

ECHO Idaho: Behavioral Health in Primary Care

Sleep Disorders — Evidence Based
Pharmacologic Interventions

June 19, 2019

Tara Whitaker, MD

Learning Objectives

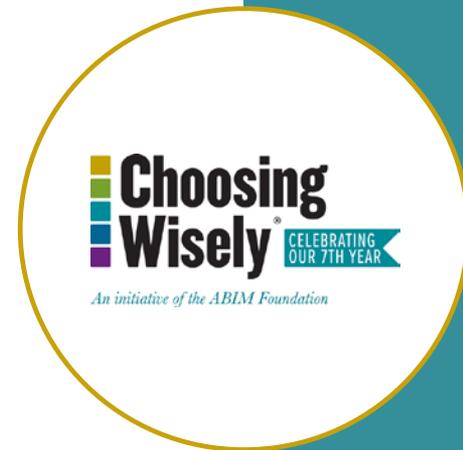
- Review evidence for the use, risks and limitations of pharmacologic therapies for insomnia
- Review resources available for reference and future learning
- Convince you to just re-watch Kyle Davis's lecture from 2 weeks ago on CBT for insomnia and apply all of his tips prior to using any medications

Insomnia

- Accounts for 5.5 million visits in primary care
- Particularly common in adults over 65
 - Up to 65% report problems with sleep in some studies
- More women affected
- Also more common in individuals who are unemployed, divorced, widowed, separated or of lower socioeconomic status
- High risk during alcohol or opiate withdrawal

Resource Plug

- Choosing Wisely Campaign
- *Choosing Wisely* is an initiative of the ABIM Foundation that seeks to advance a national dialogue on avoiding unnecessary medical tests, treatments and procedures.
- 540 specialty society recommendations
- Additional recommendations for insomnia:
 - *Avoid use of hypnotics for chronic insomnia in adults. Instead offer cognitive behavior therapy and reserve medication as adjunctive treatment—American Acad Sleep Medicine*
 - *Do not routinely prescribe antipsychotic medications as a first-line intervention for insomnia*



Medication utilization

- Prescriptions increased from 5.3 million in 1999 to 20.8 million in 2010
- OTC use levels hard to determine
 - One study: 10% of adults 18-45 use OTC sleep aids
 - Older adults similar, but more likely to use chronically

Over-the-counter sleep aids-Antihistamines



- First generation antihistamines
 - Diphenhydramine (*Benadryl, Tylenol PM, Excedrin PM, Advil PM, ZzzQuil*)
 - *Approximate ½ life: 8.5 hours*
 - Doxylamine (*Unisom SleepTabs, Equaline Sleep Aid, Good Sense Sleep Aid*)
 - *Approximate ½ life: 10 hours*
- Marketed prior to 1972, No RCTs needed, "grandfathered"
- Subjective sleep improvement
- Residual psychomotor, cognitive impairment, particularly elderly
- Anticholinergic effects
- Consider for pregnant women (doxylamine/B6)

OTC sleep aids: Melatonin



- Regulates sleep/wake cycle
- Good for insomnia related to changing time zones/jet lag or during shift work
 - Also has been studied in children
- 2013 meta-analysis: 0.1-5 mg. Mild improvement in sleep latency (7.1 m) and total sleep time (8.3 m)
- Most studies controlled release formula
- Not FDA regulated, but may be as effective as Ramelteon, a melatonin agonist which is
- Cost per month melatonin: \$1
- Cost per month Ramelteon: \$350
- Few adverse events, not habit-forming

OTC sleep aids: Valerian

- Plant derivative widely used for sleep/anxiety
- Powder, extract
- Paucity of data supporting efficacy despite widespread use for insomnia
- Unregulated products
- Relatively benign side effect profile



Resource Plug

- Therapeutic Research Center (TRC):
Prescriber's Letter and additional role-based publications, CME, resources
- Natural Medicines database for product information available



Benzos

- Try to stop them—slow taper may be needed
- Don't start them for insomnia alone, especially in the elderly
- Choosing Wisely/American Geriatrics Society:
Do not use benzodiazepines or other sedative-hypnotics in older adults as a first choice for insomnia, agitation, or delirium

Z-Drugs

- Nonbenzodiazepine hypnotics: zaleplon (Sonata), zolpidem (Ambien, Edluar), and eszopiclone (Lunesta)
- GABA_A receptor like benzos, but more selective, less anxiolysis
- Reasonable efficacy on sleep latency
- Memory loss, dizziness, disinhibition, GI upset
- Complex sleep behaviors: new recommendation to stop medicine if this has ever happened

Resource Plug

- RESOURCE PLUG: deprescribing.org—evidence based guidelines for deprescribing appropriately

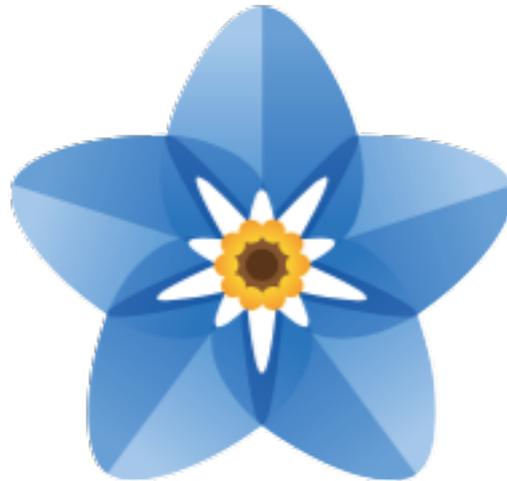


Doxepin/antidepressant notes

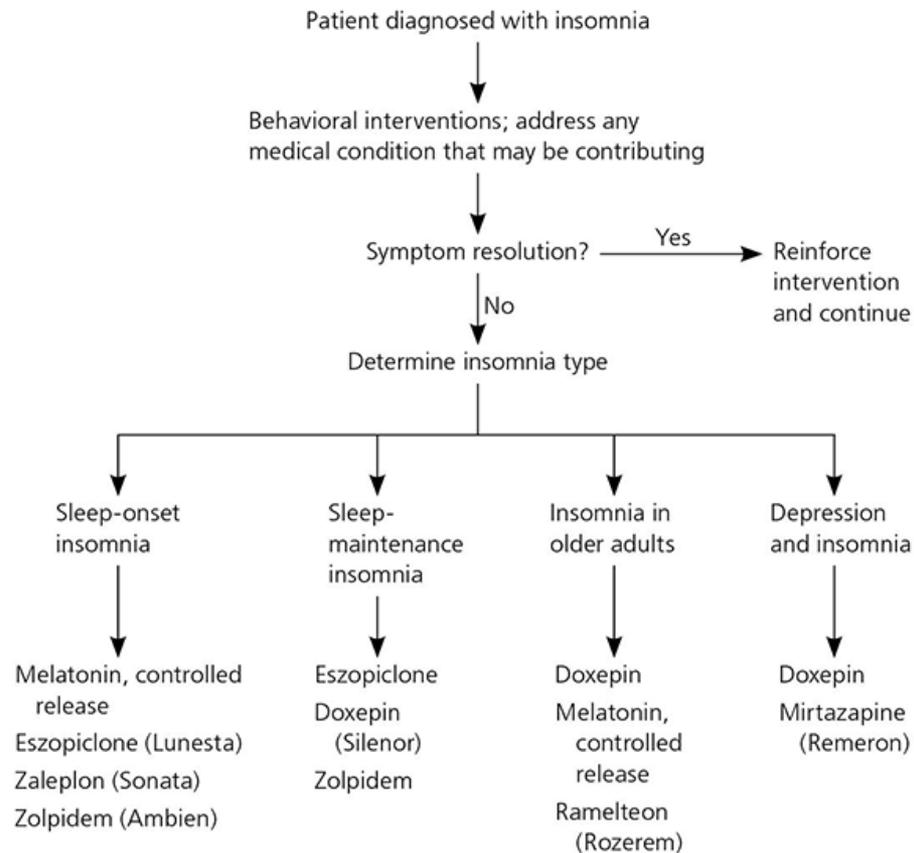
- Antidepressants widely used for sedation, but only TCA doxepin (Silenor, SINEquan) 3 mg and 6 mg is FDA approved
- Improves sleep efficiency, total sleep time, maintenance
- 6 mg dose improves sleep latency
- Adverse effects in older adults similar to placebo, BUT does have anticholinergic effects—use with caution
- 10 mg doxepin not as well studied, but much cheaper
- Evidence for trazodone is weak, not considered first line
- Consider along with mirtazapine, amitriptyline and nortriptyline only if there is another indication

Resource plug

- Anticholinergic burden calculator:
 - acbcalc.com – Calculates anticholinergic burden in patients over 65. 3+ is high risk.



Treatment of insomnia: One approach



NOTE: Medications are listed in order of preference for each indication.

Resource plug

- THE PLACEBO EFFECT
 - 2014 study: Migraine sufferers given migraine medications. One group took the drug labeled with the drug's name, one took a drug labeled placebo and one took nothing. Placebo 50% as effective as migraine medication
 - Harness it and help patients harness it.
 - Provider relationships
 - Patient self care
 - Ritualized healing

Key Points

- Behavioral strategies first, second, third
- Medicate gently and rarely
- Ensure safe prescribing practices by using evidence-based resources
- Ask about sleep and OTC product use regularly at office visits based on provider role

References

- Albert, SM et al. Sleep Health and Appropriate Use of OTC Sleep Aids in Older Adults— Recommendations of a Gerontological Society of America Workgroup. *Gerontologist* 2017, Vol. 57, No. 2, 163-170
- Culpepper, L and Wingertzahn MA. Over-the-Counter Agents for the Treatment of Occasional Disturbed Sleep or Transient Insomnia: A Systematic Review of Efficacy and Safety. *Prim Care Companion CNS Disord.* 2015; 17(6)
- Kam-Hansen, S et al. Altered Placebo and Drug Labeling Changes the Outcome of Episodic Migraine Attacks. *Science Translational Medicine* 08 Jan 2014:Vol. 6, Issue 218, pp. 218ra5
- Matheson, E and Hainer, B. Insomnia: Pharmacologic Therapy. *Am Fam Physician.* 2017 Jul 1;96(1):29-35.
- Professional Resource, Melatonin for Insomnia. Pharmacist's Letter/Prescriber's Letter. July 2016.
- PL Detail-Document, Comparison of Insomnia Treatments. Pharmacist's Letter/Prescriber's Letter. July 2014.
- Additional resources available upon request