Sleep Disorders in Palliative Care

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Disclosures

• None relevant to this topic

Prescribing

• Many off-label uses to be described, marked in many places, but read your med insert
• Black box warnings with opioids and BZ
• Black box warnings on suicide risk with AD
• Rare head-to-head RCT
Objectives

• Accurately screen and assess for sleep disorders in hospice and palliative care settings
• Identify common co-existing symptoms with sleep disorders
• Develop a plan for patients implementing both pharmacologic and non-pharmacologic modalities

Classification of Sleep Disorders

• Insomnia
• Sleep-related breathing disorders*
• Central disorders of hypersomnolence
• Circadian rhythm sleep disorders
• Parasomnia
• Sleep-related movement disorders
• Other

*Some unique pediatric diagnoses
Focus for Today

• Insomnia
• Obstructive sleep apnea
• Restless leg syndrome

Insomnia

• Acute
  – <3 months
• Chronic
  – >3 months
  – Not related to sleep restriction

Insomnia

• Advanced cancer and Palliative Care Unit
  – 61% consistent sleep disturbances, 47% mod-sev
  – Associated with anxiety and depression
• Pulmonary disease – more than 50%
• Heart failure – more than 30%
• Chronic pain – higher than general population

Mercadante, 2015; Renom-Guiteras, 2014
Insomnia – Risk Factors

- Previous insomnia
- Family history of insomnia
- Poor self-rated health
- Pain
- Depression
- Anxiety
- Serious illness

Insomnia - Assessment

- Ideal sleep time
- Sleep history
- Sleep initiation & maintenance
- Daytime function and somnolence
- Risk factors and co-morbidities, substance use
- Activity monitors and/or sleep diary
- Neck circumference
- Medication review

Mercadante, 2015; Renom-Guiteras, 2014
Insomnia Causing Medications

• CNS stimulants (caffeine, methylphenidate, amphetamine and modafinil)
• Steroids associated w/ increased wakefulness
• Calcium channel blockers
• SSRI>>SNRI
• Beta antagonists
• Respiratory stimulants (theophylline)

Insomnia and Psychologic Morbidity

• Bidirectional impact
• Can look alike given insomnia, daytime fatigue and difficulty concentrating are 3 of 8 criteria for depression
• Insomnia co-exists in 80% of people with depression
• Also look for PTSD, anxiety

Krystal 2006

Insomnia and QOL

• Impacts QOL
  – Increased fatigue
  – Increased confusion
  – Increased daytime somnolence
  – Increased anxiety
  – Increased depression
• At risk for accidents, work absence, poor health, self-medication
Insomnia and Health

- Losing restorative nature of sleep
- Impacts
  - Cardiac function (increased HTN, CV mortality)
  - Metabolic changes (increased DM)
  - Hormone patterns
  - EEG patterns
  - Psychological function (depression/anxiety)
    - Bidirectional

Li, 2014; Alvaro, 2013

Insomnia - Locations

- ICU – Poor sleep quality increases delirium
- Hospital
  - multiple interruptions for vital signs
  - 0300-0400 lab draws
  - Heavily studied – sleep bundle interventions
  - Real-world follow-through?
- Palliative Care Unit
  - 47% mod-sev insomnia, 79% nocturnal rumination

Mercadante 2015; Renom-Guiteras, 2014

Insomnia – Self-Medication

- Alcohol
  - 28% have tried as a treatment
  - Short-term
    - Increased sleep latency
    - Increased fragmented sleep
    - Increased early morning awakening

Costa 1996
Insomnia – Non-Pharm Treatment

• Nighttime environmental changes
  – Cool temp
  – Well ventilated
  – Low light
  – Limit blue light (computer, tablet, smartphone)
  – No caffeine, no tobacco, no alcohol
  – Add white noise
  – Minimize disruptions (esp in facilities)
  – Timed double void before bed

Stanchina 2005

Insomnia – Non-Pharm Treatment

• Daytime environmental changes
  – Bright natural light (OPEN THE BLINDS!)
  – Moderate physical exercise as tolerated
  – Avoid daytime naps
  – Avoid caffeine, no alcohol, exercise, large meals
  – Add white noise

Insomnia – Non-Pharm Treatment

• Cognitive behavioral therapy
• Mindfulness meditation
• Relaxation techniques

Gong, 2016
Insomnia - Medications

- Special populations
  - Pregnancy – Increase risk of fetal malformations 1st trimester
  - Alcohol consumption – Risk of excessive sedation and respiratory suppression
  - Renal/hepatic disease – Most undergo hepatic and renal clearance. Delay leads to accumulation and excessive sedation.
  - Pulmonary disease or sleep apnea – Respiratory suppressant risk
  - Nighttime decision makers – cause excess sedation/impair decision-making.
  - Older adults – Incr risk of adverse effects, esp older than 75 years

- Antidepressants
  - Mirtazpine (REMERON*)
  - Doxepin (SILENOR)
  - Trazadone (OLEPTRO*)

* off-label for insomnia

- Non-benzodiazepine hypnotics (Z-drugs)
  - Zolpidem (AMBIEN, EDLUR, ZOLPIMIST, INTERMEZZO)
  - Zaleplon (SONATA)
  - Eszopiclone (LUNESTA)
Insomnia - Medications

• **Benzodiazepines**
  – Caution in COPD or respiratory compromise
  – Caution when prescribing with opioids (Black Box warning FDA 2016)
  – Reduce sleep latency, prolong sleep time, reduce REM
  – Short-acting: triazolam
  – Intermediate-acting: estazolam, lorazepam, temazepam
  – Long-acting: flurazepam, quazepam

* off-label for insomnia

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Insomnia - Medications

• **Melatonin**
  – Lack of prospective data
  – Lack of double-blinded RCT
  – Minimal harm
  – May reduce sleep latency
  – May reduce frequent awakenings
  – Dose and quality inconsistencies
  – 0.1-0.3mg before bedtime

* off-label for insomnia
Mean Serum Melatonin after 11:45a

Dollins 1994

OSA - Assessment

- STOP-BANG
- Epworth Sleepiness Scale
- Neck circumference
- Simple and can be done by palliative care
- Also present in pediatrics
  - Form a partnership
  - Desensitization
  - PAP Nap

1. Snoring
   Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
   Yes/No

2. Tired
   Do you often feel tired, foggyhead, or sleepy during daytime?
   Yes/No

3. Observed apnea
   Has anyone observed you stop breathing during your sleep?
   Yes/No

4. Blood pressure
   Do you have or are you treated for high blood pressure?
   Yes/No

5. BMI more than 35 kg/m²?
   Yes/No

6. Age
   Age over 50 yr old?
   Yes/No

7. Neck circumference
   Neck circumference greater than 40 cm?
   Yes/No

Gender
   Gender male?
   Yes/No

High risk of OSA: answering yes to three or more items
Low risk of OSA: answering yes to fewer than three items
Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations?

Use the following scale to choose the most appropriate number:

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No chance</td>
<td>slight chance</td>
<td>moderate chance</td>
<td>high chance</td>
</tr>
<tr>
<td>Sitting and reading</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Sitting inactive, in a public space</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Sitting quietly after a lunch without alcohol</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>As a passenger in a car for an hour without a break</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>In a car, while stopped for a few minutes in traffic</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

0-10 Normal; 10-12 Borderline; 12-24 Abnormal

OSA - Treatment

- BiPAP
- CPAP
- Work with Sleep Disorders clinic or Sleep Medicine specialist
- Significant requirements to get covered by insurance and CMS
- Ask about usage and barriers

OSA - Treatment

- Inspire
  - Monitors your breathing
  - Stimulates the hypoglossal nerve
  - Turn on before bed
  - Available at KU Sleep Disorders Center
Restless Leg Syndrome

- Unpleasant sensations in the legs
  - Itch you can’t scratch, buzzing sensation, tickle that won’t stop, crawling feeling, limb jerking
- Urge to move legs
- Worse at rest
- Worse at night
- Temporary relief with movement

Intl RLS Study Group / NIH Criteria

Allen, 2003

Restless Leg Syndrome

- Incidence: 5-10% (2-4% in pediatric ages)
- Peaks at ages 40-60
- 2:1 female:male ratio
- Commonly seen in:
  - Advanced cancer
  - ESRD/Hemodialysis
  - Parkinson’s
- AKA Wilks-Ekbom disease (WED)

Restless Leg Syndrome

- Primary RLS – cause ?, possibly genetic
- Secondary RLS
  - Iron-deficiency
  - Hyper-/Hypo-thyroidism
  - Medications
    - SSRI, SNRI, neuroleptic, DA-blockers, anti-histamines, z-drugs
  - Habits (nicotine, caffeine, alcohol)
  - Rheumatologic
    - RA, Sjogren’s, Fibromyalgia
  - Multiple sclerosis, Parkinson’s, Spinal cord disorders

Yeh 2012
RLS - Assessment

• Medication review
• Labs: Serum ferritin (<75), TSH, T4, BUN/Cr
• If female: consider pregnancy (usu 3rd tri)
• No need for polysomnography (Choosing Wisely)
• Differential
  – Volitional/semi-volitional movements
  – Akathisia
  – Nocturnal leg cramps
  – Peripheral neuropathy
  – Myoclonic jerks

RLS - Medications

• Supplemental iron* (with Vitamin C)
• Dopamine-agonist (severe RLS)
  – Ropinirole (REQUIP)
  – Pramipexole (MIRAPEX)
  – Rotigotine (NEUPRO)
• Gabapentinoids^ (co-morbid pain, anxiety, insomnia)
  – Gabapentin (HORIZANT, NEURONTIN*, GRALISE*)
  – Pregabalin (LYRICA*)

*aka α2δ calcium-channel ligands * = off-label

RLS - Other Medications

• Minimal efficacy (all off-label) or low evidence
  – Carbidopa/Levodopa (SINEMET) – intermittent RLS
  – Benzodiazepines
    • Clonazepam (KLONOPIN) best studied
  – Opioids
  – Carbamazepine (TEGRETOL)
  – Clonidine
  – Amantadine
  – Magnesium replacement
RLS – Non-Pharmacologic

- Stop caffeine
- Stop tobacco
- Physical exercise
- Relaxation techniques
  - Deep breathing, meditation, yoga
- Massage
- Shorter, more frequent HD

RLS - Pediatrics

- Polysomnography may help rule out PLMD
- Associated with ADHD, anxiety, depression
- Low iron still a factor to consider
- No FDA-approved medications
- Therapy
  - 1st line gabapentin
  - Alternates – benzodiazepines, clonidine, DA-agonists (effective studies but risk of augmentation)

RLS – Relaxis Pad

FDA-approved 2014 – vibratory counterstimulation (costs around $50/month)
Sleep Disorders in Caregivers

- Sleeping with one eye open
- 39% of caregivers at home ESS>11
- Shared sleeping environment
- Highly correlated dyad
- Check in with your caregivers
- Be vigilant for medication sharing

Hearson 2011

Summary

- Look for OSA, depression, anxiety w/insomnia
- Sleep environment and habit changes require collaboration, written materials
- Have your assessment tools ready
- Stress non-pharmacologic options first
- Melatonin – over-dosed?, over-utilized?
- Use side effect profiles to patient advantage
- RLS – HPM meds=bad; add iron, non-pharm

Recommended Reading

- Fast Fact 101: Insomnia – Patient assessment
- Fast Fact 104: Insomnia – Non-pharm tx
- Fast Fact 105: Insomnia – Drug therapies
- Fast Fact 88: Nightmares
- Fast Fact 217: Restless Leg Syndrome
- Choosing Wisely - AASM
References