Insomnia and Sleep Impact on Chronic Disease
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Objectives
• At the end of the presentation the participant will be able to:
  – define insomnia
  – analyze current research demonstrating sleep's impact on chronic disease
  – summarize current best evidence for treatment of insomnia

Disclosures
• none
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Sleep Facts
Interesting Facts about Sleep

- 40% state they did not get enough sleep on workdays
- Less women were getting sleep needs met
- Gap widened for weekends for those with needs met by two hours

Source: [https://sleepfoundation.org/sleep-polls-data/other-polls/2012-bedroom-poll](https://sleepfoundation.org/sleep-polls-data/other-polls/2012-bedroom-poll)

Interesting Facts about Sleep

- Sleep duration decreased by 1.5-2 hours 1960 – 2000
- >30% of adults report <6 hrs/night per night
- 90% of Americans used some type of electronics at least a few nights per week within 1 hr of bedtime

Epidemiology and Risk Factors

- 30% general population have sleep disruption - 10% sx daytime impairment
- Risks
  - Older age
  - African Americans
  - Increased stress
  - Lower income
  - Night shift or major time work shift

Sleep Scales
• Epworth Sleepiness Scale
• Athens Insomnia Scale
• Insomnia Severity Index
• Sleep Disordered Questionnaire
• Insomnia Symptom Questionnaire
• Brief Insomnia Questionnaire
• Pittsburgh Sleep Quality Questionnaire
• STOP/BANG

Chronic Disease and Sleep

Chronic Disease
• Inadequate or poor sleep
  – increase risk of chronic disease
    • increased BP
    • impaired blood glucose
    • increased inflammation
    • change in hormone levels
Chronic Disease

• Poor sleep and Obesity
  • increase in cortisol
  • increase in secretion of insulin
  • lower levels of leptin
  • higher levels of ghrelin

Chronic Disease

• Poor sleep and Diabetes
  • increased risks of Type 2 DM
  • processing of glucose impaired

Chronic Disease

• Poor sleep and Heart Disease
  • increased risk of CHD in women
  • Sleep apnea increases HTN, CVA, CHD and arrhythmias
Chronic Disease

• Poor sleep and Heart Disease
  • sympathetic nervous system
  • Normal sleep – plasma renin activity & sympathovagal balance, blood pressure, renin & aldosterone
  • Sleep disturbance
    • = increase in renin, aldosterone, as well as C-reactive protein, interleukin-6
  • Insomnia link to change in lifestyle may add to HD affect

Chronic Disease

• Poor sleep and Mood Disorders
  • less happiness
  • increased anger and exhaustion

INSOMNIA
Clinical Diagnosis

• ICSD-3 (2014) Chronic Insomnia
  – AKA Chronic, primary, secondary, comorbid, behavioral insomnia of childhood, sleep-onset association disorder, limit-setting sleep disorder
  1. difficulty initiating, maintaining, or waking up too early
  2. despite adequate opportunity
  3. daytime impairment
  4. not better explained by another sleep disorder
  5. Occurs at least 3 times a wk for 3 mos

• ICSD-3 (2014) Short Term Insomnia
  – AKA Acute, adjustment
  1. difficulty initiating, maintaining, or waking up too early
  2. despite adequate opportunity
  3. daytime impairment
  4. not better explained by another sleep disorder
  5. Occurs at less than three months

• ICSD-3 (2014) Other Insomnia
  – AKA none
  – difficulty initiating & maintaining sleep
  – do not meet full criteria of chronic or short-term
  • DSM5
    – complaint of dissatisfaction with sleep quantity or quality
    – sleep disturbance causes clinically significant distress or impairment
    – same timeline as chronic
    – listed under sleep-wake disorders

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Coding Insomnia

- ICSD-3 (2014 update)
  - Chronic insomnia
  - Acute insomnia
  - Other insomnia
- DSM-5
  - Insomnia Disorder
- ICD-10
  - Insomnia, unspecified G47.00
  - Insomnia due to medical condition G47.01

Insomnia Pathophysiology

- increased physiological arousal
  - elevated cortisol, adrenocorticotropic hormone and CRF levels
  - increased frequency EEG activity during NREM sleep
  - Increased SNS activity and HPA axis
- no structural brain pathology

Differential Diagnosis

- Other sleep disorders
  - Sleep apnea
  - Circadian Rhythm Sleep Disorders
  - Movement Disorders
  - Parasomnias
- Comorbid conditions
  - Medications
  - Medical conditions – TREAT both
Evaluation

• Clinical history
  • Structured interview
  • Review of PMH
  • Review of medications
  • Consider use of sleep questionnaires
    • http://www.stopbang.ca=os/a/screening.php
    • VA site Insomnia Severity Index

Insomnia Evaluation

• Sleep log – paper or apps
  – Difficulty falling asleep
  – Difficulty staying asleep
  – Combination
• Consideration of referral for Polysomnography or sleep specialist
Treatment Options

Treatment Goals
- improve
  - sleep quality
  - related daytime impairments

Insomnia Treatment
- Sleep Hygiene
- CBT-I
- Pharmacology
Sleep Hygiene
- Creating a good sleep setting
- Having a calming bedtime routine
- Avoiding naps
- Minimizing nighttime light
- Exercising earlier
- Avoid caffeine late in the day
- Limiting alcohol
- Eating light dinner
- Avoid nicotine in the evening

CBTi
- modifies perpetuating factors to intervene
  - Sleep consolidation
    - consolidated then incrementally increased
  - Stimulus control
    - associations between bed and sleep
  - Sleep hygiene
  - Cognitive therapy
    - identifying and modifying maladaptive thoughts about sleep
  - Relaxation training

CBT-I
- In person
  - Resources
    - https://www.behavioralsleep.org/index.php/united-states-absm-members
- On line
  - www.shutl.me (evidence based program)
  - http://www.cbtforinsomnia.com/
Pharmaceutical Options

Pharmacology
- benzodiazepine receptor agonists
- nonbenzodiazepine receptor agonists
- selective melatonin receptor agonist
- orexin receptor antagonist
- others

Benzodiazepine receptor agonists
- intermediate-acting forms
  - temazepam
  - estazolam
- short-acting forms
  - triazolam (Halcion)

PEARL:
Nonbenzodiazepine Receptor Agonists

- eszopiclone (Lunesta)
- zolpidem (Ambien, Ambien CR, Intermezzo, Zolpimist, Edluar)
- zaleplon (Sonata)

PEARLS:

Selective melatonin receptor agonist

- ramelteon (Rozerem)

PEARLS

Orexin receptor antagonist

- suvorexant (Belsomra)

PEARLS
Others

- Sedating antidepressants
  - only doxepin has evidence – most insomnia endpoints improved – doses 1-6mg (Roth, et al and Krystal, et al 2010)
- Antihistamines
  - most common OTC – significant next day sedation

Others

- Melatonin
  - +/- evidence

- Alternative and herbal medications
  - Valerian root most studied with conflicting results

Others

- Acupressure
- Devices
  - Cerêve Sleep System
    - reduce latency to stage 1 & 2 by cooling forehead
Referrals

• CBTI
• Concern for other sleep disorder
• CBTI and a trial of medication ineffective
• History of long term chronic insomnia
• Comorbid conditions – especially substance abuse or psychiatric disorders

Case Study

• 39 yom travel nurse
• social single parent – 17 yo and 14 yo
• PMH: hypothyroidism (stable 10 yrs) - synthroid 125mcg
• BMI of 27
• Sleep hx: Difficulty getting to sleep; lays awake sometimes for “hours”; often wakes & unable to get back to sleep easily
• Tried numerous OTC & trazadone w/o success
• Sleep Hygiene for 2 months
• Trouble sleeping 4-5 nights out of 7
• Denies snoring (states ex-wife nor children complained of any snoring)

Case Study

• Decision tree for treatment
References


References

References


LIMITED PRESCRIBING INFORMATION AS A REFERENCE

Benzodiazepine receptor agonists

- **temazepam**
  - BBW: Risk with concomitant opioid use
  - Adult dosing: 7.5-30 mg q hs
  - Contraindication/Caution: pulmonary impairment, seizure hx, alcohol use or abuse, drug abuse hx, renal/hepatic impairment, elderly, hx of depression, CP450 3A medications
  - Adv rx: WD with abrupt dc, seizures, hypotension, complex sleep-related behavior, COMMON: fatigue, headache, confusion, anxiety, libido changes, appetite changes, constipation
  - Pregnancy Category X
  - Schedule Category: IV
  - Monitoring: LFTs and CBC if prolonged use

- **estazolam**
  - BBW: Risk with concomitant opioid use
  - Adult dosing: 1-2 mg qhs prn – start 0.5 mg in elderly
  - Contraindication/Caution: pulmonary impairment, seizure hx, alcohol use or abuse, drug abuse hx, renal/hepatic impairment, elderly, hx of depression, caution if smoking habit changes, CP450 3A medications
  - Adv rx: WD with abrupt dc, seizures, hypotension, complex sleep-related behavior, COMMON: fatigue, headache, confusion, anxiety, libido changes, appetite changes, constipation
  - Pregnancy Category: X
  - Schedule Category: IV
  - Monitoring: CBC if prolonged use
Benzodiazepine receptor agonists

- triazolam
  - BBW: Risk with concomitant opioid use
  - Adult dosing: 0.25 mg q hs – start with 0.125mg (max 0.25mg in elderly) – shorter acting
  - Contraindication/Caution: pulmonary impairment, seizure hx, alcohol use or abuse, drug abuse hx, renal/hepatic impairment, elderly, CP450 3A medications
  - Adv rx: hypotension, complex sleep-related behavior COMMON: drowsiness, HA, dizziness, nervousness, coordination disorders, GI (N/V)
  - Pregnancy Category X
  - Schedule Category: IV
  - Monitoring: CBC if prolonged use

Limited information ONLY Source: epocrates, drugs.com, and product insert

Nonbenzodiazepine Receptor Agonists

- eszopiclone
  - BBW: none
  - Adult dosing: 1-3 mg q hs
  - Contraindication/Caution: impair daytime functioning, should not exceed 2 mg in patients with severe hepatic impairment, depression, CYP3A4 medications concomitantly
  - Adv rx: thrombophlebitis, anorexia, anemia, WD with abrupt dc, complex sleep-related behavior, abnormal gait, COMMON: HA, dry mouth, dyspepsia, N/V, dizziness, nervousness, unpleasant taste, peripheral edema
  - Pregnancy Category: C
  - Schedule Category: IV
  - Monitoring: for prolonged use CBC

Limited information ONLY Source: epocrates, drugs.com, and product insert

Nonbenzodiazepine Receptor Agonists

- zolpidem
  - BBW: none
  - Adult dosing:
    - Women
      - sleep onset – 5 mg spec (max 15mg), 6.25 – 12.5mg (IR: must be at least 7 hours before planned awakening)
      - deep maintenance – 5 mg (IR: must be at least 7 hours before planned awakening)
      - middle of night awakening 1.75mg SL x 1 per night prn (may repeat if more than 4 hours left before planned awakening) reevaluate if more than 7-10 days
    - Men
      - sleep onset – 5 – 10 mg (max 15mg), 6.25 – 12.5mg (IR: must be at least 7 hours before planned awakening), use start low at 5 (IR: may repeat if more than 4 hours left before planned awakening)
      - deep maintenance – 5 mg (IR: must be at least 7 hours before planned awakening)
      - middle of night awakening 3.5mg SL x 1 per night prn (may repeat if more than 4 hours left before planned awakening) reevaluate if more than 7-10 days
    - Elderly
      - sleep onset – 5 mg spec (max 15mg), 6.25 – 12.5mg (IR: must be at least 7 hours before planned awakening)
      - deep maintenance – 5 mg (IR: must be at least 7 hours before planned awakening)
      - middle of night awakening 1.75mg SL x 1 per night prn (may repeat if more than 4 hours left before planned awakening) reevaluate if more than 7-10 days

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Nonbenzodiazepine Receptor Agonists

- zolpidem
  - Contraindication/Caution: impair daytime functioning, pulmonary impairment, depression, CYP3A4 medications concomitantly
  - Adv rx: WD with abrupt dc, complex sleep-related behavior, hypotension, allergic rx, tachycardia, anxiety, anemia. COMMON: HA, drowsiness, dizziness, diarrhea, dry mouth, back pain, lethargy, pharyngitis, ataxia, confusion, euphoria, arthralgia
  - Pregnancy Category: C
  - Schedule Category: IV

- zaleplon
  - BBW: none
  - Adult dosing: 5-10 mg qhs max 20 mg (elderly max 10mg)
  - Contraindication/Caution: impair daytime functioning, pulmonary impairment, hepatic impairment, elderly, depression, CYP3A4 medications concomitantly
  - Adv rx: complex sleep-related behavior, allergic rx, aggressive behavior, suicidality, hallucinations COMMON: HA, dizziness, nausea, paresthesia, dysmenorrhea, tremor
  - Pregnancy Category: C
  - Schedule Category: IV

Selective melatonin receptor agonist

- ramelteon
  - BBW: none
  - Adult dosing: 8mg PO qhs (avoid with high fat meal)
  - Contraindication/Caution: History of angioedema with previous ramelteon therapy (do not rechallenge); concurrent use with fluvoxamine, severe hepatic impairment, significant number of medication interactions
  - Adv rx: complex sleep-related behavior, prolactin levels increased, testosterone levels decreased COMMON: dizziness, somnolence, fatigue, insomnia worsened, depression, nausea, taste changes, myalgias
  - Pregnancy Category: C
  - Schedule Category: rx
Orexin receptor antagonist

- **suvorexant**
  - BBW: none
  - Adult dosing: 10 mg qhs (max 20mg) for sleep onset or maintenance; give > 7h before planned awakening – give w/o food for faster onset.
  - Contraindication/Caution: narcolepsy, CYP3A inhibitors, obesity (especially women), significant med-med interactions, drug abuse hx, severe hepatic impairment, pulmonary impairment
  - Adv rx: REM sleep effects, sleep-related activities, daytime fatigue, sleep paralysis, COMMON: drowsiness, HA, dizziness, abnormal thinking, diarrhea, cough
  - Pregnancy Category: C
  - Schedule Category: IV

Sedating antidepressant

- **doxepin**
  - BBW: increased suicidality in children, adolescents and young adults with MDD
  - Adult dosing: 10-50mg qhs (reduce in elderly), taper gradually to d/c
  - Contraindication/Caution: acute-angle glaucoma, bipolar disorder, CYP450 interactions,
  - Adv rx: skin rash, eosinophilia, bone marrow depression, COMMON: dry mouth, blurred vision, constipation, urinary retention, hypotension, N/V, indigestion, taste disturbances, wt gain
  - Pregnancy Category: B
  - Schedule Category: RX
  - Monitoring: CBC with prolonged use