Management of Insomnia

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Learning Objectives

- Characterize insomnia and its negative effects
- Discuss the goals of treatment
- Summarize guidelines of management of insomnia including non-pharmacologic and pharmacologic therapies

Insomnia: Definitions

- Insomnia:
  - Trouble initiating or maintaining sleep or inability to regain sleep after waking that are associated with daytime complications
- Chronic:
  - Symptoms that last for at least 3 months or 3 of more times per week
- Short term:
  - Symptoms of insomnia but < 3 months duration

Sateia. J Clin Sleep Med, 2017.

Impact of Chronic Insomnia

- Functional status impairments
- More work absenteeism
- Development of mood disorders, relapse of depression, alcoholism
- Associate with hypertension and cardiovascular disease

Baglioni. J Affect Disord, 2011.
Breslau. Biol Psychiatry, 1996.
Spiegelhalder. Nat Sci Sleep, 2010.

Goals of Therapy

- Improve sleep quality
- Improve insomnia related daytime complications

Measurement of Goals

- Sleep latency (SL)
  - Time it takes to fall asleep
- Total Sleep Time (TST)
- Wake After Sleep Onset (WASO)
  - Time it takes to fall back asleep after waking up
- Sleep Efficiency (SE)
  - Percentage of time in bed asleep
- Number of Awakenings (NOA)

Sateia et al. J Clin Sleep Med 2017

Types of insomnia

- Failure to fall asleep (SL)
- Inability to stay asleep (SE, NOA)
- Inability to fall back asleep upon awakening (WASO)

Sateia et al. J Clin Sleep Med 2017

Underlying Causes of Insomnia

- Treat the underlying illness or condition
  - Pain, allergies, infections, reflux, etc.
  - Medication induced: steroids, stimulants, etc.
- Understand that primary insomnia may also be present and treat accordingly

Schutte-Rodin et al. J Clin Sleep Med 2008

American Academy of Sleep Medicine

- Recently published updated guidelines
  - Cognitive and behavioral therapy (CBT) remain first line treatments
  - More discussion provided on pharmacotherapy options

Sateia. J Clin Sleep Med, 2017.

Treatment Options: Overview

- CBT and Non-pharmacologic therapy
- Pharmacologic therapy

Cognitive and Behavioral Therapy

- First line therapy-American Academy of Sleep Medicine (AASM)
- Multiple methods of approach to this
  - Stimulus Control
  - Relaxation Therapy
  - Sleep Restriction Therapy
  - Sleep Hygiene

Schutte-Rodin et al. J Clin Sleep Med 2008
Sateia et al. J Clin Sleep Med 2017

Stimulus Control

- Go to bed only when sleepy
- Use bed only for sleep
- Get out of bed if unable to fall asleep in 20 minutes
- Set a consistent morning alarm
- Do not nap during day

Bootzin. J Clin Psychiatry, 1992.
Pallesen. Behav Res Ther, 2003.
Espie. Behav Res Ther, 1989.
Engle-Freidman. J Clin Psychol, 1992.

Relaxation Therapy

- Progressive Relaxation:
  - Beginning with muscles in face work downwards contracting and relaxing
  - Improves sleep: not daytime symptoms
- Relaxation Response
  - Lying or sitting with closed eyes and controlled abdominal breathing
  - Helps with sleep quality but only modestly

Means et al. Behav Res Ther 2000
Edinger et al. JAMA 2001
Tsai et al. Psychophysiology 2015

Sleep Restriction Therapy

- Decreasing time spent in bed to what patient sleeps
- Steps:
  - Determine average time patient sleeps
  - Use average sleep time for amount allowed
  - Titrate sleep based upon sleep efficiency (above 90% increase 15-30 min, <85% decrease 15-30 min)

Spielman et al. Informa 2010
Epstein et al. Sleep 2012

Sleep Hygiene

- Sleep only as much as patient feels is needed
- Keep regular sleep schedule
- Exercise regularly 4 to 5 hours before bedtime
- Avoid caffeine later in day
- Avoid alcohol near bedtime
- Do not go to bed hungry
- Avoid large meals right before bed
- Avoid smoking or nicotine intake near bedtime
- Avoid prolonged use of light emitting devices
- Avoid napping during day

Edinger. Sleep, 2003.

CBT

- Combination of the previous treatments
  - Most efficacious long term treatment
  - Moderate to high quality evidence
- Involves talking to a sleep therapist
  - Manage anxiety
  - Sometimes hard to find trained therapists

Trauer et al. Ann Intern Med 2015
Kyle et al. Sleep 2014

Pharmacologic Therapy

- Pharmacologic therapy is not considered first line in patients, but should be used:
  - As additional therapy if CBT is ineffective
  - If patient still has symptoms with CBT
  - As a temporary adjunct to CBT
- Most medication options have low quality of evidence and come with a weak recommendation

Schutte-Rodin et al. J Clin Sleep Med 2008
Sateia et al. J Clin Sleep Med 2017

Benzodiazepines (BZDs)

- AASM: Weak evidence but benefits outweigh harm:
  - Triazolam: sleep onset
  - Temazepam: sleep onset and maintenance
- Decreases SL (4.2-10 min)
- Increases TST 61.8 min
- Half life/ duration of action affects sleep time
- Concerns
  - Long term use:
    - Efficacy: 6 months to 1 year
  - Side effects
  - Daytime "hangover"

Sateia et al. J Clin Sleep Med 2017
WU et al. Psychother Psychosom 2006
Holbrook et al. CMAJ 2000
Mitchell et al. BMC Fam Pract 2012
Morin et al. JAMA 1999

BZDs

	Onset	Duration	Available Doses	Hypnotic Dose	Preg. Category	Notes
Alprazolam	30-60 min	Intermediate	0.25, 0.5, 1, 2 mg	0.25-2mg	D	Not preferred for sleep
Clonazepam	30-60 min	Long	0.5,1,2 mg	0.5,1,2 mg	D	
Diazepam	15-30 min	Long	2,5,10 mg	5-10 mg	D	Not preferred for sleep
Lorazepam	30-60 min	Intermediate	0.5, 1, 2 mg	1-4 mg	D	No active metabolite
Oxazepam	45-60 min	Short	15 mg	15-30 mg	D	No active metabolite
Temazepam	**45-60 min**	**Intermediate**	**7.5, 15, 22.5, 30 mg**	**15-30 mg**	**X**	**AASM Preferred**
Triazolam	**15-30 min**	**Short**	**0.125, 0.25 mg**	**0.125-0.25 mg**	**X**	**AASM Preferred** Rebound Insomnia

Drugs for Insomnia. Treate Guidel Med Lett, 2009.
Roehrs. Psychopharmacology, 2001.
Glass. J clin Psychopharmacol, 2008.
Wu. Psychother Psychoom, 2006.

Z drugs (Non-BZD Agonists)

- AASM: Weak evidence more benefit than harm:
  - zaleplon: sleep onset
  - eszopicolone and zolpidem: sleep onset and maintenance
- Decrease SL, NOA and increase TST
- Evidence of efficacy for up to a year of use
- Half life/ duration of action affects sleep time
- Concerns
  - Long term use:
    - Efficacy: 6 months to 1 year
  - Side effects
  - Daytime "hangover"

Sateia et al. J Clin Sleep Med 2017
Jabcobs et al. Arch Intern Med 2004
Mitchell et al. BMC Fam Pract 2012
Wilt et al. Ann Inern Med 2016

Z Drugs

	Onset	Duration	Dosage	Notes
Eszopiclone	15-30 min	Intermediate	1,**2**,**3** mg	Good for SL and NOA, WASO
Zaleplon	15-30 min	Short	**5**, **10** mg	Okay for SL
Zolpidem	15-30 min	Short ER available	5,**10** mg 6.25,12.5 mg ER	Good for SL

Krystal. Sleep, 2003.
Walsh. Sleep, 2007.
Roth. Sleep Med, 2005.

Melatonin Analogues

- AASM: Weak evidence more benefit than harm for ramelteon
  - OTC melatonin- Weak evidence more harm than benefit
- Marginal SL improvement
- Concerns:
  - Cost
  - Lack of efficacy melatonin

Sateia et al. J Clin Sleep Med 2017

Melatonin Analogues

	Onset	Duration	Dosage	Notes	Efficacy
Ramelteon	30 min	Short	8mg	Liver metabolism Can't take with fluvoxamine	Weak AASM treatment 12 months
Tasimelteon	Weeks-months	Long	20mg	For non-24 hour sleep wake cycles primarily in blind	
Melatonin	45- 60 min	Short	2mg		Questionable evidence at best

Erman. Sleep Med, 2006.
Neubauer. Neuropsychiatr Dis Treat, 2008.
Lemoine. J sleep Res, 2007.
Wilt et al. Ann Inern Med 2016
Kuriyama et al. Sleep med 2014

Antidepressants

- AASM:
  - Doxepin: more benefit than harm (weak)
  - Trazodone: more harm than benefit (weak)
- Benefits in sleep maintenance
- Good if patient has concomitant depression or neuropathic pain
- Concerns
  - Polypharmacy
  - Dependence

Sateia J Clin Sleep Med 2017
Mendelson. J Clin Psychiatry 2005
Yeung. Sleep Med Rev, 2015.

Antidepressants

	Onset	Duration	Dosage	Notes
Doxepin	3.5 hours	Long	3-6 mg	Sleep maintenance Brand name only
Amitriptyline	4 hours	Long	25-150 mg	Limited use
Mirtazipine	Hours	Long	7.5-15 mg	Not recommended
Trazodone	1 hour	10 hours	50-100 mg	Not recommended, For depressed? Tolerance problems?

Krystal. Sleep, 2011. Walsh. Hum Psychopharmacol, 1998. Yeung. Sleep Med Rev, 2015.
Hamonen. Br J Rheumatol, 1998. Mouret. Psychopharmacology, 1988.
Mertz. Am J Gastroenterol, 1998. Mendelson. J Clin Psychiatry 2005

Suvorexant

- AASM:
  - Use for sleep maintenance insomnia (Weak)
- Evidence for TST and SL
- Efficacy for up to 1 year
- Concerns:
  - Efficacy above approved dose
  - Newer agent (cost, insurance)
  - Side effects

Herring. Neurology, 2012. Wilt et al. Ann Inern Med 2016
Herring. Biol Psychiatry, 2016 Kishi et al. PLoS One 2015
Sateia et al. J Clin Sleep Med 2017

Suvorexant

	Onset	Duration	Dosage	Notes
Suvorexant	30 min	12 hours	5-20 mg	3A4 Metabolized

Herring. Neurology, 2012.
Herring. Biol Psychiatry, 2016
Sateia et al. J Clin Sleep Med 2017

Over the Counter Options

- AASM:
  - Avoid the use of diphenhydramine, valerian root, L-tryptophan (Weak)
- Concerns
  - Anticholinergic effects
  - Lack of improvement in symptoms
  - Long term efficacy lacking

Glass. J Clin Psychopharmacol, 2008. Oxamn. Plos One, 2007.
Morin. Sleep, 2005. Hudson. Nutr Neurosci, 2005.

Over the Counter Options

- AASM: Weak evidence to avoid the use of diphenhydramine, valerian root, L-tryptophan

	Onset	Duration	Dosage	Notes	Efficacy
Diphenhydramine	0.5- 2 hours	8.5 hours	50 mg	Lack of controlled trials Anticholinergic effects	Good for pregnant since helps with nausea
Valerian Root	Hours	Hours	Varies 225-1215mg	Lack of clinical evidence Potentially hepatotoxic	No major side effects over placebo
L-tryptophan	Long	Unknown	250 mg	Lack of controlled trials or evidence	

Glass. J Clin Psychopharmacol, 2008. Bent. AM J Med, 2005.
Morin. Sleep, 2005.
Oxamn. Plos One, 2007.

Summary

- CBT options are best
- Failing these include pharmacologic intervention
  - Doxepin and Z drugs show best amount of evidence for longer term use but still have concerns
  - Lack of evidence for melatonin and trazodone
  - Pharmacological treatments have some efficacy up to 1 year

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