therapeutics letter

THERAPEUTICS INITIATIVE Evidence Based Drug Therapy

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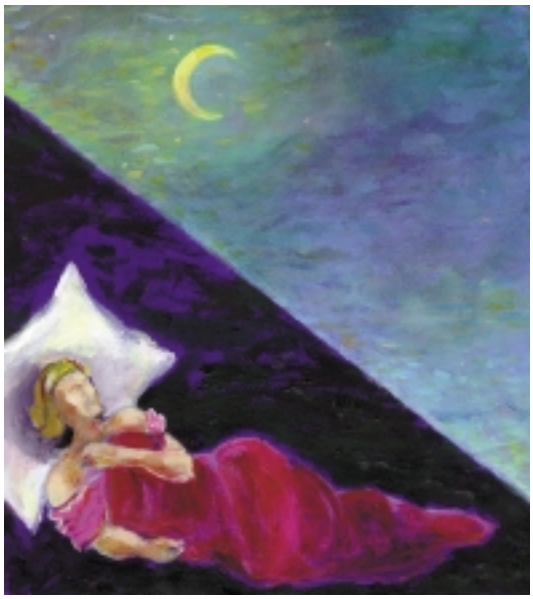
To Sleep or not to Sleep
Here are your Questions



Many psychiatric and medical disorders present with symptoms of insomnia and associated daytime impairment. It is essential to first identify such disorders if present (e.g. depression, chronic anxiety or obstructive sleep apnea) so that they can be treated specifically. The remaining cases represent primary transient or chronic insomnia. An approach to management of this common condition in the primary care setting follows.

• What are the goals of therapy in managing a patient with transient or chronic insomnia?

- To promote a sound and satisfying sleep.
- To decrease daytime drowsiness and impairment.
- To reinstate a normal sleep pattern without medication.
- To prevent dependence on drug therapy.

• What approaches are essential in managing all patients?

An improvement in sleep habits is the initial and continuing goal in all patients. This includes appropriate caffeine, alcohol and nicotine restriction, daily physical aerobic exercise, **regular sleep and awakening times (including weekends)**, avoidance of large meals late in the evening, and maintaining a good sleep environment. Counseling, encouragement and reinforcement are essential to achieve compliance with this program.[1]

• What non-prescription drugs are useful in treating insomnia?

Most over-the-counter hypnotics are antihistamines in which sedation is a significant dose related side effect. Anticholinergic side effects also occur with these drugs, including confusion, especially in the elderly. The principles for their appropriate use are similar to prescription hypnotics; **never combine hypnotic drugs.**

Alcohol does not improve sleep; despite initial sedation, alcohol is associated with an increased number of awakenings.[1]

• Are there clinically significant differences between available prescription hypnotics?

The recommended drugs, benzodiazepines and zopiclone, have a similar mechanism of action on the benzodiazepine receptor complex in the brain. They differ in potency, duration of effect (half-life), side effects and cost (see Table). The difference in duration of effect is the most clinically relevant property. The drugs with the shortest half-lives (2-3 hours) are more appropriate when the main difficulty is falling asleep. Drugs with intermediate half-lives (4-10 hours) are more appropriate when the goal is to reduce nocturnal awakenings. Drugs with half-lives >10 hours are likely to have residual effects after awakening and to be associated with accumulation if taken on a daily basis. They should be limited to patients with chronic anxiety (commonly presenting with insomnia as a symptom) when one wants an anxiolytic effect the next day. The fact that a benzodiazepine, (eg. oxazepam) is marketed as an anxiolytic, does not diminish its usefulness as a hypnotic.

• What pharmacological actions of these drugs are important to appreciate before prescribing?

Objective evidence of effectiveness of hypnotics in double-blind placebo controlled sleep laboratory trials is small; total sleep duration is at most 15 minutes longer with active drug than with a placebo.[2] Because of the development of tolerance, most hypnotic drugs rapidly lose effectiveness with continuous nightly use. It makes sense, therefore, to prescribe hypnotics to be taken intermittently for short periods **(eg. once every second or third night for 1-3 weeks).** This approach is widely recommended,[3] but randomized controlled trials of the effectiveness of this approach are needed.

The major adverse effect of hypnotics, residual or carry-over effects upon awakening, should be avoided as much as possible. The potential risks of residual effects are manifest in the Saskatchewan study,[4] which showed that current users of long half-life benzodiazepines have a 1.7-fold relative risk of hip fracture as compared to current users of short half-life drugs. To minimize such risks use short half-life drugs in the lowest effective dose; start at 1/2 of the usual recommended dose as shown in Table, when possible. Remember that the response rate to placebo in chronic insomnia is high (~33%) so you can anticipate a good rate of response to low doses.

•How should I manage a new patient with insomnia?

Work on long term improvements in sleep habits. If adjunctive medication is needed in the short term use low doses and explain why it should be taken intermittently to maintain effectiveness. Don't prescribe enough for continuous nightly use. A major goal in new patients is to avoid regular nightly use.

•How should I manage the patient who is taking a hypnotic every night?

The patient who is already a nightly user is a more difficult problem. Some of these patients can be motivated to stop (as mentioned above the medication is unlikely to be improving the duration of sleep). Before stopping, the dose must be reduced by 1/2 every 1-2 weeks until the lowest dose in the dose range (see Table) is achieved. Even after tapering, the patient should be warned that they might experience mild rebound insomnia for the first 2-3 nights after stopping.[3]

•What about older sedative-hypnotics?

The following drugs are still prescribed in British Columbia, in order of decreasing use for 1994 : chloral hydrate (Noctec), secobarbital (Seconal), meprobamate (Equanil), ethchlorvynol (Placidyl), butabarbital (Butisol), pentobarbital (Nembutal), and amobarbital (Amytal). **These drugs are dangerous in overdose, have no advantages over benzodiazepines and are not recommended.**

•Conclusions:

Manage insomnia in your practice by education and encouragement of appropriate sleep habits. If indicated prescribe hypnotics with short half-lives, in low doses, for short duration, and **not** for regular nightly use.

Table: Sedatives-Hypnotics in British Columbia

Generic Name	Trade Name	Dose Range	Mean Elim* t 1/2 (hr)[5]	Cost✦ for Single Lowest Dose ($)
Triazolam	**Halcion/Novotriolam**	**0.062 - 0.5 mg**	**3**	**0.03**
Zopiclone	**Imovane**	**3.75 - 7.5 mg**	**5**	**0.34**
Oxazepam	**Serax**	**7.5 - 30 mg**	**7**	**<0.01**
Alprazolam	Xanax	0.125 -1.0 mg	12	0.05
Bromazepam	Lectopam	0.75 - 6.0 mg	12	0.06
Temazepam	Restoril	7.5⌘ - 30 mg	13	0.20
Lorazepam	Ativan	0.25 - 2.0 mg	14	0.03
Estazolam	Prosam	0.5 - 2.0 mg	15	0.22
Clonazepam	Rivotril	0.25 - 2.0 mg	23	0.08
Nitrazepam	Mogadon	2.5 -10 mg	26	0.08
Diazepam	Valium	2.0 -10 mg	43	<0.01
Ketazolam	Loftran	7.5⌘ - 30 mg	43	0.62
Chlordiazepoxide	Librium/Corax/Solium	5.0 - 25 mg	64	<0.01
Clorazepate	Tranxene/Novoclopate	1.9⌘ - 15 mg	64	0.08
Flurazepam	Somnol/Dalmane	7.5⌘ - 30 mg	74	0.04

* Ranked according to half-life of most slowly eliminated active metabolite.
✦ 1994 Pharmacare Data.
⌘ Appropriate low starting dose for this drug is not possible, as it is only available as a capsule.

References

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