



Dealing with comorbid sleep disorders in pediatrics: are we doing enough?

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Practice points

- Pediatric health professionals need to be aware that sleep disturbance is a common problem with wide-reaching effects for many children. It is especially likely to be present in children with intellectual disabilities and those with medical, neurological and psychiatric conditions.
- Parents (and children) may not always ask for help with sleep, even when sleep problems are severe, adversely affecting the child and placing considerable caring burden on their families. Clinicians need to routinely ask a few simple screening questions to see if a more detailed follow-up assessment/referral is required.
- Consideration of predisposing, precipitating and maintaining factors should include a combination of the child's underlying condition, its pharmacological management and family and environmental issues.
- Multiple sleep disorders may be present in one child and each one might require different forms of assessment and management.
- Although some children may require referral to multidisciplinary tertiary sleep clinics, many could be being helped at the primary and secondary care level if sleep problems were identified and trained personnel were available to assess and manage sleep, and support families.
- Behavior therapy has a prominent role to play in the management of many common sleep disorders.
- Some sleep problems could be prevented by increasing parent education and providing support in the early years, with relevant advice for parents of children at greatest risk of sleep disturbances.

SUMMARY Sleep disturbance is a common problem for many children and especially likely to be present in children under the care of pediatric health professionals, although many intervention/prevention opportunities are being missed. This is worrying in view of the fact that resolving or mitigating sleep disturbance is likely to benefit the child and family, and for some children with multiple and complex problems, might be one of the most easily treatable problems with which they present. In considering ways in which sleep disturbance is commonly comorbid with other pediatric clinical conditions (or aspects related to these

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conditions), examples of the multiple and reciprocal relationships between sleep and children's health are highlighted and the fact that attention to children's sleep should be central to optimal pediatric clinical services is therefore emphasized. Suggestions for ways in which this can be achieved include increased education (for parents and professionals), routine preliminary screening for vulnerable children, the development of clear guidelines for assessment, management and referral for use in primary- and secondary-level services and, ultimately, an increased number of tertiary pediatric multidisciplinary sleep clinics.

Pediatric sleep disorders: their nature & significance

The International Classification of Sleep Disorders describes over 80 different sleep disorders grouped into the following broad categories [1]: insomnia (difficulty with sleep initiation, duration, consolidation or quality, and resulting in daytime impairment); sleep-related breathing disorders (disordered respiration during sleep); hypersomnias of central origin (primary complaint of daytime sleepiness not due to disturbed nocturnal sleep or a circadian rhythm sleep disorder); circadian rhythm sleep disorders (misalignment between the individual's endogenous circadian clock and the exogenous factors that affect the timing of sleep-wake, or alteration of the circadian timing system); parasomnias (disorders that intrude into the sleep process; usually manifestations of CNS activity); and sleep-related movement disorders (primarily characterized by relatively simple, often stereotyped movements that disturb or are associated with sleep, resulting in daytime sleepiness/impairments).

The prevalence of different sleep disorders within these categories among children of course varies, depending on the disorder and particular features of the child (e.g., age). However, in broad terms, disturbances of sleep affect approximately 30% of infants [2], school-aged children [3] and adolescents [4,5]. Problems are frequently long-standing with sleep difficulties at 6 months of age being associated with sleep problems at 5 years, which in turn increases the risk of children having sleeping problems at 10 years of age [6]. Most of the children who are under the care of pediatric clinical services (i.e., children with medical, psychiatric and neurodevelopmental disorders) are part of the 'at-risk' populations that are known to be particularly vulnerable to various forms of often severe and persistent sleep disturbance [7,8].

The high rates of pediatric sleep disturbance are significant in view of the fact that in both typically and atypically developing populations, sleep disturbance has a number of wide-ranging

negative associations including cognitive deficits, poorer academic performance, behavioral problems, increased reports of depressed mood and irritability and increased body weight [9-12], and may even be predictive of a poor psychiatric state in adulthood [13,14]. Furthermore, disturbed sleep in children is frequently associated with impairments that extend beyond the child; associations between childhood sleep problems and general family stress, marital discord and parenting difficulties have been found [15,16]. As such, the need to identify, assess and manage pediatric sleep disturbance (or even, where possible, to prevent sleep disturbance in the first place) is paramount.

Many of the adverse effects can be reversed by removal of the sleep disturbance (see [17,18] for a discussion), emphasizing the importance of addressing sleep as a means of improving overall functioning of the child and family. Indeed, for some children with complex and/or multiple clinical conditions, sleep disturbance may be one of their more easily 'treatable' problems, with benefits not only for the child, but also for the entire family.

Management of pediatric sleep disorders: barriers & service limitations

Unfortunately, there is a strong suggestion that many children who have sleep problems do not receive adequate or appropriate help for addressing them. Reasons for this are likely to be multiple and varied. For example, Blunden *et al.* found that Australian school-age children's sleep problems were considerably under-reported by parents during general practice consultations [19]. Reasons for not seeking help has been investigated among parents of children with developmental disorders, where habituating to long-standing difficulties, mistakenly believing that sleep problems were an inevitable and untreatable part of the child's basic condition, and unawareness of the problem – the latter perhaps particularly likely with certain sleep disorders (e.g., sleep-related breathing disorders) – were all apparent [20,21].

There also appear to be gaps in clinical knowledge among medical practitioners who may not enquire about or recognize sleep problems in children [22]. Chervin *et al.* found that US pediatricians discussed sleep problems in only 16 out of 103 cases over 2 years, treating only three of these [23]; Owens reported that there were significant gaps in US pediatricians' knowledge with only 34% of 626 pediatricians confident about evaluating children's sleep problems and only 25% confident about approaching treatment [24]. This study also highlights the relatively common use of prescription medication for the treatment of sleep disorders (when other approaches have a stronger evidence base) and, in other cases, the low levels of knowledge about sleep disorders that are potentially likely to respond to medication (e.g., periodic limb movement disorder or restless legs syndrome). Such findings fit with parents' reports that medication was commonly prescribed for their child's sleeplessness, although its effectiveness was poorly rated by them [21], and that parents often rate treatments poorly, regardless of their type [20]. Such inadequacies in the services received by families are perhaps unsurprising given that professional training in this field appears to be limited [25].

Such service limitations are of special concern because many possible sleep disorders may have the same key presenting symptoms and it is, therefore, imperative that a diagnostically driven approach to assessment and management, rather than a symptomatically driven approach, is adopted to ensure success. For example, 'difficulty getting off to sleep' is a presenting symptom that might be caused by a number of sleep disorders (each requiring a different focus of intervention), including those relating to anxiety, poor limit setting on the part of carers, an inappropriate sleep environment or disruption to the child's body clock. Making the correct diagnosis (and management decision), therefore, requires a sophisticated and broad level of knowledge so that one can consider appropriate differential diagnoses.

It seems likely that the variable availability of appropriate sleep services and specialists may also play a role in maintaining the situation, whereby pediatric sleep disorders are not optimally identified, assessed and managed. Sleep disorder medicine is a broad field that falls across many different health-related specialties (e.g., psychiatry, neurology, psychology and respiratory

medicine); it is therefore not surprising that a wide range of intervention approaches might be used [10,26,101]. A co-ordinated multidisciplinary approach to assessment and management is the ideal for optimal outcomes [27]. However, the sheer number of affected children realistically means that not all children will be able to (or need to) access tertiary sleep disorder services and a tiered approach is probably more appropriate. In order for such a system to work, one key aspect is that primary and secondary care services need to be alert to identifying sleep disturbance and equipped with the skills to make basic assessments and, where appropriate, provide preliminary management advice or suitable referral. Because behavior therapy is likely to play a prominent first-line approach for many common pediatric sleep disorders and might be used preventively [28], efforts should be made to ensure it can be accessed by families.

Considering comorbidity as a means of improving patient care

An appreciation by clinical staff and service planners of the multiple and reciprocal relationships between sleep and child health is a precursor to improved services for the identification and management of comorbid sleep disturbance where they are integrated into routine pediatric services. The following sections will highlight how attention to children's sleep should be central to optimal pediatric clinical services by considering, with some specific examples, ways in which sleep disturbance is commonly comorbid with other pediatric clinical conditions (or aspects related to these conditions).

■ Comorbidity with other medical & neurological conditions

It is perhaps difficult to think of an example where sleep has been shown to be unaffected by the presence of a pediatric medical condition [29]. Sometimes, the sleep disturbance is directly caused by the medical condition, but the cause may also be associated pain or discomfort (e.g., for children with juvenile rheumatoid arthritis, headache or eczema) [30,31], associated psychological distress or a combination of these things (e.g., in children with cancer [32]).

It should be noted that different types of epilepsy can be associated with sleep in a number of ways [33,34]. Sleep may induce (or suppress) seizure activity, sleep loss may lead to increased seizure frequency, seizures can occur

predominantly (or exclusively) during sleep, seizures may hinder sleep onset, disrupt sleep during the night, impact upon sleep architecture, reduce sleep duration and be associated with daytime sleepiness (as a result of impaired night sleep, daytime seizures or as a consequence of anti-epileptic medication side effects). Electrical status epilepticus during sleep, which in itself may be asymptomatic, is associated with neuropsychological impairment such as cognitive regression, behavioral disturbance and motor impairment; the link between the duration of electrical status epilepticus during sleep and neuropsychological outcome highlights the importance of early recognition and effective treatment [35].

The hospital environment itself might contribute to children's (and parents') sleep disturbance, causing fear and anxiety (either while staying in hospital or in anticipation of an outpatient visit), or disturb sleep because of nighttime noise and light levels [36,37]. It has been noted repeatedly that the disruptive effects on sleep can persist after discharge [38,39], highlighting the need for post-discharge monitoring of sleep.

The link between sleep and a child's medical state and care is of significance to pediatrics, not only because of the importance of good sleep for the child's general physical and psychological functioning, as outlined above, but also because reduced sleep or sleep disruption can predict health outcomes. For example, in children with asthma, sleep quantity predicted next day peak expiratory flow and self-reported sleep quality predicted the severity of asthma symptoms; asthma symptomatology was not predictive of sleep measures, indicating the potential benefits of targeting sleep behaviors as a means to improve asthma control rather than the other way around [40]. Furthermore, poor sleep adversely affects children's perceptions of pain and may contribute to the difficulties they have coping with their medical condition [41], although this relationship may be partially mediated by mood [42]. In addition, where children's sleep disturbance impacts upon parents' sleep this is likely to further reduce the families coping resources and place the unit under additional strain, as discussed further below.

■ Comorbidity with intellectual disabilities

High rates of sleep problems in children with intellectual disabilities probably arise due to a

combination and interaction of physical and psychosocial factors, including medical, neurological and psychiatric problems (and their treatment).

Some sleep disorders may be specifically related to the child's particular underlying condition [8]; for example, Down's syndrome is associated with hypotonia and also a number of other risk factors for narrowed airways such as midfacial and mandibular hypoplasia, large posteriorly placed tongue, upper respiratory tract infections causing enlarged tonsils and adenoids, and a congenital narrowing of the airway. It is, therefore, perhaps unsurprising that obstructive sleep apnoea hypopnea syndrome is frequently described in children with Down's syndrome [43]. Sometimes there is an interaction between atypical physical functioning and psychosocial factors; for example, an abnormal endogenous melatonin rhythm (in terms of production, secretion, distribution or metabolism) has been described in association with particular syndromes, likely with a genetic basis (e.g., an inverted rhythm in Smith Magenis syndrome [44], a 'flattened' profile in autism [45]), which in itself is likely to predispose to problems with sleep timing and/or continuity. However, the circadian clock is influenced by both endogenous and exogenous factors. Exogenous factors that may play a particular role include reduced exposure to daytime light in some care environments where outdoor exposure is limited, reduced differentiation between 'daytime' and 'night-time' in terms of extent and nature of activities and the environment in which they occur, reduced flexibility to link key time-giving cues (e.g., bed times and meal times) to each individuals' particular sleep-wake rhythm for children living in group residential settings and impaired learning of the association between social time cues and sleep.

Normal sleep patterns and behavior are both biologically and socially determined, so in addition to atypical functioning of the structures and processes involved with the control of sleep and wake states, the learnt elements of sleep (e.g., where one sleeps and how one falls asleep), which vary from family to family and culture to culture [18,28,46], must also be considered. These learnt elements may be more challenging to learn for children with intellectual disabilities or may be more challenging to 'un-learn' once inappropriate sleep-related behaviors have been established.

■ Comorbidity with psychiatric & behavioral disturbance

Bidirectional links between psychiatric conditions (which are more common in children with intellectual disabilities) and various types of sleep disturbances have been noted. For example, anxiety and mood disorders may be associated with sleep disturbances including insomnia, nightmares and bedtime refusals [47]. Sleep disordered breathing, motor restlessness during sleep, periodic limb movement disorder and sleeplessness can occur at higher rates in ADHD [48]; it has even been suggested that for some children with ADHD, their daytime symptoms of attention difficulties and hyperactive behavior are caused by a primary sleep disorder [49], with 'ADHD symptoms' reversed by treatment of the sleep disorder [50–53].

It should be emphasized that challenging daytime behavioral and emotional disturbance may well arise as a consequence of sleep disturbance (if sleep is compromised in terms of quality or quantity) and that successful treatment of sleep disturbance has been seen to be associated with improvements in daytime behavior. In addition to numerous positive anecdotal reports, assessments of daytime behavior, utilizing questionnaires and analog rating scales, have shown improvements following behavioral interventions for sleeplessness problems [54–56]; although not all studies support the idea that improved sleep results in improvements in daytime behavior [55–58].

■ Medication effects on sleep

A further consideration, is of course that medications for co-existing medical, neurological and psychiatric conditions may in themselves have a disruptive effect on sleep in various ways [59,60]. For example, classic anti-epileptic medications (e.g., phenobarbital, carbamazepine, valproate and phenytoin) have been associated with reduced sleep latency, more slow wave sleep and daytime sleepiness. Newer anti-epileptic medications (e.g., gabapentin, lamotrigine, vigabatrin and zonisamide) tend to have less of a sedating effect after the medication is established but may still have variable effects on sleep architecture [33]. Antidepressant drugs, such as selective serotonin reuptake inhibitors, are frequently associated with insomnia and periodic limb movements [61,62], and methylphenidate for the treatment of ADHD appears to increase sleep latency although sleep may be

consolidated [63]. Antihistamines may be associated with sedation [64], whereas corticosteroids tend to be associated with increased wakefulness during sleep and increased alertness during the day [65,66]. Theophylline (a respiratory stimulant and bronchodilator) has been associated with insomnia [67,68]. Studies with adults (limited in number) suggest that the action of analgesics depends on the compound used; nonsteroidal anti-inflammatory drugs may increase wakefulness [69] whereas opioids are associated with sedation and, importantly, respiratory depression during sleep [70]. Pseudoephedrine and phenylpropanolamine (used to treat nasal congestion and available in many over-the-counter preparations) have also been associated with increased wakefulness in adults [71].

Although there are gaps in knowledge about sleep-related medication effects in pediatrics, existing literature suggest that mindful monitoring of the effects of a child's medications on their sleep should be an important part of their overall care, with attempts to maximize management of their condition while minimizing associated sleep disturbance where possible.

■ Comorbidity & the family

The impact of sleep disturbance in children frequently extends beyond the child, affecting parents and other family members [18]. Studies of parents of sleepless, crying infants suggest that profound parental reactions are evoked, including actually hitting, shaking or smothering a child during the episodes [72], or having fantasies about harming (and even killing) the child [73]. It is also well documented that mothers of sleepless children (both typically and atypically developing children) have higher rates of stress, irritability, anxiety and depression, and have more negative views about themselves, their child and their spouses [56,74–80]. For some children with chronic illnesses, it may be the need for parents to provide nocturnal care/monitoring, rather than the presence of a sleep disturbance *per se*, that disrupts the parents' sleep [81]. Either way, the impact on the child (and the family unit) of resultant sleep disturbance in the parents, and its negative sequelae, should not be underestimated.

Assessment of a child's sleep should, therefore, include assessment of the impact upon the family as this might suggest areas of clinical need in the parents (successful treatment for which might be expected to have knock-on

benefits for the child), and might also have implications for the feasibility of any indicated interventions. For example, behavioral interventions, often suggested as a first-line treatment for many common childhood sleep disorders, require considerable time and energy commitment from the families to be successfully implemented. Getting families to the stage where they have the resources to undertake behavior therapy (perhaps by using other short-term interventions or respite services) might be an important stage in management. The clinical relevance of parenting factors for child sleep should not be underestimated and attention needs to be paid to all family members [82].

■ Comorbidity among sleep disorders

It should be remembered that multiple sleep disorders can exist in one child, with some combinations being particularly likely. This highlights the need for broad screening of problems in at-risk groups and in children presenting with any one sleep complaint. The combination of sleep disorders present might be those that are thought to share a common pathophysiology (e.g., periodic limb movement disorder and restless legs syndrome), or those with unrelated underlying etiology (e.g., behaviorally based sleep disorders may be present in children with other sleep disorders of more physiological origins or arise as a secondary problem); high rates of co-occurring sleep disorders have been documented in children with sleep disordered breathing, with other commonly reported sleep difficulties including behaviorally based insomnia, as well as enuresis, bruxism and arousal disorders [83,84]. Of course, in such cases it may be necessary to use multiple forms of treatment to address individual sleep disorders, emphasizing the ideal for sleep disorder services to be multidisciplinary and have a co-ordinated approach.

Conclusion & future perspective

The field of sleep disorder medicine continues to grow and, over the last decade, there have been significant developments in public and professional awareness of the area. However, given the widespread nature of the problems, the implications they have for child and family health (mental and physical) and the gaps in service provision, there remains a need to build upon this and to ensure that all children and their families are able to access appropriate services and support, not just those who are fortunate enough to be

associated with services where there are individuals who have taken a special interest in the field. Examination of the many and multiple ways in which sleep disturbance is comorbid with child health issues emphasizes the need for assessment and management of sleep to be considered as a key and routine part of the child's overall holistic care at every level.

Awareness raising and education about ways to promote good sleep, and also the significance and nature of sleep disturbance and intervention possibilities needs to continue and be directed at both parents and school staff. This should help to ensure that some problems are prevented/curtailed and that help is sought when appropriate. The widespread availability of advice material for families will help achieve this [102,103].

Greater emphasis on sleep disorder medicine (and integration of sleep across topics) in teaching curricula for doctors, nurses, psychologists and other child health workers is needed. Across general practice and pediatric services (including school nurses and educational psychologists), the routine screening of sleep for children who may be particularly prone to suffer from sleep disturbance could help to avoid intervention opportunities from being missed. Mindfulness of the conditions and factors associated with comorbid sleep disturbance will help to alert professionals and to direct enquiries. Brief screening tools, such as the BEARS sleep screening instrument [85], are practical and quickly administered.

Positive responses to preliminary enquiries need to be followed by more detailed enquiry and referral to specialist services where appropriate. Given the high rates of sleep disturbance (especially in some clinical groups), it is unrealistic (and perhaps inappropriate) to expect that all children would be referred to specialist sleep disorder services. The delineation of clear assessment, management and referral pathways, tailored to incorporate key factors of particular relevance to specific clinical groups, would facilitate a tiered system to the clinical process. The Autism Treatment Network Sleep Committee have drafted such guidelines for insomnia symptoms in children with autism and are currently evaluating their feasibility and usefulness; the approach and development process should serve as an excellent model to be applied to other clinical groups/sleep disorders [104].

While practitioners in every field probably consider that their specialty needs more representation in pediatrics, it is argued that sleep

medicine should be considered a high priority because of the sheer number of affected children and the inter-relationships between sleep and various aspects of child and family physical and mental health. To that end, the identification of a dedicated 'sleep specialist' in each pediatric service would allow this person to be trained (in fundamentals of assessment and management, which would be appropriate/possible in nonspecialized settings, and also in local tertiary referral options) so that they could act as a source of information and support for families and their clinician-colleagues alike. Such an approach would also reduce the demand on overstretched tertiary sleep services, although ultimately one would hope for a greater number of multidisciplinary pediatric sleep disorder services given the scope of the problem and diverse nature of sleep disorder medicine.

Although ensuring that families can access appropriate support and advice should be a service priority, an investigation of how to improve

access (e.g., with brief forms of treatment, low-cost delivery methods and identifying active therapeutic components and their efficacy for particular groups of children and different sleep disorders) should be a key research target for the future along with further exploration of the potential for objective screening methods (e.g., urinary protein analysis for the detection of obstructive sleep apnoea) [86,87], which could have a significant impact upon clinical practice and the lives of children and their families.

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