Overview of Insomnia and the use of Sedative-Hypnotic Medication

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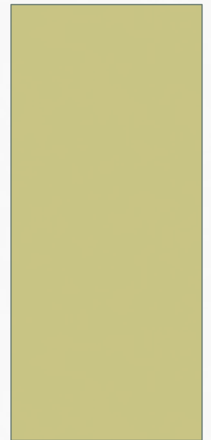

Learning Objectives

1. To review the differential diagnosis and assessment issues for insomnia

2. To review and consider evidence-based choices for sedative-hypnotic medications

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Faculty/Presenter Disclosure

Faculty: Dr. Murray W. Enns

Relationships with commercial interests: None

Outline

- DSM-5 criteria
- Differential diagnosis of insomnia
- Assessment issues
- Medication treatment considerations
- Cases and questions

Insomnia Disorder (DSM-5)

A. Poor sleep quality or quantity (beginning, middle or end of night)
B. Causes distress or impairment
C. At least 3 nights per week
D. Present for at least 3 months
E. Sleep problems despite adequate time allotted
F. Not due to another primary sleep disorder
G. Not due to a substance (e.g. Rx or drug of abuse)
H. Not explained by other mental/medical disorder

American Psychiatric Association, DSM-5

Insomnia Differential Dx (DSM-5)

A. **Narcolepsy**
B. **Sleep breathing disorder (Obstructive Sleep Apnea)**
C. **Restless legs syndrome +/- periodic limb movements**
D. Substance/medication induced sleep disorder
E. Circadian rhythm sleep disorders
    - Sleep phase delay
    - Sleep phase advance
    - Irregular sleep-wake type
F. Many mental health disorders include sleep disturbance as a criterion:
   e.g. Major Depressive Disorder, Generalized Anxiety Disorder, Post-Traumatic Stress Disorder

American Psychiatric Association, DSM-5

Medication-induced insomnia

Psychiatric medications may be implicated:

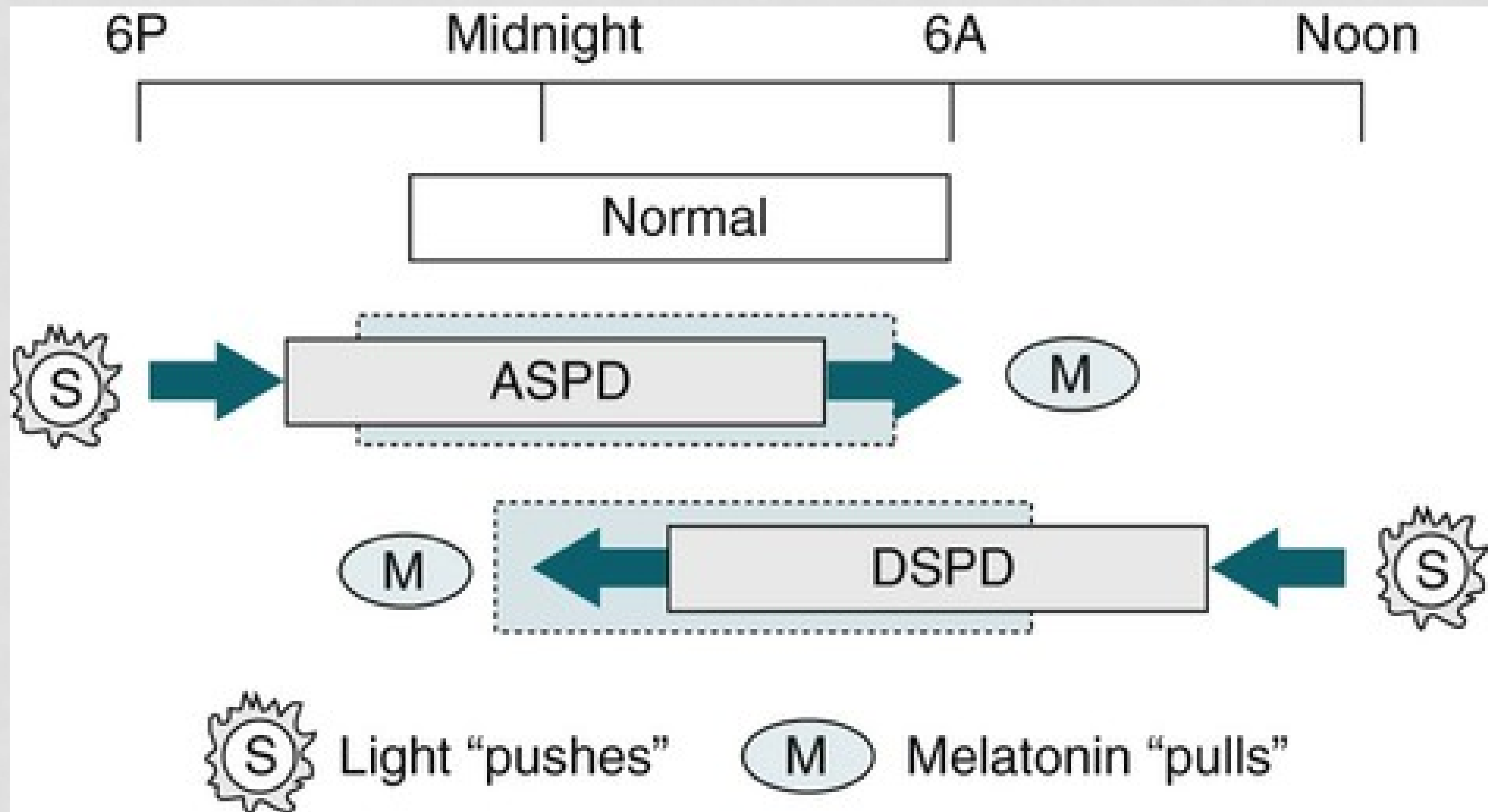
-SSRIs/SNRIs, bupropion, MAOIs, & stimulants can be excessively activating

-SSRIs/SNRIs, TCAs, & antipsychotics can cause or worsen restless legs

-Antipsychotics can cause akathisia

-Antidepressants or antipsychotics may be associated with vivid dreams or nightmares

Circadian Phase Disorders



Assessment Issues I

a. Patients may not be aware that they snore loudly, waken with a gasp, or kick their legs in bed at night

b. "Sleep-state misperception" is common

c. So… collateral history from a bed partner can be important diagnostically

Assessment Issues II

a. Excessive sleepiness may not be accurately perceived (see Epworth Scale)

b. A sleep history must be inclusive and systematic to characterize the problem (often need a Sleep Diary – see later)

c. Sleep lab assessment – can be long wait times – much can be done without… (or while waiting)

RUSH

SLEEP DIARY

⇐ COMPLETE THIS SECTION AFTER GETTING OUT OF BED ⇒								⇐ COMPLETE AT END OF NEXT DAY ⇒		
Day & Date	Unusual stressors, time of alcohol & sleep medications	Time you went to bed	Time it took you to fall asleep	# of awakenings	*Amount of time awake	Time you got up for the day	Total sleep time	Sleepiness Rating (see below)	Fatigue Rating (see below)	Napping: time of day & sleep amount
Sunday 5/20/00	*argument at dinner, 2 beers 6-8pm, Ambien 10 mg at 9:30pm*	*10pm*	*30 min*	*3*	*30 min*	*6am*	*7 hr*	*75*	*45*	*3pm 1 hr*

* **Amount of time awake**: this is all the time you spent awake during the night, from the first time you awakened to the time you got out of bed. It does not include the time it took you to fall asleep initially

SLEEPINESS AND FATIGUE RATING SCALE: (AVERAGE RATING FOR THE WHOLE DAY FOLLOWING A GIVEN SLEEP EPISODE)

	0	25	50	75	...100
SLEEPINESS:	Extremely sleepy	Sleepy	Neither	Alert	Very alert
FATIGUE:	Extremely fatigued	Fatigued	Neither	Energetic	Very energetic

The Epworth Sleepiness Scale

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

Choose the most appropriate number for each situation:

0= would never fall asleep

1= slight chance of falling asleep

2= moderate chance of falling asleep

3= high chance of falling asleep

Activity	Score
Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public place (theater, meeting, ect.)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting quietly after lunch without alcohol	_____
Sitting and talking to someone	_____
In a car, while stopped for a few minutes in traffic	_____
Total	_____

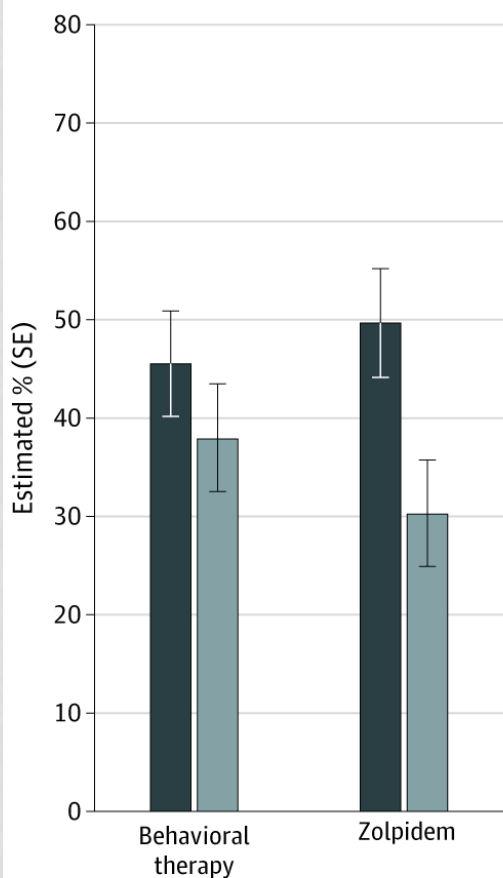
Sedative-hypnotic medication: challenges and concerns

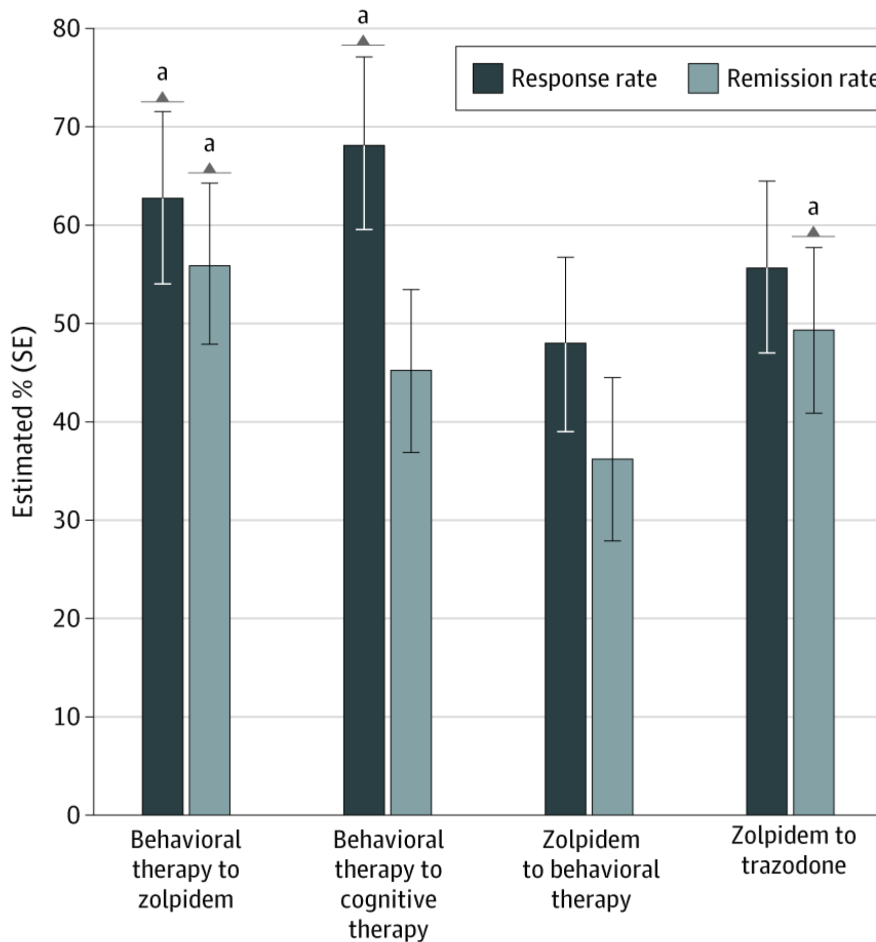
a. Tolerance and tachyphylaxis
b. Daytime sedation or impairment (consider half-life)
c. Instant “negative reinforcement”
d. No perception of control over sleep
e. Rebound insomnia (implications for discontinuation)
f. Loss of accurate perception of sleep
g. Unhelpful sleep habits (falling asleep while reading/watching TV etc.)
h. Risk of abuse or diversion (esp. BZDs)
i. Medical hazards, particularly in the elderly

CBTi is a *highly effective first line* treatment, so why not stop prescribing?

a. Not everyone can access CBTi
b. Drop out rates in CBTi trials are commonly 22-30% (Harvey & Tang, 2003)
c. 19-26% of insomnia patients do not respond (Trauer et al, 2015)
d. CBTi is like Buckley's Cough Syrup…
"It tastes awful. And it works"…
e. Severe insomnia - Very short sleep (<6 hrs) ± physiologic-hyperarousal is less responsive to CBTi (Vgontzas et al, 2013)
f. Insomnia tends to be persistent over 5 year follow-up (Morin et al, JAMA Network Open, 2020)

Morin et al, JAMA Psychiatry 2020
Effectiveness of Sequential Therapies for Insomnia





Extensive medication options…which ones should be chosen?

a. BZDs with varying half-lives
b. Zopiclone (t-1/2 = 5-6 hours) (or Lunesta ® = eszopiclone)
c. Zolpidem (Sublinox®, t-1/2 = 2 - 3 hours)
d. Trazodone (t-1/2 = 10 – 12 hours)
e. Tryptophan (5-HT precursor - weak but "natural")
f. Doxepin (low dose) (t-1/2 = 15 hours)
g. Other antidepressants (e.g. mirtazapine, amitriptypine)
h. Low dose antipsychotics (e.g. quetiapine, olanzapine)
i. Melatonin
j. Melatonin agonists (Rozerem ® = Ramelteon)
k. Orexin antagonists (Belsomra ® = Suvorexant)

The foregoing is just a list, not recommendations

Recommended medication options I*

Z-drugs (non-BZD GABA agonists)

Zolpidem 5 – 10 mg (sleep onset)

Zopiclone 3.75-7.5 mg (onset and maintenance)

Benzodiazepines

Triazolam 0.125 – 0.25 mg (sleep onset)

Temazepam 15 – 30 mg (onset and maintenance)

Recommended medication options II*

<u>Low Dose Doxepin</u>

Effective for sleep maintenance insomnia

Does not require "antidepressant" doses

Silenor ® (US) 3 – 6 mg;
generic doxepin in Canada – use up to 10 mg

<u>Other antidepressant Rxs</u>

Trazodone 50 – 150 mg (especially with PTSD)

Amitriptyline (*only if* chronic pain syndrome)

Mirtazapine (*only selected* depression cases)

Not recommended*

Low dose antipsychotics

E.g. quetiapine or olanzapine

Poor risk-benefit balance due to metabolic SEs and tardive dyskinesia

(*Except* - when there is a specific indication for an antipsychotic drug)

Long half-life benzodiazepines

E.g. clonazepam, diazepam

(*Except* – when there is a specific indication for a non-antidepressant anxiolytic e.g. social anxiety disorder, generalized anxiety disorder)

Ramelteon and Suvorexant?

a. Better than placebo
b. Different mechanisms
(melatonin agonism; orexin antagonism)
c. Important as “proof of concept”
d. Not demonstrated to be more efficacious than other agents
e. May be less problematic for “rebound” insomnia
f. May be lower risk of abuse
g. Not currently available in Canada –
cost effectiveness concerns

Recent review: Dujardin, Pijpers, Pevernagie. Prescription Drugs Used in Insomnia. Sleep Med Clin 15 (2020) 133–14

Always combine Rx for insomnia with attention to sleep behavior

a. Choose a standard wake-up time and stick to it every day
b. The bed is for sleep and sex only
c. Never stay in bed for extended periods without being asleep
d. Do not worry or do other thinking while in bed
e. Avoid all daytime napping
f. Do not retire to bed too early, and do not sleep-in

CBT for insomnia works in psychiatric disorders too!
Jansson-Frojmark and Norell-Clarke, 2016

ILLUSTRATIVE CASES

Case 1

- 40 y/o RCMP officer, on leave from work
- Multiple traumatic exposures over 18 year career
- Diagnosed with PTSD
- Chronic low back pain – work related
- Current problems:
  nightmares, middle insomnia ++, pain,
  hyperarousal, depressed and anxious mood
- Current Rx: prazosin 6 mg hs; reluctant for any Rx

Case 2

- 54 year-old married homemaker
- Longstanding mild initial/middle insomnia
- Much worse for 3 months
- Depressed mood, loss of interests, low NRG, poor concentration, loss of appetite (also 3 months)
- No other mental health history
- Uses OTC sleep meds, 2-3 drinks/day, ⇧ caffeine
- Retires to bed 10:00 pm, rises at 8:00 am.
- Insomnia much worse with amitriptyline 10 mg hs

Case 3

- 39 year old unemployed man on social assistance
- Longstanding schizoaffective disorder, relatively stable on quetiapine 100 mg bid and 400 mg hs, plus zopiclone 15 mg hs
- Still complains bitterly "can't stay asleep at night" but acknowledges that he feels sleepy/medicated
- Trials of clonazepam, trazodone, lorazepam - no sustained help, and ++++ daytime sleepiness
- Extensive weight gain since diagnosis, BMI = 36

Case 4

- 21 yoa unmarried student, lives independently
- Severe difficulty initiating sleep, often 3 – 4 hours
- Tosses & turns for hours, falls asleep at 3-4:00 am
- Repeatedly late for classes ("can't get going")
- He feels excessively sleepy most days
- On weekends, he sleeps in until noon
- Neither OTC sleep meds nor alcohol use are helpful
- Sunday night is his worst night of insomnia

*Recent Reviews of Medication Management for Insomnia

- Sateia MJ et al, Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med, 2017, 13(2):307-348

- Rios P et al, Clinical Evaluation of Interventions for the Management of Insomnia: A Review of Reviews. Ottawa. Canadian Association for Drugs and Technology in Health (CADTH), September 2018.

- Hassinger AB et al, Selecting a Pharmacotherapy Regimen for Patients with Chronic Insomnia. Expert Opin Pharmacother, 2020, 21(9): 1035-1043.

Questions
(after Dr. N. Vincent)