Respiratory/Sleep Disorder Breathing (SDB)

Definitions

“SDB is highly prevalent, under recognized, under reported and under treated”

Central
1. Central sleep apnea (CSA) is defined by the cessation of air flow without respiratory effort. CSA is relatively uncommon, as compared with OSA. However, considerable overlap exists between CSA and OSA, from the standpoint of pathogenesis as well as disease manifestations. (Respir Care. 2010 Sep; 55(9): 1168–1178.)

Obstructive:
1. OSA is defined by the American Thoracic Society (ATS) as “a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction (obstructive apnea) that disrupts normal ventilation during sleep and normal sleep patterns.” (Epi of Ped OSA)

Outcomes

• Primary: Improve recognition of signs and symptoms of sleep disordered breathing across the lifespan, recognizing that symptoms important for its recognition in infants will be different than in adults
• Secondary: Implement a strategy to identify sleep disordered (SDB) in the clinical setting through a reliable screening method (not currently available) that improves appropriate referral for additional appropriate assessment (polysomnography)
• Tertiary: Minimize the adverse impact of unrecognized SDB on physical well-being (including sudden, unexplained death) and neurocognitive function.

Infancy

1. Clinical Questions
   a. Is there any predictable sequence to cranial nerve dysfunction (is eating affected before facial weakness and / or respiratory regulation), and each child different?
   b. Is there any anatomic (imaging) or physiologic marker that identifies children at greatest risk for SDB?
   c. Does any observed sign / symptom predict a greater need for specific interventions (shunting, foramen decompressions)?
2. Guidelines
   a. Have a low threshold for assessment of SDB in infants with evidence of other cranial nerve dysfunction - poor feeding, respiratory distress, facial weakness / tongue fasciculations
   b. There is insufficient evidence to support routine sleep studies on every infant with a NTD (I think there are, however, centers doing this)
   c. There is not sufficient evidence to suggest that the need for a specific intervention being required or not being required (shunt, decompression) that can be based solely the results of a sleep study.
   d. Do not presume that specific MR findings either confirm or rule out SDB as a diagnosis in the individual child.
   e. Discuss sleep disordered breathing with parents and care providers so they can better observe for early symptoms or changes

Toddler
Preschool
1. Clinical questions
   a. Is there a sufficiently sensitive and specific method (questionnaire, test before polysomnography) that would support routine screening of children with NTD for SDB?
   b. Is there a clinical profile (signs, symptoms, other risk factors like obesity, hypertension) that would warrant a higher priority referral?
2. Guidelines
   a. Recognize the symptoms of SDB in children (mouth breathing, a history of delayed growth, features of inattention and hyperactivity) are different compared to adults (snoring or excessive daytime sleepiness).
   b. Providers should ask about questions related to sleep quality, quantity and other possible symptoms at every visit (at least annually). Screening questionnaires for SDB in children may not be sensitive or specific enough for clinical settings (have been used in research settings with some success) Changes in respiratory status / function should be evaluated further as NTD is not a progressive disorder.
   c. Discuss sleep disordered breathing with parents and care providers so they can better observe for early symptoms or changes

Schoolage
- Same as Preschool

Teenage
1. Clinical questions
   a. Are asymptomatic individuals with NTD really asymptomatic or are they only unrecognized?
   b. What is the effect of SDB on morbidity and mortality?
2. Guidelines
   a. Because patients are unlikely to discuss sleep related symptoms spontaneously with a primary care provider, these should be queried at each visit (at least annually)
   b. Recognize clinical findings that may either contribute to or be the result of sleep disordered breathing: hypertension, obesity.
   c. Improve patients’ awareness of this condition, its presentation and it adverse impact on quality of life.

Adult
- Same as teenage

Research Gaps
1. Is the frequency of or reasons for sleep disorders in the NTD population truly greater / different than the general population?
2. Are these differences related to the Chiari malformation and / or brain stem dysfunction?
3. Does unrecognized sleep disordered breathing contribute to the neurocognitive profile / decline in individuals with a NTD?
LITERATURE REVIEW

Population Data

General Population Children
1. Obstructive sleep-related breathing disorders (SRBDs) are common but usually undiagnosed among children.
   a. Survey of Sleep Disturbances in Children (Gen Ped Clinics J Peds 2002) used the Pediatric Sleep Questionnaire (>1000 children).
      Symptoms reported Included:
      Habitual snoring – 17%
      Criterion scores suggestive of sleep-disordered breathing – 11% overall; 29% in clinic for neurologic indications; 21% in children at the clinic for noninfectious respiratory.
      Insomnia was reported in 430 (41%) of the children;
      ≥2 symptoms were present in 18% of the children.
      Excessive daytime sleepiness was suggested in 14% of the children
      38% had symptoms of sleep terrors, sleepwalking, or nocturnal bruxism.

2. Methods to help identify SRBDs without the expense of polysomnography could greatly facilitate clinical and epidemiological research. The Pediatric Sleep Questionnaire scale for childhood SRBDs, snoring, sleepiness, and behavior is a valid and reliable instrument that can be used to identify SRBDs or associated symptom-constructs in clinical research when polysomnography is not feasible. This study demonstrates the validity and reliability of PSQ scales for childhood SRBD, snoring, excessive daytime sleepiness, and inattentive/hyperactive behavior (PSQ Sleep Medicine 2000)

3. Ample evidence exists that Sleep Related Breathing Disorder symptoms differ between children and adults. Important that awareness of several childhood symptoms that may not be as prominent in adults, including mouth breathing, a history of delayed growth, and especially features of inattention and hyperactivity. (Sleep Med 2000). There are also symptoms that are common in adults that may not be as common in children (excessive daytime sleepiness).

General Population Adults
1. 4% prevalence estimate of SDB in the general population
2. Wisconsin Sleep Study: OSA is present in 9% of women and 24% of men; reaches moderate or worse severity in 4% women and 9% of men. (USPSTF)
3. 1990’s data – adults 10% with mild OSA (AHI 5 <15) and 3.8 – 6.5% for moderate (AHI 15<30) to severe (AHI >30) OSA. (USPSTF)
4. Identified risk factors for OSA in adults – male sex, older age (40-70 years old), postmenopausal status, higher BMI, craniofacial and upper airway anomalies. (USPSTF)
5. Rates may be higher with greater obesity (an issue in individuals with SB). The role OSA plays in increasing overall mortality is clear. Whether it is independent from other risk factors (older age, higher BMI, and other cardiovascular risk factors) is less clear. (USPSTF)
6. 80% of adults with some degree of OSA remain undiagnosed. Symptoms listed in adults: snoring, witnessed cessation of breathing, gasping or choking at night, excessive daytime sleepiness, impaired cognition, and mood changes. (USPSTF)
7. Patients are unlikely to discuss sleep related symptoms spontaneously with a primary care provider. (Estimate about 20%) (USPSTF)
8. 75% of adults with OSA do not report daytime sleepiness (most commonly reported symptom) (USPSTF)

In the NTD Population

1. Sleep disordered breathing (SDB) is not well defined in the NTD population. There appears to be a higher prevalence of sleep disordered breathing in the NTD pediatric population than in the general pediatric population.
   a. With more SB patients observed to have obstructive sleep apnea than central, perhaps the lower cranial nerve dysfunction plays a larger role than central respiratory center dysfunction.

2. The prevalence of moderate to severe sleep-disordered breathing (SDB) in patients with myelomeningocele may be as high as 20%.
   a. The prevalence of SDB seems to be directly related to the frequency of testing for SDB.
   b. Obstructive sleep apnea and central apnea may occur more frequently than central hypoventilation even in this population. (Rx of SDB in MM Ped Pulm 2000)

3. In children with SB/MM, three types of SDB are known:
   a. prolonged pauses in respiratory effort (central apnea)
   b. persistent low tidal-volume breathing or bradypnea causing hypercarbia and hypoxemia (central hypoventilation syndrome)
   c. episodes of partial or complete airway obstruction (obstructive hypopnea or obstructive apnea respectively).
   d. Patients with a NTD may also have restrictive pulmonary disease as a result of kyphoscoliosis and/or diminished respiratory muscle strength due to lower motor-neuron lesions (Developmental Medicine & Child Neurology 1999, 41: 40–43)

4. The survival (increased mortality) of children with myelodysplasia is adversely affected by Central Ventilatory Dysfunction independent of adjustments for sensory level, motor level and birth head-circumference.
   a. Survival did not appear to be affected by any one form of therapy.(Hays / McLaughlin DMCN)

5. Less is known about the effect of neurosurgical intervention (hydrocephalus intervention, CM-II decompression) on sleep hygiene / SDB. In their study of symptomatic patient referral (about 10% of the patient population), this is likely an underestimate. In the referred group, about 31% of the identified sleep apnea was in the moderate to severe range. (Patel JNS)

6. The clinical course of infants and children with myelomeningocele and central respiratory control abnormalities is variable.

7. Sleep disturbances are common and persistent in adolescents with SB. They experienced greater sleep disturbances compared with their typically developing peers during early adolescence. Sleep assessment and management are important clinical and research priorities in this population (Journal of Pediatric Psychology, 41(6), 2016, 631–642)

8. Potential mechanisms (Risk factors of sudden death)
   a. Midbrain elongation – might reflect an impaired ability of the mesencephalic reticular activating system to regulate arousal and modulate respiratory and cardiovascular rhythms.
   b. Some patients with MM have a slower hyperventilation response to hypercarbia, suggesting intrinsic dysregulation of reticular activating system mediated respiratory control
   c. May also be an abnormal response to hypoxia

9. Another study on potential mechanisms because of the proximity and subsequent distortion of brainstem and other structures (Mechanisms for SDN in patient with MM)
a. Compression of the respiratory nuclei in the medulla and impingement of the lower cranial nerves controlling vocal cords and bulbar muscles involved in pharyngeal airway patency.

b. Children with SB have dysfunction of central and peripheral chemoreceptors causing deficits to respiratory stimuli. Appear to have normal breathing during wakefulness but exhibit prolonged expiratory apnea with cyanosis during sleep that presents as an obstructive problem.

c. Symptoms reported in their patients: apnea, blue spells, SOB, snoring, excessive daytime sleepiness, choking, irritability (these are similar to those in the general population)

10. Patients with MMC should be closely monitored for indications of sleep disordered breathing, and polysomnography and peripheral oxygen may be beneficial in improving sleep and cognition.

a. Asymptomatic infants with myelomeningocele have a high incidence of ventilatory pattern abnormalities during sleep. The clinical significance of the abnormalities of the ventilatory pattern that we have documented, in the absence of clinical symptoms, is not known with certainty. (J PEDIATR 1986;109:631-4)

b. Adolescents and young adults with myelomeningocele have abnormalities in control of ventilation during sleep and wakefulness. Thought to be the result of their Arnold-Chiari malformation that interferes with central chemosensitivity (hypercapnic ventilatory response) and central integration of chemoreceptor output. The abnormalities persist. (J PEDIATR 1989;115:898-903)

In the NTD Population Adults

1. Occasional occurrence of sudden unexplained death in young adult patients with NTD – factor identified included female sex, sleep apnea and midbrain elongation (cumulative). (Risk factors of sudden in death in YA with SB)

2. The death rate from age 5 to 40 for individuals with SB is over 10 times the national average. Half these deaths were sudden and unexpected. (Developmental Medicine & Child Neurology 2010,52:749–753)

3. Young adult women with myelomeningocele are at significantly increased risk of sudden death in the setting of midbrain elongation and sleep apnea.

a. Increased risk of 24 xs compared to males, without sleep apnea and without midbrain elongation.

b. Incidence of sleep apnea greater in women which is the opposite of sleep apnea in the general population (male dominance) (Risk factors of sudden in death in YA with SB)

4. SDB and sudden unexplained death during sleep as frequent causes of death among children with SB/MM, representing up to 21.8% of the reported deaths. Reports of patients with SB/MM followed over time describe mortality rates of 14.0 to 18.6%, with most deaths occurring between birth and 30 months of age. Many reports have implicated progression of brain-stem/cranial-nerve dysfunction as an important cause of death. (Developmental Medicine & Child Neurology 1999, 41: 40–43)

Identification of SDB

1. Screening for SDB in Children

a. Questionnaires - A large number of questionnaires have been used in an attempt to identify snoring and SDB among children. However, in the absence of any universally accepted objective definition of snoring, parental reports of snoring, elicited through variously phrased question items, generally have not been validated against an external gold standard. (Epi of POSD)
b. Frequency of excessive daytime sleepiness is unknown in children with OSA. It is actually infrequent and tends to develop among more severe and/or obese patients. (Pediatrics 2001 Objective Sleep Measures)

c. A study demonstrates the validity and reliability of PSQ scales for childhood SRBD, snoring, excessive daytime sleepiness, and inattentive/hyperactive behavior in a typical patient population. Use in clinical practice should probably await studies of whether these scales distinguish between referred patients with SRBDs and those without SRBDs, and between patients with SRBDs and those with other causes of excessive daytime sleepiness. (Sleep Medicine 1 (2000) 21-32)

2. **Testing for SDB in Children**
   a. Practice Parameters for the Respiratory Indications for polysomnography (PSG) in children (Sleep, 2011) provides some indications for PSG in children with suspected sleep related breathing disorders
      1. When the clinical assessment suggests a dx of OSA syndrome (OSAS)
      2. When the clinical assessment suggests the diagnosis of congenital central alveolar hypoventilation syndrome or sleep related hypoventilation due to neuromuscular disorders or chest wall deformities.
   3. Task force identified certain conditions associated with elevated prevalence of sleep related disordered breathing including OSAS – this list included Chiari malformation and MM
   4. Abbreviated PSG is not recommended for the evaluation of OSAS in children
   5. Clinical evaluation alone does not have sufficient sensitivity or specificity to establish a Dx of OSAS (history, PE, audio or visual recordings standardized questionnaires) Snoring and other nocturnal symptoms did not consistently identify OSAS compared to PSG. Questionnaires had low sensitivity but had better specificity but could not separate primary snoring from OSAS
   6. Obesity is an independent risk factor for having SRDB. SRDB is an independent risk factor for hypertension
   b. The gold-standard investigation for identification of SDB is overnight observed PSG. This involves measurements of respiratory variables – carbon-dioxide levels, oxygen saturation, sleep state – and electromyogram recordings of respiratory muscles, including the diaphragm and intercostal muscles

3. **Testing for SDB in Children with NTD**
   a. One article proposes that all children with CMII should be screened / tested at regular intervals using PSG to detect SDB as early as possible. (Peds Int)
      1. Better identify children at risk
      2. Guide the decision process on the need for surgical intervention
      3. ID children at risk for post-op respiratory complications
   b. Have looked at pneumograms and carbon dioxide challenges to evaluate the predictability of AC deformity or brain stem dysfunction in affected infants. These 2 tests were not predictive of symptoms related to AC deformity. (Peterson Wolraich)

4. **Screening for SDB in Adults**
   a. Critical evidence gap in the use of validated screening questionnaires for OSA in asymptomatic adults (USPSTF)
   b. No screening instrument assessed by the task force has been adequately validated in a primary care setting. (USPSTF).
   c. Found no studies that directly evaluated the effect of screening for OSA on health outcomes (mortality, quality of life, cardiovascular events, cerebrovascular events) (USPSTF).
   d. Some evidence of treatment benefit on intermediate outcomes (AHI, ESS, blood pressure)
e. Excessive daytime sleepiness (EDS) in adult patients with OSA occurs frequently. In adults, EDS is positively correlated with the number of arousals, but not with the respiratory disturbance index or the degree of hypoxemia. Pediatrics 2001 (Objective Sleep Measures)

f. Recent publication by USPSTF (JAMA 2017) reviewed screening for OSA in asymptomatic adults. It concludes that “the current evidence is insufficient to assess the balance of benefits and harms of screening for OSA in asymptomatic adults, including those with previously unrecognized symptoms”

5. Testing for SDB in Adults with NTD

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