Sleep Issues in Children with Autism Spectrum Disorders Treatment

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April 21, 2016

Conflict of Interest

☐ Mead Johnson provided ferrous sulfate for a government funded trial of iron to treat insomnia in children with ASD.
☐ We will discuss non-evidence based treatments.
Learning Objectives

☐ At the end of this session, participants will be able to:
  ▪ Discuss sleep concerns in children with ASD.
  ▪ Consider medical and behavioral causes of sleep difficulties in children with ASD.
  ▪ Discuss behavior interventions and strategies for sleep difficulties in children with ASD.
  ▪ Discuss the role of melatonin and medications to treat sleep concerns in children with ASD.

Robert

☐ 5-year-old with ASD and fluent speech
☐ Mother has concerns about depression due to new onset irritable behavior and poor sleep
☐ Falls asleep easily but waking 2-3 times/night.
☐ Family recently moved
☐ Bedtime routine the same, settles more quickly because now has his own room
☐ Mother no longer working outside the home
☐ New school has a better student/teacher ratio.
Robert

☐ Differential:
  ■ Distress due to changes related to the family’s move/change in routine
  ■ Depression due to move
  ■ Anxiety now that he is sleeping alone in his own room
☐ Next Questions?

Robert

☐ Robert has constipation which developed shortly after the move. Since mother was no longer working outside the home, she wanted to work on toilet training
☐ Robert did well with voiding but refused to have a bowel movement in the toilet. His stools are hard and difficult to pass. He is now withholding
Robert

- Disposition: Robert’s mother allowed him to have a diaper every afternoon after preschool and his behavioral therapist implemented a desensitization procedure for sitting on the toilet. Additionally, a stool softener was initiated. Once Robert’s constipation resolved, his sleep improved significantly as did his irritability.

Behavioral Impact of Poor Sleep

- All Children
  - Attention
  - Irritability
- ASD
  - Self injury
  - Repetitive Behaviors
  - Aggression
- Parents
  - Greater Stress
Physical Impact of Poor Sleep

- Neural Plasticity  (Picchioni 2014)
- Memory Consolidation
- Obesity  (Hill 2015, Dreyer 2015)
- Cardio-metabolic  (Quist 2015)
  - Cortisol
  - Insulin resistance
  - Sympathetic tone
- Immune Function  (Careaga, 2015)

Prevalence of Sleep Disorders in Children

- Autism Spectrum Disorders: 50-80%
- Developmental Disabilities: 30-80%
- Typical Development:
  - Ages 1-5 years: 25-30%
  - School age: 10-12%
- Objective measures (conflicting data)
  - Meta-analysis (Elrod 2015)
Sleep 101: Sleep Cycles

- Circadian Rhythms
- Ultradian Rhythms
- Wake/sleep cycle
Sleep 101: Circadian Disorders

- We entrain a 24 hour sleep/wake cycle with environmental cues ("zeitgebers")
  - Light/Dark
  - Social Interaction
  - Noise
  - Ambient Temperature
  - Core Body Temperature
  - Hunger/Pain
  - Hormones/Melatonin

Biological Differences
Melatonin Pathways

1. Tryptophan
2. Serotonin
3. N-acetylserotonin
4. Melatonin
5. 6-sulfoxymelatonin

AA-NAT
ASMT
CYP1A2
Biological Differences

Melatonin

Behavioral/Sensory Differences

- **Behavioral:** *Sleep is the Ultimate Transition!*
- **Arousal Dysregulation:** Difficulty Calming (Mazurek, 2013)
- **Lack of entrainment:** Social Cues, Communication
Medical Conditions may affect Sleep

- **Gastrointestinal**: Reflux/Constipation/Pain
- **Seizures**
- **Snoring/Disordered Breathing**: Allergies/Congestion
- **Nighttime Coughing**: Asthma/Sinusitis
- **Pain/Itching**: Dental/Hunger/Eczema
- **Nutrition**: Iron intake/Restless Sleep
- **Medication**: Side effects

Gastrointestinal

- Association between GI and Sleep issues in AGRE, Simons Simplex, and AS-ATN
- Constipation
- GERD
- Eosinophilic Esophagitis

(Aldinger, 2015, Hollway, 2013)
Sleep Disordered Breathing

- OSA in 1-5% of children
- Criteria for workup of OSA includes daytime dysfunction
- Risk Factors
  - Craniofacial abnormalities
  - Adeno/tonsillar hypertrophy (peak ages are 2 to 6)
  - Nasal obstruction (allergies)

Lumeng & Chervin, 2008; Marcus et al., 2012

Polysomnography

- Preparation is the Key
  - Tours of Sleep Lab
  - Visual Schedules
CPAP

Desensitization is the Key

Restless Leg Syndrome/Periodic Limb Movement Disorder

- RLS: Uncomfortable sensation in legs, urge to move, worse at night, 2% of children
- PLMD: periodic extension of the toe and flexion of the ankle and knee
- PLMI elevated in 0-38%
  - 35% ASD, 44% DD, 17% TYP

(Lane 2015)
Psychiatric Conditions

- Anxiety and ADHD common in ASD
- Depression/Mood
- DSM-5 recommends diagnosis and management of sleep issues separate from other diagnoses

Insomnia Practice Pathway

All children with autism spectrum disorder present for evaluation

Screen child for insomnia

Yes

Assess for medical contributors affecting insomnia

Medical Contributors Present

Yes

A. Initiate evaluation/treatment for medical contributors
   and/or
   B. Consultation/referral to appropriate sub-specialist for medical contributors

No

Assess if family able and willing to use educational approach

Initiate Sleep Education Program (Toolkit)

Yes

A. Plan for toolkit follow-up to reassess insomnia
   or
   B. Consider consultation to sleep specialist if family unwilling or unable to use educational approach

No

Return in 1 year for reassessment and deep screening follow up (re-enter algorithm at Box 2 at time of 1 year reassessment)

Insomnia Resolved?

Yes

No

A. Consider sleep medication
   and/or
   B. Consultation/referral to sleep specialist for insomnia

Arrange timely follow up

Insomnia resolved?

Yes

No
Sleep Education

- Effective for children with DD and ASD
  - Sleep
  - Daytime behavior
  - Parenting sense of competence
- Modifications and Creativity are key!

(Jan 2008; Moss 2014; Malow, 2014; Johnson 2013; Vriend, 2011)

AIR-P Sleep Study

- Sleep Education Training:
  - Group intervention with a psychologist x 2
  - 1 hour visit with a trained educator with phone follow up
- Actigraphy before and after intervention
- Sleep latency significantly reduced

Malow et al, (2014)
Daytime

- Caffeine
- Light
- Exercise
- Bedroom use
- Naps

Sensory Considerations

- Temperature
- Texture
- Sound
- Light
Visual Supports

Autism Speaks Toolkits

Timing

- Sleep needs for children with ASD
- When is bedtime?
- The forbidden zone
Strategies for Bedtime Resistance

- Extinction
- Rocking chair method
- Rewards
- Bedtime Pass

Safety Issues

- Child-proof doors and cabinets
- Baby monitor
- Alarm or bell on child’s door
- Medical Bed

Resources

Autism Speaks Toolkits available at www.autismspeaks.org
Medications

- No hypnotic adequately studied in children
- **Everything “Off Label”**
- Risk vs. Benefit
- Behavioral intervention
  - Try first if possible or along with meds

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Melatonin

- Meta-analysis
  - sleep latency: mean 34 min (p<0.001)
  - sleep time: mean 50 min (p<0.001)
  - night waking (p<0.05)
- Open Label Trial
  - Most responded to 1 or 3 mg
  - Maintained improvement
  - Well tolerated

Wiebe Braam (2009), Malow (2011)
Clonidine

- Older retrospective chart reviews
- Central $\alpha_2$ adrenergic receptor agonist, $\downarrow$ release of NE
- Used for sleep onset insomnia
- May $\uparrow$ SWS, $\uparrow$ REM
- Overdose is a concern

Low Iron Stores/Low Ferritin

- Associated with RLS and PLMD (Dosman et al, 2007)
- $\geq 8\%$ with ASD (Reynolds, 2012)
- Associated with ADHD (Konofal 2008)
- Ferritin levels & restless sleep responded to iron treatment
  - Open label/subjective report
  - ASD (Dosman 2007)
## Gabapentin

- Designed as a precursor of GABA: mechanism unknown.
- Retrospective chart review/23 children:
  - Most with DD
  - 78% reported improvement at follow up
  - 6 had side effects
    - 5 with agitation and difficulty falling asleep
    - 1 with agitated awakenings
- Few drug interactions.

## Antihistamines

- Reduce sleep onset latency and night waking
- CNS H1 subtype histamine receptor
- Minimal effect on sleep architecture
- May see side effects
  - Daytime drowsiness
  - Appetite loss, nausea, vomiting, constipation
  - Anticholinergic side effects (dry mouth, urinary retention)
  - Paradoxical behavioral excitation
Herbal Supplements

- None tested in children
- Valerian root: efficacious in adults
- Lavender: concerns about precocious puberty in children
- Lemon balm, chamomile, and passion flower: not efficacious in adults
- Significant safety concerns with Kava-Kava (hepatitis) and tryptophan (myalgia)

Challenges/Next Steps

- Etiology
  - Biological Differences/Pharmacogenomics
- Measurement: Screening/Outcomes
  - Subjective vs. Objective
  - Measurement of Severity
  - Overall Improvement
- Clinical Trials
  - Placebo
  - Complexity: Meds, Co-occurring conditions, Environmental changes
Thank You

- **Patients and Families**
  - University of Colorado Denver
    - Terry Katz, PhD, Ann Halbower, MD
  - Vanderbilt University
    - Beth Malow, MD, Karen Adkins, RN
  - University of Rochester
    - Susan Hyman, MD, Heidi Connolly, MD
  - SEED
    - Susan Levy, MD, Susan Hepburn, PhD
    - Norbert Soke, MD, PhD
  - CCTSI/CTRC