## **Non-benzodiazepine hypnotics (Z-drugs)**

* Examples: zolpidem, zaleplon, eszopiclone
* Prefer zolpidem to help fall asleep and stay asleep or zaleplon to help fall asleep or fall back asleep if having periodic nighttime awaking
* Avoid eszopiclone if possible due to its longer half-life (6–9 hours) and patients commonly reporting a metallic taste and headaches with use
* Class has minimal effects on sleep architecture and the best long-term data (6–12 months)
* Must allow for 7–8 hours of total sleep time
* Precautions: next day impairment and CNS depression, parasomnias, abnormal thinking, and behavioral changes

## **Melatonin Agonists**

* Examples: melatonin and ramelteon
* Potentially consider melatonin first due to cost, but caution purity concerns with over the counter medications
* Evidence is much more impressive for circadian rhythm disorders (e.g., jet lag, shift work) than insomnia, but they may decrease sleep latency (7–10 minutes) and increase total sleep time (8–10 minutes) based on data from ramelteon
* Nice alternative in older adults with concerns for over sedation
* Precautions with ramelteon: hyperprolactinemia, drug-drug interactions

## **Antidepressants**

* Examples: doxepin, nortriptyline, mirtazepine, SSRIs, trazodone
* Best to assess depression or psychiatric disorders objectively to determine treatment goals (e.g., depression remission, intermittent use to decrease sleep latency), follow measurements over time, and identify the importance of behavioral health intervention
* If truly treating major depressive disorder, typically shoot for max tolerated doses with the goal of depression remission
* Keep in mind side effects, treatment response, cost, comorbid conditions, interactions
* Avoid widespread use of trazodone due to side effects (e.g., orthostatic hypotension, priapism) and beware use of brand doxepin (Silenor) because a generic drug is available

## **Antihistamines**

* Examples: diphenhydramine, chlorpheniramine, doxylamine, hydroxyzine
* Evidence of benefit is less robust than many FDA approved treatments; short term it may slightly reduce sleep latency, but consistent long-term use may result in tachyphylaxis
* Precautions: anticholinergic side effects (e.g., dry mouth, constipation, urinary retention), cognitive impairment in older adults, delirium, may impair sleep architecture

## **Orexin receptor antagonists**

* Example: suvorexant
* Similar evidence of benefit to the non-benzodiazepine hypnotics with many similar risks (e.g., behavior changes, parasomnias, CNS depression, depression, abuse)
* Thought to have less effects on sleep architecture, but there is a caution for REM sleep changes resulting in sleep paralysis and cataplexy; note narcolepsy is a contraindication!
* Watch out for significant drug interactions (e.g., CYP3A4 interactions, CNS depressants)

## **Benzodiazepines**

* Examples: lorazepam, temazepam
* 2nd or 3rd line therapy because of safety concerns although more reasonable if treating co-morbid psychiatric disorders like anxiety
* Will increase total sleep time and decrease sleep latency although thought to negatively impact sleep architecture
* Potentially quite helpful in rhythmic movement disorders of sleep
* Precautions: physical dependence, abuse, daytime somnolence, amnesia, anticholinergic side effects, CNS depression, & cessation rebound effects (e.g., insomnia, anxiety, seizures)

## **References**

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