffeine use) factors that promote optimal sleep. Furthermore, it should be emphasized that behavioral (i.e., nonpharmacologic) treatment approaches to bedtime struggles and night waking in children have a well-documented empirical basis and are the mainstay of treatment and that pharmacologic approaches should be largely considered adjuncts in the treatment of pediatric insomnia. Principles of sleep hygiene are listed in Table 1, and a list and brief description of the most common behavioral treatments for pediatric insomnia are included in Table 2.

CHARACTERISTICS OF THE “IDEAL” HYPNOTIC

Currently, there are no medications approved by the Food and Drug Administration for the treatment of difficulty initiating or maintaining sleep in the pediatric population. Although it is clear that the ideal pediatric hypnotic medication does not exist, the task force members agreed that it was important to consider characteristics that would be present in the optimal clinical situation, in order to allow the practitioner to compare the pharmacologic options that are currently available. Pharmacokinetic properties of the ideal pediatric hypnotic would include the high oral
bioavailability, a property that encompasses solubility, rapid absorption, stability, and invulnerability to extensive first-pass metabolism by the liver or gut, in order to ensure rapid, consistent, reliable clinical response and allow appropriate dosages to be predicted accurately.\textsuperscript{46} Metabolism should be to inactive products or to active metabolites with short half-lives, with half-lives no longer than that of the parent compound in order to minimize metabolite-associated side effects. Elimination half-life should be short (2 to 3 hours). Pharmacodynamic properties would include a rapid onset of effect, preferably within 30 minutes, so that it could be administered shortly before bedtime, and a duration of action that would be sufficiently long so that only once-nightly dosing is necessary but not excessively long so that it produces residual daytime sedation. There should also be no associated rebound, tolerance, or withdrawal and few side effects—preferably, the tolerability profile of placebo—with little or no potential for drug-drug interactions. The ideal hypnotic should also not affect sleep architecture, as changes in slow-wave sleep, for example, might lead to alterations in levels of hormones such as human growth hormone. Finally, the medication should be available in a palatable oral liquid as well as tablet or capsule formulation. Pharmacologic and clinical properties of medications currently most commonly used in the treatment of pediatric insomnia are listed in Tables 3 and 4.

It should also be noted that there are many herbal preparations that are also used for the treatment of pediatric insomnia, both by parents and practitioners. These include valerian, chamomile, kava, lavender, and, less commonly, hops, lemon balm, and passion flower.\textsuperscript{51,52} In particular, valerian root and chamomile have been shown in several studies to have sleep-promoting effects without residual daytime drowsiness or performance impairment. The long-term safety and efficacy of most herbal preparations are unknown. Table 5 lists properties of selected commonly used herbal preparations.

### General Recommendations for Use of Medications in Pediatric Insomnia

- Since the ideal pediatric hypnotic does not currently exist, rational treatment selection should be based on the clinician’s judgment of the best possible match between the clinical circumstances (type of sleep problem, patient characteristics, etc) and the individual properties of currently available drugs (onset and duration of action, safety, tolerability, etc). This principle presumes some degree of familiarity on the part of the clinician with the pharmacologic profile of the sedative/hypnotics currently available for use in the pediatric population.

- Treatment must be diagnostically driven and based on a careful clinical evaluation of the symptoms and consideration of all possible differential diagnoses. It is incumbent upon the clinician to choose the most appropriate pharmacologic or behavioral therapies, or a combination thereof, based on the actual diagnosis rather than the symptom complex. For example, sleep-initiation insomnia may be due to a primarily behavioral sleep disorder (eg, limit-setting sleep disorder), a physiologically based sleep disorder (eg, restless legs syndrome, delayed sleep phase syndrome), or a combination (eg, psychophysiologic insomnia), each necess-

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**Table 1**—Principles of Good Sleep Hygiene

**Sleep schedule**

Bedtime and wake-up time should be about the same time everyday. There should not be more than an hour difference in bedtime and wake-up time between school nights and nonschool nights. Sleeping in on weekends to “catch-up” on sleep should be avoided.

**Bedtime routine**

Establish a consistent 20- to 30-minute bedtime routine. The routine should include calm activities, such as reading a book or talking about the day, with the last part occurring in the bedroom.

**Bedroom**

The bedroom should be comfortable, quiet, and dark, except for a dim nightlight. Room temperature should be cool (less than 75 degrees). Using the bed for activities (studying, talking on the phone) other than sleeping should be avoided.

**Meals**

Heavy meals within an hour or 2 of bedtime may interfere with sleep. However, a light snack (such as milk and cookies) before bed is acceptable to avoid going to bed hungry.

**Caffeine**

Caffeine should be avoided for at least 3 to 4 hours before bed. Caffeine can be found in many types of soda, coffee, iced tea, and chocolate.

**Alcohol**

Alcohol may shorten sleep onset but disrupts sleep later in the night and, thus, should be avoided.

**Smoking**

Nicotine is a stimulant and may disturb sleep.

**Evening activities**

The hour before bed should be a quiet and calm time. High-energy activities and heavy exercise and stimulating activities, such as playing computer games, should be avoided during that time.

**Electronic media**

Television sets, computers, etc. should be kept out of the bedroom to avoid establishing television viewing and playing video or computer games as a learned sleep-onset association. These activities are also often highly stimulating.

**Naps**

In young children, naps should be geared to the child’s age and developmental needs. In older children and adolescents, naps should generally be avoided, as prolonged daytime sleep can contribute to difficulty initiating and maintaining nocturnal sleep.

**Exercise**

Time should be spent outside every day, with a period of daily exercise.

**Sunlight**

Spending time outside every day, especially in the morning, and exposure to sunlight helps maintain normal sleep-wake circadian rhythms.
sitting a different treatment approach.

- Sleep problems in infants and very young children are almost always related to “developmental asynchrony” between the child’s sleep development and parental expectations (eg, development of nocturnal-diurnal sleep-wake rhythms, “sleeping through the night”). Therefore, medication is rarely, if ever, indicated in this age group.
- In almost all cases, medication is not the first treatment choice nor the sole treatment strategy. Medication use, except for very self-limited circumstances such as travel, should be viewed only within the context of a more comprehensive treatment plan.
- Medication should always be used in combination with nonpharmacologic strategies (behavioral interventions, parent education, etc). This is analogous to a number of other conditions in children, such as attention-deficit/hyperactivity disorder, in which a combination of pharmacologic and behavioral strategies are often superior to drug treatment alone.
- Prior to consideration of pharmacologic treatment, sleep hygiene should be always be optimized. All sleep disorders in children may be exacerbated by poor sleep habits, such as excessive caffeine use and irregular sleep-wake schedules, which must be addressed before medication is recommended.
- Treatment goals should be realistic, clearly defined, and discussed and agreed upon with the family before treatment is initiated. In addition, there must be clear plan for follow-up and reassessment of therapeutic goals. In particular, the parental expectations regarding the degree of amelioration of the sleep problem by medication and the anticipated duration of drug treatment should be clearly established.
- Medication use should be short term; no prescription refills should be given without reassessment of the target symptoms and assessment of patient compliance with both pharmacologic and behavioral management.
- Adolescents should be screened for alcohol and drug use and pregnancy prior to initiation of therapy. Many recreational substances may have synergistic clinical effects when combined with sedatives/hypnotics. In addition, hypnotics with high toxicity levels in overdose should be used with extreme caution in situations in which there is any risk of nonaccidental overdose.
- Patients should also be screened for concurrent use of self-initiated nonprescription sleep medications (Excedrin PM, melatonin, herbal remedies). Some of these medications have similar ingredients (eg, diphenhydramine is the soporific ingredient in both Benadryl and Tylenol PM); while generally viewed by parents as “safe,” the potential drug-drug interactions between most herbal preparations and sedative/hypnotics are largely unknown.
- Medication selection, particularly in terms of duration of action, should be appropriate for the presenting complaint—ie, for problems with sleep onset, a shorter-acting medication is generally desirable. For problems with sleep maintenance, longer-acting medications may be considered but are more likely to result in “hang-over” effects the following morning.
- All medications should be used with caution and monitored closely for efficacy and side effects. Since there are so few data on safety and efficacy of these medications in children, a conservative approach, similar to that which should be exercised with any pediatric off-label drug use, is warranted.

### Table 2—Summary of Empirically Based Nonpharmacologic Treatments for Pediatric Insomnia

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Target problems</th>
<th>Description</th>
<th>Selected references</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extinction</td>
<td>Bedtime disturbances/night wakings</td>
<td>Putting the child in bed and systematically ignoring inappropriate child behaviors (eg, crying) until morning.</td>
<td>Rickert VI31</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Seymour FW32</td>
</tr>
<tr>
<td>Graduated extinction</td>
<td>Bedtime disturbances/night wakings</td>
<td>Combining extinction with scheduled parental checks</td>
<td>Reid MJ33</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hiscock H14</td>
</tr>
<tr>
<td>Early intervention/parent education</td>
<td>Bedtime disturbances/night wakings</td>
<td>Education of parents in the establishment of appropriate sleep habits (eg, sleep routines, put to bed awake) to prevent the development of sleep problems.</td>
<td>Wolfson A35</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adair R36</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Kerr SM37</td>
</tr>
<tr>
<td>Scheduled awakenings</td>
<td>Bedtime disturbances/night wakings</td>
<td>Parent awakening child 15-30 minutes before usual spontaneous awakening or parasomnia.</td>
<td>Rickert VI18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Durand VM39</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Frank NC40</td>
</tr>
<tr>
<td>Extinction with parental presence</td>
<td>Bedtime disturbances/night wakings</td>
<td>Parent feigns sleep while staying in child’s room and ignoring inappropriate child behaviors (extinction).</td>
<td>Sadeh A41</td>
</tr>
<tr>
<td>Positive bedtime routines</td>
<td>Bedtime disturbances</td>
<td>Parent developing a set bedtime routine that the child enjoys and associating these routines with positive behaviors (eg, falling asleep quickly).</td>
<td>Adams LA42</td>
</tr>
<tr>
<td>Phase advance or delay chronotherapy</td>
<td>Delayed sleep phase syndrome</td>
<td>Systematically advancing or delaying child’s sleep phase to desired sleep-wake schedule.</td>
<td>Okawa M45</td>
</tr>
</tbody>
</table>

For an extended review see Mindell JA44 and Kuhn BR.45

*Journal of Clinical Sleep Medicine, Vol. 1, No. 1, 2005*
Table 3—Pharmacology of Selected Medications Used for Pediatric Insomnia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-life (T½)</th>
<th>Onset of action/peak level, min</th>
<th>Class</th>
<th>Mechanism of Action</th>
<th>Metabolism</th>
<th>Drug-Drug Interactions</th>
<th>Effects on Sleep Architecture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>19-60 h</td>
<td>20-60</td>
<td>Rapid absorption; slowed by food</td>
<td>Benzodiazepine (BZD)</td>
<td>Hepatic</td>
<td>ETOH/ barbiturates</td>
<td>Suppresses SWS; reduces frequency of nocturnal arousals</td>
</tr>
<tr>
<td>Flurazepam (Dalmane)</td>
<td>48-120 h</td>
<td>20-45</td>
<td>Rapid absorption; bioavailability 100%; onset action within 1 hr; peak effects 2-4 h</td>
<td>Alpha-receptor agonists</td>
<td>Hepatic</td>
<td>no active metabolites</td>
<td>Increases CNS depression; may alter effects of anticoagulants</td>
</tr>
<tr>
<td>Quazepam (Doral)</td>
<td>48-120 h</td>
<td>20-45</td>
<td>Rapid absorption; bioavailability 100%; onset action within 1 hr; peak effects 2-4 h</td>
<td>alpha-adrenergic receptor agonists; (guanfacine more selective) decrease NE release</td>
<td>Hepatic</td>
<td>no active metabolites</td>
<td>Decreases SOL</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>3-25 h</td>
<td>45-60</td>
<td>Biphasic; first T ½ 3-6 hours (sustained; 3 min and 45 min; 90% excreted in 4 h)</td>
<td>Hormone analogue</td>
<td>Hepatic</td>
<td>Largely unknown; NSAID, ETOH, caffeine, BZD may interfere with normal melatonin production</td>
<td>Decreases SOL; main effect on circadian rhythms</td>
</tr>
<tr>
<td>Triazolam (Halcion)</td>
<td>8-24 h</td>
<td>15-30</td>
<td>Rapid absorption; bioavailability 100%; onset action within 1 hr; peak effects 2-4 h</td>
<td>Antihistamines</td>
<td>Hepatic</td>
<td>ETOH/CNS depressants</td>
<td>Decreases SOL; may impair sleep quality</td>
</tr>
</tbody>
</table>

SWS refers to slow-wave sleep (stage 3-4); SOL, sleep-onset latency; BZD, benzodiazepine; GABA, gamma-aminobutyric acid; CNS, central nervous system; NSAID, nonsteroidal anti-inflammatory drug; NE, norepinephrine; ETOH, alcohol; REM, rapid eye movement sleep.
Potential Indications for Hypnotic Use in Otherwise Normal Children (Generally Short-Term Use)

- The safety or welfare of the child is threatened—eg, parent is overwhelmed or unable to implement nonpharmacologic interventions. Because of their rapid onset of action, medications may assist in “breaking the cycle” and allow for the implementation of effective behavioral strategies.
- There is a failure of or inability to comply with an adequate trial of accepted nonpharmacologic/behavioral treatment, eg, the older child or adolescent with psychophysiological insomnia who fails to respond to standard behavioral management such as stimulus control and sleep restriction.
- Medication is used as an adjunct to sleep hygiene/chronotherapy in circadian rhythm disturbances; eg, in an otherwise normal adolescent with delayed sleep phase syndrome.
- The insomnia occurs in the setting of medical illness with

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosing range (mg/d)</th>
<th>Formulation</th>
<th>Side effects</th>
<th>Development tolerance/ withdrawal effects</th>
<th>Safety profile/ (overdose)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonazepam</td>
<td>0.5-2.0</td>
<td>Tablets</td>
<td>Residual daytime sedation, rebound insomnia on discontinuation, psychomotor/ cognitive impairment, anterograde amnesia (dose dependent); impairment respiratory function</td>
<td>No, especially with shorter acting BZD; withdrawal effects include seizures</td>
<td>Marked abuse potential</td>
<td>Also used to control partial arousal parasomnias (night terrors, sleep walking); use short half-life BZD for sleep onset; longer half-life for sleep maintenance</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>15-30</td>
<td>Tablets</td>
<td>Insomnia on withdrawal effects</td>
<td>No</td>
<td>Poor tolerability safety profile; overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Reports of possible liver toxicity; respiratory depression limits use</td>
</tr>
<tr>
<td>Quazepam</td>
<td>7.5-30</td>
<td>Tablets</td>
<td>Insomnia on withdrawal effects</td>
<td>No</td>
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<td>Insomnia on withdrawal effects</td>
<td>No</td>
<td>Poor tolerability safety profile; overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Reports of possible liver toxicity; respiratory depression limits use</td>
</tr>
<tr>
<td>Estazolam</td>
<td>1-2</td>
<td>Tablets</td>
<td>Bradycardia, hypotension</td>
<td>Yes</td>
<td>Poor tolerability safety profile; overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Reports of possible liver toxicity; respiratory depression limits use</td>
</tr>
<tr>
<td>Triazolam</td>
<td>0.125-0.25</td>
<td>Tablets</td>
<td>Bradycardia, hypotension</td>
<td>Yes</td>
<td>Poor tolerability safety profile; overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Reports of possible liver toxicity; respiratory depression limits use</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>50-75 mg/kg; max 1-2 g/dose</td>
<td>Capsules, syrup, rectal suppository</td>
<td>Respiratory depression gastrointestinal (nausea, vomiting, especially if taken without food), drowsiness/ dizziness</td>
<td>Yes, withdrawal after prolonged use may cause delirium, seizures</td>
<td>Poor tolerability safety profile; overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Reports of possible liver toxicity; respiratory depression limits use</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.025-0.3 (up to 0.8); increase by 0.05 increments</td>
<td>Tablet, transdermal patch</td>
<td>Dry mouth, bradycardia, hypotension, rebound hypertension on discontinuation</td>
<td>No</td>
<td>Narrow therapeutic index; Overdose: bradycardia, decreased consciousness hypotension</td>
<td>Also used in daytime treatment of ADHD</td>
</tr>
<tr>
<td>Guanfacine</td>
<td>0.5-2</td>
<td>Tablets</td>
<td>Bradycardia, hypotension</td>
<td>Yes</td>
<td>Narrow therapeutic index; Overdose: bradycardia, decreased consciousness hypotension</td>
<td>Also used in daytime treatment of ADHD</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>5-10</td>
<td>Tablets</td>
<td>Headache, retrograde amnesia; few residual next-day effects insomnia on discontinuation</td>
<td>No</td>
<td>Narrow therapeutic index; Overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Little clinical experience in children</td>
</tr>
<tr>
<td>Zaleplon</td>
<td>5-10</td>
<td>Tablets</td>
<td>Dizziness, CNS overstimulation, cardiac arrhythmias, hypotension, priapism</td>
<td>Yes</td>
<td>Narrow therapeutic index; Overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Little clinical experience in children</td>
</tr>
<tr>
<td>Trazadone</td>
<td>20-50</td>
<td>Tablets</td>
<td>Dizziness, CNS overstimulation, cardiac arrhythmias, hypotension, priapism</td>
<td>Yes</td>
<td>Narrow therapeutic index; Overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Little clinical experience in children</td>
</tr>
<tr>
<td>Melatonin</td>
<td>2.5-5 (0.3-25)</td>
<td>Tablets; various strengths</td>
<td>Largely unknown; reported hypotension, bradycardia, nausea, headache Possible exacerbation of co-morbid autoimmune diseases</td>
<td>No</td>
<td>Narrow therapeutic index; Overdose: CNS depression, cardiac arrhythmia, hypothermia, hypotension</td>
<td>Little clinical experience in children</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>25-50 (should not exceed daily dose 300mg)</td>
<td>Tablet, capsule, syrup, injectable</td>
<td>Daytime drowsiness, gastrointestinal (appetite loss, nausea/ vomiting, constipation, dry mouth), paradoxical excitation</td>
<td>Yes</td>
<td>Overdose: hallucinations, seizures, excessive stimulation</td>
<td>Weak soporifics; high level of parental/practitioner acceptance</td>
</tr>
<tr>
<td>Brompheniramine</td>
<td>4</td>
<td>Tablets</td>
<td>Bradycardia, hypotension</td>
<td>Yes</td>
<td>Overdose: hallucinations, seizures, excessive stimulation</td>
<td>Weak soporifics; high level of parental/practitioner acceptance</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>4</td>
<td>Tablets</td>
<td>Bradycardia, hypotension</td>
<td>Yes</td>
<td>Overdose: hallucinations, seizures, excessive stimulation</td>
<td>Weak soporifics; high level of parental/practitioner acceptance</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>25-100; 0.6mg/kg (children)</td>
<td>Tablets</td>
<td>Bradycardia, hypotension</td>
<td>Yes</td>
<td>Overdose: hallucinations, seizures, excessive stimulation</td>
<td>Weak soporifics; high level of parental/practitioner acceptance</td>
</tr>
</tbody>
</table>

BZD refers to benzodiazepine; CNS, central nervous system; ADHD, attention-deficit/hyperactivity disorder.
associated issues, including pain control, concomitant medications, hospitalization, eg, the child on steroids for chronic asthma.

- The insomnia occurs in the context of an acute stressor, eg, a death in the family.
- The insomnia occurs or is anticipated in the context of travel, eg, a prolonged plane ride with accompanying time change.

Contraindications to Hypnotic Use in Otherwise Normal Children

- The insomnia occurs in the presence of untreated sleep-disordered breathing, eg, obstructive sleep apnea. Not only is hypnotic medication often inappropriate for treating the underlying condition, but sedatives with respiratory-depressant properties (eg, chloral hydrate) may be dangerous in the situation of a comorbid sleep-related breathing disorder.
- The insomnia is due to a developmentally based normal sleep behavior; for example, there are inappropriate expectations regarding the child’s sleep behaviors from the parent or practitioners.
- The insomnia is due to a self-limited condition that temporarily results in night wakings, eg, teething.
- There are potential drug interactions with concurrent medications (eg, opiates) or unrecognized substance abuse or alcohol use.
- There is limited ability to follow up with and monitor the patient, eg, parent frequently misses scheduled appointments.

Pharmacologic Treatment of Pediatric Insomnia in Children with Special Needs

Sleep disturbances are a prominent part of the morbidity of neurobehavioral, psychiatric, and chronic medical conditions. Whether as a primary condition or secondary to the chronic condition, pediatric insomnia may contribute to exacerbation of these conditions and have an adverse impact on the quality of life for the child and family. Children with chronic medical and development conditions are particularly prone to insomnia because of unique combinations of family stresses, caregiver interactions, social (peer) relationships, medical needs, sedating or activating medications, physical challenges, or psychiatric co-morbidity. For example, factors common to many medical conditions that can also create or exacerbate insomnia include pain, pruritus, cough, abnormal movements, and other disturbances. The physician must consider each of these potential factors, realizing that several may coexist and frustrate therapeutic interventions.

Because the neural and cognitive requisites to develop and express most sleep symptoms are basic, children with chronic medical and developmental conditions are susceptible to the same emotional, behavioral, medical, and circadian sleep disorders as normal children. Therefore, these common causes of insomnia should be considered first in children with chronic health conditions and developmental disabilities and treated appropriately. As is the case with normal children, it is preferable to identify and control the underlying process that creates a sleep disturbance instead of simply prescribing symptomatic therapy for insomnia. However, sleeplessness may overshadow other indicators of primary medical and psychiatric disorders and, thus, appear to arise de novo in an otherwise healthy child. For example, insomnia is often a presenting symptom of many psychiatric disorders such as depression, posttraumatic stress disorder, and generalized anxiety disorder. If not carefully sought, other symptoms of psychiatric and medical conditions may be missed, and an opportunity to eliminate the basis of the insomnia would be lost.

Children with neurologic injury and specific genetic, psychiatric and behavioral syndromes and conditions are particularly susceptible to specific types of insomnia. Examples include autism and pervasive developmental disorder, blindness (circadian rhythm disorders), Smith-Magenis syndrome (severe insomnia), Williams syndrome (periodic limb movement disorder), Rett syndrome (prolonged sleep-onset latency, sleep fragmentation), and Tourette syndrome (increased nocturnal movements and awakenings). Children with attention-deficit/hyperactivity disorder are often reported by parents to have sleep-onset difficulties and restless sleep and present one of the more common chronic conditions for which sedatives are recommended by pediatric practitioners. Children with asthma and atopy, renal failure, and epilepsy are also highly prone to sleep disruption related to the underlying chronic condition, medication, or both. Thus, the physician may be guided by literature relevant to the specific diagnosis.

The approach to insomnia in children with underlying medical conditions and developmental disabilities and treated appropriately. Because the neural and cognitive requisites to develop and express most sleep symptoms are basic, children with chronic medical and developmental conditions are susceptible to the same emotional, behavioral, medical, and circadian sleep disorders as normal children. Therefore, these common causes of insomnia should be considered first in children with chronic health conditions and developmental disabilities and treated appropriately. As is the case with normal children, it is preferable to identify and control the underlying process that creates a sleep disturbance instead of simply prescribing symptomatic therapy for insomnia. However, sleeplessness may overshadow other indicators of primary medical and psychiatric disorders and, thus, appear to arise de novo in an otherwise healthy child. For example, insomnia is often a presenting symptom of many psychiatric disorders such as depression, posttraumatic stress disorder, and generalized anxiety disorder. If not carefully sought, other symptoms of psychiatric and medical conditions may be missed, and an opportunity to eliminate the basis of the insomnia would be lost.

Table 5—Pharmacology and Clinical Properties of Selected Herbal Preparations Used for Pediatric Insomnia

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Scientific Name</th>
<th>Mechanism of Action</th>
<th>Sleep Architecture Effects</th>
<th>Usual Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valerian</td>
<td>Valeriana officinalis</td>
<td>Binds BZD receptors</td>
<td>Decreases SOL, improves sleep continuity; increases SWS</td>
<td>2-3 g in tea every day to t.i.d; extract equivalent to 2-3 g</td>
<td>Reported toxicity rare; effects may take several weeks</td>
</tr>
<tr>
<td>German chamomile</td>
<td>Matricaria recutita</td>
<td>Binds BZD receptors</td>
<td>Decreases SOL</td>
<td>1-3 g in tea t.i.d</td>
<td>Weak hypertensive effect; may cause contact allergies</td>
</tr>
<tr>
<td>Kava</td>
<td>Piper methysticum</td>
<td>CNS depressant</td>
<td>Improves sleep quality</td>
<td>60-120 mg every day</td>
<td>May have anxiolytic effects; does not appear to potentiate alcohol, BZD effects</td>
</tr>
<tr>
<td>Lavender</td>
<td>Lavandula angustifolia</td>
<td>CNS depressant</td>
<td>Improves sleep quality, Essential oil; decreases restless sleep inhalation</td>
<td></td>
<td>May potentiate effects alcohol</td>
</tr>
</tbody>
</table>

SWS refers to slow-wave sleep (stage 3-4); SOL, sleep-onset latency; BZD, benzodiazepine; CNS, central nervous system.
or developmental conditions must take into account expected efficacy in light of a patient's behavioral strengths and challenges, capabilities and needs of families and caregivers, healthcare priorities or urgencies that may temporarily supersede long-term interests, and impact of insomnia therapy on underlying medical conditions and concurrent medications. For example, a teenager with mild mental retardation might not be able to take a hypnotic in a reliable manner, a family in crisis may need the rapid effect of a hypnotic until behavioral interventions take effect, and melatonin has the potential to lower the seizure threshold in a child with an underlying seizure disorder. In addition, because of frequent concurrent use of other medications and the idiosyncratic response that these children may have to sedative/hypnotics, extreme caution should be exercised in regard to medication choice and monitoring of side effects.

The task force therefore recommends that specific history about quality of sleep be an integral part of the evaluation and maintenance care of children with chronic medical and mental health conditions. Pharmacologic therapy should be considered for sleep problems as part of the overall management strategy, in conjunction with behavioral therapy and sleep hygiene. Sleep problems in these children should be managed aggressively to avoid exacerbation of the underlying condition and improve overall quality of life; longer duration of drug therapy is often necessary in these children. Consultation with a pediatric neurologist, developmental behavioral pediatrician, or sleep specialist is often warranted.

**RESEARCH NEEDS**

The lack of well-designed controlled studies concerning the efficacy, tolerability, dosing, and safety profile of soporific drugs in children impedes the rational clinical management of childhood insomnia. The recommendations that are presented here are of necessity based on clinical experience and at this time cannot be evidence based. Further research based on well-designed controlled studies is necessary to develop standards of practice for this important pediatric problem. Concerning pediatric insomnia, health professionals responsible for the care of children should set as goals the comprehensive understanding of this problem; the establishment of an evidence-based understanding of appropriate treatment choices for this problem, especially pharmacologic treatment for childhood sleep problems; and the education of themselves and society in general. The task force recommends that research studies be designed to address the following specific questions.

**What is the Spectrum of Childhood Insomnia?**

Development of a consistent nosology takes into consideration the possibility of different patterns of insomnia, as these may vary depending on developmental status and age of the child. Other factors may influence the character of these patterns and warrant investigation. These include parental expectations concerning childhood sleep, as well as the impact of cultural background, socioeconomic status, and environment on insomnia. This knowledge will be important to identify at-risk children. Of particular interest are studies of special needs groups, including children with chronic pain syndromes, attention-deficit/hyperactivity disorder, psychiatric problems such as depression or anxiety, bipolar disorder, and pervasive developmental-autism spectrum disorders. These children appear to be at high risk for developing or having sleep problems and may benefit from the use of medications in addition to traditional behavioral approaches.

**How Do We Assess Pediatric Insomnia?**

The diagnosis of childhood insomnia is a clinical diagnosis. Overnight sleep studies are useful to rule out other causes of nighttime sleep problems such as sleep apnea but not for the diagnosis of insomnia. Questionnaires and tools such as sleep diaries play an important role in this diagnosis. Instruments specifically addressing childhood insomnia are lacking. Validated instruments should be developed that can screen large populations of children of all ages and developmental status, reliably identify at-risk children, and assess severity. These instruments should include those with sufficient rigor for the researcher, as well as those that can be reasonably used to screen children seen by pediatricians and family practice physicians. There is a need to develop outcome measures specific to childhood insomnia. These will depend on a clear understanding of the natural history and long-term outcome of this problem, as well as the impact on the daytime cognitive and behavioral function of the child and on the quality of life of the child and of the family.

**What Drugs Are Efficacious and Safe to Treat Childhood Insomnia?**

The current use of pharmacologic agents to treat children with sleep problems lacks a sound basis to guide the rational choice of a specific medication, dose of that medication, or duration of therapy. To address these concerns, research efforts should be directed to evaluate currently used medications. These include prescription medications such as clonidine, trazodone, and chloral hydrate; nonprescription medications such as diphenhydramine, melatonin, and valerian; and medications with currently established indications in adults such as zolpidem and zaleplon. Clinical trials of these drugs should establish the effective dose, address safety issues, and determine efficacy for inducing sleep. Additionally, withdrawal and discontinuation effects need to be examined. Outcome measures should also include the impact of the specific drug on daytime cognitive and behavioral functioning. The development of new drugs that meet the "ideal" hypnotic profile should be supported. There is a need to evaluate the impact on sleep and sleep-related outcome measures of nonhypnotic drugs, such as stimulants and antidepressants.

**What Education Programs Need to Be Developed and Who Will Benefit from These Programs?**

A simple answer is any health professional involved in the care of children. Our current knowledge base suggests that pediatric insomnia is a common and pervasive problem among children of all ages and significantly impacts on the child's sleep and daytime cognitive and behavioral functioning, and the quality of life of the child and the family. The impact of the knowledge gained from the suggested research will be only as good as our ability to disseminate that information to health professionals. Currently, for those involved in the day-to-day care of children, few hours are spent in training programs and during continuing medical
education efforts concerning childhood sleep problems in general and pediatric insomnia in specific. The significance of this problem merits the development of education programs addressing pediatric sleep issues for health professionals in training as well as primary care practitioners.

SUMMARY

The use of pharmacotherapy in the treatment of pediatric sleep disorders presents both opportunities and challenges for the practicing community-based physician, for sleep specialists, for providers of special needs populations, and for the pharmacologic research community. These task force recommendations are the first steps in an ongoing effort to maximize care for children with serious sleep complaints and their families. This effort will necessarily include generating the data needed to produce evidence-based guidelines and developing the methodology to ensure appropriate outcomes in clinical practice. It is our hope that by highlighting the clinical needs, summarizing the current research and clinical “state of the art,” and providing a template for future research, these task force recommendations will move the field closer to achieving these goals.

REFERENCES

38. Rickert VI, Johnson CM. Reducing nocturnal awakenings and cry-


