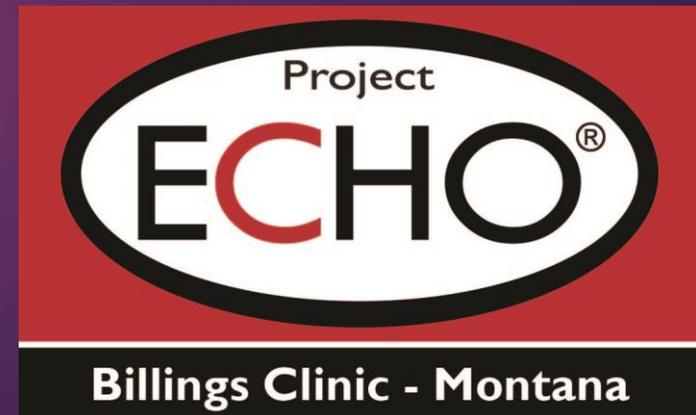


# Medications for Insomnia in Children

PROJECT ECHO BILLINGS CLINIC

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# Take-Home Points

- ▶ - most youth with sleep disorders improve with proper treatment.
- ▶ - Sedation is not the equivalent of normal, refreshing sleep.
- ▶ - Behavioral treatment is first line. Pharmacotherapy is second line, and combination treatment may be needed.
- ▶ - Clonidine is commonly prescribed despite the lack of RCT's in youth and there is no such indication in adults either.
- ▶ - Watch for paradoxical drug reactions related to incorrect dosing or timing of administration.

# Sleep-related Behaviors

- ▶ - A lot of sleep is behavioral. Children learn how to sleep from their families, including key associations with sleep.
- ▶ - If child associates activity or attention from parents with sleep, then awakenings during the night may require lots of attention from parents. This adds to the family burden related to youth insomnia.

# Associated Variables

- ▶ - Need to consider cultural background of the family and sleep-related expectations. What was sleep and sleep-related behavior like for parents and grandparents?
- ▶ - 2 separate homes? Will interventions be done in both homes?
- ▶ - Do parents have sleep problems, making them more vulnerable to complaints related to youth sleep disruption?

# National Data

- ▶ National Ambulatory Medical Care Survey (NAMCS)
- ▶ - 19 million patient visits
- ▶ - 81% of children and 48% of adults received sleep meds.
- ▶ - In children, antihistamines and clonidine were most commonly rx'd.
- ▶ - Very concerning uptick in using antipsychotics, especially quetiapine, for sleep.

# Sedation vs. Sleep

- ▶ - Key principle in sleep pharmacology is to NOT equate sedation with good sleep. ETOH is a perfect example.
- ▶ - There could be an overreliance on the effects of medication without good understanding of the cause of the sleep problems.

# Paradoxical Reactions?

- ▶ Pedi Sleep Medication Reactions
  - ▶ - "He did not sleep at all!"
  - ▶ - "She became hyper!"
  - ▶ - Insufficient dose or incorrect timing is more likely a problem.
  - ▶ - Circadian surge in the evening: if meds given too early, has to counter the surge and child could become disinhibited, behave inappropriately, have scary hypnagogic hallucinations.
  - ▶ - Give hypnotics on an empty stomach to boost absorption.

# Dosing

- ▶ Dosing
- ▶ - Don't underdose! Youth have faster hepatic metabolism, leading to faster elimination.
- ▶ - Low dose may alter behavior, but not help the child fall asleep. Could lead to what appears to be "paradoxic" reactions.
  
- ▶ Insomnia
- ▶ - Treatment-seeking is led by parents. Need to ask what their sleep was like before having kids.
- ▶ - If parents had impaired sleep, they may struggle to handle TYPICAL sleep disruptions in children.
- ▶ - Medications should be considered second-line and adjunctive.

# Diphenhydramine

- ▶ Antihistamines
- ▶ - Diphenhydramine is a competitive H1 histamine receptor blocker, rapidly absorbed. Peak blood and tissue levels happen within 2hrs of ingestion.
- ▶ - 4-6 hrs of activity with normal dosing. Half-life in children is 5.4 hrs (sd 1.8hrs).
- ▶ - A study in infants showed it was no better than placebo and had to be stopped.
- ▶ - Adverse effects: at therapeutic doses, it's impaired consciousness; in overdose, it's anticholinergic effects (fever, mydriasis, blurry vision, dry mouth, constipation, urinary retention, tachycardia, dystonia, confusion).

# Melatonin

- ▶ Melatonin
- ▶ - The physiologic increase in nocturnal blood melatonin concentration (10x to 15x increase) seems to happen 1-2hrs before bedtime
- ▶ - Circadian rhythm of melatonin develops b/w 2nd and 3rd month of life; neonates and infants depend on mom's rhythm through milk
- ▶ - Best time to give melatonin is around 5-6hrs before dim light melatonin onset (DLMO), or about 9-10hrs after awakening
- ▶ - on average, melatonin shortens sleep latency by about 16min and increase sleep time by 28min

# More Melatonin...

- ▶ - usual dose in trials is 5mg; melatonin AND behavioral changes can lead to improvement in sleep structure over time
- ▶ - National Sleep Foundation has warned against using melatonin in patients with immune disorders, lymphoproliferative disorders, corticosteroids, immunosuppressants; melatonin can enhance immune function
- ▶ - melatonin can be most effective in children struggling with circadian factors, including delayed sleep phase syndrome and blind children;
- ▶ - a double-blind PBO controlled trial of 5mg melatonin in children 6-12 yo with sleep-onset insomnia showed 63min decrease in sleep latency and increased sleep time of 41 min

# ...and Melatonin

- ▶ - long term trial of melatonin is well-tolerated; survey of parents who have children with ADHD and chronic sleep-onset insomnia, treated for 3.7yrs, reported no serious adverse events or treatment related co-morbidities

# Ramelteon and Clonidine

- ▶ Ramelteon

- ▶ - consider using in adolescents with sleep-onset insomnia or delayed sleep phase syndrome
- ▶ - melatonin type 1 and type 2 receptor agonist approved for patients 18+ yo
- ▶ - case reports in younger children have demonstrated some success

- ▶ Clonidine

- ▶ - no RCTs for children with insomnia
- ▶ - central  $\alpha_2$ -adrenergic receptor agonist
- ▶ - half-life is 6-24hrs
- ▶ - onset of action is within 1hr, peak effects at 2-4hrs
- ▶ - s/e: hypotension, bradycardia, irritability, anticholinergic effects, REM suppression
- ▶ - rebound HTN and REM rebound with rapid discontinuation

# Non-Benzo Hypnotics

- ▶ Zolpidem, zaleplon, eszopiclone
- ▶ - non-benzo hypnotics
- ▶ - off-label in children, so no dosing guidelines
- ▶ - preserve overall sleep architecture
- ▶ - not known to have rebound insomnia when these meds are stopped
- ▶ - should be given as child is being put to bed; don't give and then wait to take effect

# Non-Benzo Hypnotics

- ▶ - Zaleplon only helps with sleep onset, has half-life of 1 hr in adults
- ▶ - zolpidem can also help with some maintenance, has half-life of 2.5hrs
- ▶ - open label study in children with insomnia showed zolpidem was well-tolerated, and led to recommended dose of 0.25mg/kg, with max of 20mg
- ▶ - giving children a lower dose is likely to lead to more problems than benefit b/c they are cleared more rapidly in children (zolpidem clearance is 3x higher in children)
- ▶ - eszopiclone has longer half-life at 6hrs; no studies done in children