Sleep and the Special Needs Child

Shana Hansen, M.D.
Pediatrics
Adolescent Medicine
Sleep Medicine

Disclosure

- Shana Hansen, MD, has no relationships with commercial companies to disclose.
- There will be reference to unlabeled/unapproved uses of drugs or products in my presentation.

Learning Objectives

At the end of this presentation the participant will be able to:

1. Discuss normal sleep and why children with specific chronic illnesses are at higher risk for developing sleep disorders.
2. List and screen for sleep disorders associated with specific neurobehavioral disorders and syndromes.
3. Understand basic management principles for common sleep problems in children with chronic illness.

Normal Sleep

- Sleep is a reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment
- NREM (non-rapid eye movement) sleep is a relatively inactive, yet actively regulating brain in a movable body
  - Stages 1-3
  - Stage 3 = slow wave sleep = recovery sleep
- REM (rapid eye movement) sleep is a highly active brain in a paralyzed body

Factors Modifying Normal Sleep

- Age
  - Infancy
    - Newborns transition from awake to sleep through REM and have a 50 to 60 minute NREM-REM cycle
    - They develop the consolidated sleep cycle by 6 months
  - Childhood
    - Increased slow wave sleep (stage 3) during early childhood with reduction of SWS to adult level by 13 years

Factors Modifying Normal Sleep

“Normal”

Normal circadian sleep rhythm. Sleep urge is greatest at night with a small increase at mid day. Sleep need increases throughout the waking hours and is replenished during sleep.
Factors Modifying Normal Sleep

- Melatonin levels peak in the middle of the night.
- The pineal gland begins producing melatonin in the evening.
- Melatonin levels decline to low daytime amounts.

Prevention of Sleep Disorders

- Primary
  - Avoids development of disease
  - Diet, Exercise, Stress Reduction
- Secondary
  - Early disease detection to prevent progression
  - Screening for those at risk
- Tertiary
  - Reduces morbidity by restoring function and avoiding complications
  - Behavioral/cognitive
  - Medical: HTN, Cardiac Disease, Cerebrovascular Disease
  - Adverse events such as MVAs

Sleep and Chronic Illness

- Need for ongoing screening due to high prevalence
  - 30-80% with sleep disturbance
  - Severity and frequency correlates with type/severity of disability
  - Less likely to improve
- Negatively effects:
  - Physical symptoms (lower seizure threshold)
  - Cognitive, emotional, and social development
  - Daytime behavior
  - May have multiple sleep disorders and heterogeneous etiologies
  - Lack of solid clinical research

Risk Factors in Special Needs Population

- Medical/Neurological Co-morbidities
- Sensory Dysfunction
  - Vision Deficit → Circadian Rhythm
  - Sensitivity to social/environmental cues
  - Decreased
  - Increased: Autism and PDD → Night awakenings
- Daytime Behavioral Problems
- Cognitive Impairment
- Co-Morbid Psychiatric Disorders
- Age
  - Younger are more likely to have sleep issues

Risk Factors in Special Needs Population

- Parenting Related Variables
  - Difficulty with Limit Setting
  - High Levels of Family Stress (Expressed Emotion)
  - Expectations regarding sleep
- Pain
- Adverse effects of medication
  - Commonly used in this patient population
  - May further disturb sleep and alter sleep patterns
  - Environment
Neurodevelopmental Disabilities
- Etiology is varied
  - HIE, CNS malformation, trauma, infection, metabolic, genetic, degenerative
- Causes of sleep disturbances complex
  - Severity/location
  - Associated sensory loss
  - Pain
  - Environment
  - Parenting

Autism
- High incidence of sleep disturbances
  - 40-80% estimated
- Study of 146 autistic kids: parent questionnaire
- Bedtime resistance-56%
- Insomnia-initiation and maintenance-54%
- Parasomnias-53%
- SDB-25%
- Difficulty waking up in am-45%
- Daytime sleepiness-31%
- More severe autism → more severe sleep issues
- Sleep problems → worsened daytime behaviors, social skills

Autism
Etiology of sleep problems?
- Altered circadian rhythms
  - Clock gene anomalies
  - Early morning awakenings
  - Poor sleep maintenance
  - Abnormal melatonin release
  - Supplementation benefits seen in small studies
  - Primary arousal dysfunction
    - May be associated with co-morbid anxiety and O-C symptoms

Autism
Managing sleep issues
- Depakote in those with co-morbid epilepsy
- Melatonin
- Other meds?
- Bright light
- Avoidance of stimulating meds
- Behavioral therapy
  - Lower response rate
  - Identified as the highest priority in terms of clinical trials for sleep medication*

ADHD and sleep
- Many with parent-reported sleep problems: 25-50%
  - Onset, night awakenings, restless, nightmares, sleepwalking, enuresis, early awakening, sleeping less, sleeping more, daytime sleepiness
  - Multifactorial/directional
  - Sleep disorders are associated with inattention and hyperactivity → mistaken for ADHD
  - Symptoms resolve after T/A
  - Symptoms overlap
  - Important to screen for sleep issues

ADHD and sleep
- Hyperactivity
  - Inattention
  - Poor organization
  - Impulsivity
  - Disruptive Behavior
- Disrupted sleep
  - Bedtime resistance
  - Poor limit setting
  - Poor sleep hygiene
  - Insufficient Sleep
ADHD and sleep

Objective findings
- PSG findings: inconsistent
  - Increased movement
  - Sleep onset latency?
  - Total sleep time?
  - Sleep stages unchanged
  - Increased intra-individual day-to-day variability
- Recent studies:
  - Decreased TST and sleep efficiency
  - Increased arousals and sleep fragmentation
  - Increased sleep onset latency

Recent studies: Decreased TST and sleep efficiency, increased arousals and sleep fragmentation. Sleep inertia and increased daytime sleepiness. Intrinsic dysregulation of arousal? Some studies have failed to associate sleepiness with poor sleep quality/quantity, specific subtype?

ADHD and sleep

Subtype
- ADHD-C vs ADHD-I vs controls
- ADHD-I
  - Fewer sleep problems than ADHD-C, same as controls
  - Better sleep efficiency, less fragmented sleep
  - Greater daytime sleepiness
  - Global physiologic ’underarousal’?
- ADHC-C
  - Slept less
  - Increased movement during sleep


ADHD and sleep

Severity
- Parental report of severity of sleep problems correlates with ADHD symptoms
  - Supports hypothesis that poor sleep negatively affects daytime functioning
  - Does not mean sleep problems are primary cause of ADHD symptoms
- Sleep problems and ADHD likely have common neurophysiologic etiology

AdHD and sleep disordered breathing

Retrospective study 3-16 yr with ADHD
- 24% OSA, 24% upper airway resistance syndrome
- More likely to be obese
- Did they all really have ADHD?
- 1980s
  - ADHD kids found to have OSA; improved after treated
  - Small study: 12 SDB, 11 snorers, 10 control
  - Parental scales and performance test improved after T/A in SDB, no change in other group


ADHD and sleep disordered breathing

- OSA leads to mood, behavior, memory, sleepiness
- Is OSA an independent risk factor for ADHD?
  - Inconsistent data
  - Likely co-exist
  - SCREEN for OSA when assessing for ADHD
ADHD and Restless Leg Syndrome/Periodic Limb Movement Disorder

- PLMS
  - 117/129 kids referred to sleep clinic/confirmed to have PLMS also met criteria for ADHD
  - Hyperactivity associated with RLS/PLMS
  - 866 subjects: 13% overall had high hyperactivity indices
    - 8% of those with ‘restless legs in bed’
    - 12% of those without restless legs
    - OR of PLMS was 1.6
    - Small study showed improvement in behavior after RLS treatment

Further studies on PLMD and RLS in children with ADHD. Mov Disord 1999;14:1000-1007

Do Sleep Disorders Cause Cognitive and Behavioral Morbidity?

- Evidence suggests they may contribute
  - ‘Combined OR for neurobehavioral ‘problems’ in SDB = 3
  - NO RCT to support this
  - Lack of proof that a substantial % of kids with neurobehavioral deficits have undiagnosed sleep disorders
  - No direct association between apnea severity and hyperactivity
  - Studies linking SDB with poor school performance have been correlational and have confounders ($)


ADHD and sleep Medications: Risk vs Benefit

- Stimulants
  - Sleep onset latency increased
  - Total sleep time and sleep efficiency decreased
  - Subjective increase in sleep problems
  - ‘medicated children may have more severe ADHD’
  - Recent study which controlled for severity
    - No change in parent report, arousals, early awakening, TST
    - Sleep onset latency was increased
  - Extended-release
    - 12% report insomnia


ADHD and sleep Medications: Risk vs Benefit

- Methylphenidate in afternoon
  - Decreased movement, increased sleep quality and consolidation (44)
  - Different forms, doses, schedules
  - Co-morbidities
  - Most studies use subjective measures
  - Treat side effect with more meds?


ADHD and sleep Treatment

- Melatonin
  - Improved sleep-onset latency and TST (3-6 mg)
  - Behavioral interventions
  - Many other meds tried
    - Clonidine, trazodone, TCAs, diphenhydramine.....

Epilepsy

- Onset of sleep can trigger inter-ictal spikes
  - May be the only abnormality on EEG in new onset dz
- Sleep deprivation triggers increased inter-ictal epileptiform discharges
- Prolonged seizure activity interferes with neuronal processing and learning
- Frequent seizures ➜ sleep fragmentation ➜ sleepiness
- Sleep disorders affect seizure control
  - Treating OSA improves it
Childhood sleep-related epilepsy syndromes

- Nocturnal frontal lobe epilepsy
  - Hypermotor behaviors occur randomly during sleep
  - 20-30 sec
- Benign rolandic epilepsy
  - Seizures with drooling, aphasia, facial twitching
  - Centrotemporal spikes on PSG
  - AD, onset 5-14 yrs, normal child, good prognosis
- Juvenile myoclonic epilepsy
  - Myoclonic jerks and generalized tonic-clonic seizures upon morning wakening
  - AD, onset 12-18 yrs, normal child, life-long disorder

Landau-Kleffner Syndrome

- Regression in language function (auditory verbal agnosia)
- Continuous epileptiform activity during REM and NREM Sleep

Benign Rolandic Epilepsy

- Seizures with drooling, aphasia, facial twitching
- Centrotemporal spikes on PSG
- AD, onset 5-14 yrs, normal child, good prognosis

Juvenile Myoclonic Epilepsy

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Chiari Malformation

- Chiari Type I
  - Descent of cerebellar tonsils below foramen magnum
  - No hydrocephalus and normal 4th ventricle
  - Incidental MRI finding
  - HA, dizziness, nystagmus, VCP
  - Rare central and obstructive apnea
  - AD transmission
  - Symptomatic at birth or short after, few late-onset
  - Daytime respiratory function may be normal initially
  - Hypoventilation, decreased RR, hypercarbia, hypoxia
  - Pulmonary hypertension, cyanosis
  - Mortality at young age common

Neuromuscular Disorders

- Spinal muscular atrophy, Duchenne MD, Myotonic MD, congenital nonprogressive myopathies
  - 75% have sleep disordered breathing
  - Weak intercostal, diaphragm, and upper airway muscles
  - Hypoventilation
    - Repeated hypoxia
    - Retained CO2
  - OSA
  - Worsens during REM
  - Nocturnal SDB proceeds daytime respiratory failure
  - CPAP, BiPAP, tracheostomy

Congenital Central Hypoventilation Syndrome

- Defective autonomic control of breathing
  - Abnormal output from respiratory center in brainstem
  - Insufficient ventilatory effort
  - AD transmission
  - Symptomatic at birth or short after, few late-onset
  - Daytime respiratory function may be normal initially
  - Hypoventilation, decreased RR, hypercarbia, hypoxia
  - Pulmonary hypertension, cyanosis
  - Mortality at young age common
**Congenital Central Hypoventilation Syndrome**
- Associated with:
  - Hirschprung’s disease - 20%
  - Ganglioglioma - 5%
  - Neuroblastoma - 10%
- Secondary causes:
  - Brainstem malformations
  - Head injuries
  - Poliomyelitis
  - Arnold Chiari type II
  - Mitochondrial disorders

**Cerebral Palsy**
- Static insult to the developing CNS
- Muscle tone
- Resting posture
- Muscle coordination
- Joint functioning
- Sleep disordered breathing very common
- NM incoordination
- Craniofacial abnormalities
- Adenotonsillar hypertrophy
- Immobility

**Cerebral Palsy**
- Daytime irritability
- Nocturnal hypoxia
- Fragmented sleep
- If OSA is treated with CPAP or T/A, improved:
  - Sleep consolidation
  - Daytime functioning
  - Caregiver concern

**Cerebral Palsy - Co-morbidities**
- Epilepsy
- Increased sleep fragmentation, daytime symptoms
- Dilantin - increased adenotonsillar hypertrophy risk
- Severe perinatal brain injury
- Visual impairments
- Irregular sleep/wake cycles
- Disorganized, undifferentiated sleep stages
- Myelomeningocele
- OSA, hypoventilation
- Arousal deficits to normal respiratory stimuli

**Craniofacial anomalies**
- Upper airway skeletal and muscular development and neuromuscular coordination determine patency and function of upper airway
- Abnormal development/obstruction can occur at many sites
- Genetic
- Acquired
  - Intrauterine compression
  - Trauma
  - Nasal allergies
  - Deviated septum
  - Post-op cleft palate repair
  - Macroglossia due to storage dz
Craniofacial anomalies

Chooanal atresia stenosis

Maxillary hypoplasia

CHARGE
Crouzon, Apert, Stickler, Pfeiffer
Down Syndrome
Achondroplasia

Mandibular hypoplasia

Oronasopharyngeal tissue hypotrophy

Treacher Collins, Pierre Robin,
Nager, Goldenhar, Craniosynostosis

Beckwith-Wiedemann

Achondroplasia

- Most common disorder with disproportionate short stature
  - Normal trunk length,
    Underdeveloped bones that ossify in cartilage → narrow foramen magnum, Short Limbs, Macrocephaly

- Infant Sleep Issues:
  - Central Sleep Apnea with SIDS
  - Though to be related to stenosis of foramen magnum
  - Restrictive Lung Disease
  - Desat during feeding

- Child-Adult Sleep Issue: SRBD
  - Midface Hypoplasia
  - Tonsilar/Adenoid Hypertrophy

Down Syndrome

- OSA (may be as high as 50%)
  - Macroglossia, Midface Hypoplasia, Hypotonia
  - May have co-existing obesity
  - Chronic Hyperventilation
  - Hypotonic intercostal and diaphragmatic muscles
  - CO2 retention
  - Central Sleep Apnea

- May have residual SDB after T/A
- Abnormal Sleep Architecture
  - Decreased sleep efficiency
  - Increased arousals
  - Suppression of both SWS and REM Sleep

Prader-Willi Syndrome

- Congential Hypotonia, FTT, Hypogonadism, Cognitive Dysfunction, Obesity
- Microdeletion of paternally contributed region of chromosome 15q11.2-q13
- 50% have excessive daytime sleepiness

- Hypothalamic Dysfunction
  - Low Level of GH, Hypocretin – ‘wake’ NT
  - Early childhood: increased appetite → hyperphagia → obesity
  - Elevated ghrelin levels

- Ventilatory Abnormalities
  - Hypoventilation
  - OSA
  - Central apneas

- OSA (and Sudden Death) associated with Growth Hormone Rx?

Sickle Cell

- High stroke risk (25% SS, 10% SC dz by 45 yr)
- Nocturnal hypoxia common (40%)
- Sickling → vaso-occlusion
- OSA exacerbates hypoxia
- Prevalence in SS unknown (one study 36%)
- 15/18 patients had reduced nocturnal hypoxic events after T/A
- Increased sickle cell crisis
- Risk for more complications after T/A
- Fever, atelectasis, pneumonia, sickle crisis
Management Considerations

- Sleep Hygiene
- Behavioral
- Pharmacological
- Light

Sleep Hygiene

- Consistent Scheduling
- Structured Bedtime Routine
  - Specific and Predictable
  - Positive Reinforcement
  - Expectations Communicated and Consistently Enforced
- May need transitional objects
- Avoid daytime sleeping

Behavioral Management

- Similar techniques as with other children
- Unmodified Extinction or extinction with parent present
- Bedtime Fading
  - Set bedtime to current sleep onset time
  - Gradually advance (fade) to desired bedtime
- Insufficient evidence to recommend a single therapy over another

Pharmacologic

- Often needed in combination with behavioral intervention
- Potential Pitfalls of Hypnotics in this population
  - Unpredictable side-effects
  - Development of tolerance
  - Paradoxical Effects
  - Withdrawal Effects
  - Rebound Sleep Onset Delay on D/C
- Melatonin: Best studied Rx in this population
  - Improvements in sleep onset, night awakenings, early awakenings, and efficiency in variety of disorders
  - Low report of side effects

Melatonin

- Secreted by pineal gland
- Works best for delayed phase
  - Children with CNS pathology and insomnia*
  - Decreased SOL 63 mins
  - Increased TST 46 mins

- Delayed phase sleep disorder*
  - Dosage: 0.5-1 mg QHS; many studies use 3-5 mg
  - 5-6 pm
  - Decreased SOL slightly (16 min)
  - Increased TST (28 min)
- Best dose and time not known
  - 3-5 mg 1 hr before bed for initiation insomnia
- ADHD
  - Decreased SOL and increased TST **
  - No change in ADHD symptoms, may improve mood


Melatonin

- Neurodevelopmental disabilities-RCT crossover trial *
  - Sleep onset latency decreased by 30 mins
  - Self reported sleep efficiency improved
  - Reduced family stress
- Autism-RCT placebo control trial
  - SOL decreased 28 mins, TST increased 21 mins


Antihistamines

- Diphenhydramine
- Doxylamine
- Hydroxyzine

- Efficacy questionable
- Side effects: dry mouth, urinary retention, blurred vision, dizziness, sedation

Trazodone

- Most commonly prescribed agent for treating insomnia across all classes of medications
- Used at lower doses for insomnia than depression (0.5-2 mg/kg/day; 25-100 mg)
- Lack of sound research to support its use
- Major side effects: sedation, dizziness, dry mouth, orthostatic hypotension, priapism (rare)

Alpha Agonists

- Clonidine (0.05-0.4 mg/day)
- Guanfacine (0.5-4 mg/day)

- Commonly used in ADHD/devo patients with sleep onset insomnia
- Little/no evidence to support efficacy and safety
- SE: anti-cholinergic, irritability, dysphoria, rebound hypotension

The Tricyclics

- Amitriptyline (0.25 mg/kg/day-1 mg/kg/day)
- Doxepin (3-6 mg/day)

- Used at much lower doses for insomnia than depression
- Side effects: dry mouth, urinary retention, dizziness, daytime sedation

Mirtazapine

- Noradrenergic, specific serotonergic antidepressant
- 15-45 mg (adult dosing)

- Associated with weight gain, increased appetite, daytime sedation and dizziness
Antipsychotics
- Typically used at doses much lower than those for treating psychosis
- Very sedating
- Weight gain, increased risk for diabetes, high blood pressure, restless leg syndrome, muscle spasm or Parkinson-like symptoms

FDA Indications
Adults
- Sleep onset only:
  - Zolpidem
  - Zaleplon
  - Remeron
- Sleep onset and sleep maintenance:
  - Zolpidem ER
  - Eszopiclone
  - Doxepin

Take Home Points: Choosing a med
- Symptom pattern
- Treatment goals → Realistic!
- Patient preference
- Past treatment
- Co-morbid conditions → OSA?
- Other meds/drugs
- Side effects

Take Home Points: Choosing a med
- Melatonin
- Alpha-agonists
- SHORT-TERM treatment (2-4 weeks)
  - Non-Benzos
  - Ramelteon
  - Trazodone, TCAs, Mirtazapine
  - OTC (Benadryl) - not recommended

Take Home Points: Choosing a med
- Frequency
  - Nightly
  - Scheduled intermittent (2-5 nights/week)
    - May prevent tolerance, dependence, abuse
- Duration
  - Prior 2005: labeling recommended short-term
  - Now: no mention/guidelines
  - Recent RTC of non-Benzos for 6 months show continued efficacy and low complication rate

Take Home Points: How long do you treat?
- Chronic meds for severe/refractory or those with chronic co-morbid conditions
- Nightly or intermittent
Take Home Points

- Discontinuation
  - Rebound insomnia (1-3 days)
  - Withdrawal
  - Recurrence of insomnia
  - Taper hypnotics every 2-3 nights by smallest increment possible

Light Therapy

- Appropriate timing is key
  - Different sleep lengths/times in children
  - Morning light for delayed phase
  - Daytime bright light for irregular sleep/wake

- Children prone to circadian rhythm disturbances especially sensitive to circadian desynchronization
  - Jet Lag
  - Daylight Savings Time

Conclusions

- Children with special needs have complex sleep problems
- Treatments are disease and patient specific
- Pediatric sleep disorders is an area where much research needs to be done

Questions?

References

- Further studies on PLMD and RLS in children with ADHD. Mov Disord 1999;14:1000-1007.