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FAST FACTS AND CONCEPTS #105

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Introduction *Fast Facts* #101 and #104 reviewed assessment of insomnia and its non-pharmacological therapy. This *Fast Fact* focuses on the pharmacological treatment of insomnia. Prior to pharmacological treatment, it is important to improve sleep hygiene and treat any contributing underlying medical conditions (e.g. depression, pain, worsening CHF or COPD).

Non-Specific Drug Treatment

1. **Benzodiazepines** have been successfully used for short term insomnia, although there are no systematic studies on long-term use and rare studies in palliative care. The mechanism of action is unclear with the drugs causing subjective rather than objective improvement in sleep. All drugs are dosed orally, at bedtime. Most commonly used are temazepam (start 7.5 mg), flurazepam (15 mg), estazolam (0.5 mg) and triazolam (0.125 mg). The first three are medium half-life benzodiazepines (10-15 hours); triazolam has a short half-life (<12 hours). All three undergo hepatic metabolism; flurazepam and triazolam have active metabolites. Benzodiazepines have a high incidence of amnesia and rebound insomnia, particularly in anxious patients, and may cause paradoxical agitation, especially in the elderly. Other side effects include tolerance and dependence with long-term use and additive CNS and respiratory side effects when used with other drugs. Triazolam is metabolized by cytochrome P450 3A4 and thus has numerous drug-drug interactions.
2. **Benzodiazepine receptor agonists** of the g-aminobutyric receptor complex. These are rapidly absorbed, metabolized by the liver, do not have active metabolites, and have low abuse potential. Zolpidem (5-10 mg) and Zaleplon (10-20 mg), both dosed at bedtime, are ultra-short acting agents that restore sleep in patients with nocturnal awakenings.
3. **Antidepressants** such as trazadone (25-100 mg), doxepin (10-50 mg), and imipramine 10-75 mg) are commonly used for insomnia due to their sedative properties.
4. **Miscellaneous Sedative Hypnotics** Choral Hydrate has moderate short term efficacy but is more toxic than benzodiazepines. Barbiturates are effective in short term treatment, but tolerance develops rapidly. Once commonly used for insomnia, these drugs are no longer used except in rare circumstances.
5. **Antihistamines and Over-The-Counter drugs** Diphenhydramine or other classical anti-histamines have sedative properties, but they are generally not preferred in the elderly due to anticholinergic properties and drug interactions. Diphenhydramine (25-100 mg) has been shown to increase sleep duration and quality; duration of action is 4-6 hours. Most over the counter products contain diphenhydramine or a similar sedating antihistamine, including products such as Unisom, Tylenol PM, and Nyquil.
6. **Melatonin** is used for circadian rhythm sleep disorders and is less effective for chronic insomnia.
7. **Herbal remedies** In one study Valerian (oral extract 400-900 mg QHS) was as effective as oxazepam. The major side effects are hepatotoxicity, cardiotoxicity and delirium. There is less data regarding kava.

Drugs for specific sleep disorders Restless leg syndrome is treated with dopaminergic agents such as pergolide (start 0.05 and increase to 0.2-0.5 mg taken in divided doses before bedtime). Side effects of pergolide include abdominal pain, nasal stuffiness, nightmares, and recurrence of symptoms earlier in the day (see *Fast Fact* #217). Other dopamine agonists such as bromocriptine, pramipexole, and ropinirole can also be used. There

are pharmacologic therapies for narcolepsy; addressing these is beyond the scope of this *Fast Fact*.

References

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