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REVIEW

Clinical practice

Sleep problems during infancy

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Abstract Sleep problems are very prevalent during infancy. The most common problems are those related to night wakings and sleep-disordered breathing (SDB). Most common night waking problems do not have identified physiologic etiology. Their causes appear to be behavioral or developmental by nature, and they usually respond well to behavioral interventions. SDB may result from a variety of anatomic and neurologic factors and is associated with a variety of medical and developmental disorders. Because of the high prevalence of sleep problems during infancy, their persistence, their potential adverse developmental effects, and the positive treatment outcomes, pediatricians should serve as the primary address for screening and referral to proper assessment and treatment.

Keywords Sleep · Infants · Interventions · Behavioral · Apnea · Breathing

Abbreviations

SDB	Sleep-disordered breathing
PSG	Polysomnography
GER	Gastroesophageal reflux
OSA	Obstructive sleep apnea

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Sleep problems during infancy may have serious adverse developmental and functional implications. Sleep problems may interfere with child growth and development and disrupt family functioning and parental well-being [7, 19, 22].

Sleep problems during infancy have multiple etiological sources that can be divided into three broad domains: (a) developmental or maturational delays, (b) behavioral and environmental factors, and (c) medical and physiological factors. In many cases, a potential overlap between these sources exists and, therefore, full identification of these underlying factors is a real challenge for proper diagnosis and interventions. In the present review, we cover common sleep problems during infancy, their potential causes, and related interventions.

Difficulties falling asleep and night wakings

Sleep-wake patterns evolve very rapidly during the first year of life. The most striking maturational process is the consolidation of nighttime sleep. The newborn spends an average of 16 h of sleep in multiple and relatively short sleep episodes around the clock [30]. During the first 6 months, nocturnal sleep is extended and becomes more consolidated; whereas, daytime sleep diminishes. During the second half of the first year, most infants achieve the goal of a reasonably consolidated sleep during the night. However, many infants continue to wake up frequently during the night, which is a major source of distress to parents and one of the most common complaints in pediatrics [1, 3, 26, 32].

Developmental studies using objective measures to document sleep (video recordings or actigraphy) have shown that most healthy infants continue to wake up with an average of two to three wakings per night during early

childhood [3, 6, 33]. A major difference between infants who are referred because of excessive night wakings and non-referred infants lies in the phenomenology of night wakings. Non-referred infants are more likely to resume sleep without or with minimal parental help and awareness; whereas, referred infants are more likely to have difficulty resuming sleep and require more elaborated parental interventions to resume sleep [31].

Excessive night wakings can result from a variety of medical issues (listed below), but most often, no medical cause is identified. Research has shown that in most cases, there are strong associations between the frequency of night wakings and parental bedtime behaviors [1, 4, 34, 37]. Infants who fall asleep with physical contact and/or parental active involvement are more likely to wake up more often and to require help to resume sleep. This is why these sleep problems fall under the category of "behavioral insomnia" and could be defined as sleep-onset association type or limit-setting type depending on the specific characteristics and age [2]. Clinical research has shown that behavioral interventions based on encouraging infants to fall asleep and resume sleep in their crib with minimal parental involvement are very effective in resolving night-waking problems in infancy [14, 20, 29]. It has also been demonstrated that instituting a consistent nightly bedtime routine (without additional behavioral components) is beneficial in improving sleep in infants and toddlers [21]. Because of the high success rates of behavior-based interventions and the fast response, they should be considered as the treatment of choice during infancy [25, 27]. Medication should be considered in extreme cases that do not respond to behavioral interventions or when other medical issues are involved [24].

Night terrors

During night terror events (also referred to as pavor nocturnus or sleep terrors), infants wake up abruptly and scream as if they suffer from a terrible pain. They appear terrorized and may sweat or show other signs of autonomic discharge. Furthermore, they are likely to respond negatively and fight against caregiver's attempts to console them. In unusual presentations such as events that include repetitive, stereotypic, or tonic-clonic movements; color change; or apneas; seizures should also be considered. Night terrors are considered among the disorders of arousals and occur during slow wave sleep. Therefore, these events are more likely to occur during the first half of the night when slow wave sleep is more prevalent.

Night terrors can start during the second half of the first year of life and are very common as isolated events during infancy and toddlerhood [23]. The underlying causes for night terrors have not been identified, although a genetic risk has been reported [23]. In most cases, the sporadic events disappear with maturation. It is suspected that stress and insufficient sleep can exacerbate the problem. When the clinical picture includes only isolated events in otherwise healthy infants, the parents should be educated about the benign nature of these events and encouraged to let the event run its course, or alternatively, to wake up the child more firmly to terminate the event. Sometimes, the events occur at a relatively fixed schedule at night (e.g., around 1 A.M. or 2 h after sleep-onset). In these cases, clinical experience has shown that scheduled brief awakenings of the child prior to the anticipated time of the events can prevent them from happening and resolve the problem after seven to ten consecutive days of practice [6].

Sleep-disordered breathing

Sleep-disordered breathing (SDB) encompasses a spectrum that includes primary snoring, upper airway resistance syndrome, obstructive hypoventilation, and obstructive sleep apnea (OSA). SDB is clinically manifested as snoring and obstructive sleep hypoventilation/apnea and arousals. The epidemiology of pediatric SDB shows a three-peak distribution. By prevalence order, the 2–6 years peak is due mainly to adenotonsillar hypertrophy; the adolescent peak is related to the epidemic of teenage overweight and a smaller peak occurs during the first year of life. SDB in infants is frequently associated with anatomic narrowing of the upper airways [11] secondary to congenital anatomic deformities resulting mainly from osseous malformations, enlargement or functional disturbance of soft tissues, and neurologic disorders (Table 1).

Craniofacial malformations

Craniofacial anomalies are important risk factors for OSA in infants with an incidence of 15–90% depending on the anomaly [10]. These disorders include a variety of syndromes and non-syndromatic anomalies of the face. Mandibular involvement is manifested as micrognathia and retrognathia causing glossoptosis. Examples are congenital syndromes such as Treacher Collins and Nager acrofacial dysostosis and the more common non-syndromatic Pierre Robin sequence. The latter may result in physiologically significant and life-threatening hypoxic obstructive apneas in the neonatal and infant period and is often treated by tracheostomy. The experience acquired with mandibular distraction osteogenesis suggests this technique as an early and best approach [18].

Another group of congenital anomalies with a high rate of SDB involve maxillary hypoplasia. Most are syndromatic. Main examples are Crouzon, Apert, Pfeiffer, and achondroplasia. Midfacial hypoplasia, depressed nasal base, small

Table 1 Causes and abnormalities associated with sleep-disordered breathing and obstructive sleep apnea in infants

Congenital anatomic malformations	Enlargement of soft tissue	Functional	Neurologic
Craniofacial anomalies: Apert, Crouzon, Pfeiffer, and achondroplasia	Macroglossia	Laryngomalacia	Glossoptosis
Micrognathia	Down's syndrome	Pharyngomalacia	Down's syndrome
Cleft palate	Beckwith–Wiedemann	Gastroesophageal reflux	Chiari malformation
Pierre Robin sequence	Storage diseases (mucopolysaccharidosis)		Hydrocephalus
Choanal atresia	Swelling secondary to allergy (rhinitis)		Increased ICP
	Adenotonsillar hypertrophy		Vocal cord paralysis
	Acute infections (retropharyngeal abscess and infectious mononucleosis)		Brain tumors
	Hypothyroidism		Familial dysautonomia
			Cerebral palsy
			SMA I (Werdnig–Hoffmann)
			Muscular dystrophy

Some diseases such as Down's syndrome have more than one mechanism responsible for upper airway obstruction during sleep

ICP intracranial pressure

narrowed nasal airways, and diminished oropharyngeal depth predispose these infants to SDB. While in the formers, SDB becomes clinically significant early, in achondroplasia, SDB usually develops in later years with a rate of at least 40%. Early occurrence does occur [33]. A study of 17 infants with achondroplasia and respiratory difficulties showed that in addition to the maxillary hypoplasia, "relative" adenotonsillar hypertrophy, muscular and neurological factors resulting from small foramen magnum, and hydrocephalus contributed to SDB [34].

Since surgical correction is usually possible only after several years, intervention at early age may be confined to tracheostomy. Treatment with continuous positive airway pressure may not be tolerated by infants. These infants with SDB present as continuous hypoventilation and may thus be successfully treated with nocturnal supplemental oxygen without the need for tracheostomy while waiting for reconstructive surgery after 4 years of age. Monitoring for hyperoxia-induced hypoventilation may be required.

Due to the high incidence of SDB in infants with craniofacial anomalies, we recommend that even in mild presentation of noisy breathing or other clinical signs of SDB, periodic reassessment of gas exchange and sleep be accomplished by polysomnography to identify the evolution of these problems since in many cases, especially in syndromes of mid-face hypoplasia, the airway narrowing worsens over time. Even mildly enlarged adenotonsillar tissue may contribute to the increased airway resistance, hence, our practice is to evaluate each case with SDB by an ear, nose, and throat (ENT) specialist and recommend adenotonsillectomy as a first step also in these cases.

SDB due to cleft palate is probably under-reported and under-treated [17]. Interestingly, repair of the cleft palate has been associated with increased risk or worsening. Macroglossia is another risk factor for SDB in infants. Examples are Beckwith–Wiedemann and Down's syndromes.

Congenital brain stem malformations

Malformations involving the posterior cranial fossa, brain stem, and upper cord may cause sleep apnea. Both central sleep apnea and OSA complicate Chiari malformations I and II [5, 36]. The mechanisms are compression and ischemia of the respiratory center in the medulla and traction of the lower cranial nerves. Resolution should be expected with early or prompt intervention.

Adenotonsillar hypertrophy

Although uncommon, SDB due to hypertrophic adenoids and tonsils does occur in infants. SDB in infants share a few common characteristics with older children. Unique characteristics for this age group include male predominance, high incidence of preterm infants, failure to gain weight, and high recurrence rate after surgery [8]. In a series of 29 infants younger than 18 months, SDB due to hypertrophic adenoids and tonsils started at a mean of 6 months with an average delay in diagnosis of 6 months due mainly to a low suspicion index [8].

Acute infection

Acute infections, for example, retropharyngeal abscess and acute swelling of the adenotonsillar tissue in infectious mononucleosis, may cause acute upper airway obstruction with severe sleep apnea. These situations require prompt

treatment (corticosteroids in mononucleosis, antibiotics, and drainage in retropharyngeal abscess) and may constitute medical emergencies.

Gastroesophageal reflux

Gastroesophageal reflux (GER) is common in infancy. SDB may constitute the only clinical presentation in infants. However, established GER by esophageal pH monitoring or other techniques in an infant who has SDB proven by polysomnography (PSG) during a different session does not confirm that GER is the cause of the breathing disorder. Hence, simultaneous recording of PSG and esophageal pH may be required.

The mechanism behind "GER respiratory events cycle" is bidirectional. GER causes airway obstruction, and OSA can lead to GER [11]. Infants born preterm are at a higher risk for SDB induced by GER. The addition of pH monitoring to PSG should be considered in infants presenting with unexplained SDB [9].

Several clinical entities occur almost exclusively in infants during sleep—sudden infant death syndrome, apparent life-threatening event, and congenital central hypoventilation syndrome. Nevertheless, they are beyond the scope of this review.

Sleep problems caused by other medical issues

A variety of medical disorders affect sleep in infants and children. Among the most common are asthma, itching due to atopic dermatitis, colic, and cow's milk allergy.

Colic

Colic is a symptom of paroxysmal abdominal pain and crying occurring in infants during the first few months. The attack usually begins suddenly and may persist for several hours. Sometimes, the passage of feces or flatus provides relief. Colic starts at 2–3 weeks of age. In most cases, the attacks tend to occur predominately during the evening and last until midnight or shortly after. In about 15% of the infants, the attacks start during sleep as well. Colic gradually disappears by 4 months of age. The effects of colic on sleep are still controversial. Several studies using diary recordings suggest that infants with colic sleep less during the colicky period especially during the day, while night sleep is relatively impaired. Data suggest that infants who suffered from colic have higher rate of night wakings and less nocturnal sleep [15, 37]. Colic may be associated with a disruption and delay in maturation of circadian rhythm and sleep-wake organization which resolve when colic disappears. Other studies based on 24-h ambulatory polysomnographic assessment have shown that excessively crying infants with colic do not sleep less compared to non-colic infants and have normal sleep structure at the age of 9 weeks and 7 months [12, 13]. It has been argued that sleep difficulties in the "post-colic" period is due mainly to parents' attitude, interpretation, and practices acquired during the colic phase rather to intrinsic sleep problems. Nevertheless, this may lead to a failure in the establishment of good sleep hygiene. Hence, instructing parents of infants with colic and post-colic sleep problems with implementation of good sleep practices (see below) is usually recommended.

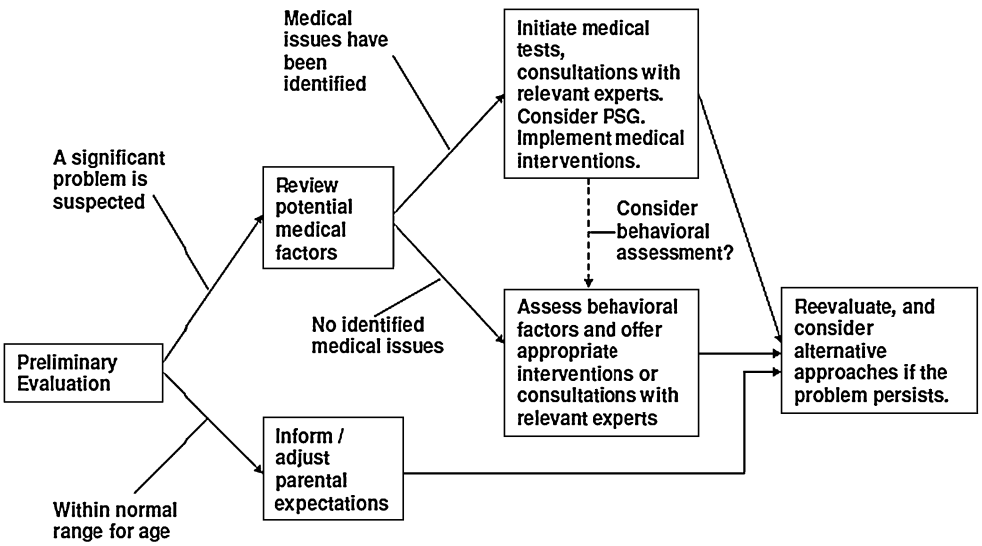

Fig. 1 Outline of the main stages in addressing sleep complaint in infants

Cow's milk allergy

Milk allergy has been implicated in infant sleep problems. It has been demonstrated that cow's milk allergy can cause persistent sleep problems, and that a milk-free diet can lead to a significant improvement in sleep [15, 16]. When suspected, a milk-free diet trial for a number of nights with accompanied sleep assessment (parental reports or objective assessment) is recommended.

Another common problem that has been frequently associated with sleep difficulties in infants includes atopic dermatitis [4]. Teething is often considered as a significant factor in sleep problems in infancy. However, research has shown that the influence of teething on sleep is very limited (usually within a range of 1 or 2 days before and after tooth eruption) if it exists at all [16, 35].

Basic guidelines for establishing good sleep practices

Pediatricians are primary sources of professional information for parents of sleep-disturbed infants. Therefore, providing guidance in basic principles for good sleep practices is a valuable clinical service for the parents. Most infants presenting sleep difficulties can benefit from the following guidelines (when applicable, considering the specific infant's and parents' characteristics):

- Establish regular sleep schedule and bedtime routine considering the infant's biological signals.
- Provide appropriate sleep environment (i.e., relatively quiet and dark room). No need for a total soundless environment because this may sensitize the infant to normal noises occurring at night. Total darkness may also trigger fears in some infants.
- Encourage the infant to fall asleep in the crib (or other appropriate sleep surface) with minimal parental assistance.
- Gradually increase nocturnal feeding intervals and eliminate nocturnal feeding and sweet drinks when the infant is mature enough (i.e., 6–12 months of age for most healthy infants).
- Gradually minimize all rewarding parental behaviors during the night (i.e., holding, rocking, feeding, and playing).
- If separation fears are suspected, parental passive presence can provide reassurance without compromising the other guidelines.

Most behavioral interventions are elaborations and derivatives of these basic guidelines. It is beyond the scope of this paper to describe these behavioral interventions in detail, but more detailed descriptions are available in the literature [20].

Conclusions

Sleep problems are very common complaints to pediatricians during infancy. Although maturational processes lead to improvement in sleep in most children, sleep problems are persistent and may have adverse developmental effects.

Because of the significant adverse effects of infant sleep problems and the overall positive outcomes of tailored interventions, it is important to address these problems appropriately in clinical settings. Figure 1 outlines the main stages in addressing sleep complaint in infants:

1. Assess the severity of the problem and potential underlying factors. Standardized screening questionnaires can provide comparisons to normative data [e.g., 28, 32]
2. If a medical disorder is suspected, an appropriate assessment should be implemented. For instance, if SDB is suspected, this assessment should include ENT consultation and a polysomnographic study.
3. When there are no indications for underlying medical problems or when an additional behavioral etiology is suspected, a full behavioral evaluation or expert consultation and intervention should be considered.

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